

**“FINAL PAPER”**

**The Effects of Pharmacist Intervention on Depression  
Medication Adherence: A Systematic Review**

**A Pharmacy Practice Paper**

**Josephene N. Lee, RPh**

**Karen Riley, PharmD, Facilitator  
University of Florida  
College of Pharmacy  
WPPD Program**

**October 2006**

## **Background**

Depression, a leading mental health disease, is the leading cause of disability in the United States. By the year 2020, the World Health Organization projects depression to be the second leading cause of global disease, behind ischemic heart disease, for all ages and sex.<sup>1</sup> Patients with depression have been reported to have direct medical costs approximately 3 times higher than patients without mental health disorders.<sup>2</sup> There are about 17 million depression patients in the United States, costing about \$80 billions annually in lost productivity and other indirect costs and \$70 billions in medical cost plus an additional \$7 billions because of medication nonadherence.<sup>3,4</sup>

Medications, regardless of how effective they are, do not work in patients who do not take them. Poor adherence to prescribed medication regimens has been a well-recognized problem in all of medicine, and disappointingly low among mental disorder patients.<sup>5</sup> Patients with chronic conditions, such as depression, are less likely to follow prescription orders than those with acute conditions. Although the efficacy of adherence enhancing strategies have been extensively researched over the last few years, the rates of adherence have not changed much over the past few decades.<sup>6</sup> Several studies<sup>2,7</sup> have reported that the medication adherence rate of depression patients was about 72% within the first month of treatment and dropped sharply to about 43% after 6 months of treatment.

With growing pressure to shorten hospital stays and reduce the intensity of outpatient treatment today, contact between patients and healthcare providers may become increasingly restricted. As a result, encouraging patients on medication adherence may become more important than ever before.

## **Pharmacist Medication Intervention**

Poor rates of medication adherence by psychiatric patients have led the healthcare providers to focus on enhancing intervention methods. Numerous intervention approaches among patients with depression have suggested that enhanced depression intervention with psychotherapy education is effective primarily for patients who complain of psychological symptoms.<sup>8,9</sup> Psychotherapy is warranted as the preferred first-line treatment when the depression is mild and the patient is motivated to work on psychological issues.<sup>10,11</sup> Psychotherapy alone is not sufficient to treat severe major depression. For major depression, pharmacotherapy remains a vital part of treatment. A combination treatment of pharmacotherapy and psychotherapy recommended by the American Psychiatric Association for patients with moderate to severe depression was reportedly very effective.<sup>12</sup>

The role of pharmacists in the medical field has recently grown well beyond dispensing function and expanded to clinical trials, health economics, patient educations, and others.<sup>13</sup> The specialized skills of clinical pharmacists have proved to be beneficial for improving treatment outcomes in a variety of health care settings. Because of their skills in identifying drug interactions, their excellent position of direct patient contact and their trust by patients, pharmacists can help patients remove evident adherence barriers and incorporate interventions into the care of their patients with use of tactics described

in Table 1.<sup>14</sup> Studies<sup>15,16</sup> have reported that patients prescribed by pharmacists were found functioning as well as or better than those prescribed by other providers.

The American College of Physicians and the American Society of Internal Medicine have jointly endorsed in a position paper the role of pharmacists in collaborative patient care arrangement.<sup>17</sup> Several studies<sup>18,19</sup> included pharmacists in the test of the effects of the collaborative care processes on medication adherence rates, clinical outcomes, provider and patient satisfaction, medical resource utilization, and quality of life.

Depression has been associated with low quality of life in patients, and improvement on depression through medication adherence can improve patients' health-related quality of life (HRQL), which is a multidimensional construct to assess the physical, mental and social functioning of patients. Although prior pharmacist interventions did not assess impacts of medication adherence in the trials, they demonstrated improvements, inconsistently, on the HRQL of patients with other diseases.<sup>20</sup>

Cost is one side of the appropriateness of care coin, with the other side being the derived benefits of treatment. While identifying the outcomes of care is important, there is increased focus on measuring the costs associated with achieving the outcomes. Cost-effectiveness analysis is increasingly used in health care to help determine which health interventions provide the most effective care. This is especially important when available resources are scarce and restricted. The costs associated with interventions by pharmacist should be analyzed and compared with the costs by other providers.

The purpose of this report was to summarize related studies and determine whether pharmacist intervention would 1) improve depression patients in adherence to medications; 2) improve health-related quality of life; and 3) reduce the health care cost.

## Method

Finley et al<sup>21</sup> have searched electronically through the PubMed database and manually through various journals for studies examining the impacts of clinical pharmacists on the care and outcomes of patients with mental disorders from 1972 to 2002. As a result, they identified sixteen articles for detailed review and assessment to determine the impacts of pharmacist intervention on mental disorder patients. Five of the sixteen studies were related to depression intervention. Bell et al<sup>22</sup> also searched articles involving community pharmacist intervention in antidepressants and identified four additional studies, which were not previously reported by Finley et al. Their search findings that were related to antidepressant intervention were included for review.

