Evidence-based strategies to reduce polypharmacy: A review

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Abstract

Introduction
Polypharmacy, a preventable and significant contributor to morbidity and mortality in the geriatric population, is best defined as any number of medications that exceed medical necessity. A multi-pronged approach using evidence-based interventions is needed to effectively address polypharmacy and prevent downstream harm to patients. Resources and interventions should target patients, situations, and prescribing practices associated with higher risk of experiencing an adverse drug event. Liberalizing clinical targets in the elderly and drawing from palliative care concepts can pave the way for rational discontinuation of multiple medications. Many of these strategies are employed by interdisciplinary teams and models of care that have proven to be effective in minimizing polypharmacy.

Conclusion
This review summarizes current evidence-based strategies for addressing polypharmacy and reducing medication-related harm to vulnerable populations such as the elderly. Future investigations should validate risk assessment tools and evaluate interdisciplinary models of care in geriatric populations and settings.

Introduction

Polypharmacy is widely recognized as a contributor to adverse outcomes in geriatric populations. As the proportion of elderly people (≥65 years of age) in the population continues to grow, the burden of associated comorbidities managed with medications will increase1. The traditional and perhaps most widely used definition of polypharmacy is of five or more medications, possibly implying that patients using fewer medications are not at risk for adverse drug events (ADE).

Viktil et al. instead found a linear relationship between number of ADE and number of drugs used2. As such, recent research has shifted to a relative definition of “more medications than clinically indicated.” Reports describe between 44% and 59% of elderly patients taking ≥1 medications unnecessarily3,4,5.

Significant consequences of undue medications in the elderly include increased risk of ADE, drug-drug interactions, geriatric syndromes, medication non-adherence, and both direct and indirect costs4.

Reducing polypharmacy in vulnerable populations demands a multi-pronged approach that includes risk identification, strategies to minimize medications, and interdisciplinary teamwork. This review draws upon existing literature to suggest evidence-based strategies to minimize polypharmacy.

Discussion

Strategies to Decrease Polypharmacy

Risk Identification: High-Risk Patients and Situations
One essential strategy is to identify, stratify, and target individual patients at higher risk of polypharmacy and ADE.

Multiple studies have identified risk factors associated with polypharmacy and patients who develop ADE7,8. These patient characteristics can be classified into three groups: 1) demographic (increasing age, white race, female gender, higher levels of education), 2) health status (general poor health, cardiovascular disease, hypertension, asthma, diabetes), and 3) access to health care (increased number of health care visits, multiple providers, type of insurance)6.

Moreover, patients with a history of ADE were also more likely to suffer from subsequent ADE9.

Geriatric patients are also particularly vulnerable to the effects of polypharmacy due to comorbidity- and age-related functional decline of the kidney and liver affecting metabolism and clearance of drugs10. Additionally, decreased lean body mass and total body water with a relative increase in total body fat can further alter drug kinetics. Consequently, medications used in the elderly may have faster onset, higher bioavailability, and longer duration of action11. When prescribing medications, providers should pay particular attention to these variable factors in the elderly that can lead to ADE and other complications.

More recently, a risk score known as the GerontoNet ADR Risk Score was developed through analysis of a large Italian database of 5,936 hospitalized geriatric patients. It predicts risk of ADE by including many of the above risk factors such as number of comorbidities, presence of heart failure and liver disease, number of drugs, previous ADE, and renal failure. The tool’s area under the receiver operator characteristic curve (ROC) of 0.71 was subsequently validated in four European academic hospitals and found to have similar predictive ability12.

However, further studies are needed in order to apply this tool to different populations and settings such as

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nursing homes and ambulatory clinics.

Situations that involve transitions of care, such as a hospital discharge or transfer to nursing home, place a patient at higher risk of ADE and should also be a target for intervention. According to a cross-sectional study by Hajjar et al. that looked at rates of polypharmacy in elderly hospitalized patients at discharge, 41.4% were on 5-8 medications and 37.2% were on 9+ medications.

Furthermore, 58.6% of patients took one or more unnecessary medications. The nursing home is another setting that requires careful attention to reduce polypharmacy. The 2004 United States Nursing Home Survey found that 39.7% of nursing home patients were on 9 or more medications. Careful medication reconciliation encouraged at these transitions will be a key aspect of limiting polypharmacy.

Another high-risk scenario occurs when patients are treated by multiple providers. As elderly patients have increasingly complicated medical issues, the number of subspecialists involved in their care is also likely to increase. The number of prescribers has strongly been shown to be an independent risk factor for ADE. Adjusted analyses of 405 elderly patients in a cohort study showed that each additional prescriber significantly increased the odds of self-reporting an ADE by 29%.

