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Polypharmacy and Inappropriate Drug Use among Older People—a Systematic Review

Söuve Elmståhl and Henrik Linder

Department of Health Sciences, Division of Geriatric Medicine, Lund University, Skåne University Hospital, Malmö, Sweden. Corresponding author email: solve.elmstahl@med.lu.se

Abstract

The use of medication and polypharmacy are increasing among older people and inappropriate drug use (IDU) and drug related side effects have been discussed more intensively. Although definitions of polypharmacy and IDU differ, the last decade criteria have been established which enables comparison of published studies. The aim of this study was to determine the frequency of polypharmacy and IDU among subjects ≥ 65 years.

Fourteen studies fulfilled criteria for polypharmacy and prevalences ranged from 27% to 59% in primary care patients compared to 46%–84% in hospital care. Furthermore, drug treatment tends to increase over time. Ten studies fulfilled the criteria for IDU with prevalences from 27% to 56%.

Conclusion: Polypharmacy and IDU is a common phenomenon among older people but IDU did not differ between primary care and hospital patients. There is a need for prospective studies on drug use among older persons.

Keywords: prevalence, frequency, hospital, primary care, medication

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Introduction

Intensive medical progress has been accomplished over the last few decades. Today, physicians can treat far more diseases than in the past. Older adults ≥ 65 years are treated with an increasing number of drugs. Multimorbidity in the general elderly population currently ranges from 40% to 80% and is expected to become a major health consideration in the coming years.^{1,2} Taking this into consideration, as well as the fact that the older populations in many European countries are increasing, polypharmacy is an important research field. The objectives of this paper are to determine the prevalence of polypharmacy in the general older adult population ≥ 65 years, and to determine the prevalence of inappropriate drug use in the same group. This review will focus on published studies over the last ten years. There are several definitions of polypharmacy. In this review, the use of five or more drugs was chosen as the definition. The term "older people" is defined according to the World Health Organization [WHO] definition. Elderly people of 65–79 years are considered to be the younger elderly, while persons 80 years and older are classified as older elderly.³

Materials and Methods

A search for published articles was performed in the medical database Pub Med [www.ncbi.nlm.nih.gov/pubmed/] on the 14th of September, 2009. A combination of the following MeSH-terms was used: polypharmacy, prevalence, inappropriate drug use, aged, and aged 65 and over (see Table 1). The inclusion criteria were: age ≥ 65 years, abstract written in English, abstract describes polypharmacy prevalence, and study size of 40 patients or more.

Table 1. The structured article review included the following descriptors.

Purpose	Not described	Incomplete	Clear
Study design	Retrospective	Prospective	
Selection description	Not described	Incomplete	Clear
Drop out	Not described	>20%/5%–20%	<5%
Analysis of drop out	No	Yes	
Results description	Missing	Incomplete	Clear
Conclusion	Missing	Incomplete	Clear

There was a ten-year time limit on articles. If the article headline was in accordance with the objectives, the abstract was read. Furthermore, if the objective was answered in the abstract, the article was read. Articles were categorized and described according to the descriptors given in Table 1. Out of 52 reviewed papers on the prevalence of polypharmacy, 38 were excluded, 28 because their purpose, including polypharmacy, was lacking, 8 because they did not fulfill inclusion criteria, and 2 due to double publication of results (see flow diagram in Fig. 1). Thirty-two papers were reviewed on inappropriate drug use, of which 22 articles were excluded; 17 lacked purpose, 3 did not fulfill inclusion criteria and 2 were double publications (see Fig. 1).

According to the STROBE statement on checklist for observational studies, we have described settings and participants.³ Cohort studies, cross-sectional studies and longitudinal studies are included and eligibility criteria of polypharmacy are as follows. Polypharmacy can be defined in many ways. The most common definition, the use of five or more drugs, was adopted in this review. Another definition is "the prescription and administration of more medicines than are clinically indicated to a given patient".^{4,5} Information on the sampling strategy for the included studies is lacking. Characteristics of study participants, including number, age, gender and proportion of dropouts, if stated, are presented in Tables 2 and 3.

