Polypharmacy in Elderly Patients

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ABSTRACT

Background: Polypharmacy (ie, the use of multiple medications and/or the administration of more medications than are clinically indicated, representing unnecessary drug use) is common among the elderly.

Objective: The goal of this research was to provide a description of observational studies examining the epidemiology of polypharmacy and to review randomized controlled studies that have been published in the past 2 decades designed to reduce polypharmacy in older adults.

Methods: Materials for this review were gathered from a search of the MEDLINE database (1986–June 2007) and International Pharmaceutical Abstracts (1986–June 2007) to identify articles in people aged >65 years. We used a combination of the following search terms: polypharmacy, multiple medications, polymedicine, elderly, geriatric, and aged. A manual search of the reference lists from identified articles and the authors’ article files, book chapters, and recent reviews was conducted to identify additional articles. From these, the authors identified those studies that measured polypharmacy.

Results: The literature review found that polypharmacy continues to increase and is a known risk factor for important morbidity and mortality. There are few rigorously designed intervention studies that have been shown to reduce unnecessary polypharmacy in older adults. The literature review identified 5 articles, which are included here. All studies showed an improvement in polypharmacy.

Conclusions: Many studies have found that various numbers of medications are associated with negative health outcomes, but more research is needed to further delineate the consequences associated with unnecessary drug use in elderly patients. Health care professionals should be aware of the risks and fully evaluate all medications at each patient visit to prevent polypharmacy from occurring. (Am J Geriatr Pharmacother. 2007;5:345–351) Copyright © 2007 Excerpta Medica, Inc.

Key words: polypharmacy, older adults, morbidity, mortality.
INTRODUCTION
People aged ≥65 years are one of the most rapidly growing age groups in the United States. In 2005, there were ~27 million adults in this age group, with the number of women outweighing men. Many older adults have multiple medical conditions, such as hypertension, arthritis, heart disease, cancer, and diabetes mellitus, which require multiple medications for proper treatment. The use of multiple medications is often referred to as polypharmacy, but a standard definition is not used. A second and perhaps more important definition is the administration of more medications than are clinically indicated, representing unnecessary drug use. Unfortunately, using multiple medications may cause problems such as the increased risk of inappropriate use of medications (including drug–drug interactions and duplication of therapy), nonadherence, and adverse effects.

The objective of this review was to provide a description of observational studies examining the epidemiology of polypharmacy and to review randomized controlled studies that have been published in the past 2 decades designed to reduce polypharmacy in older adults.

MATERIALS AND METHODS
The MEDLINE database (1986–June 2007) and International Pharmaceutical Abstracts (1986–June 2007) were searched to identify articles on polypharmacy in the elderly. We used a combination of the following search terms: polypharmacy, multiple medications, polymedicine, elderly, geriatric, and aged. We also conducted a manual search of the reference lists from identified articles and the authors’ article files, book chapters, and recent reviews to identify additional articles. Articles were included only if they were: (1) in English; (2) involved those aged ≥65 years; (3) not a review; or (4) observational or randomized trials that either quantified the multiple use of medications and their consequences or described interventions to reduce polypharmacy.

RESULTS
Drug Utilization Studies
Twenty-one studies were examined. There is not a consistent cut point that defines polypharmacy. Previous studies have used 2, 4, 5, and 9 medications to identify polypharmacy. Surveys of community-based elderly patients show that 2 to 9 prescription medications on average are taken per day. A national survey by Kaufman et al found that 57% of US women aged ≥65 years took ≥5 prescription medications and 12% took ≥10 medications. This is consistent with results from a large study in Europe (N = 2707; mean age, 82.2 years), which found that 51% of patients took ≥6 medications per day.

It is also important to evaluate the use of nonprescription medications in older adults. A study of 1059 rural community-dwelling elderly patients (mean age, 74.5 years) found that almost 90% took ≥1 and almost 50% took 2 to 4 over-the-counter medications. Another study of 2590 noninstitutionalized patients reported that 47% to 59% of older patients took a vitamin or mineral and 11% to 14% took herbal supplements. Data also suggest that polypharmacy may be increasing in the elderly, especially in those aged ≥85 years.