Literature searches further continued through 2006 by use of the Medscape and Google Scholar for articles of randomized controlled trials involving pharmacist intervention in adherence to medications for depression patients. The text words used in the searches included *pharmacist intervention, medication intervention, depression, medication adherence, cost, resource utilization, quality of life, psychiatric disorder, health-related quality of life, and antidepressants*. The University of Florida Health Science Center Library was also utilized to obtain the identified articles whose free full texts were not available from the Medscape, Google Scholar and the Detroit VA Medical Center

Library. In addition, manual searches were also performed through the various journals available at the Detroit VA Medical Center Library. Studies of pharmacist interventions on healthcare costs and health-related quality of life were also searched.

The inclusion criteria for this assessment must be that each study included a randomized controlled trial identifying the apparent impacts of pharmacist intervention on a patient population (intervention group) with depression. Also included are the interventions that could be applied directly toward the patient population (both groups) or healthcare providers who deliver care. For collaborative care models, the clinical pharmacists' role must be prominent, and the results of the pharmacists' intervention must be compared with a distinct control group of patients who do not receive comparable health care. For the purposes of this review, historic control studies with a before-after design were also included.

## **Results**

Twelve published articles involving the pharmacist intervention of antidepressant adherence rate, cost of care, and/or quality of life that satisfied the inclusion criteria were summarized in Table 2. Three studies<sup>19,24,30</sup> simultaneously reported the impacts of intervention on medication adherence, cost of care and health-related quality of life. Detailed findings of the studies related to each individual subject are described in the following subsections.

### ***Medication Adherence***

Nine of the twelve intervention studies are related to medication adherence. The most common intervention strategy that clinical pharmacists utilized was a combination of drug monitoring (baseline assessment and treatment follow-up), drug counseling by telephone and personal interviews, and patient education (drug side effects). Three investigations<sup>18,19,30</sup> reported that pharmacists were authorized to prescribe medications and change doses under the supervision of psychiatrists or physicians. Two<sup>23,28</sup> interventions analyzed the impact on reduction in number of drugs for elderly people. One study<sup>29</sup> evaluated the impact on adherence of patients with recurrent depressive episodes.

Numerous measurements can be utilized by researchers in measuring the outcomes of medication adherence. These measurements include patient self-report, pill counts, and prescription claims. While lack of a standard measurement has led to widely mixed results among the interventions, the cumulative results reported in these investigations were overwhelmingly positive. Five studies<sup>24,26,29,30,31</sup> determined the medication adherence rate by use of the patient self-report approach, using questionnaires and surveys by mail, telephone or personal interview. Finley et al<sup>18,19</sup> used pharmacy records including prescription refill and paid prescription claims to calculate medication possession ratio and determine the adherence rate. One study<sup>32</sup> utilized the pill count method in determining the adherence. Three studies<sup>24,26,28</sup> used clinical outcomes, such as drug attitude inventory and depression rating, to qualitatively assess the adherence. One study<sup>29</sup> further sub-grouped the trial patients in both groups and

assessed how the intervention affected those who took antidepressants at entry of the trial and those who did not.

Medication adherence is defined as the degree to which patient's behavior corresponds with the treatment regimens prescribed by the healthcare providers. The improvement in medication adherence by these pharmacist interventions was summarized in Table 3. Five investigations reported an improvement varying from 15% to 19% and three investigations reported the adherence qualitatively. However, one investigation<sup>30</sup> reported no statistical difference for all outcome measures because patients in both groups were exposed to the same available resources (a Hawthorne effect).

### ***Health Related Quality of Life***

Eleven studies measured functional outcomes (physically and psychologically) which can serve as indicators for assessing the HRQL. The findings of these studies were summarized in Table 4. Common outcome measures used in determining HRQL included physical functioning and psychological functioning. Majority of the pharmacist interventions in this review monitored the psychological function such as depression symptoms and mood disorder. Seven studies reported no statistical difference in improvement of HRQL between the pharmacist intervention group and the control group. Four investigations<sup>18,19,24,26</sup> reported a HRQL improvement at various levels, using various indexes. One study<sup>25</sup> reported that improvement in HRQL depended largely upon the type of drugs prescribed, but not the providers who prescribed.

### ***Economic Impact***

Four studies that qualitatively or quantitatively measured cost of care (resource utilization) were identified and summarized in Table 5. The cost of care includes not only the intervention cost but also total related medical costs, which are generally affected by frequency of hospital and clinic visits, days of hospitalization, and medication cost. Two investigations<sup>19,23</sup> reported a decreased total healthcare cost in the intervention groups and one study reported no significant difference in total cost of care. In contrast, one study<sup>24</sup> reported a significant increase in total cost of care in the intervention patients, however, the cost per successful outcome was only 30% of the cost for the control patients. This study also included the cost of pharmacists for the intervention patients in the analysis. Only one study<sup>23</sup> pharmacist intervention studies reported complete medical costs, thus limiting the usefulness of these data.

