Polypharmacy and medication errors: Stop, Listen, Look, and Analyze...

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ABSTRACT
Polypharmacy and adverse drug events (ADE) continue to be difficult problems in modern healthcare despite continuing efforts to reduce their occurrence. The incidence of polypharmacy is increasing dramatically in the geriatric population, especially when considering that this 15% segment of the United States population accounts for nearly one third of all prescription medications. Increased incidence of adverse drug events has been associated with a variety of healthcare environments, including the intensive care unit (ICU) and various emergency settings (i.e., acute care surgery, emergency rooms, trauma care). This article reviews the incidence, etiologic factors, and potential solutions toward reducing both polypharmacy and ADE.

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INTRODUCTION
Prevention of adverse drug events (ADE) and emphasis on patient safety belong to some of the top priorities for the Joint Commission for the Accreditation of Health Care Organizations. 1 To some, polypharmacy is defined as the concurrent use of multiple medications, whether prescription or over-the-counter, by a single patient. 2 For others, polypharmacy is defined as unnecessary use of multiple and/or redundant medications in management of the same condition. Certain expert groups regard polypharmacy as unnecessary or excessive use of medications, even going as far as calling it “an uncontrolled experiment”. 3,4

POLYPHARMACY AND THE ELDERLY
It is well established that older adults are more likely to be affected by multiple chronic conditions, thus increasing the likelihood that they take several or more medications concurrently (Table 1). While only approximately 15% of the United States population is ≥65 years of age, this age group accounts for over 30% of medication consumption. In fact, studies show that an average geriatric patient takes anywhere between 2 to 6 prescription medications and 1 to 3 non-prescription medications simultaneously. 5 From the pharmacologic standpoint, when an elderly patient is concurrently taking approximately 10 medications, our current research and monitoring tools are not sophisticated enough to provide a meaningful estimation of the clinical effect of such polypharmacy. 6,7

Several factors that have been postulated to contribute to polypharmacy in the elderly. 2,5 As patients age, the incidence of chronic health conditions (CHC) increases gradually, with over 90% of patients over the age 65 years having at least one CHC and approximately 30% having more than one chronic medical diagnosis. 6,7 A number of different alternative medications may be used to treat these chronic health conditions, and although all prescribed medications may be clinically justified, many patients often have more than one medical care provider treating their CHC with a variety of prescription and non-prescription medications. To further compound the problem, patients often receive multiple prescriptions from various care providers with little or no coordination or communication between these providers (Table 1). 2 In one study, predictive factors for the development of polypharmacy included the number of medications at baseline (i.e., at the time of initial contact with a

FACTORS ASSOCIATED WITH GERIATRIC PATIENT POLYPHARMACY
- Availability of nonprescription drugs
- High cost of prescription medications (leads to use of up to several other “alternatives” to reach same effect)
- Hoarding of old medications
- Inadequate patient knowledge of medications and medical conditions
- Increasing number of chronic health conditions
- Patients being treated by multiple prescribing physicians
- Patients using different sources of medication, often with little or no co-ordination between these sources
- Taking at least one medication for every diagnosis
- Tendency toward self-treatment/self-medication

Table 1. Factors associated with the development of polypharmacy in the geriatric population. Modified from Reference 29.

Figure 1. Incidence of minor polypharmacy (concurrent use of 2-4 drugs) by age group. 26 Male patients = light blue; Female patients = red.
given health care provider), patient age, presence of diabetes, coronary ischemic disease, heart failure, hypertension, atrial fibrillation, diseases of the esophagus and stomach, and drug use without an indication.3

MEDIATION RELATED ERRORS

Medication-related errors (MRE) and inappropriate medication utilization contribute to more deaths than breast cancer or HIV-related complications, accounting for anywhere between 44,000 and 98,000 fatalities per year.7 There is a growing body of evidence demonstrating the true breadth of this problem within the healthcare system. Although national patient safety standards are being implemented, the issue remains a significant concern.

