

Review

The effects of pharmacist interventions on patients with polypharmacy

Elinor C. CHUMNEY, Leslie C. ROBINSON

ABSTRACT*

Polypharmacy, the state of being prescribed or taking more medications than clinically appropriate, can result in a variety of negative outcomes for both patients and healthcare facilities. These include negative outcomes such as adverse drug effects, hospitalizations, and poor patient health, as well as economic outcomes such as increased drug cost and costs associated with increased utilization of health services. Available data suggests pharmacists have the potential to have a large effect in combating this problem through a variety of interventions such as reducing the number of medications taken, reducing the number of doses taken, increasing patient adherence, preventing adverse drug reactions (ADRs), improving patient quality of life and decreasing facility and drug costs. A small number of studies have been performed on the pharmacists' role in addressing the problem of polypharmacy; however, they include various populations, settings, and measured outcomes. Furthermore, some of the results are conflicting. Nonetheless, this review of the available literature concludes that pharmacist interventions can improve patient outcomes. With the ever-increasing costs of healthcare, the substantial cost savings for patients as well as institutions provided by these interventions are further justification for widespread implementation of pharmacist interventions at healthcare institutions.

Keywords: Pharmacists. Polypharmacy, Drug Therapy.

RESUMEN

La polimedición, estado de tener prescrito o estar tomando más medicamentos de los clínicamente apropiados, puede producir diversidad de resultados negativos tanto para los pacientes como para los centros sanitarios. Estos incluyen resultados negativos como efectos adversos de los medicamentos, hospitalizaciones y mala salud de los pacientes, así como resultados económicos como coste aumentado de medicamentos y costes asociados con el aumento de la utilización de servicios. Los datos disponibles sugieren que los farmacéuticos tienen la posibilidad de tener un gran efecto para combatir este problema a través de una variedad de intervenciones, tales como reducir el número de medicamentos usado, aumentar el cumplimiento del paciente, prevenir las reacciones adversas medicamentosas (RAM), mejorar la calidad de vida de los pacientes y disminuir los costes de medicamentos del centro sanitario. Se han realizado algunos estudios sobre el papel del farmacéutico afrontando el problema de la polimedición; sin embargo incluyen diversas poblaciones, ámbitos, y resultados medidos. Incluso, algunos de los resultados son contradictorios.

Esta revisión de la literatura concluye que las intervenciones del farmacéutico pueden mejorar los resultados de los pacientes. Con los costes de sanidad permanentemente al alza, los ahorros conseguidos por estas intervenciones para los pacientes y para las instituciones son una justificación adicional para la implantación masiva de las intervenciones de farmacéutico en las instituciones sanitarias.

Palabras clave: Farmacéuticos. Polimedición. Farmacoterapia.

(English)

INTRODUCTION

Although the term polypharmacy has evolved over time and is often used to mean many different things in different situations, its basic definition is quite simple - more drugs are prescribed or taken than are clinically appropriate.¹ The specific number of drugs taken is not itself indicative of polypharmacy as all of the drugs may be clinically necessary and appropriate for the patient; however, as the number of prescribed drugs increases, so do

*Elinor C. CHUMNEY. PhD, MSc. Department of Pharmacy Practice. South Carolina College of Pharmacy. Charleston, South Carolina (USA).
Leslie C. ROBINSON. PharmD Candidate. Department of Pharmacy Practice. College of Pharmacy. Medical University of South Carolina. Charleston, South Carolina (USA).

the chances of polypharmacy. A 2002 national survey indicated that 25% of the overall population takes 5 or more medications per week. When specifically considering the population 65 years of age and older, this percentage increases to about 50%, with 44% of men and 57% of women taking 5 or more medications per week and 12% of both sexes taking 10 or more prescriptions per week.² The most worrisome consequence of polypharmacy is the occurrence of adverse drug reactions (ADRs), but increased drug costs and patient quality of life are also significant issues.

Due the fact that people are living longer, the elderly population, which often suffers from multiple chronic diseases requiring multiple medications, continues to increase. These patients are much more likely to experience polypharmacy and its negative consequences, especially adverse drug reactions (ADRs). ADRs are one of the most troubling issues surrounding medication use in the elderly, as this patient population is more likely to have poor outcomes than others.³ They affect approximately 10-20% of hospitalized patients and around 7% of the general population; this number increases when the population of interest is limited to the elderly.⁴ Because the elderly are much more likely than other populations to have poor outcomes as a result of polypharmacy due to their generally poorer overall health status, it is crucial to consider any intervention that has the potential to reduce this problem – a role that pharmacists are well trained to fill.

