Depression remains one of the most common conditions seen in primary care settings. Antidepressant medications (ADMs) are considered standard treatment for moderate to severe depression, and in some instances, for minor depression. When ADM adherence is low, patients are at risk for treatment failure and poor quality of life. Nurses may be key in ensuring the success of ADM therapy; however, little is known about the interventions nurses use or the consequent patient outcomes. The objectives of this article were to identify studies in which nurses managed ADM adherence and to collect evidence about the efficacy of these interventions. A systematic literature review of clinical trial studies was conducted, which specifically included the role of the nurse. Nurse interventions identified were: patient care management, medication monitoring, depression education, and referrals to specialty providers. Nurses use a range of interventions to manage ADM adherence. In most studies, these approaches, including collaborative care, were efficacious. [Journal of Psychosocial Nursing and Mental Health Services, 52(4), 48-57.]
The purpose of this systematic review was to identify research in which nurses played a role in managing antidepressant medication (ADM) adherence. Additionally, evidence was sought regarding the specific nursing components of these interventions that produced improved outcomes.

The treatment of depression lies largely with primary care providers (PCPs). Treatment for depression may include psychotherapy, medication, or both, depending on symptom severity, chronicity, comorbidities, stressors, cultural beliefs, and patient preferences (Agency for Healthcare Research and Quality, 2012). Although PCPs prescribe 62% of ADMs, there is concern that depression continues to go untreated, undertreated, or that ADMs might be prescribed without a corresponding psychiatric diagnosis (Mark, Levit, & Buck, 2009; Mojtabaie & Olfson, 2011). ADMs are part of a standard approach to treating depressive disorders, with more than 20 ADMs currently available worldwide. These medications can, singularly or in combination with other ADMs or antipsychotic medications, relieve the disabling effects of depression. Treatment of adults with depression who use the ADMs is efficacious; however, suboptimal ADM therapy remains a serious concern. Reported levels of non-adherence to ADMs have been consistently high (Akincigil et al., 2007; Cantrell, Eaddy, Shah, Regan, & Sokol, 2006; Demyttenaere et al., 2001).

A brief review of terminology is warranted. Compliance is seen as an outdated paternalistic term that refers to the extent that the patient’s behavior conforms to the prescriber’s recommendations (Aronson, 2007). Adherence was introduced as a term that also describes how well the patient’s behavior matches the prescriber’s recommendations but implies a level of mutual agreement on the part of the patient. Adherence is the term often used in research because specific tools have been developed to measure adherence, which is not yet the case for concordance outcomes. Concordance takes an additional step toward patient-centeredness, implying shared decision making and consensus agreement (De las Cuevas, 2011). Medication persistence refers to the duration of time that a patient takes a particular medication (Cramer et al., 2008).

Non-adherence to ADMs results in suboptimal treatment and can increase the probability of relapse and poor quality of life. Even partial non-adherence can be detrimental, although might not always result in ill effects (Mitchell & Selmes, 2007). Patients who only partially follow or discontinue their ADM regimen frequently make that decision without physician consultation (Sawada et al., 2009). Nurses in primary care settings are in key positions to alter the course of non-adherence and modify the disruptive consequences of suboptimal treatment of depression.

A number of studies have addressed the barriers to ADM compliance and adherence including drug characteristics, patient beliefs, patient-provider relationships, and systems of care (Brown et al., 2005; Bultman & Svarstad, 2000; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Lamb, Bower, Rogers, Dowrick, & Gask, 2011; van Servellen, Heise, & Ellis, 2011). Less attention has been given to specific elements of interventions that seem to be effective (Chong, Aslani, & Chen, 2011). Although interventions that reportedly promote ADM adherence vary (e.g., pharmacist-based interventions, telehealth, educational mailings, or primary care nursing staff), there are few primary care ADM adherence enhancement programs that focus on the components of nurse interventions that add to the success of ADM adherence both in the short and long term.

Careful analysis of specific nursing interventions in ADM adherence is absent in the literature; there are two articles that help show, at least in general terms, that nurses play an important role in ADM adherence for patients with depression. First, Fortney et al. (2007) created and examined a program that achieved significantly better adherence and response to treatment by 6 months and remission, which used a nurse case management approach. A second article identified the frequency that nurses are employed in ADM adherence enhancement trials. Chong et al. (2011) summarized the literature on multifaceted depression interventions from January 1990 to December 2010 and reported that
30% (n = 6) of these studies included the specific discipline of nursing, and when an intervention used mixed professional groups, this frequency increased to 45% of all studies reviewed. Thus, nurses in primary care settings are in key positions to promote ADM adherence due to nurses’ accessibility, amount of time spent with patients (Jacobs, 2005), and the general level of trust and confidence they encourage in patients. Lacking in the literature is a description of the components of the nursing role that might be associated with adherence and clinical outcomes.