Inappropriate drug use was defined according to the use of a standardized protocol. Included articles in this report used the following established protocols for unsuitable medication for the elderly and stated information on prevalence. These include the criteria according to Beers,^{6–8} McLeod,⁹ Zahn¹⁰ and the Swedish National Board of Health and Welfare Quality indicator.¹¹ The Beers (1997)⁷ criteria include 13 different drug categories, while Beers (2003)⁸ is expanded to 20 categories including barbiturates, diuretics (ethacrynic acid), H2 antagonists, hypoglycemics, muscle relaxants, sedatives, stimulants, and vasodilators. Antihypertensive, antipsychotic, laxantia and antibiotic drug categories were also added. McLeod's (1997)⁹ criteria were comprised of 12 categories, but hypoglycemic and anticholinergic drugs were not included. The Swedish Quality Indicator¹¹ lists drugs that should be avoided such as

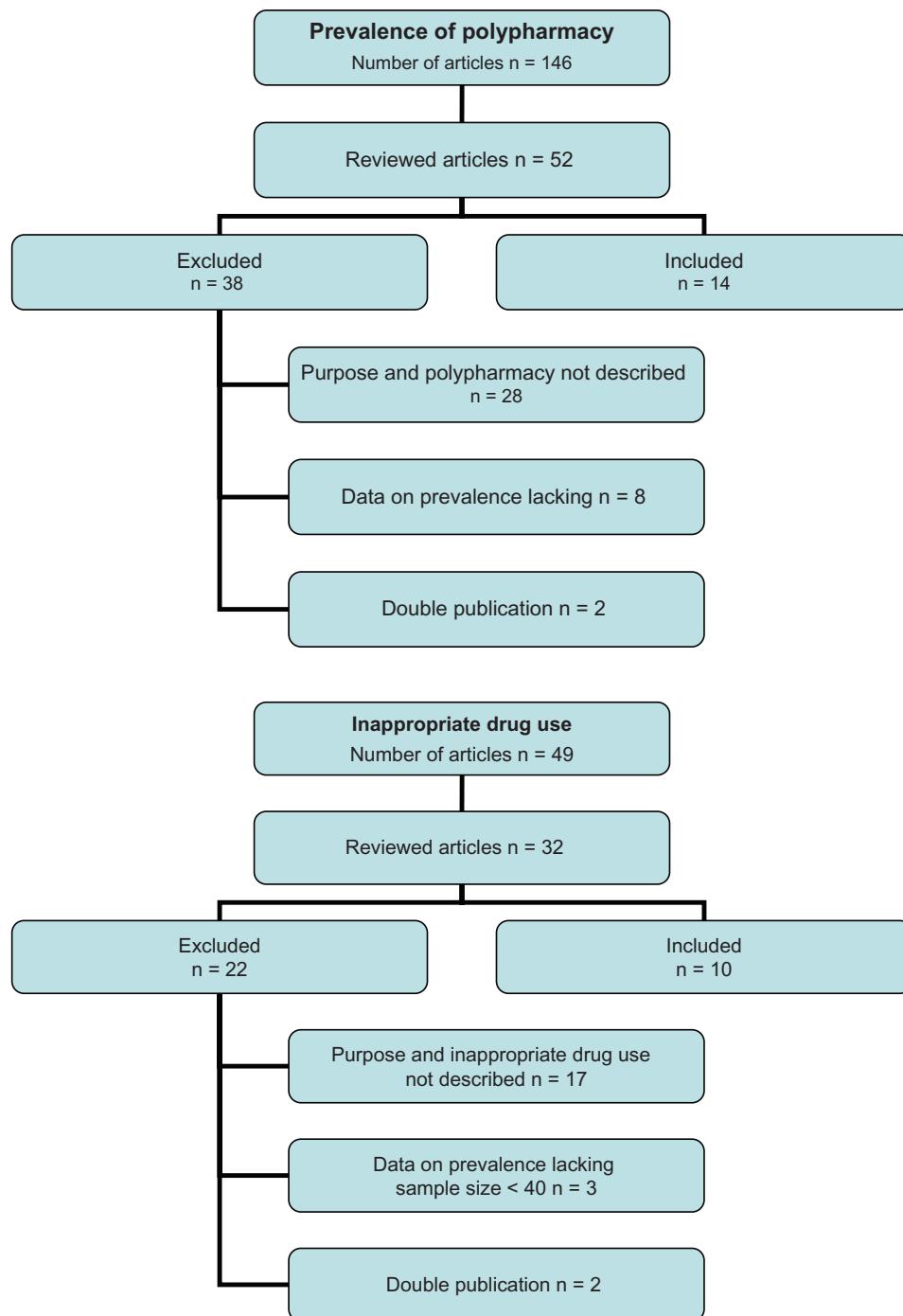


Figure 1. A flow diagram of included studies on polypharmacy (MeSH search terms polypharmacy, prevalence, aged) and inappropriate drug use (MeSH terms inappropriate drug use, polypharmacy, aged).

sedatives, barbiturates and drugs that are rarely appropriate or that can have inappropriate doses. The prevalence for at least one inappropriate drug has been presented separately for the polypharmacy group and the none polypharmacy group (<five drugs) if presented by the authors. None of the selected studies included any analysis of dropout.