Historically physicians have been entirely responsible for management of their patient's chronic diseases and complex medication regimens. Today pharmacists are increasingly responsible more managing patients' medication regimens by providing comprehensive medication reviews and educational services for both patients and physicians. A number of studies have examined pharmacist interventions to reduce polypharmacy and the outcomes that these interventions have upon humanistic and clinical factors. Specifically, studies have considered the number of medications and doses taken, patient adherence, social and functional abilities, and ADRs, in addition to economic factors such as costs to the patient and the institution. Many of these studies show positive findings when examining patient outcomes which could indicate publication bias. As well, several have also been published that show a null effect of pharmacist interventions. This leads us to conclude that the risk of publication bias is minimized.

When researching the literature on patient outcomes of pharmacist interventions in polypharmacy, it was noteworthy that there is no available synthesis of data examining multiple patient outcomes. This lack of data may be hampering the widespread implementation of pharmacist interventions. It was therefore important to examine the available literature to determine and evaluate the effects of pharmacist interventions in polypharmacy on humanistic, clinical, and economic outcomes. A meta-analysis was not possible

because none of the published studies considered common measures of effect; however, a critical review of available literature was performed and the varied outcomes were assessed to highlight any potential benefits.

METHODS

A search was performed using Ovid Medline to identify articles that discussed the effects that pharmacist consults have on patient outcomes and polypharmacy. The keywords that were used were 'polypharmacy' in combination with either 'pharmacist' or 'drug therapy.' Of the 49 originally retrieved studies 38 were excluded because they did not specifically look at pharmacist interventions or did not focus on polypharmacy. Review of the references used in the 11 identified articles led to the identification of 6 additional articles. Of the included studies, 10 were performed in a primary care or ambulatory outpatient setting,^{1,5-13} 3 examined patients in a nursing home or long-term care facility,¹⁴⁻¹⁶ 1 involved hospital inpatients,¹⁷ and 2 considered patients in a community setting.^{18,19} The outcomes examined by the included studies are humanistic, clinical, and economic (see Table 1).

In all of the included studies, a pharmacist medication review to identify drug related problems was the cornerstone of the pharmacotherapy consult or intervention.^{1,5-19} The medication reviews included factors such as patient interviews by a pharmacist to evaluate medication use and adherence,^{5-9,11,12,14,16,18} patient use of health and human services,⁵ a quality of life survey,^{5,8,9} or other physical and mental assessments,^{6,8,14} the cost of the patients' medications,^{5,7,8,12} and any patient reported problems with medications.^{7,9,11,12,14} In addition to medication reviews, the pharmacist interventions in four of the studies were more extensive.^{6,10,16,17} In one study the pharmacist made rounds with the medical team⁵ and in others the pharmacist was available for consult to the physicians and nursing staff throughout the day and provided educational sessions for other healthcare professionals.^{6,10,16,17}

From the information obtained through the medication reviews and patient interviews, pharmacists developed pharmaceutical care plans and medication recommendations that were submitted to the patient's physician.⁵⁻¹⁹ In some interventions pharmacists counselled patients on any accepted changes^{5-9,11-13,16} in addition to other important issues such as adherence and medication safety.^{7-9,11,12,16,18}

RESULTS

Clinical Outcomes: Decreased number of medications or doses

Elderly patients afflicted with multiple chronic conditions usually see many different physicians for treatment and require multiple medications to manage. Polypharmacy is a common result with duplicate or interacting medications. Inappropriate drug therapy can result in poor outcomes for

patients and adverse reactions, which is especially true for elderly patients due to poorer health status overall. Comprehensive medication therapy management services provided by pharmacists for patients taking multiple medications for chronic disease states may improve overall drug therapy.¹¹ Pharmacist interventions have been shown to help decrease the total number of drugs taken in addition to the number of doses taken per day.^{1,6,7,11,14,18,19} Some researchers have concluded that an intervention of any kind by a pharmacist can reduce the number of drugs that a patient is taking.^{6,18}

Seven studies found a decrease in the number of prescriptions taken by patients as a result of pharmacist intervention.^{1,6,7,11,14,18,19} These studies showed a range of 17.6% to 52.2% decrease in the average number of prescriptions per patient. Four studies examined the change in daily doses taken and found decreases of 21.5% to 29.8% after the pharmacist interventions.^{1,6,7,19} For contrast, two studies found that there was no change in either the number of prescriptions taken or the number of doses taken per day.^{10,12}