LITERATURE SEARCH

The studies for this systematic literature review were derived from the following databases: CINAHL, MEDLINE, PubMed, and PsycINFO. Search terms included patient compliance, medication adherence, persistence, non-persistence, concordance, patient refusal, patient dropouts, termination, discontinuation AND depression, depressive disorder, antidepressive agents AND intervention, therapy, management, program outcomes, treatment outcomes, primary care. Previous comprehensive literature reviews focused on general medication adherence interventions as summarized in a Cochrane Review (Haynes et al., 2008) or for ADM adherence interventions specifically (Chong et al., 2011; Lingam & Scott, 2002; Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2002; Vergouwen, Bakker, Katon, Verheij, & Kessels, 2003). No literature review was found that examined the nurse’s role in ADM adherence enhancement programs.

Search inclusion criteria contained peer-reviewed articles written in English and published between January 2002 and January 2012; a clear measure of adherence; a standardized measure of depression; and research objectives that included direct investigation of ADM adherence management programs. The initial search was supplemented with an additional retrieval of articles for the same period that focused on the role of nurses in ADM adherence enhancement.

Articles from peer-reviewed journals were excluded if they did not describe the use of a standardized measure of depression; clearly identify how a judgment of whether a patient was adherent versus non-adherent was made; or did not include nurses as part of the adherence enhancement intervention. Articles directed at treatment of other psychiatric illnesses (e.g., schizophrenia, bipolar disorder) or medical illnesses (e.g., HIV/AIDS, diabetes) were excluded from this review. Also, articles examining ADM treatment efficacy trials or dosing schemes for one or more antidepressant agents were omitted from the review. To confirm thoroughness of the review, previously published systematic reviews on topics related or semi-related to the current focus were also examined.

A university research librarian assisted the authors in conducting the database literature search. This search was then cross-checked by title and abstract. The authors independently reviewed the titles and abstracts of these articles to determine whether studies met inclusion criteria, then met to resolve any discrepancies. Following this, relevant articles were retrieved in full and the authors again reviewed these to determine whether studies met inclusion criteria.

The initial search yielded 277 articles, and when narrowed for duplicate citations, the total decreased to 250. Eliminating articles that did not meet inclusion criteria reduced the total to 71 articles that investigated outcomes of ADM adherence enhancement programs. Studies that did not provide a standard measure of adherence, depression, or focused on interventions not using nurses decreased the total to 10 studies.

The next step of the review was to abstract data from the studies. Data were extracted in order of (a) intervention focus; (b) author, date, and country of the study; (c) intervention nurse’s title as specified in the article; (d) population and sample characteristics; (e) measure(s) of adherence used; and (f) study outcomes. A description of the data abstracted on review checklists is summarized in Table A (available in the online version of this article). To examine the role of the nurse in each study, data on program focus, program objectives, role, and key intervention components of the adherence enhancement programs were summarized (Table).

RESULTS

This systematic review identified 10 articles that met study inclusion criteria and evaluated ADM adherence enhancement programs employing nurses. All studies were published between January 2002 and January 2012 and were conducted in the United States. There were nine randomized control trials (RCTs) and one quasi-experimental study (Table A). Sample sizes in these studies generally ranged from 30 to 218; however, one multisite RCT included 1,801 participants (906 intervention and 895 usual care patients). All participants included in these studies were adults recruited from outpatient clinics or primary care practices.

There was some variability in how depression was evaluated in study participants. The most frequent measure was the Patient Health Questionnaire used either alone (Deen, Fortney, & Pyne, 2011; Dietrich et al., 2004; Edlund, Fortney, Reaves, Pyne, & Mittal, 2008; Fortney et al., 2007) or with other measures (e.g., Symptom Checklist [SCL-20, SCL-90 Depression subscale] [Unützer et al., 2002], Hopkins Symptom Checklist [Dobscha et al., 2006]). The remaining three studies used different measures such as a diagnosis of depression or a new prescription of an ADM (Simon, Ludman, & Operskalski, 2006; Simon et al., 2011) or the Diagnostic and Statistical Manual of Mental Disorders fourth edition, text revision criteria for a diagnosis of depression (Jacobs, 2005). The commonly used Beck Depression Invento-
ry for symptom severity (Beck, Steer, Ball, & Ranieri, 1996; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Steer, Cavalieri, Leonard, & Beck, 1999), the Center for Epidemiologic Studies Depression Scale (Lewinsohn, Seeley, Roberts, & Allen, 1997; Radloff, 1977), and the Hospital Anxiety and Depression Scale (Bjelland, Dahl, Haug, & Neckelmann, 2002; Zigmond & Snaith, 1983) for symptoms of depression were not used by any study.