Results

Fourteen studies on polypharmacy, listed in Table 2, fulfilled the study criteria. The prevalence of polypharmacy ranged from 19% to 83% depending on care setting, study design and year of publication.

5 population studies were gathered from our search in the Pub Med database. In a Swedish study

**Table 2.** Prevalence of polypharmacy among older people ≥ 65 years.

First author, year, country	Study design	Care setting	Number of participants	Age (year)	Percent women	Drop out	Polypharmacy prevalence
Haider et al, 2008, Sweden ¹²	Cross-sectional	Population	621	≥ 77	59%	–	43%
Klarin et al, 2005, Sweden ¹³	Cohort	Population	785	≥ 75	58%	33%	40%
Fialová et al, 2005, Europe ¹⁴	Retrospective	Population	2707	≥ 65	74%	–	50%
Jyrkkä et al, 2006, Finland ¹⁵	Prospective	Population	Year 1998: 601 Year 2003: 339	≥ 75 ≥ 75	– –	14% 44%	1998: 54% 2003: 67%
Linjaku et al, 2001, Finland ¹⁶	Cross-sectional	Population	Year 1990–91: 1196 Year 1998–99: 1260	≥ 65	57% 58%	7% 18%	1990–91: 19% 1998–99: 25%
Schuler et al, 2008, Austria ¹⁷	Prospective	Hospital care	543	≥ 75	60%	–	65%
Wawruch et al, 2008, Slovakian ¹⁸	Retrospective	Hospital care	600	≥ 65	59%	43%	60%
Gallagher et al, 2007, Ireland ²²	Prospective observational	Emergency care	597	≥ 65	56%	–	46%
Cannon et al, 2006, USA ²³	Retrospective	Hospital/home health care	786	≥ 65	64%	–	73%
Chan et al, 2009, Taiwan ¹⁹	Longitudinal observational	Long-term care	11338	≥ 65	61%	4%	84%
Junis-Walker et al, 2006, German ²⁵	Cross-sectional	Primary care	466	≥ 70	60%	35%	27%
Buck et al, 2009, USA ²⁶	Cross-sectional	Primary care	Center 1: 37247 Center 2: 24004	≥ 65	59% 60%	–	Center 1: 46% Center 2: 58%
Flaherty et al, 2000, USA ²⁰	Retrospective chart review	Hospital/self care/family care	833	≥ 65	–	–	Hospital: 66% Self/family care: 59%
Mamun et al, 2004, Singapore ²¹	Observational	Nursing home	454	≥ 65	–	11%	59%

by Haider et al,¹² the polypharmacy prevalence was 43%. A similar prevalence of 40% was seen in another Swedish population study.¹³ Fialová et al investigated homecare patients in a number of European countries and 50% had polypharmacy.¹⁴ In the Finnish longitudinal population study, the prevalence increased from 54% in the year 1998 to 67% in 2003.¹⁵ In a similar way, a rise in prevalence can be seen in a study by Linjakumpu et al.¹⁶ In the years 1990 to 1991 the prevalence was 19%, and in 1998 to 1999 it was 25%.

Five reviewed hospital studies had a somewhat higher polypharmacy prevalence (46% to 66%) than that found in studies of the general population, and the two recent reports from Austria and Slovakia showed a prevalence of 65% and 60%.^{17,18}

The highest reported prevalence of 84% was found by Chan et al¹⁹ in a study regarding frail Taiwanese elderly with long-term care needs (Table 3). In contrast, primary care settings show a lower prevalence of between 27% and 59%. Flaherty et al²⁰ compared patients discharged from home care and returned to self care/family care or hospital. In the first group the prevalence was 66%, while in the second group the prevalence was 59%. When Mamun et al investigated long-term care in Singapore, the prevalence was 59%.²¹

