Published in final edited form as:
Expert Opin Drug Saf. 2014 January ; 13(1): . doi:10.1517/14740338.2013.827660.

Clinical Consequences of Polypharmacy in Elderly

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Abstract

Introduction—Polypharmacy, defined as the use of multiple drugs or more than are medically necessary, is a growing concern for older adults.

Areas Covered—We present information about; 1.) Prevalence of polypharmacy and unnecessary medication use. ; 2.) Negative Consequences of Polypharmacy; 3.) Interventions to improve polypharmacy.

Expert Opinion—International research shows that polypharmacy is common in older adults with the highest number of drugs taken by those residing in nursing homes. Nearly 50% of older adults take one or more medications that are not medically necessary. Research has clearly established a strong relationship between polypharmacy and negative clinical consequences. Moreover, well designed inter-professional (often incuding clinical pharmacist) intervention studies that focus on enrolling high risk older patients with polypharmacy have shown that they can be effective in improving the overall quality of prescribing with mixed results on distal health outcomes.

Keywords

aged; drug utilization; polypharmacy; suboptimal drug use

1.0 Introduction

Given the rising tide of persons over the age of 65 worldwide, polypharmacy is a becoming more prevalent in older adults. Examining the definition as it appears in a standard medical dictionary reveals that the word “poly” is derived from the Greek word meaning more than one and that “pharmacy” referring to the Greek word for drug “pharmacon”[1]. Unfortunately, there is no standard cut point with regard to the number of medications that is agreed upon for the definition of polypharmacy. To operationalize this definition, researchers have arbitrarily chosen various cut points. An alternative definition for polypharmacy is the use of more medications than are medically necessary [2]. For this

definition, medications that are not indicated, not effective, or constitute a therapeutic duplication would be considered polypharmacy. Although this definition is more clinically relevant, it does necessitate a clinical review of medication regimens.

This review will begin with information about the prevalence and types of medications taken by older adults with polypharmacy. This section will also highlight the prevalence and types of unnecessary drugs as well. The next section will detail the epidemiology of adverse health outcomes resulting from polypharmacy. Following this, evidence from randomized, controlled intervention trials that included older adults with polypharmacy showing how medication use can be improved will be presented. We will then finish with an expert opinion and conclusion sections.

2.0 Polypharmacy in the Various Settings (Table 1)

There have been numerous studies that have documented the rates of polypharmacy defined as multiple drugs in various settings. Fewer studies have focused on the use of unnecessary drugs.

2.1 Ambulatory Care

Many studies in ambulatory care define polypharmacy as a medication count of five or more medications. However, current medical practice guidelines often require multiple medications to treat each chronic disease state for optimal clinical benefit. Therefore, an elderly patient with at least two disease states, such as heart failure and chronic obstructive pulmonary disease, will usually exceed this arbitrary threshold of > five medications [3]. For example, a 2005-2006 study from the USA reported by Qato et al used a population-based survey of community dwelling persons 57-85 years of age [4]. Overall 37.1% of men and 36% of women between 75 and 85 years of age took at least five prescription medications. **Table 1** shows the most common prescription medications reported. Moreover, among this older age group taking at least one prescription medication, 47.3% reported the use of an over-the-counter medication and 54.2% a dietary supplement. The use of unnecessary drugs was studied in 128 older male outpatients from the United States [5]. Overall 58.6% of patients took one or more unnecessary prescribed drug. The most commonly prescribed unnecessary drugs are summarized in **Table 1**.

2.2 Hospital Setting

Few studies have examined the issue of polypharmacy in the hospitalized elders. A study by Hajjar and colleagues looked at both definitions of polypharmacy at hospital discharge [6]. Among 384 patients studied, it was reported that 41.4 % were on at least 5-8 medications, and 37.2% were on 9 or more. Overall 58.6% of patients took one or more unnecessary prescribed drug. **Table 1** lists the most common unnecessary medication classes and individual agents. An Italian study in 2011, examined the prevalence of polypharmacy in the hospital setting both at admission and discharge [7]. They found that on admission 51.9% of patients were on greater than five medications with an average of 4.9 medications and 5.2 diagnoses. At discharge this rate increased to 67% with an average of 6.0 medications and 5.9 diagnoses. **Table 1** provides information about the most common drug classes that patients were on at discharge.