The most frequently used approach to document adherence was patient self-report (interview or question-
naire), either as the only measure or in conjunction with pharmacy refill data. Pharmacy refill data provide information on how frequently a patient refilled his or her ADM prescription. Patient self-reports were used in seven studies with questions specifically designed for the study. None used well-known self-report questionnaires (e.g., Medication Adherence Questionnaire [Morisky, Ang, Krousel-Wood, & Ward, 2008] or the Medication Adherence Rating Scale [Thompson, Kulkami, & Sergejew, 2000]). Two studies using self-report measures also used them in conjunction with another measure (e.g., pharmacy refill records [Deen et al., 2011; Fortney et al., 2007]). Two studies used pharmacy refill data exclusively (Simon et al., 2006; Simon et al., 2011). One used self-report and electronic record monitoring (Edlund et al., 2008).

**Summary of Studies Employing Nurses**

The literature reviewed, primarily RCTs, varied in study purpose, sample, intervention tested, and findings. The majority of these trials reported significant positive outcomes in adherence. Three studies reported significant adherence results using some form of collaborative care (Deen et al., 2011; Fortney et al., 2007; Unützer et al., 2002) with nurse case managers or nurse practitioners.

Unützer et al. (2002) tested the Collaborative Care Model of Late Life Depression in Primary Care Settings, referred to as the Improving Mood—Promoting Access to Collaborative Treatment (IMPACT). In this multisite RCT, the intervention consisted of nurses or psychologists working as care managers who were specifically educated for the study as depression clinical specialists. The intervention group was more likely to show a great-
er reduction in depression severity and symptoms, express more satisfaction with depression care, and exhibit less functional impairment.

Fortney et al. (2007) reported a telemedicine-based collaborative care model in which the intervention patients were twice as likely to be adherent and response to treatment improved. Researchers determined that the active intervention component was telephone-based supervised nurse case management. The authors concluded that outcomes can be modestly improved by implementing a nurse case management system without the use of elaborate and expensive interactive video equipment or reorganization of care to duplicate a team-based environment. A collaborative care model using telemedicine, such as the one tested, could be successfully adapted for primary care clinics without an on-site psychiatrist. Edlund et al. (2008) used this same sample to report adherence results and examined the idea that positive changes in beliefs about depression and its treatment might be associated with higher rates of ADM initiation, adherence, and treatment response. Results indicated that beliefs were not associated with adherence.

Deen et al. (2011) performed an RCT of seven Veterans Affairs community outpatient clinics. The intervention using a nurse care manager as part of a team approach predicted higher treatment adherence (odds ratio = 2.11; 95% confidence interval [1.02, 4.36]; p = 0.04). Intervention status also significantly predicted higher health care satisfaction and perceived patient-centeredness.

A structured telephone-based care management program using nurses was shown not to be effective (Simon et al., 2006). The care management program had no significant effect on

### TABLE (CONTINUED)

**SUMMARY OF NURSE ROLE AND COMPONENTS OF INTERVENTION PROMOTING ANTIDEPRESSANT MEDICATION (ADM) ADHERENCE ENHANCEMENT (N = 10)**

<table>
<thead>
<tr>
<th>Adherence Enhancement Program</th>
<th>Program Objectives</th>
<th>Nurse Role and Key Intervention Components</th>
</tr>
</thead>
</table>
| Re-engineering Systems for Primary Care Treatment of Depression (Dietrich et al., 2004) | Test effectiveness of evidence-based model for management of depression in primary care with support from quality improvement resources | Care Managers  
  - Telephone support  
  - Assistance in overcoming barriers  
  - Support self-management practices (e.g., exercise or social activities)  
  - Present new patients and follow ups to psychiatrists |
| Interactive Response System to Enhance ADM Compliance (Stuart, Laraia, Ornstein, & Nietert, 2003) | Evaluate use of innovative interactive voice response (IVR) system to increase patient compliance with ADMs prescribed in primary care settings | Nurses in Primary Care Settings  
  - Specially designed information to participate in IVR system  
  - Inform IVR system of patients’ enrollment |
| Collaborative Care Management Model of Late-Life Depression in Primary Care Settings (Unützer et al., 2002) | Determine effectiveness of improving Mood-Promoting Access to Collaborative Treatment (IMPACT) collaborative care management program for late-life depression | Nurse Practitioners  
  - Conduct an initial clinical and psychosocial history  
  - Review educational materials  
  - Discuss preferences for depression treatment  
  - Discuss needs for treatment adjustment with supervising psychiatrist and liaison PCP  
  - Refer to additional health or social services as clinically indicated  
  - Conduct follow up to 12 months monitoring treatment response with use of web-based questionnaire and clinic information system follow-up contacts every other week, decreasing to monthly as clinically indicated |
ADM adherence despite making significantly more medication management visits over 6 months than with the usual care group. The active components of the intervention were follow-up telephone calls, care coordination, and the addition of cognitive-behavioral therapy.