Table 3 presents the 10 studies on inappropriate drug use that fulfilled the study criteria. As expected, the frequency of inappropriate drug use was higher in study groups with polypharmacy (≥ 5 drugs), being 27% to 56%, compared to groups without

**Table 3.** Frequency of inappropriate drug use ≥ 65 years with polypharmacy.

First author, year, country	Protocol polypharmacy prevalence	Study design	Care setting	Number of participants	Age (year)	Percent women	Drop out	At least one inappropriate drug*	At least one inappropriate drug**
Haider et al, 2009, Sweden ^a	a ♀ 58% ♂ 52%	Cross-sectional	Population	626 258	75–89	60%	2.3%	—	—
Klarin et al, 2005, Sweden ^{b,c,d}	b 40% b,c,d 50%	Longitudinal cohort	Population	785	≥ 75	58%	33%	♀ 36% ♂ 32%	10%
Fialová et al, 2005, Europe ^e	c 50%	Retrospective cross-sectional	Population	2 707	≥ 65	74%	—	—	13%
Schuler et al, 2008, Austria ^f	c 65%	Prospective cohort	Hospital care	543	≥ 75	60%	—	39%	—
Wawruch et al, 2008, Slovakian ^g	c 60%	Retrospective	Hospital care	600	≥ 65	59%	43%	27%	13%
Gallagher et al, 2008, Ireland ^h	c 46%	Prospective	Emergency care	597	≥ 65	56%	—	46%	—
Cannon et al, 2006, USA ⁱ	b 73%	Retrospective	Hospital care/ home care	786	≥ 65	64%	—	37%	19%
Buck et al, 2009, USA ^j	c,e 46%/58% b,e —	Cross-sectional	Primary care	(C1) 37 247 (C2) 24 004	≥ 65	59%	—	Center 1: 55% Center 2: 51%	Center 1: 23% Center 2: 23%
Simon et al, 2005, USA ^k	—	Cross-sectional	Population	157 517	≥ 65	57%	—	49%***	—
Heikka et al, 2008, Finland ^l	c 43%	Retrospective cross-sectional	Nursing home	1 987	≥ 65	81%	4.7%	56%***	—

Notes: Used protocol to define inappropriate drug use: (a) Indicator Swedish Health Welfare; (b) Beers 1997; (c) Beers 2003; (d) McLeod 1997; (e) Zahn 2001; * prevalence of inappropriate drugs in the group with polypharmacy ≥ 5 drugs; ** prevalence of inappropriate drugs in the group with polypharmacy < 5 drugs; *** prevalence of inappropriate drugs in the total study group.



polypharmacy (<5 drugs), for which the prevalence of inappropriate drug use was 10% to 23%.

In 3 newly published reports from 2008, with the same protocol for definition of inappropriate drug use and the same hospital care settings, the noted frequency ranged from 27% to 46%, indicating that this is a common finding. The highest frequency, being 56%, was noted among nursing home patients.

No gender differences in inappropriate drugs use were indicated in a population-based study by Haider et al;¹² it was found that this occurred with similar frequency in women (36%) and men (32%).

Discussion

The term polypharmacy has its limitations. Polypharmacy dose not include qualitative differences between different drug classes and inappropriate drug use. Furthermore, there are different definitions of polypharmacy. Before Beers' study in 1997⁷ there has been a lack of established protocols for inappropriate drug use.⁷ The Beers protocol was updated in 2003.⁸ Patients with inappropriate drug use can thus be underestimated in earlier reports using the Beers protocol from 1997.⁷ This might explain the lower prevalence of polypharmacy noted by Klarin and Junis-Walker,^{13,25} using the 1997 protocol. As a consequence of different definitions, a comparison has to be made with caution.

This article shows that a large number of elderly people are treated with many drugs, and that the reported prevalence of polypharmacy depends on the care setting. In primary care, the prevalence ranges from 27% to 59%. In hospitalized patients, the polypharmacy prevalence ranges from 46% to 84%. A higher multimorbidity and frailty among hospitalized patients might explain these results. Furthermore, drug use tends to increase over time. The Jyrkkä et al study is one example¹⁵ in which the polypharmacy prevalence increased from 54% in the year 1998 to 67% in the year 2003. The implementation of guidelines on secondary prevention will inevitably contribute to this phenomenon.