2.3 Nursing Home Setting

Polypharmacy in nursing homes has been an ongoing concern over the past four decades. In the late 1990's, the US Center of Medicare and Medicaid Services felt this to be such an important issue that it implemented a quality indicator measure targeting patients on 9 or more medications. A study using data from the 2004 United States Nursing Home Survey

found that 39.7% had polypharmacy defined by this quality indicator measure [8]. Of note the group with the lowest rate of polypharmacy was those patients age 85 years or older (34.8%). **Table 1** shows the top ten most common medication classes used among this nursing home population. In contrast, a study of 64,395 Canadian nursing home patients studied reported that only 15.5% were on > 9 medications [9]. The top therapeutic drug classes prescribed to this cohort can be seen in **Table 1**. To the best of our knowledge no multisite study has been conducted examining unnecessary drug use in older nursing home patients [2].

3.0 Consequences of Polypharmacy

Unfortunately, there are many negative consequences associated with polypharmacy. , Specifically, the burden of taking multiple medications has been associated with greater health care costs and an increased risk of adverse drug events (ADEs), drug-interactions, medication non-adherence, reduced functional capacity and multiple geriatric syndromes.

3.1 Increased Healthcare Costs

Polypharmacy contributes to health care costs to both the patient and the healthcare system. A retrospective cohort study found that polypharmacy was associated with an increased risk of taking a potentially inappropriate medication and an increased risk of outpatient visits, and hospitalization with an approximate 30% increase in medical costs [10]. Another study conducted in Sweden reported that those taking 5 or more medications had a 6.2% increase in prescription drug expenditure and those taking 10 or more medications had a 7.3% increase [11].

3.2 Adverse Drug Events

In 2005, it was estimated that over 4.3 million health care visits were attributed to an ADE [12]. It has been reported that up to 35% of outpatients and 40% of hospitalized elderly experience an ADE. Furthermore, approximately 10% of emergency room visits are attributed to an ADE [13]. In a population based study, outpatients taking 5 or more medications had an 88% increased risk of experiencing an ADE compared to those who were taking fewer medications [12]. In nursing home residents, rates of ADEs have been noted to be twice as high in patients taking 9 or more medications compared to those taking less [14]. Another study evaluating unplanned hospitalizations in older veterans found that a patient taking more than 5 medications was almost 4 times as likely to be hospitalized from ADE [15]. As one might expect, common drug classes associated with ADEs include anticoagulants, NSAIDs, cardiovascular medications, diuretics, antibiotics, anticonvulsants, benzodiazepines, and hypoglycemic medications [13,15,16].

3.3 Drug-Interactions

Older adults with polypharmacy are predisposed to drug- interactions [17]. In a prospective cohort study of older hospitalized adults taking 5 or more medications, the prevalence of a potential hepatic cytochrome enzyme-mediated, drug-drug interaction was 80%. The probability of a drug-drug interaction increased with the number of medications. Specifically, a patient taking 5-9 medications had a 50% probability whereas the risk increased to 100% when a patient was found to be taking 20 or more medications [18]. In a study of community-dwelling elderly adults, almost 50% of patients had a potential drug-drug interaction [19]. Drug-drug interactions are a frequent cause of preventable ADEs and medication-related hospitalizations [16,20]. , Thus practitioners should keep the possibility of a drug-drug interaction in mind when prescribing any new medications.

Studies have reported the prevalence of drug-disease interactions to be 15-40% in frail elderly patients. Risk of drug-disease interactions has been shown to increase with increased numbers of medications [21,22]. With patients living longer with more chronic disease states requiring drug therapy, the risk of drug-disease interactions should be a concern for healthcare providers.