<table>
<thead>
<tr>
<th>Predictors of polypharmacy</th>
<th>Odds ratio for major polypharmacy</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular drugs</td>
<td>4.5</td>
<td>3.9-5.2</td>
</tr>
<tr>
<td>Drugs for anemia</td>
<td>4.1</td>
<td>2.7-6.1</td>
</tr>
<tr>
<td>Anti-asthma drugs</td>
<td>3.6</td>
<td>3.1-4.1</td>
</tr>
<tr>
<td>Diabetic medications</td>
<td>1.7</td>
<td>1.4-2.0</td>
</tr>
<tr>
<td>Analgesic medications</td>
<td>1.7</td>
<td>1.5-1.9</td>
</tr>
<tr>
<td>Psychotropic drugs</td>
<td>1.2</td>
<td>1.1-1.5</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>1.8</td>
<td>1.6-2.0</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.2</td>
<td>1.1-1.3</td>
</tr>
</tbody>
</table>

Table 2. Predictors of polypharmacy.26 Note that cardiovascular drugs, pharmacology for anemia, and medications for pulmonary disease are most prominently associated with polypharmacy.

Among clinical settings that are often affected by polypharmacy and inappropriate medication use are emergency, trauma, and the intensive care unit (ICU). In these settings, patients who frequently require the highest acuity of care are likely to be simultaneously treated with multiple pharmacologic agents, by multiple healthcare providers. To further exacerbate the problem, these patients often have pre-existing medical conditions and acute/chronic organ dysfunction that can affect physiologic response to pharmaceuticals and drug metabolism. Moreover, many patients present to these clinical settings without a complete and/or accurate list of their current medications.

Medication errors have been well studied within the context of the healthcare system. Nearly 40% of errors originate with the prescribing physician/provider, resulting in approximately 50% of all ADE.13-14 The common types of errors associated with prescribing include overdose in one study were overdose 41%, underdose 17%, allergy 13%, wrong dosage form 12%, wrong drug 5% and duplicate therapy 5%.15 Order transcription errors account for about 12% of errors and 11% of ADE.14 Pharmacy dispensing errors constitute a total of 11% of medication errors and are associated with 14% of ADE.14 Finally, drug administration itself is associated with nearly 40% of MRE and 26% of ADE.13-14 Medication errors can be further divided into those involving: (a) wrong dosing; (b) incorrect frequency of administration; (c) prescribing ineffective medication; (d) prescribing the wrong medication; and (e) duplicate therapy. The most common type of medication error is administration of improper dose (incidence of ~ 41%), followed by administration of the wrong drug (19%) and the wrong route of administration (about 9%).16 The most common root causes of medication errors include performance and knowledge deficits (44%) and errors in communication (nearly 16%).16 Certain medications have been identified as associated with greater potential of ADE, and are usually characterized by narrow therapeutic windows, clear and measurable toxicities, or a high frequency of drug-specific complications.14 This “high-alert” list includes adrenergic agonists, aminoglycosides, benzodiazepines, calcium, potassium,
chemotherapeutic agents, chloral hydrate, digoxin, anticoagulants including warfarin, oral glycemic agents, short- and long-acting insulin, lidocaine, narcotics and opiates, neuromuscular blocking agents, antiepileptic drugs, to name just a few.\textsuperscript{14,29}

**STRATEGIES TO REDUCE MEDICATION RELATED ERRORS/ADVERSE EVENTS**

Numerous attempts at reduction of MRE and ADE have been made, many of which resulted in noticeable decrease, but not in complete elimination of these errors.\textsuperscript{17} Some of the most promising tactics for potentially reducing medication errors revolve around moving toward computerized physician order entry systems and changing the leadership approach and the “blame culture” within the healthcare system.\textsuperscript{12,14,17} Patient safety should be embedded within the entire design and structure of the healthcare organization.\textsuperscript{14} This begins with changes in attitudes and values that promote the “safety culture” in the workplace – reducing “blame and shame”, eliminating excessive fear of punishment, encouraging teamwork, eliminating “production pressure”, as well as proactively addressing worker fatigue and stress.\textsuperscript{14}

**POLYPHARMACY: USEFUL SCREENING QUESTIONS FOR THE PRACTITIONER**

- Does the patient take any dietary supplements, herbal medications, vitamins, or over-the-counter drugs?
- What pharmacies (both traditional and internet-based stores) did the patient use to fill prescriptions during the last two years?
- How many practitioners does the patient currently go to? What medications does each respective practitioner prescribe?
- Is the patient able to clearly read and understand labels on prescription medications that he/she is taking? Is the patient able to easily open the medication vial and appropriately take prescribed doses?
- When does the patient take his/her medications? Of those times, when are they more likely to forget to take medications? How often does he/she forget to take medications?
- Does the patient have any concerns or questions about his or her medication regimen?