Table 1: Outcomes examined by study

Study	# of Patients	# of Medications	# of Doses	Adherence	Quality of Life	ADRs	Facility Costs	Drug Costs
Zarowitz 2005 ¹	6693 6039	X X	X X					X X
Krska 2001 ⁵	332				X			X
Galt 1998 ^b	336	X	X	X			X	X
Jameson 1995 ⁷	56	X	X	X	X	X		X
Jameson 2001 ⁸	268					X	X	X
Hanlon & Weinberger 1996 ⁹	172					X		
Allard 2001 ¹⁰	266	X						
Farrell 2003 ¹¹	170	X			X	X		
Lim 2004 ¹²	126			X		X		X
Hanlon & Landsman 1996 ¹³	105					X		
Furniss 2000 ¹⁴	330	X						
Trygstad 2005 ¹⁵	7362							X
Christensen 2004 ¹⁶	6344				X			X
Leape 1999 ¹⁷	150					X	X	
Doucette 2005 ¹⁸	150	X					X	
Schrader 1996 ¹⁹	289	X	X	X	X			X

For one study, investigators assessed a group of patients before and after an intervention by a pharmacist and found that the average number of prescriptions taken decreased from 5.7 to 4.4 (22.8%).¹⁹ This study also showed that 35% of the intervention patients had a dosage reduction for at least 1 of their medications.¹⁹ A study that consisted of two waves of identical interventions separated by one year found that there was a decrease in the average number of prescriptions per patient per month (PPPM) from 4.6 to 2.2 (52.2%) during the first wave and a decrease from 4.5 to 4 (11.1%) during the second wave.¹ Researchers believe that the smaller reduction that was seen in the second wave of the intervention was most likely due to the fact that 91% of these patients also participated in the first wave of the intervention, which indicates that appropriate drug therapy changes were probably already made.¹ Although the number of drugs taken PPPM decreased after each intervention, it appears that the positive effects of an isolated intervention were not sustained over time as the number of drugs taken PPPM before the second intervention was almost identical to the number taken before the first intervention.¹ This would suggest that pharmacist interventions are effective, but their needs to be a sustained pharmacist presence. A study of nursing home residents found that pharmacist intervention resulted in a decrease in prescriptions from 5.1 to 4.2 (17.6%) versus a decrease from 4.9 to 4.4 (10.2%) in the control group. Similarly, pharmacist

interventions were shown to decrease the average number of prescriptions from 10.4 to 8 per day (23.1%) and decrease the number of doses taken per day from 23.5 to 16.5 (29.8%) at a Veteran Affairs Medical Center (VAMC).⁶ A final study of the average number of prescriptions taken by patients after a pharmacist intervention found a 1.1 decrease in the average number of prescriptions taken per day from 6 to 4.9 (18.3%) and a decrease in the average number of doses per day of 2.15, from 10 to 7.85 (21.5%).⁷

It is important to take into consideration that it may not be appropriate to simply reduce the number of drugs a patient is taking as opposed to optimizing the drug therapy, as all of the drugs prescribed may be necessary and appropriate for the patient.^{7,20} It is also important to note that the optimization of therapy may include switching a patient to a more appropriate drug, so the number of drugs will not decrease, but the instance of polypharmacy will.^{7,20} Pharmacist interventions are able to target high risk patients for therapy alterations to prevent adverse drug reactions.⁸

While most studies have found a decrease in the overall number of drugs in the intervention group as compared to the usual care group, one study did find that there was no decrease in the number of drugs prescribed between groups; however, there was a decline in both groups compared to baseline.¹⁰ The limitation of this study was that not everyone in the experimental group received the full

intervention so the result may not fully reflect the effects of the pharmacist intervention.¹⁰ A second study also found no change in the average number of prescriptions taken after an intervention by a pharmacist, but there were other positive outcomes such as increased adherence and medication knowledge.¹²

Clinical Outcomes: Increased Adherence

For patients with chronic diseases and multiple medications adherence is essential for effective treatment. By employing comprehensive pharmacist interventions that include patient education and follow up, patients could become more adherent and feel empowered to take their health into their own hands. Also, by simplifying the drug regimen, patients may be better able to understand their treatment and the importance of remembering to take their medications.⁷ Studies have shown that using pharmacist interventions and education can increase a patient's adherence with his or her medication regimen.^{7,12} It is important for patients to understand why they are using their medications and how they work, as this can increase their involvement in their own healthcare and encourage them to learn about their condition and take charge of their disease.²¹ It can also help prevent therapeutic duplications by prescribers.