### **Discussion**

Most intervention studies did not measure the effectiveness in preventing relapse of depression because of the short follow-up periods, 12 months or less. A relapse was reported within two years of treatment among more than 35 percent of elderly patients with major depression.<sup>33</sup> Questions<sup>34</sup> were raised that the common practice of administering antidepressants for only 6 to 12 months may not be sufficient to prevent recurrence of depression. To assess the effectiveness of an intervention on relapse of depression, the intervention and follow-up duration should be extended to at least 2 years.

The results of these studies, thus, cannot be applied to general population because of population selection bias. Most of these trials were not blinded since both patients and providers knew the trials during the tests. Majority of the patients in the trials were female and white. Women reportedly have a poorer adherence rate than men because they have higher tendency to split the drugs in half to save money. Caucasian has a higher adherence rate than other races such as Asian, Hispanics and black.

Social economic status is also an important affecting factor on medication adherence. None of these studies evaluated the intervention impacts on the underserved groups including the elderly, homeless and low income without a medical insurance. Their adherence is expected to be very low because of concern of medication cost. An effective intervention should include innovative approaches, such as half tablet of higher doses, to relieve patients from their financial burden.

Adverse drug side effect was cited as the leading cause for early discontinuation of medication.<sup>35,36</sup> The side effects can be reduced by changing prescriptions to controlled-release medications instead of immediate-release medications because a CR medication has a reduced dose at any given time. Reduction of dosing frequency by CR medication would make it much simpler for the elderly who take multiple drugs and improve their medication adherence. Sheehan and colleagues<sup>37</sup> reported that CR medication improved medication adherence without significantly increasing the medical cost. None of these studies indicated prescription of CR medications during the trials.

A long-term treatment for depression patients is needed in order for the medication to work. Lack of this information may result in lower adherence rates. Patients may stop use of the medications when they do not see the effects immediately or when they feel better after administration of medications. Adequately educated patients on drug information will improve the adherence, and pharmacists can play a better role than other healthcare providers in drug counseling.

More than 40% of patients aged 65 years or older have been reported to take five or more drugs simultaneously.<sup>38</sup> Polypharmacy, use of multiple medications by a patient, presents a significant problem for the elderly because of potential of adverse drug reactions (ADR) and medication misadventure. Two prospective intervention studies on the elderly are noteworthy for further discussion. Furniss and colleagues<sup>23</sup> reported a reduction in the number of medicines prescribed to elderly people in nursing homes without significant impacts on their morbidity. However, this study did not demonstrate how the ADR affects the medication adherence. Bieszk and colleagues<sup>39</sup> assessed medication appropriateness and adherence through medical records, prescription claims data and patient interviews in a senior drug benefit plan intervention and reported a more than 61% of patients in medication adherence and a reduction of care cost by 10%. Since pharmacist was not involved in the trial, comparison of the outcomes with other studies was not done.

Two investigations<sup>15,16</sup> reported that pharmacists are able to provide intervention as well as or better outcomes than other psychiatrists. However, none of these identified studies directly compared the effectiveness of intervention between pharmacists

(intervention group) and other healthcare providers (control group). Future studies may focus more in this aspect.

Identifying the most cost-effective pharmacist intervention is essential when scarce resources currently encourage increasing use of mail service pharmacies and reducing time for patient counseling. Pharmacist interventions with different adherence strategies have resulted in mixed outcomes and made it difficult to identify the most cost-effective role that pharmacists may assume. A telephone call or a reminder chart was found to be an effective approach, especially affecting elderly patient's medication-taking behaviors at home.<sup>40,41</sup> Five<sup>18,19,29,31,32</sup> of six studies that included telephone contact with patients in the intervention approaches reported a substantial improvement in medication adherence. One<sup>30</sup> cited a Hawthorne effect for no significant difference in adherence between intervention and control groups.

Researchers generally hypothesize that an improvement in medication adherence will directly or indirectly improve patient's quality of life. As shown in Table 4, majority of the studies reporting improvement in medication adherence, however, failed to demonstrate an improvement in HRQL by enhanced interventions. Future studies should focus on intervention techniques that can effectively improve the HRQL.

An increase in intervention costs may be offset by other decreased medical costs as a result of improvement in medication adherence. One study<sup>42</sup> evidenced that the costs associated with improving clinical outcomes were offset by saving in medical costs. Dickinson et al<sup>11</sup> also demonstrated a decrease in total outpatient costs for depressed patients who complained of psychological symptoms. Rost and colleagues<sup>43</sup> suggested that sufficient reduction in outpatient costs to cover the program cost could only occur after the enhanced care improves patient's conditions to normal levels. They reported a cost saving starting at the second year of their study. In contrast, one intervention<sup>44</sup> reported a significantly high rate of hospital admission in the intervention patients, implying an increase in cost of care. These conflicting outcomes were also evidenced by the studies summarized in Table 5.