An important consideration in evaluating polypharmacy is the types of medications that are being consumed. A large national survey in the United States found that the most common prescription medications used in noninstitutionalized patients were estrogen products, levothyroxine, hydrochlorothiazide, atorvastatin, and lisinopril. Cardiovascular agents, antibiotics, diuretics, opioids, and antihyperlipidemics were the most frequently used classes of prescription medications in a large study of Medicare patients. Pain medications (eg, acetaminophen, ibuprofen, acetylsalicylic acid), cold and cough medications (eg, pseudoephedrine, diphenhydramine), and vitamin or nutrient products (eg, multivitamins, vitamins E and C, ginseng, Ginkgo biloba extract) were the most common nonprescription medications consumed. Analgesics, vitamins, minerals, antacids, and laxatives were also found to be commonly used nonprescription agents among the elderly.

Prevalence, Predictors, and Risks of Unnecessary Polypharmacy
Five studies have evaluated the unnecessary drug use definition of polypharmacy. A study of 236 ambulatory patients aged ≥65 years by Lipton et al found that almost 60% of patients were taking medications that were suboptimal or lacking an indication. Schmader et al had similar findings: they reported that 55% of 208 elderly patients were taking drugs without an indication. They also found that one third of patients were taking ineffective drugs, and 16% had a therapeutic duplication in their medication regimens. In a study of 834 outpatients aged ≥65 years, Schmader et al evaluated unnecessary drug use, defined by the Medication Appropriateness Index (MAI) criteria as a medication with no indication, lack of effectiveness, or therapeutic
duplication. The daily mean number of unnecessary drugs was 0.65 per person. A study in frail elderly veterans (N = 384), which also used the MAI to define unnecessary drug use, found that 44% of patients had ≥1 unnecessary medication at hospital discharge, with 25% of the patients having the medication started during the hospitalization. The reasons for the unnecessary drug use included no indication (32%), lack of effectiveness (18%), and therapeutic duplication (7%). Gastrointestinal, central nervous system, and therapeutic nutrient/mineral agents were found to be the most commonly used unnecessary drugs. Another recent study of veteran outpatients (N = 196) aged ≥65 years found a 64% prevalence of medication underuse. This study also showed that underuse and unnecessary use of medications simultaneously occurred in 42% of patients.

No studies were found in the literature search linking unnecessary drug use with health outcomes. However, it is likely that unnecessary drug use would be related to increased drug expenditures.

Risk Factors for Polypharmacy
Nine studies were assessed to determine the risk factors for polypharmacy. Many risk factors for polypharmacy have been identified and can be classified into 1 of 3 groups: demographic, health status, and access to health care characteristics. Increased age, white race, and education are demographic characteristics associated with polypharmacy. Poorer health, depression, hypertension, anemia, asthma, angina, diverticulosis, osteoarthritis, gout, diabetes mellitus, and use of ≥9 medications are the health status characteristics associated with polypharmacy. Predictors of polypharmacy related to access to health care characteristics include number of health care visits, supplemental insurance, and multiple providers.

Consequences of Polypharmacy
Eighteen studies examined the consequences associated with polypharmacy. There may be many consequences associated with polypharmacy. Patients are at an increased risk of receiving an inappropriate medication and having an adverse drug reaction (ADR), which may impact a patient’s adherence to his or her medication regimen. Polypharmacy has also been reported to increase the risk of geriatric syndromes and morbidity/mortality.

Adherence
Polypharmacy creates complex medication regimens that make nonadherence a common problem in the elderly, with prevalence rates averaging 50%. However, elderly patients are adherent with ~3 out of every 4 of their individual medications. The elderly also have adherence rates similar to younger patients when number of drugs is taken into account.

Inappropriate Prescribing
Studies have shown that the use of multiple medications increases the risk of inappropriate prescribing. Hanlon et al found that both the number of prescription (odds ratio [OR], 1.28; 95% CI, 1.21–1.36) and nonprescription (OR, 1.17; 95% CI, 1.12–2.35) medications increased the risk of inappropriate prescribing as defined by the MAI in frail elderly veterans. A cross-sectional study in 786 patients (mean age, 78 years) receiving home health care reported that polypharmacy increased the risk of potentially inappropriate medications, as defined by the Beers criteria, and the risk of potentially dangerous drug interactions.