The following workplace environment characteristics have been associated with improved patient safety: (a) encouraging free flow of information; (b) voluntary and confidential non-punitive reporting; (c) emphasis on teamwork as a highly valued characteristic; and (d) providing ample training aimed specifically at promoting patient safety.\textsuperscript{14} After addressing the “human factors”, consideration should be given to technology-driven measures and improving the physical characteristic of the workplace that could further enhance patient safety. Enhancements in work area should involve: (a) reduction in clutter; (b) limiting through traffic; (c) reduction of distractions; (d) enhancement of workflow; (e) provision of adequate space with optimized lighting and temperature control; and (f) access to tools that could further enhance patient safety such as providing techniques for optical magnification and electronic drug referencing systems.\textsuperscript{14} Perhaps the most dramatic reduction in MRE has been observed after implementation of computerized physician order entry. In one study, the incidence of errors in a computerized unit was only 3.4%, while a paper-based order entry resulted in 27% medication prescription errors at the same institution during the same time period.\textsuperscript{17} Moreover, computer order entry was associated with significantly fewer ADE.\textsuperscript{17} Considering the fact that majority of serious medication errors involved either performance lapse, lack of knowledge, or failure of communication, emphasis should be placed on education, fostering openness about clarifying medication names, dosages, and routes of administration, and encouraging consultation from qualified pharmacy personnel in a non-judgmental multidisciplinary setting.\textsuperscript{14,16}

Also crucial in preventing MRE are initiatives such as medication name alerts, education regarding common automated dispensing cabinet stocking errors, and unsafe medication marketing practice alerts.\textsuperscript{18} Further safety measures include strategies and systems that: (a) prevent dosage calculation errors; (b) reduce dispensing errors on the part of the pharmacy by using computerized, centralized, and automated medication dispensing systems; (c) encourage independent “check and verify procedures”; and (d) reduce or altogether eliminate verbal medication orders.\textsuperscript{14} In addition, the importance of adequate and timely documentation cannot be overemphasized.\textsuperscript{14} Medication reconciliation is another concept that is closely related to both polypharmacy and medication errors. It may contribute to reduced medication errors and drug-drug interactions if appropriately instituted, maintained, and enforced.\textsuperscript{19}

**POLYPHARMACY: ASSOCIATION WITH ADVERSE PATIENT OUTCOMES**

<table>
<thead>
<tr>
<th>Adverse drug reactions</th>
<th>Drug-drug interactions (often very complex)</th>
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<tbody>
<tr>
<td>Arhythmia</td>
<td>Increased costs of medication and/or treatment</td>
</tr>
<tr>
<td>Balance/gait disturbances (resulting in falls/injuries)</td>
<td>Increased risk of hospitalization</td>
</tr>
<tr>
<td>Cognitive changes/confusion</td>
<td>Patient nonadherence (increased with complex regimens)</td>
</tr>
<tr>
<td>Constipation</td>
<td>Various medication errors</td>
</tr>
<tr>
<td>Cutaneous reaction/rash</td>
<td></td>
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<tr>
<td>Gastric ulcers/bleeding</td>
<td></td>
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<tr>
<td>Hypotension or hypertension</td>
<td></td>
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<tr>
<td>Neurologic dysfunction (i.e., pseudoparkinsonism)</td>
<td></td>
</tr>
<tr>
<td>Psychiatric side effects (depression, suicidal ideation, etc)</td>
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<tr>
<td>Unexpected treatment failure</td>
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</tbody>
</table>

Table 4. List of potential adverse outcomes associated with polypharmacy. Modified from reference 28.