## **Conclusion**

The studies supported the roles of clinical pharmacists in providing intervention on medication adherence in collaborative care models for patients with moderate to severe depressions. To further evaluate whether a pharmacist intervention has superior over other intervention teams in medication adherence, future collaborative care models may be designed to treat the pharmacist-led intervention group as an intervention group and other groups led by other healthcare providers as a control group. The results can then provide an indication for future trends for a cost-effectiveness pharmacist intervention program.

Three primary factors contribute to low medication adherence in depression patients. These factors are:

1. lack of drug information on adverse reactions and drug-administering schedules;
2. financial difficulty; and

### 3. complicate drug regimens.

Depending on patient's belief in their depression symptoms to measure the status of health related quality of life has resulted in inconsistent outcomes. Standardized intervention measures that can more correctively reflect patient's depression status and effectively monitor the improvement in patient's HRQL should be developed.

Increases in intervention costs are usually offset by other decreased medical costs as a result of decreases in clinic visits and emergency frequency. However, a solid determination on the benefit of intervention in healthcare expenses is not possible because of numerous factors that affect the costs.

### References

1. World Health Organization, The World Health Report 2001 – Mental health: New understanding, new hope. *Geneva World Health Organization*, 2001.
2. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analysis review of the literature. *Diabetes Care* 2000; 23(7): 934-942.
3. CIGNA Behavioral Health. Direct costs of depression in the workplace are tip of the iceberg: employers have huge stake in promoting depression treatment. *MIT Depression Symposium* October 13, 2005. (Abstract)
4. Cantrell C, Eaddy M, Shah M, Regan T, Sokol M. Methods for evaluating patient adherence to antidepressant therapy: a real-world comparison of adherence and economic outcomes. *Medical Care* 2006; 44(4): 300-303.
5. Osterberg L, Blaschke T. Adherence to medication. *New England Journal of Medicine*. 2005; 353(5):487-497.
6. Atreja A, Bellam N, Levy S. Strategies to enhance patient adherence: Making it Simple. *Medscape General Medicine*. 2005; 7(1):4–9.
7. Lin EH, Von Korff M, Katon W, et al. The role of the primary care physician in patient's adherence to antidepressant therapy. *Medical Care*. 1995; 33(1):67-74.
8. Keeley R, Smith J, Nutting P, Dickinson L, Dickinson P, Rost K. Does a depression intervention result in improved outcomes for patients presenting with physical symptoms? *General Internal Medicine* 2004; 19: 613-623.
9. Dickinson L, Rost K, Nutting P, Elliott C, Keeley R, Pincus H. RCT of a care manager intervention for major depression in primary care: 2-year costs for patients with physical vs psychological complaints. *Annals of Family Medicine* 2005; 3(1): 15-22.
10. Byrne N, Livingston G, Regan C. Adherence to treatment in mood disorders. *Current Opinion Psychiatry* 2006; 19(1): 44-49.
11. Ravindran L, Conn D, Ravindran A. Pharmacotherapy of depression in older adults. *Geriatrics Aging* 2005; 8(8): 20-27.
12. Pampallona S, Bollini P, Tibaldi G, Kupelnick B, Munizza C. Combined pharmacotherapy and psychological treatment for depression. *Archives of General Psychiatry* 2004; 61(7): 714-719.
13. Hanlon JT, Artz MB. Drug-related problems and pharmaceutical care. *Medical Care* 2001; 39 (1):109-112.