Adverse Drug Reactions
The risk of ADRs may increase with increased number of drugs taken. An ADR, as defined by the World Health Organization, is a reaction that is noxious and unintended, and which occurs at dosages normally used in humans for prophylaxis, diagnosis, or therapy. ADRs have been reported to occur in 5% to 35% of outpatients and account for as many as 12% of hospital admissions in older patients. The risk of ADRs is strongly associated with multiple comorbidities, use of specific types of drugs such as warfarin, and increasing number of drugs taken.

Geriatric Syndromes
A study by Larson et al showed an increased risk of cognitive impairment with multiple medications. A study by Ruby et al found that the use of multiple medications with urologic activity increased the risk of urinary incontinence.

A few studies have examined the impact of multiple medication use on falls. Those patients taking ≥2 psychotropic agents had a 2.4- to 4.5-fold increased risk of falling than those taking 1 central nervous system drug. A study by Agostini et al examined the risk of polypharmacy and balance in 885 community-dwelling residents aged ≥72 years. For impaired balance, adjusted ORs were 1.44 (95% CI, 0.94–2.19) for those taking 1 to 2 medications, 1.72 (95% CI, 1.09–2.71) for those taking 3 to 4 medications, and 1.80 (95% CI, 1.02–3.19) for those taking ≥5 medications. The authors concluded that a greater number of medications were...
associated with an increased risk of adverse drug outcomes.⁴⁹ Weiner et al⁵⁶ found that elderly male outpatients (N = 305; age range, 70–104 years) taking ≥2 central nervous system medications (i.e., benzodiazepines, other sedative/hypnotics, antidepressants, antipsychotics, opioid analgesics) had a 2.37-fold increased risk of falls.

**Morbidity/Mortality**

There are data which suggest that, even after controlling for multiple comorbidities, polypharmacy is associated with a decline in physical and instrumental activities of daily living.⁵¹ Polypharmacy is also associated with negative consequences, such as increased risk of mortality.⁵² In addition, polypharmacy increases medical costs. Older patients with heart failure taking 11 doses per day were found to have annual drug costs >83800 in 2001.⁵³

**Interventions to Reduce Polypharmacy**

Five studies were found that met our inclusion criteria (Table). The overall 3 studies were conducted in managed care populations that used prescriber education as the intervention to reduce polypharmacy.²⁰,²⁸,⁵⁶ Another study utilized a medication grid to alert providers as to how many drugs were being administered.⁵⁶ Finally, the last study was a randomized controlled trial that evaluated the use of geriatric evaluation and management (GEM) on inpatient and outpatient care.²⁸

Although there are a number of studies that have targeted older patients taking multiple medications, polypharmacy may not be reduced if one improves both unnecessary use and underuse simultaneously, as no difference in overall medications will be found.¹¹ Several studies have proposed possible methods of reducing the number of medications for elderly patients. Muir et al⁵⁶ supplied a medication grid to medical resi-