The authors of this study felt this finding was likely related to poor communication and deficiencies in care coordination. Consolidation of care through a central primary care provider may help mitigate this problem.

**Risk Identification: high-risk prescribing practices**

Recognization of inappropriate prescription medications is acknowledged to be an important indicator of quality of care tied to clinical outcomes, and is used as a benchmark in older patients enrolled in Medicare and other managed care plans.

In practice, researchers and clinicians use several measures to identify potentially inappropriate medications (PIMs). The oldest and most well-known of these is the Beers criteria. The criteria consist of a list of medications to potentially avoid or replace in patients ≥65 years of age.

It is simple and can be applied to large populations but has several limitations including: 1) the inclusion of obsolete drugs, 2) a need for periodic updating, 3) some controversial contraindications, 4) omission of drug-drug interactions or drug duplications, and 5) overlooking medication omission errors.

A study using the 2003 Beers criteria found a non-significant increase in the odds of having an ADE when exposed to a drug on the list.

Another study defined inappropriate medications using the Beers criteria in combination with other explicit criteria (that accounted for drug-drug interactions and therapeutic duplication) and found a significantly increased association with ADE (adjusted odds ratio [OR]: 2.14; 95% confidence interval [CI]: 1.01-2.61).

The Screening Tool of Older Persons Potentially Inappropriate Prescriptions and Screening Tool to Alert Doctors to the Right Treatment (STOPP/START) criteria were developed and validated to address the limitations of the Beers criteria. STOPP/START criteria are organized by system, list drug-drug and drug-disease interactions to avoid (e.g. thiazide diuretic with history of gout), and address therapeutic duplication and omission errors. Hamilton et al. prospectively studied 600 consecutive elderly inpatients and found the adjusted odds ratios for serious avoidable ADE were 1.85 (95% CI: 1.51-2.26) and 1.28 (95% CI: 0.95-1.72) with application of STOPP criteria and Beers criteria, respectively, suggesting that STOPP/START may more accurately predict ADE.

In contrast, the Medication Appropriateness Index (MAI) is considered an implicit tool because it incorporates clinical judgment. The tool consists of 10 questions that are to be applied to each medication, for example: “Is there an indication for the drug? Is it effective for the condition? Is there unnecessary duplication with other drugs?” The MAI focuses on the patient-medication interaction rather than solely the medication and is able to detect change over time. Lund et al. found that a modified MAI scoring approach (allowing clinicians to decide which MAI items were appropriate) significantly predicted ADE risk (OR: 1.13; 95% CI 1.02-1.26), while Beers criteria and the original MAI scoring approach did not.

The ideal measure would be simple, easy to calculate, patient-centred, and validated in both inpatient and outpatient settings. While none of the existing measures are perfect, the explicit tools are easier to implement and can even be incorporated into an electronic medical record.

Considering the Beers criteria was designed as a research tool, the STOPP/START criteria may be more practical at flagging high-risk prescribing in clinical practice. The MAI, although more time-consuming, may have promise as a predictive tool for ADE when used by well-trained clinicians.

**Strategies to minimize medications**

**Altering clinical targets**

Most clinical trials upon which clinical targets are based exclude elderly and cancer patients: two groups identified as at particular risk of ADE. However, a growing body of evidence suggests that maintaining these strict goals (e.g. hemoglobin A1c <7 in diabetes or tighter blood pressure control based on comorbidities) may in fact be harmful in the elderly. The widely-cited Action to Control Cardiovascular Risk in
Diabetes (ACCORD) trial demonstrated no decrease in MI, stroke, or cardiovascular death with tight glycemic control, but rather an increased risk of hypoglycemia, adverse events, and death\textsuperscript{25}.

In a retrospective study examining healthcare claims data of over 860,000 diabetic patients over age 18, researchers noted an association between hypoglycemic events and hospital admissions for cardiovascular events (e.g. MI, CAGB, revascularization, PCI, unstable angina)\textsuperscript{26}.

Even the Hypertension in the Very Elderly Trial (HYVET), a randomized controlled trial that showed reduction in stroke and overall mortality in very elderly patients (>80 years old) with blood pressure management, showed benefit at a goal blood pressure of 150/80--higher than oft-cited goal blood pressures\textsuperscript{27}. By liberalizing our clinical targets, we may be able to minimize morbidity and decrease usage of medications such as sulfonylureas or antihypertensives that may have more potential to harm than help.