14. Kenreigh C, Wagner L. Medication Adherence: a literature review. *Medscape Pharmacists* 2005; 6(2) (Abstract).
15. Rosen C, Holmes S. Pharmacist's impact on chronic psychiatric outpatients in community mental health. *American Journal of Hospital Pharmacy* 1978; 35(6): 704-708.
16. Stimmel, McGhan W, Wincor M, Deandrea D. Comparison of pharmacist and physician prescribing for psychiatric inpatients. *American Journal of Hospital Pharmacy* 1982; 39(6): 1483-1486.
17. Keely JL. Pharmacist scope of practice. *Annals Internal Medicine* 2002; 136(1): 79-85. (position paper).
18. Finley P, Rens H, Pont J, Gess S, Louie C, Bull S, Bero L. Impact of a collaborative pharmacy practice model on the treatment of depression in primary care. *American Journal of Health-System Pharmacy* 2002; 59(16): 1518-1526.
19. Finley P, Rens H, Pont J, Gess S, Louie C, Bull S, Lee J, Bero L. Impact of a collaborative care model on depression in a primary care setting: a randomized controlled trial. *Pharmacotherapy* 2003; 23(9): 1175-1185.
20. Pickard A, Johnson J, Farris K. The impact of pharmacist interventions on health-related quality of life. *The Annals of Pharmacotherapy* 1999; 33: 1167-1171.
21. Finley P, Crismon M, Rush J. Evaluating the impact of pharmacists in mental health: A systematic review. *Pharmacotherapy* 2003; 23(12): 1634-1644.
22. Bell S, McLachlan A, Aslani P, Whitehead P, Chen T. Community pharmacy services to optimize the use of medications for mental illness: a systematic review. *Australia and New Zealand Health Policy* 2005; 2(1): 29-39.
23. Furniss L, Gurns A, Craig A, Scobie S, Cooke J, Faragher B. Effects of a pharmacist medication review in nursing homes: randomized controlled trial. *British Journal of Psychiatry* 2000; 176(6): 563-567.
24. Canales P, Dorson P, Crismon M. Outcome assessment of clinical pharmacy services in a psychiatric inpatient setting. *American Journal of Health-System Pharmacy* 2001; 58(13):1309-1316.
25. Taylor A, Spruill W, Longe R, Wade W, Wagner P. Improved health-related quality of life with SSRIs and other antidepressants. *Pharmacotherapy* 2001; 21(2): 189-194.
26. Bultman D, Svarstad B. Effects of pharmacist monitoring on patient satisfaction with antidepressant medication therapy. *Journal of American Pharmacists Association*. 2002; 42(1):36-43.
27. Brook O, van Hout H, Nieuwenhuysen H, Haan M. Effects of coaching by community pharmacists on psychological symptoms of antidepressant users; a randomized controlled trial. *European Neuropsychopharmacology* 2003; 13(5): 347-354.
28. Brook O, van Hout H, Nieuwenhuysen H, Heerdink E. Impact of coaching by community pharmacists on drug attitude of depressive primary care patients and acceptability to patients: a randomized controlled trial. *European Neuropsychopharmacology* 2003; 13(1): 1-9.
29. Adler D, Bungay K, Wilson I, Pei Y, Supran S, Peckham E, Cynn D, Rogers W. The impact of a pharmacist intervention on 6-month outcomes of depressed primary care patients. *General Hospital Psychiatry* 2004; 26(3): 199-209.
30. Capoccia K, Boudreau D, Blough D, Ellsworth A, Claker D, Stevens N, Katon W, Sullivan S. Randomized trial of pharmacist interventions to improve depression

- care and outcomes in primary care. *American Journal of Health-System Pharmacy* 2004; 61(2): 364-372.
31. Rickles N, Svarstad B, Statz-paynter J, Taylor L, Kobak K. Pharmacist telemonitoring of antidepressant use: effects on pharmacist-patient collaboration. *Journal of American Pharmacists Association* 2005; 45(3):344-353.
  32. Brook O, van Hout H, Stalman W, Nieuwenhuysen H, Bakker B, Heerdink E, de Haan M. A pharmacy-based coaching program to improve adherence to antidepressant treatment among primary care patients. *Psychiatric Services* 2005; 56(4): 487-489.
  33. Reynolds C, Dew M, Pollock B, Mulsant B, Frank E, Miller M, Houck P, Mazumdar A, Butter M, Stack J, Schlernitzauer M, Whyte E, Gildengers J, Karp J, Lenze E, Szanto K, Bensasi S, Kupfer D. Maintenance Treatment of Major Depression in Old Age. *New England Journal of Medicine* 2006; 354(11): 1130-1138.
  34. Reifler B. Play it again, Sam – Depression is recurring. *New England Journal of Medicine* 2006; 354(11): 1189-1190.
  35. Tabor P, Lopez D. Comply with us: improving medication adherence. *Journal of Pharmacy Practice* 2004; 17(3): 167-181.
  36. Keene M. Confusion and complaints: the true cost of noncompliance in antidepressant therapy. *Medscape Psychiatry & Mental Health* 2005; 10(2).
  37. Sheehan D, Eaddy M, Sarnes M, Vishalpuria T, Regan T. Evaluating the economic consequences of early antidepressant treatment discontinuation: a comparison between controlled-release and immediate-release paroxetine. *Journal of Clinical Psychopharmacology* 2004; 24(5): 544-548.
  38. Kaufman D, Kelly J, Rosenberg L, Anderson T, Mitchell A. Recent patterns of medication use in the ambulatory adult population of the United States. The Slone survey. *Journal of the American Medical Association* 2002; 287(3): 337-344.
  39. Bieszk N, Bhargava V, Pettita T, Whitelaw N, Zarowitz B. Quality and cost outcomes of clinical pharmacist interventions in a capitated senior drug benefit plan. *Journal of Managed Care Pharmacy* 2002; 8(2): 124-131.
  40. Cargill J. Medication compliance in elderly people: influencing variables and interventions. *Journal of Advanced Nursing* 1992; 17(4): 422-426.
  41. Fulmer T, Kim T, Montgomery K, Lyder C. What the literature tells us about the complexity of medication compliance in the elderly. *The American Society on Aging* 2003; 4(1): 43-48.
  42. Katon W, Unutzer J, Fan M, Williams J, Schoenbaum M, Lin E, Hunkeler E. Cost-effectiveness and net benefit of enhanced treatment of depression for older adults with diabetes and depression. *Diabetes Care* 2006; 29(2):265-270.
  43. Rost K, Pyne J, Dickinson L, LoSasso A. Cost-effectiveness of enhancing primary care depression management on an ongoing basis. *Annals of Family Medicine* 2005; 3(1) 7-14.
  44. Barclay L. Pharmacist review may not reduce hospital admissions in older patients. *BMJ Online* First January 21, 2005.