3.4 Medication Non-adherence

Non-adherence with drugs in older adults has been associated with complicated medication regimens and polypharmacy [23-27]. Non-adherence rates in community dwelling elderly adults has been reported to be between 43-100% [24,25]. The large variance in the non-adherence rates may be attributed to different methods, tools, and thresholds for categorizing adherence as well as the variety of populations studied. In one study, the rate of patient non-adherence was 35% when a patient was taking 4 or more medications [28]. Medication non-adherence is associated with potential disease progression, treatment failure, hospitalization, and ADEs, all of which could be life-threatening [24,27,28].

3.5 Functional Status

Polypharmacy has been associated with functional decline in older patients. In a prospective study of community-dwelling older adults, increased prescription medication use was associated with diminished ability to perform instrumental activities of daily living (IADLs) and decreased physical functioning [29]. A study using data from the conducted aWomen's Health and Aging Study, found that use of 5 or more medication was associated with a reduced ability to perform IADLs [30]. A prospective cohort of approximately 300 older adults found that patients taking 10 or more medications had diminished functional capacity and trouble performing daily tasks [31]. As part of the Women's Health Initiative Observational study, polypharmacy was associated with incident disability in older women [32]. In patients who have reported falling in the past year, higher medication use was found to be associated with functional decline [33]. Prescribers should be aware of the risk of functional decline in patients taking multiple medications.

3.6 Cognitive Impairment

Cognitive impairment, seen with both delirium and dementia, has been associated with polypharmacy. A study in hospitalized older adults reported that the number of medications was a risk factor for delirium [34]. In a prospective cohort study of 294 elders, 22% percent of patients taking 5 or less medications were found to have impaired cognition as opposed to 33% of patients taking 6-9 medications and 54% in patients taking 10 or more medications [31].

3.7 Falls

Falls are associated with increased morbidity and mortality in older adults and may be precipitated by certain medications. A study comparing patients who have not fallen compared to those who have fallen once and those multiple times , reported that the number of medications was associated with an increased risk of falls [35]. A study in older adult outpatients asas the number of medications increased, the falls risk index score increased and the duration of the one-leg standing test duration decreased [36]. In a prospective cohort study, the use of 4 or more medications was associated with increased risk of falling and the risk of recurrent falls [37]. A study in elderly patients with dementia reported that those patients who reported a fall had an increased prevalence of polypharmacy [38]. In a study of institutionalized older adults the risk of experiencing a fall within the previous 30 days was by 7% for each additional medication [39]. Given the serious consequences of falls in older

adults, caution should be used in prescribing new medications to those who are at risk of falling.

3.8 Urinary Incontinence

Urinary incontinence is yet another problem that is associated with the use of multiple medications. In a population-based, longitudinal study of women aged 70 years and older, polypharmacy was associated with an increased risk of lower urinary tract symptoms [40]. Many medications are known to exacerbate urinary incontinence, so a medication review should be performed to evaluate both the number of medications as well as the specific types of medications a patient is taking.

3.9 Nutrition

Polypharmacy has also been reported to affect a patient's nutritional status. A prospective cohort study found that 50% of those taking 10 or more medications were found to be malnourished or at risk of malnourishment [31]. A survey of community-dwelling elders older adults found that polypharmacy was associated with a reduced intake of fiber, fat-soluble and B vitamins, and minerals as well as an increased intake of cholesterol, glucose, and sodium [41].

4.0 Evidence that Unnecessary Drug Use Can Be Improved

Recently a comprehensive review was published on this subject [2]. They included 36 studies of which 15 were randomized controlled trials (RCTs). Only two RCTs measured unnecessary drug use as defined by a valid implicit measure (i.e., 3 items from the MAI) [42,43]. The study by Schmader et al included 430 frail hospitalized patients in the Geriatric Evaluation and Management (GEM) care intervention group and 404 frail patients were in the control group [42]. On average those inpatients randomized to the intervention group took 10.4 medications which was similar to the 10.2 medications randomized to the control group. The number of unnecessary medications taken by the intervention group at hospital discharge was significantly reduced in comparison to those in control group patients (-0.5 vs 0.1). Another randomized controlled trial by Spinewine et al. examined the value of adding a clinical pharmacist to an inpatient GEM team care had on unnecessary drug use [43]. The sample consisted of 186 patients aged 70+ years of age. The rate of decline in patients with unnecessary drug use was greater in the intervention vs the control group (46.9% vs 6.6%).