The prevalence of inappropriate drug use in elderly individuals with polypharmacy ranges from 27% to 56% among the paper-fulfilling criteria. At present, few studies have been published concerning inappropriate drug use among elderly individuals with fewer than five prescriptions. Taking this into

consideration, it is difficult to estimate any trends regarding the prescription of less than five drugs and inappropriate drug use in an elderly population.

Polypharmacy might occur more in the elderly for several reasons. Since many chronic conditions like stroke, cardiovascular diseases, musculoskeletal disorders and dementia are highly age dependent, an ageing population will exhibit an increased prevalence of polypharmacy. Implementation of guidelines concerning secondary prevention as well as evolving treatment levels for problems concerning blood pressure, diabetes, lipids and osteoporosis will lead to attribution of a higher proportion of prescriptions to elderly subjects and thereby increase the proportion who have polypharmacy. For example, a recent report from US prescription drug data in 2007 and 2008 showed that the use of five or more drugs the last 10 years has almost doubled from 6% to 11%.²⁹ A Danish study using a nationwide prescription database reported an increased statin use following acute myocardial infarction from 13% in 1995 to 61% in 2002.³⁰ In these situations, it is important to avoid inappropriate drug use. Another potential factor that could influence drug prescription is differences in health policies and subsidization of drugs between countries.

However, the present studies do not consider potential adverse drug events from high doses due to impaired renal function with age. We have previously reported from a national population-based cohort, ie, Good Aging in Skåne, that the occurrence of chronic kidney disease, defined as glomerular filtration rate (GFR) less than 30 mL/min/1.73 m² increases from 12% among 80–89 year old subjects to 27% among elderly individuals > 90 years.²⁴ Too high of a dosage in relation to renal function is not taken into consideration in the protocol of inappropriate drugs use. Therefore, the present findings most likely underreport inappropriate prescription drug use.

Limitations and Strengths

MeSH terms in the Pub Med database have been used in order to standardize the selection of articles for this review. Selected articles were examined with help from a modified article review to standardize the selection procedure. The numbers of patients in the reports were limited to at least 40 patients, because of difficulties making conclusions based on



small samples. The use of only one database (Pub Med) and the time limit of the past ten years might have restricted identification of relevant epidemiological studies. However, dropout rates in the included articles were not accounted for. It can only be speculated on whether there could be systematic underestimation of detected polypharmacy in the published studies due to selection bias of the most diseased subjects suffering from multimorbidity. The studied papers lacked information on confound-adjusted estimates and the varying study designs, including retrospective chart review and prospective designs, might explain the wide range of polypharmacy. Meta-analysis was not used because of the heterogeneity of study design and care settings, as well as the high variation in drop-out rates. Polypharmacy and inappropriate drug use are recent concepts that have emerged over the two past decades; therefore, there are few published papers. The clinical relevance of these concepts is strengthened by studies showing associations to outcomes like hospitalization and mortality.³¹ An Irish national population study reported that 9% of overall expenditures on pharmaceuticals went towards inappropriate prescribing among those > 70 years.³² Polypharmacy has also been found to be an important predictor of drug-drug interactions (DDI)³³ and DDI is associated with length of hospital stay and cost of hospitalization.³⁴ Recently in 2012, a task force supported by the American Geriatric Society has updated the Beers criteria and increased it to include 53 medications or classes categorized into three groups, including potentially inappropriate medications in general, or related to one's disease, and medications that should be avoided.³⁵ The ambition to include a grading of evidence in conjunction with the intent to update these criteria is a great advantage compared to other criteria. More widespread use of these updated criteria will facilitate follow-up and comparison between health care providers and societies.

Conclusion

In this study, the polypharmacy prevalence was found to range from 19% to 83% and the corresponding prevalence of inappropriate drug use was found to range from 27% to 56%. Thus, polypharmacy and inappropriate drug use are common phenomena among the elderly and drug treatment tends to increase over time, although few prospective studies

have been published. There is a need for prospective studies on drug use among elderly persons.

Author Contributions

Conceived and designed the experiments: SE. Analyzed the data: SE, HL. Wrote the first draft of the manuscript: HL. Contributed to the writing of the manuscript: SE, HL. Agree with manuscript results and conclusions: SE, HL. Jointly developed the structure and arguments for the paper: SE, HL. Made critical revisions and approved final version: SE, HL. All authors reviewed and approved of the final manuscript.

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Competing Interests

Author(s) disclose no potential conflicts of interest.

Disclosures and Ethics

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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