**Table 1. Pharmacist Intervention Tactics**

- Educating patients about the importance of adherence
- Identifying ways to help patients avoid running out of medications
- Providing strategies for improving adherence with medication aids, such as dosing calendar and pill boxes
- Identifying confounding factors that may adversely affect adherence
- Explaining to patients the side effects of medications and review the regimens to identify possible simplification strategies

**Table 2. Effects of Pharmacist Intervention on Depression Patients**

Source	Pharmacist Intervention	Sample size		Follow-up	Outcome measures	Findings
		Intervention	Control			
Furniss et al 2000 <sup>23</sup>	Review of medical history, medication and current medical problems 2 times; Initial assessment of depression symptom scales	158	172	8 mos	Depression symptoms; Quality of life; Number of drugs filled; Cost of care	<ol style="list-style-type: none"> <li>1. There was a decline in the total MMSE scores for intervention group (12.5 vs 13.8 at baseline)</li> <li>2. No statistically different changes were observed in depression scores.</li> <li>3. The intervention reduced total healthcare cost by 19%.</li> <li>4. Mean number of prescribed drugs for elderly patients was reduced.</li> </ol>
Canales et al, 2001 <sup>24</sup>	Performing baseline assessment and weekly review; Attending morning report and staff brief; Reviewing medical history and drug administration records; Monitoring drug reactions; Providing treatment recommendation; Conducting patient drug education weekly and counseling;	45	48	NA	Depressive symptoms; Cognitive function; Quality of life; Thought disorder; Mood disorder	<ol style="list-style-type: none"> <li>1. A significant difference between the groups was observed for baseline MMSE scores, but the improvement in MMSE scores did not differ significantly between the group (10 vs 12);</li> <li>2. Hamilton Psychiatric Rating (HAM) scores improved significantly more for mood disorder (65% vs 9%);</li> <li>3. Discharge scores (thought disorder) improved significantly more in intervention group (93% vs 23% for patients with 20% improvement and 62% vs 0% for 30% improvement)</li> <li>4. Total healthcare cost increased in intervention group by 21% during the trial, but cost effectiveness ratio (cost/ successful outcome) decreased by 70%.</li> </ol>
Taylor et al 2001 <sup>25</sup>	Selecting patients with medication adherence rate > 80%; Reviewing patient's demographic and medication records; Assisting patients completing SF-36 form;	35	22	N/A	HRQL factors including: Physical functioning; Physical role; Bodily pain; General health; Vitality; Social functioning; Emotion; Mental health	<ol style="list-style-type: none"> <li>1. Physical HRQL for patients receiving SSRIs is better than those taking other antidepressants (50 vs 39).</li> <li>2. No statistical difference in improvement in mental HRQL was observed between the groups.</li> <li>3. No statistical differences in the individual scale score, physical and mental summary scales, were observed on the basis of providers (psychiatrist vs non-psychiatrist).</li> </ol>

**Table 2. Effects of Pharmacist Intervention on Depression Patients**

Source	Pharmacist Intervention	Sample size		Follow-up	Outcome measures	Findings
		Intervention	Control			
Bultman and Svarstad 2002 <sup>26</sup>	Identifying patients meeting study criteria; Performing patient interviews twice to assess medication history, drug knowledge, and drug belief, patient satisfaction, medication adherence; Patient selection (taking new antidepressant; older than 18 and understanding English); Monitoring patient behavior;	100	100	2 mos	patient beliefs; patient knowledges; patient satisfaction with therapy; adherence rate	<ol style="list-style-type: none"> <li>1. High percentage (87%) of patients satisfied with antidepressants treatment at baseline.</li> <li>2. Medication adherence rate was observed to be 76% within 3 months.</li> <li>3. 24% of patients reported discontinuation of medication within 3 months.</li> <li>3. Pharmacist monitoring positively influenced adherence for patients taking antidepressants for the first time.</li> </ol>
Finley et al, 2002 <sup>18</sup>	Intake and follow-up interviews (3 clinic visits and 5 phone calls); Medical history and other environmental stressors review; Drug prescribing and dose changes under protocol; Drug information counseling; Communication with PCPs	91	129	6 mos	Medication adherence rate; Patient satisfaction; Clinic visit frequency; Resource utilization	<ol style="list-style-type: none"> <li>1. Medication adherence rate improved 15% at end of study (81% vs 66%).</li> <li>2. Patient's recall to complete 6-month treatment was different (76% vs 49%).</li> <li>3. Clinic visit decline was different (39% vs 12%).</li> <li>4. patients were more satisfied in intervention group.</li> </ol>
Finley et al, 2003 <sup>19</sup>	Drug monitoring; Patient education; Routine follow-up (clinic visits at weeks 6 and 24 and extensive phone calls at weeks 1,2,4, 10 and 16); Drug prescribing and medication change under protocol;	75	50	6 mos	Medication adherence rate; Patient satisfaction; Clinic visit frequency; Resource utilization	<ol style="list-style-type: none"> <li>1. Medication adherence rate increased by 19% (67% vs 48%)</li> <li>2. Intervention patients were more satisfied with treatment.</li> <li>3. Clinic visits declined by 13% (15% vs 2%).</li> <li>4. Drug cost of intervention patients increased by 42%</li> <li>5. No significant difference in improvement of depression symptom</li> </ol>