4.1 Evidence that Polypharmacy Can be Improved (Table 2)

There have been several comprehensive reviews that have summarized the data regarding the quality of prescribing for older adults enrolled randomized controlled trials receiving various interventions in different settings because they were taking multiple medications [23,44-47]. Overall these reviews highlighted data from 50 studies of which only 5 were included in two or more reviews [42,49-51]. **Table 2** summarizes these five studies. As shown, three studies were conducted in ambulatory care setting whereas the other two studies were focused in long term care facilities. Three interventions were delivered by a pharmacist and a multidisciplinary approach was used by the remaining two studies. A statistically significant improvement was seen in the four studies that used the Medication Appropriateness Index as a process measure [42,48,50,51. Only one study showed an reduction in the use of ineffective medications [49]. While three studies measured ADEs, only one showed a statistically significant reduction in serious ADEs ;42, 48, 50]. Only one study showed an improvement in pain [50].

5.0 Expert Opinion

Key research findings to date are that the percentage of older adults with polypharmacy defined by medication count varies across numerous studies and health care settings. There are few studies that have used a validated implicit measure of unnecessary drug use and examined it's predictive validity with important health outcomes. In contrast, research has clearly established a strong relationship between polypharmacy and negative clinical consequences. Moreover, well designed inter-professional intervention studies that focus on enrolling high risk older patients with polypharmacy have shown that they can be effective in improving the overall quality of prescribing with mixed results on distal health outcomes.

In the coming years it is hopeful that increased research funding will become available for the study of new and innovative interventions to reduce unnecessary drug use. . Further research work is also needed in those patients with extreme polypharmacy (e.g., 20 or more medications) since this phenomena should become more common due to greater numbers of older adults with multiple co-morbid conditions and the discoveries of novel drug therapies.

6.0 Conclusion

Polypharmacy has been and always will be common among the elderly population due to the need to treat the various disease states that develop as a patient ages. Unfortunately with this increase in the use of multiple medications comes with an increased risk for negative health outcomes such as higher healthcare costs, ADEs, drug-interactions, medication non-adherence, decreased functional status and geriatric syndromes. More implementation studies are needed to show that practical application of the methods shown to improve polypharmacy issues can be disseminated to the various medical settings where older adults receive care.

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Article Highlights Box

- Polypharmacy is defined as increase in the number of medications or the use of more medications than are medically necessary.
- Polypharmacy is common in older ambulatory care, hospital, and nursing home patients
- Polypharmacy increases the risk of numerous negative health consequences in the elderly.
- The best intervention (s) for improving polypharmacy involves an inter-professional approach that often includes a clinical pharmacist.

Table 1

Summary of Observational Studies of Polypharmacy in Older Adults

Author/Year	Setting/Country/Sample	Polypharmacy Results	Most Common Types of Medication Class/Individual Medications
Qato 2008	Ambulatory/USA/N=2976	37.1% men and 36% women aged 75+ used at least 5 RX medications; 46% took an OTC medication and 52% dietary supplements	hydrochlorthiazide, atorvastatin, levothyroxine, lisinopril, metoprolol, simvastatin, atenolol, amlodipine, metformin, furosemide
Rossi, 2007	Ambulatory/USA/ N=128	58.6% took 1+ unnecessary drugs	central nervous system, gastrointestinal, vitamins
Hajjar 2005	Hospital/USA/n=384	37.2% ≥ 9 drugs 41.4% 5-8 drugs 21.4% 1-4 drugs; 58.6% took 1+ unnecessary drugs	gastrointestinal, central nervous system, and therapeutic nutrients/minerals H_2 blockers, laxatives, genitourinary antispasmodics, tricyclic antidepressants
Nobili , 2011	Hospital/Italy/n=1332	Admission-51.9% on 5+; Discharge-67% on 5+	antithrombotics, gastrointestinal diuretics, acei, beta-blockers, lipid and non-insulin glucose lowering rxs, digoxin
Dwyer , 2009	Nursing Home/USA/N= 13,507	39.7% on 9+ meds	laxatives, acid/peptic disorders, antidepressants, antipsychotics/antimanics, non-narcotic pain relievers, antipyretics, antiarthritics
Bronskill, 2012	Nursing Home/Canada/n=64,395	15.5% on 9+ medications	diuretics, ppi, aceI, beta-blockers, benzodiazepines, ssris, ccb, antipsychotics, statins, opioids