Pharmacist interventions have been shown to help improve patient medication knowledge as well as other important factors.^{7,12} One study found that 40% of patients who participated in a pharmacist intervention stated that they were more adherent as a result of simplification of their drug regimen, and 80% said they were more adherent as a result of their increased medication knowledge.¹⁹ Another study showed that the intervention group had a similar trend towards increased adherence; however, it was not statistically significant.¹² A study at a VAMC found that the pharmacist clinic had the highest patient attendance rate out of any physician staffed clinic in the area.⁶

Pharmacists may be able to increase adherence and improve patient care simply through more frequent patient contact and follow up as patients may be more likely to go see their pharmacist than their doctor. Despite the many studies showing positive results there was one study which showed no difference in adherence between the intervention and control group. This may be due to that fact that patients in the control group received a higher level of attention from the nursing staff than would typically be seen in usual care.⁹ Because medication adherence is such an important factor in effectively treating patients to goal, any method used to increase adherence is worthy of continued research.

Humanistic Outcomes: Improved Quality of Life

While decreasing polypharmacy may have a variety of different health related benefits, it is also important to consider the effects on functional and social outcomes. One study reported that 66% of the older adults participating in the polypharmacy pharmacist intervention felt better.¹⁹ One in four felt that they had improved functioning, increased levels

of independence, fewer adverse health effects, more energy, more peace of mind, and/or increased levels of exercise tolerance;¹⁹ however, some studies also suggested that there was no difference in patients perceptions of their health related quality of life after the intervention.^{5,9} In a study of elderly outpatients at a VAMC, no improvement in health related quality of life (HRQOL) was reported by patients.⁹ The researchers believe that the results were related to the fact that veterans seen at the VAMC appeared to have a greater disease burden than their non-veteran counterparts, the study only lasted a year whereas more time may have been necessary to see the results, and the questionnaire used may not be accurate as an evaluative instrument.⁹

While patients' perception of their own health may not always be affected by pharmacist interventions, these interventions may improve their actual health. In one study, nursing home patients who received a pharmacist intervention were less likely to die over the course of the study, with a mortality rate of 2.5, than those who never received the intervention, who had a mortality rate of 8.1.¹⁴

Clinical Outcomes: Decreased Adverse Drug Reactions

The frequency of ADRs increases as the number of drugs taken increases. It has been estimated that the frequency of ADRs is 6% when a patient takes 2 drugs, 50% when a patient takes 5 drugs, and almost 100% when a patient takes 8 or more drugs.²² Due to the especially high number of medications that are required to effectively manage chronic diseases in the elderly, ADRs and other side effects of the drugs prescribed to these patients must be carefully monitored. As the prevalence of elderly patients continues to increase, ADRs must be monitored even more diligently as this population is at an even greater risk for poor outcomes as a result of these adverse reactions due their poorer overall health status.²³⁻²⁸ Recent research has shown that pharmacist interventions and pharmacotherapy consults can greatly reduce a patient's risk of experiencing an ADR.^{7,8,11,12,17} In a before and after study it was found that instances of ADRs in patients was decreased from 10.4 to 3.5 ADRs per 1000 patient days as the result of an intervention.¹⁷ Another study found that there was a relative risk reduction of 9.8% following pharmacist interventions.⁵ A group of patients receiving a pharmacist consult was found to consist of a greater number of improved patients and fewer worsened patients when their adverse effect scores were compared to patient scores in the control group.⁸ The consult group showed 54% improved 24.2% unchanged, and 21.8% worsened, where as the control group had 40.2% improved, 34.7% unchanged, and 31.9% worsened.⁸ A final study showed that a pharmacist interventions resulted in a non-significant trend towards a decrease in ADRs.⁷

It is important to consider the prescribing practices of physicians and the instances of inappropriate prescribing or pharmaceutical care issues, as these can potentially lead to serious ADRs.¹³ The authors of one study concluded that pharmacist intervention

increased the number of documented medication issues resolved, especially those related to patients' information needs, dosage, prescription problems, and monitoring to prevent ADRs.⁵ This study showed that 70% of all pharmaceutical care issues were resolved in the intervention group compared to only 14% of issues resolved in the control group.⁵ Over half (52%) of the intervention patients had no remaining issues at the end of the study period, but only 0.6% of the control group were issue-free.⁵ A randomized controlled trial of elderly outpatients with polypharmacy showed a 23% reduction in inappropriate prescribing at 12 months as well as a significant decrease in the number of ADRs experienced by patients in the pharmacist intervention group as compared to the control group.⁹ The reduction in ADRs experienced by patients can lead to reduced patient morbidity and mortality, as well as substantial cost savings by preventing future hospitalizations and drug costs.^{6,8}

Economic Outcomes: Facility Cost Savings

Pharmacist interventions not only result in positive clinical outcomes, but can also result in substantial cost savings to institutions. When patients are on multiple medications, there is a great potential for drug therapy problems. In patients that are on multiple drugs, pharmacist interventions have resulted in significant cost savings.^{6,8,17} While there are oftentimes medication cost savings it is important to take into consideration the costs of the intervention as well as the cost savings resulting from negative outcomes avoided.