**Table 2. Effects of Pharmacist Intervention on Depression Patients**

Source	Pharmacist Intervention	Sample size		Follow-up	Outcome measures	Findings
		Intervention	Control			
Brook et al 2003 <sup>27</sup>	Performed 3 drug coachings (drug use, side effects, time for drugs to work and other counseling); Provided a take-home video on depressive symptoms and reliefs, and medication adherence	69	79	3 mos and 3 mos follow-up	Mental depressive symptoms;	<ol style="list-style-type: none"> <li>1. More than two thirds of patients were in remission at the 6-month follow-up.</li> <li>2. Intervention patients improved significantly from baseline more than the control patients on depressive symptoms.</li> <li>3. No statistically significant difference on improvement in depressive symptoms between both groups.</li> </ol>
Brook et al 2003 <sup>28</sup>	Performed 3 drug coachings (drug use, side effects, time for drugs to work and other counseling); Provided a take-home video on depressive symptoms and reliefs, and medication adherence	69	79	3 mos and 3 mos follow-up	Drug Attitude; Depressive symptom;	<ol style="list-style-type: none"> <li>1. Intervention patients had more positive drug attitude than control patients (14.2 vs 9.7).</li> <li>2. A positive attitude toward ADs may improve adherence rate.</li> <li>3. A take-home informative video was effective in influencing patient's ideas about medication.</li> </ol>
Adler et al, 2004 <sup>29</sup>	Contacting patients 9 times over the 18-month study; Reviewing medication history, drug side effects and efficacy; Assisting PCP and patients in drug choice, dose and regimen; Providing social support; Educating patients to maintain AD medication;	258	249	6 mos Study period and 12 months follow-up	AD use rate (adherence rate); depression severity	<ol style="list-style-type: none"> <li>1. Intervention improved AD adherence by &gt;11% at both 3 months (60.6 vs 48.9) and at 6 months (57.5 vs 46.2).</li> <li>2. For patients using ADs at study entry, no significant differences in AD use were observed between groups at 3 or 6 months.</li> <li>3. For patients not on AD at study entry, AD use rate was higher in intervention patients at both 3 months and 6 months.</li> <li>4. Depression outcomes, both physical and mental, were no different between two groups.</li> </ol>

**Table 2. Effects of Pharmacist Intervention on Depression Patients**

Source	Pharmacist Intervention	Sample size		Follow-up	Outcome measures	Findings
		Intervention	Control			
Capoccia et al 2004 <sup>30</sup>	Performing patient follow-up by phone 11 times (weekly for the first 4 weeks followed by every other weeks through week 12 and then every 2 months for 4 - 12 months); Interviewing patients 2 times during clinic visits; Patient contact during clinic visits (week 4 and 12); Monitoring drug treatment (time drugs taken, change of drugs and other treatment); Educating patients on side effects; Providing drug refills and medication dose adjustment	41	33	12 mos	Adherence rate; Depression symptom; Patient satisfaction; Clinical visits	<ol style="list-style-type: none"> <li>1. No significant difference in medication adherence between treatment groups.</li> <li>2. No overall difference in satisfaction with depression care was observed between groups.</li> <li>3. No overall difference in improvement of depression symptoms was observed between groups.</li> <li>4. Depression symptoms improved from baseline in both groups.</li> <li>5. No difference between two groups in number of visits to all health care providers was observed.</li> </ol>
Rickles et al, 2005 <sup>31</sup>	Conducting 3 monthly phone calls to patients; During 1st call, assessing patient's drug knowledge and belief, adverse effects, drug use status, treatment goals, and self-rated depression severity; During 2nd call, reviewing previous concerns, drug adherence, progress assessment, and recommendations; During 3rd call, repeating the previous concerns	28	32	3 mos and 3 mos follow-up	Adherence rate; Frequency of feedback to pharmacist; Depression symptoms; Antidepressant knowledge; Drug belief	<ol style="list-style-type: none"> <li>1. No significant difference between two groups in adherence rate was observed for the 3-month period.</li> <li>2. Rate of missed doses rate was significantly lower in intervention group at 6 months (30% vs 49%).</li> <li>3. No statistically significant impact on depression symptom was observed between groups.</li> <li>4. Depression symptom improved from baseline in both groups.</li> <li>5. Intervention patients had higher scores in drug knowledge and belief (75% vs 48%).</li> </ol>