**Drawing from palliative care**

Palliative care teams often discontinue multiple non-essential therapies at the end of life (for instance, in patients with advanced dementia) and these strategies may be applicable to elderly patients without an end-stage diagnosis\textsuperscript{28}. Bain et al. proposed a conceptual framework that employs routine, rational discontinuation of medications. The framework includes four key steps: 1) recognize an indication to discontinue medications (e.g. diminished benefit, change in symptoms), 2) identify and prioritize medication(s) to be discontinued, 3) discontinue with proper planning, communication, and coordination with other providers, and 4) monitor for effects\textsuperscript{29}.

A group in Israel, applying similar palliative care principles to geriatric and disabled (but non-palliative care) patients, developed and tested the Good Palliative Geriatric Practice algorithm. Rooted in the notion that "less is more", their studies show that a careful discontinuation of non-essential medications can be successful. The algorithm asks, in essence, "Is there evidence for this drug in this patient's age group?" and if not, "Does benefit outweigh risk? Would an alternative be better? Would a lower dose be more appropriate?" In so doing, the algorithm guides providers through a careful analysis of each medication in the context of that patient's clinical situation. Of 70 elderly patients, an average of 4.9 drugs were discontinued in 64 patients; only 2% were restarted because of recurrence of the original indication. Not only was discontinuation not harmful, but an astounding 88% of patients also reported a global improvement in health\textsuperscript{30,31}. Applying a systematic approach may offer the freedom to discontinue multiple medications at once without fear of adverse outcome.

**In practice: interdisciplinary teams**

**Comprehensive Geriatric Assessment**

The Comprehensive Geriatric Assessment (CGA) is a global, multilevel approach that identifies medical, psychosocial, and functional limitations of elderly patients and provides integrated care through an interdisciplinary team\textsuperscript{32,33}.

These teams include at minimum a geriatrician, social worker, and nurse who follow standard protocols to 1) assess functional, cognitive, affective, and nutritional status; 2) screen for geriatric syndromes such as incontinence and falls; 3) assess caregivers and social support; and 4) develop a specific, individual plan for each patient\textsuperscript{34}. The CGA pays particular attention to medication management with goals of improving the quality of prescribing and both recognizing and preventing potential ADE\textsuperscript{31}.

CGA principles have been applied to multiple models of care, including acute care units, home geriatric assessments, and outpatient consults and clinics, which have all been widely studied. Acute Care of the Elderly (ACE) inpatient units were developed in the 1990s and have been shown to improve quality of care without increasing lengths of stay\textsuperscript{35}. A "mobile" version of this approach (that does not require a physical unit) was associated in a prospective matched cohort study with lower rates of adverse events, shorter hospital stays, and better satisfaction\textsuperscript{36}.

Similarly, a trial randomizing 834 elderly VA patients to outpatient CGA services found the intervention reduced risk of serious ADE by 35% compared with usual care in the outpatient clinical setting\textsuperscript{37}. The integrated, team-based, patient-centred model of the CGA clearly improves care for geriatric patients in multiple settings.

**Role of Clinical Pharmacists**

Incorporating pharmacist expertise is essential to reduce polypharmacy and occurs in several settings. First, a pharmacist located in the clinic is uniquely situated to educate both patients and providers and has been shown in randomized trials to decrease both the number of total prescribed medications and PIMs\textsuperscript{38}. A recent prospective study demonstrated improved clinical outcomes when a clinic pharmacist reviewed each medication regimen, counselled the patient, and provided a report to the health care provider; at 6 months not only did the number of ADE decrease from 2 to 0, but patient adherence also improved significantly\textsuperscript{39}.

Second, pharmacists in the community and at the level of managed care are able to centralize information from multiple providers. These pharmacists can thus identify PIMs and high-risk drug combinations and then alert both patients and providers. Managed care interventions targeting both patients and physicians with mailed recommendations find that between 15% and 45% of physicians report subsequent change to the medication regimen\textsuperscript{40,41}. These changes are borne out in outcomes data such as decreased polypharmacy events and lower diagnoses.
Conclusion
Polypharmacy places geriatric patients at risk of adverse events, functional decline, and geriatric syndromes. The strategies outlined above, such as use of a risk stratification tool and application of palliative care principles, represent initial steps forward to reduce polypharmacy; however, much work remains.

Future investigations should continue to develop and validate risk assessment tools in various elderly populations and settings. Some of these tools may eventually be integrated into an EMR and thus easily highlight the patients most at risk.

Future clinical trials focused particularly on the elderly could also provide data about optimal clinical targets and lenient treatment strategies. Finally, models of care utilizing the comprehensive geriatric assessment approach should become standard of care in elderly patients. In these models, pharmacists play a key role in minimizing medications and reducing errors and thereby improving patient safety and outcomes. Evidence-based strategies exist, but further implementation studies in the geriatric population are needed to evaluate utility in clinical practice.

References
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