A study examining the results of a pharmacist intervention in a nursing home found that there was a 12:1 cost-minimization ratio, with an estimated savings range for the implementation of a comprehensive pharmacist intervention of 218 US dollars to 335 US dollars per person per year when the savings on medications and the costs of the interventions were considered.¹⁶ This resulted in a savings of 1.4 to 2.1 million US dollars per year for the facility.¹⁶ The result of instituting a pharmacotherapy consult clinic run by pharmacists at the Houston VAMC found an almost 6 fold savings with a ratio of dollars saved to dollars spent of 5.8:1.⁶ The implementation of the clinic in this study estimated that the cost savings associated with the pharmacist intervention, not including cost savings of prescription drugs was 37,945 US dollars over the study period of one year with a total overall cost savings of 54,730 US dollars for the 336 patients involved in the study.⁶ The non-medication related estimated cost savings resulted from a reduction in ADR-related services such as physician visits and hospitalizations.⁶ A final study found that the inclusion of pharmacists as physicians rounded prevented 66% of ADRs which was estimated to save the hospital 270,000 US dollars per year.¹⁷ These studies support the idea that pharmacist interventions should be implemented based on cost-savings alone.^{6,16,17}

Economic Outcomes: Drug Cost Savings

While many studies have shown overall cost savings, there are conflicting results as to whether

pharmacist interventions truly decrease the total drug costs.^{7,8} There were seven studies that specifically examined the cost savings related to drug costs.^{1,6,7,12,15,16,19} These studies showed monthly cost savings that ranged from 1.53 US dollars per patient to 109 US dollars per patient. In a study at a VAMC, the implementation of a pharmacotherapy consult clinic was shown to have a cost avoidance for actual prescriptions of 16,786 US dollars over the one year period of the study, which is approximately 4.16 US dollars per patient per month (PPPM).⁶ In another study of ambulatory patients, the pharmacist intervention was found to decrease the overall drug costs by 293 US dollars over six months, which would be equivalent to 49 US dollars PPPM.⁷ It is important to note that while the drug costs decreased, it was not at the expense of good medical care, as patient outcomes were monitored and showed either no worsening or some non-significant beneficial effects.⁷

The North Carolina Polypharmacy initiative showed a relative cost reduction between the intervention and control groups of 19.04 US dollars PPPM for all patients receiving a medication review.¹⁵ This savings increased to 23.60 US dollars in the group that had pharmacist recommendations sent to the physicians and to 35.55 US dollars when drug therapy changes were made as a result of the recommendations.¹⁵ One of the studies estimated that a pharmacist intervention resulted in a cost savings of 387.38 US dollars over two months or 1.53 US dollars PPPM.¹² Another study showed that actual drug costs over two waves of identical pharmacist intervention periods were reduced by 4,777,077 US dollars for 6693 patients, or 109 US dollars PPPM, in the first intervention wave and 1,202,142 US dollars for 6039 patients, or 25 US dollars PPPM in the second intervention wave six months after each intervention took place.¹ This study showed that a pharmacist intervention in a managed care setting resulted in a nearly four-fold (389%) return on investment over the course of two intervention periods; however, non-drug costs were not included so the effect on the total cost of care cannot be determined.¹ A study of 46 patients who participated in a one-on-one pharmacist intervention found that 43% of patients reported spending less money per month on medications with an average savings of 30 US dollars PPPM.¹⁹ A final study found there was an average reduction in drug costs of 30.33 US dollars PPPM when nursing home residents received a medication profile review.¹⁶

While many studies have found a cost savings, there have been studies that found no significant difference in the average monthly cost of prescriptions per patient between the patients that received the intervention and those that did not.⁵ One study showed that there was no significant cost savings in the intervention group; however, this may be attributed to the high variability in drug costs from one year to the next for the included patients, as the standard deviation was 600 US dollars.⁸ The studies that have not shown a benefit in savings for overall drug costs have still shown benefits to the patient.

SUMMARY

There have been a number of individual studies that have documented the effect that pharmacist interventions can have on both humanistic and clinical outcomes as well as economic outcomes. Despite this preponderance of positive evidence for the implementation of pharmacist interventions and pharmacotherapy consults, these interventions are

still not widely utilized throughout the various healthcare settings. The presented studies have shown that pharmacist interventions can improve patient outcomes, and with the ever-increasing costs of healthcare, the substantial cost savings for patients as well as institutions provided by these interventions are justification enough for widespread implementation at healthcare institutions.

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