**Table 2. Effects of Pharmacist Intervention on Depression Patients**

Source	Pharmacist Intervention	Sample size		Follow-up	Outcome measures	Findings
		Intervention	Control			
Brook et al, 2005 <sup>32</sup>	Provided nontricyclic antidepressants in an electronic pill container to all patients; Offered 3 phone calls (10-20 minutes); Provided a take-home video emphasizing medication adherence; Documented number of pills, date drug was filled, date drug was refilled.	64	71	6 mos	Adherence rate by pill consumed/day; Depressive symptom	<ol style="list-style-type: none"> <li>1. No differences in improvement in adherence rate was observed between two groups per intention-to-treat analysis.</li> <li>2. Adherence rate improved 17% (90% vs 73%) per intervention protocol analysis.</li> <li>3. No improvement in depression symptoms was observed.</li> </ol>



**Table 3. Medication Adherence Statistics**

Study Source	Measurement	Adherence Rate		
		Intervention	Control	Improvement
Canales et al, 2001 <sup>24</sup>	Barnes Rating Scale	27%	-7%	Qualitative
	Simpson-Angus Rating Scale	22%	-7%	
Bultman and Svarstad 2002 <sup>26</sup>	Health Communication Model	63%	87%	Qualitative
Finley et al, 2002 <sup>18</sup>	Prescription Refills	81%	66%	15%
Finley et al, 2003 <sup>19</sup>	Prescription Refills	67%	48%	16%
Brook et al 2003 <sup>28</sup>	Drug Attitude Inventory (DAI-30)	14.2	9.7	Qualitative
Adler et al, 2004 <sup>29</sup>	Patient Self-report	60.6%	48.9%	12%
Capoccia et al 2004 <sup>30</sup>	Patient Self-report	59%	57%	No
Rickles et al, 2005 <sup>31</sup>	Patient Self-report	70%	51%	19%
Brook et al, 2005 <sup>32</sup>	Pill Count	90%	73%	17%

**Table 4. HRQL Improvement Statistics**

Study Source	Measurement	Health Related Quality of Life		
		Intervention	Control	Improvement
Furniss et al 2000 <sup>23</sup>	Mini-Mental State Exam (MMSE)	3%	-8%	No
	Geriatric Depression Scale (GDS)	10%	-4%	No
Canales et al, 2001 <sup>24</sup>	Hamilton (HAM) Psychiatric Rating	65%	9%	56%
	Clinical Globe Impression (CGI) Scale	93%	23%	70%
	MMSE (50% reduction)	10%	12%	2%
Taylor et al 2001 <sup>25</sup>	Physical Component Summaries (PCS);	50	39	Yes
	Mental Component Summaries (MCS);	45	42	No
	SF-36 Scales	67	56	Yes
Bultman and Svarstad 2002 <sup>26</sup>	Health Belief Model	Not Applicable	Not Applicable	57%
Finley et al, 2002 <sup>18</sup>	Clinic visit frequency reduction	39%	12%	27%
Finley et al, 2003 <sup>19</sup>	Clinic visit frequency reduction	15%	2%	13%
Brook et al 2003 <sup>27</sup>	Hopkins Symptom Checklist (SCL-90)	1.3	1.2	No
Adler et al, 2004 <sup>29</sup>	Modified Beck Depression Inventory (mBDI)	5.7	3.8	No
Capoccia et al 2004 <sup>30</sup>	Hopkins Symptom Checklist (SCL-20)	1.0	1.0	No
Rickles et al, 2005 <sup>31</sup>	Beck Depression Inventory-II	0%	0%	No
Brook et al, 2005 <sup>32</sup>	Hopkins Symptom Checklist (SCL-13)	1.3	1.4	No

**Table 5. Effects of Pharmacist Intervention on Healthcare Cost**

Source	drug cost % (I vs C)	Clinic Visit Cost % (I vs C)	Hospital Cost % (I vs C)	Total Healthcare Cost		
				Intervention	Control	Cost Increase
Furniss et al 2000 <sup>23</sup>	2% (£290 vs £284)	25% (£265 vs £212)	-50% (£253 vs £506)	£807.58	£1001.81	-19%
Canales et al, 2001 <sup>24</sup>	67% (\$252 vs \$151)	not reported	+19% (24 days vs 21 days)	9890	8141.44	21%
Finley et al, 2003 <sup>19</sup>	42%	13% (15% vs 2%)	(+7% vs +119%)	5%	24%	-19%
Capoccia et al 2004 <sup>30</sup>	not reported	0% (visit) (9 vs 9)	0%	not reported	not reported	No