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Setting</th>
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<th>Results</th>
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<tr>
<td>Muir et al, 2004</td>
<td>General medicine inpatient service</td>
<td>Medication grid provided to admitting residents that listed all medications and administration times for 1 week.</td>
<td>Medication grid reduced number of medications per patient in the intervention group (0.92) compared with the control group (1.65) (P &lt; 0.001).</td>
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<tr>
<td>Fillit et al, 1999</td>
<td>Medicare managed care organization</td>
<td>Mailing to elderly Medicare managed care members at risk for polypharmacy urging them to meet with their physicians and bring medications with them for review.</td>
<td>Of the 42% of the population at risk who had a medication review with their physician, 20% reported having a medication discontinued.</td>
</tr>
<tr>
<td>Fick et al, 2004</td>
<td>Medicare + Choice southeastern managed care organization</td>
<td>Physicians were mailed a list of patients taking potentially inappropriate medications.</td>
<td>Overall, 12.5% of potentially inappropriate medications were discontinued.</td>
</tr>
<tr>
<td>Zarowitz et al, 2005</td>
<td>Outpatient, managed care</td>
<td>Clinical pharmacy medication review with physician education.</td>
<td>Overall, polypharmacy event rate decreased from 29.01 to 9.43 events/1000 patients after the first mailing and from 27.99 to 17.07 events/1000 patients after the second mailing.</td>
</tr>
<tr>
<td>Schmader et al, 2004</td>
<td>Inpatient and outpatient care for veterans</td>
<td>Inpatient or outpatient GEM.</td>
<td>Unnecessary and inappropriate drug use was reduced in inpatients receiving GEM care (P &lt; 0.05).</td>
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GEM = geriatric evaluation and management.
dents caring for hospitalized elderly patients ready to be discharged to home that consisted of a listing of all medications and times of administration over the previous week. They found that the number of medications was reduced in the intervention group by 0.92 per patient compared with an increase of 1.65 medications in the control group (P < 0.001). Number of doses per day also decreased in the intervention group. A survey study in a Medicare managed care population evaluated whether a medication review by primary care physicians resulted in a change in medications. Patients were sent letters urging them to bring their medications in for a review, and primary care physicians were given clinical practice guidelines on polypharmacy. Of the 42% of patients at risk who had a medication review with their physician, 20% had a medication discontinued by their physician and almost 30% had a change in medication dose. Another study among Medicare managed care patients found that mailing physicians a list of patients who were taking a potentially inappropriate medication resulted in a discontinuation of a medication in 12.5% of cases. Zarowitz et al used clinical pharmacists to educate and aid physicians in reducing polypharmacy among outpatient managed care patients (N = 195,971). They found that the rate of patients receiving ≥5 medications decreased from 7.99 to 4.1 events/1000 patients after the intervention. It was also reported that the rate of overall polypharmacy events—defined as use of ≥5 medications, ≥2 narcotics, ≥2 benzodiazepines, ≥3 oral antidiabetic medications, or the use of sildenafil with a nitrate—was reduced from 27.99 to 17.07 events/1000 patients after a second mailing.

Only one study was found in our literature search that attempted to reduce unnecessary drug use. A multisite, randomized controlled study was reported that examined the impact of inpatient and outpatient GEM on drug-related problems in 834 patients at 11 US Veterans Affairs hospitals and clinics. They found that inpatient GEM care significantly reduced (P < 0.05) unnecessary drug use, as measured by the MAI, compared with usual care.

**Clinical Considerations for Polypharmacy**

Obtaining a thorough medication history is very important before any new medication is prescribed. Both prescription and nonprescription medications need to be taken into account and should be brought with the patient to all health care provider visits. Once the prescriber has a complete medication history, he or she can then decide whether the addition of another medication is clinically indicated and if the benefits outweigh the risk of use. Nonpharmacologic therapy, such as diet modification or exercise, may be appropriate instead of medication in some cases. If a medication is determined to be clinically necessary, the drug’s pharmacokinetic, pharmacodynamic, and adverse-event profile, along with the patient’s renal and hepatic function, must be taken into account for proper dosing. Starting doses are often lower in the elderly and may be administered differently than in younger patients to prevent toxicity from occurring. Other concomitant disease states and medications should be evaluated to prevent any drug–disease or drug–drug interactions from occurring. Educating both patients and their families verbally and in writing about their medications can improve adherence. Considering generic options, utilizing compliance aids (eg, pillboxes, medication calendars), limiting the prescribing of as-needed drugs, simplifying medication regimens to medications that can be dosed QD or BID, and encouraging family support may help enhance medication adherence. Setting sensible therapeutic goals and assessing medication regimens periodically are also very important to ensure that polypharmacy does not lead to unnecessary medical problems.

**CONCLUSIONS**

Polypharmacy is common among the elderly. Many studies have found that various numbers of medications are associated with negative health outcomes, but more research is needed to further delineate the consequences associated with unnecessary drug use. Health care professionals should be aware of the risks and fully evaluate all medications at each patient visit to prevent polypharmacy from occurring.

**REFERENCES**


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