Abbreviations- acei(ACE Inhibitors), ccb(Calcium Channel Blockers), otc(Over-the-Counter Products), ppi(Proton Pump Inhibitors), rx(prescriptions), ssri(Selective Serotonin Reuptake Inhibitors)

Expert Opin Drug Saf. Author manuscript; available in PMC 2014 January 01.

Table 2

Randomized Controlled Studies Designed to Improve Medication Quality in Older Adults using Multiple Medications

Study	Setting	Patients/Inclusion Criteria	Intervention (Duration)	Process Measures (I vs. C)	Clinical Outcome Measures (I vs. C)
Pharmacist	*Interventions*				
Hanlon, 1996	1 VA general medicine clinic, USA	208 age ≥65 taking ≥5 medications	Pharmacist review, written drug recommendations to PCP and patient counseling at each clinic visit; (12 months)	↓ MAI score (12.8 vs. 16.7, P<.001) (Lower is better)	NS differences in HRQOL or ADEs (30% vs. 40%) or; health care costs ($7873 vs. $5926)
Krska, 2001	6 general practices, Scotland	332 age ≥65 with ≥4 medications and ≥2 chronic disease states	Pharmacist review of medication related issues; pharmacist implemented recommendations agreed to by patient's GP; 3mos	↑ resolution of monitoring issues, ineffective therapy (83% vs. 41%, P<.001)	NS differences in medication costs, HRQOL, clinic visits, hospitalizations
Crotty, 2004	85 LTCFs, Australia	110 hospitalized patients age ≥65 transferred to a LTCF; Average # of medications 8.7	Pharmacist summary of medications at hospital d/c given to community pharmacist, MD and nurse; Pharmacist conducted drug review discussed at case conference	Better MAI score (2.5 vs 6.5, p<<0.001)	↓ pain, NS differences in ADEs, falls, mobility, behavior, confusion, ER/ hospitalizations
Multidisciplinary	*Team*	*Intervention*			
Schmader, 2004	Clinics at 11 VA medical centers, USA	834 frail persons age ≥65 after hospital discharge (mean ≥10 medications)	Multidisciplinary, protocol-driven GEM clinic; (12 months)	NS difference in # of unnecessary drugs, # of inappropriate drugs, or MAI score (P>.25 for each), ↓ number of conditions with omitted drugs (↓ 0.2 vs. ↑0.1, P<.001)	NS difference in all ADEs (RR 1.03; P=.75);↓ risk of serious ADEs (RR 0.65; P=. 02)
Crotty, 2004	10 LTCFs, Australia	154 patients age ≥65 with mean ≥5.9 medications	Case conference with MDs, pharmacist, care worker, dementia expert	↑ change in MAI score (4.1 vs 0.4, P<.001)	NS differences in behavior

Abbreviations: ADE(Adverse Drug Event), C (Control Group), D/C(Discontinue), GEM (Geriatric Evaluation Management), GP (General Practitioner), HRQOL(Health Related Quality of Life), I (Interventio), LTCF (Long Term Care Facility), MAI (Medication Appropriateness Index), MD (Doctor of Medicine), NS (Non-significant), PCP(Primary Care Physician), RR(Relative Risk), VA (Veteran's Administration), MOS (months)