Participation of clinical pharmacists is another strategy that can reduce or prevent both MRE and ADE. In both the ICU and
general hospital ward, participation of clinical pharmacist on daily physician rounds decreased \textit{ADE} by 66\% in the ICU and by 78\% on general medicine units.\textsuperscript{10-21} Common pharmacist interventions included: (a) order clarification, including wrong dose, wrong frequency, inappropriate drug choice and duplicate therapy; (b) providing drug information and education, (c) recommending alternative therapy; (d) identification of actual or potential drug interactions; and (e) identification of drug allergies.\textsuperscript{21} In nursing homes, participation of \textit{clinical pharmacist} decreased use of medications that were not indicated from 19\% to 11\%, and the use of inappropriate medications from 37\% to 20\%.\textsuperscript{22}

\textbf{MEDICATION RECONCILIATION}

\textit{Medication reconciliation} is an important part of the new healthcare paradigm aimed at reducing \textit{MRE, ADE}, and any forms of inappropriate medication use. In order for \textit{medication reconciliation} to be truly effective in preventing \textit{MRE}, all prescribing and dispensing entities should participate in an information sharing system that can facilitate this complex task on local, regional, and even on national scale. For example, significant problems have been reported with regards to community and internet-based pharmacies that may be uneasy with regards to sharing information about a patient’s current medications.\textsuperscript{18} One study of \textit{medication reconciliation} performed at the time of hospital admission found that 54\% of patients had medication discrepancies, of which nearly 60\% could result in potential harm if not discovered.\textsuperscript{23} The effectiveness of \textit{medication reconciliation} is clearly demonstrated by one study in the critical care setting, where errors at the time of discharge from a critical care unit were virtually eliminated by a reconciliation process.\textsuperscript{24} Evidence is also emerging that \textit{medication reconciliation} is best performed in a multidisciplinary setting.\textsuperscript{19} According to one report, the number of medication discrepancies decreased from an average of 0.5 per patient to zero per patient before and after the implementation of \textit{multidisciplinary medication reconciliation} process.\textsuperscript{19}

\begin{table}[h]
\centering
\begin{tabular}{|c|}
\hline
\textbf{POLYPHARMACY: IMPORTANT STRATEGIES FOR PREVENTING ADVERSE OUTCOMES} \\
\hline
\textbullet Assist patients with making a comprehensive list of their prescription and over-the-counter medications. This should include the dose, frequency, strength, and duration of therapy \\
\textbullet Educate patients that medication nonadherence may lead to unnecessary medication changes \\
\textbullet Encourage patients to carry the list of their medications to every physician appointment and update this list whenever changes are made to their medication regimen \\
\textbullet Encourage patients to read all labels carefully and to use only one pharmacy (or as few pharmacies as possible) \\
\hline
\end{tabular}
\caption{Table 5. Proposed patient-centered strategies for reducing complications associated with polypharmacy. Modified from reference 28.}
\end{table}

Process recommendations for \textit{medication reconciliation} programs include some combination of the following components: (a) identification process for patients at risk; (b) performance of reconciliation by a pharmacist or a nurse as soon as possible after admission; (c) pharmacist or nurse reconciliation of any unintended or unanticipated variances via discussion with physician; and (d) written instructions regarding pre-admission medications included with discharge prescriptions.\textsuperscript{25} Again, one of the crucial aspects that will be required if large-scale \textit{medication safety and reconciliation programs} are to be effective will be the implementation of widespread, standardized, universally compatible, adequately monitored, and easy-to-use communication systems.\textsuperscript{14} \textit{Medication reconciliation} is not without certain disadvantages. These drawbacks include: (a) labor intensive nature of the overall process; (b) the fact that many of the identified errors are not clinically significant; and (c) the still imprecise quantification of the true beneficial effect of \textit{medication reconciliation} on patient outcomes.\textsuperscript{25}

\textbf{CONCLUSIONS}

Medication related errors constitute a serious problem within our healthcare system. Geriatric patients are at especially high risk of \textit{MRE} both because of the high incidence of \textit{polypharmacy} in this group and because of the inadequacy within the current medication/prescription information sharing systems that can further exacerbate the effects of \textit{polypharmacy}. Measures aimed at reduction of \textit{MRE} and \textit{ADE} should involve a combination of human- and technology-based measures. Among those measures, \textit{computerized medication order entry and medication reconciliation} appear to provide the most promise. Although institution-specific medication safety systems should be able to freely interface within regional and/or national medication safety systems, such an extensive undertaking may be very costly and difficult to implement because of patient privacy issues and likely requirement for new legal framework and/or changes to existing laws.

![Figure 4. Frequencies of medication errors during different phases of the medication management cycle. Note that prescribing and administration errors constitute approximately 90\% of all medication errors.\textsuperscript{30}](Image 318x125 to 558x374)
REFERENCES