This study can be compared with another approach by the same investigators to evaluate an online management messaging follow-up program (Simon et al., 2011). This study, using specially educated psychiatric nurses, showed that the intervention group had higher rates of adherence (prescription refill data) at 3 months, lower SCL scores, and greater satisfaction with treatment compared to the usual care group.

The difference between persistence and adherence became evident in one study. When examining specifically persistence in taking ADMs over time, Dietrich et al. (2004), in a cluster RCT, examined the relative effectiveness of adding care managers to the treatment of patients with depression receiving primary care. Care managers were nurses who promoted self-management, counseled patients in overcoming barriers to adherence, provided telephone support, and provided feedback to psychiatrists. This study measured persistence in medication taking, not what is commonly referred to as adherence.

Two studies examined variations of their own programs by analyzing the relative effectiveness of different adherence enhancement approaches. Jacobs (2005) conducted a quasi-experimental study of split versus integrative approach to adherence management. Jacobs (2005) used advanced practice nurses (APNs) with prescriptive authority and psychiatrists to test the premise that outcomes might differ by health care professional and whether care was split between pairs of practitioners performing psychotherapy and medication monitoring or not. There were no significant differences in ADM adherence whether the participant was seen by a psychiatrist or APN ($\chi^2 [3, N = 122] = 4.699, p = 0.001$).

One last study examined the relative effectiveness of ADM enhancement strategies. Stuart, Laraia, Ornstein, and Nietert (2003) compared the effectiveness of three approaches to enhance adherence. They experimented with an interactive voice response (IVR) system to enhance ADM adherence using PCP nurses who provided educational materials and follow-up telephone calls in two of the three approaches. Three strategies were tested for their relative effectiveness in enhancing adherence: (a) education alone; (b) education and telephone calls; or (c) education, calls, and IVR. No significant differences in adherence outcomes were noted across the different treatment strategies. Patients’ anecdotal comments suggested that they would prefer to receive rather than make calls to the automated IVR system and they would prefer to speak to a live person.

In summary, analyses of the results of RCTs revealed positive findings in studies using nurses or nurse practitioners in the role of care manager. However, three studies reporting positive effects used the same sample with the same intervention from the Collaborative Care Model research (Deen et al., 2011; Edlund et al., 2008; Fortney et al., 2007). Only one article reported no significant differences, and this study’s outcome was persistence, not adherence. Even with those showing effectiveness, only cautious conclusions about achievements of superior adherence when involving nurses in care can be made. Because of the limited number of studies and disparities in designs, confidence in interventions is tentative.

**DISCUSSION**

In the majority of ADM adherence enhancement programs, nurses were reported to use multifaceted intervention strategies. For example, care management including patient medication follow up and education were most frequently mentioned. The Table displays each study, the objectives of the adherence enhancement program, and the intervention components of the nurses’ roles.

**Care Management, Patient Medication Monitoring, and Follow Up**

Care management was an integral part of ADM intervention and a role that nurses played in all studies. Their involvement varied. In some cases, nurses were the primary member of a team, and in other instances, they

---

**Suboptimal treatment of depression in primary care settings threatens the significant value of the many ADMs available.**
were supportive to mental health professionals. For example, in the study by Deen et al. (2011), nurses were off-site care managers along with a team of clinical pharmacists and telepsychiatrists. Along with the nurse, the team focused on barriers to care, education, activation, monitoring for symptoms and side effects, and medication adherence. In the study by Edlund et al. (2008), off-site nurse depression care managers also monitored patients over time in the acute and continuation phases of treatment.

The care manager role (usually performed by an RN) included monitoring symptoms and beliefs about depression and depression treatment. When a patient endorsed a barrier to medication adherence, the care manager would follow with a semi-structured interview—a combination of short scripts read to the patient verbatim and bulleted lists that guided the care manager's response to selected scenarios. Intervention scripts also included asking the patient to role play conversations or think how treatment could improve his or her life. In the study by Fortney et al. (2007), nurses were also off-site care managers and worked closely with a team of clinical pharmacists and telepsychiatrists. Nurses focused on barriers to care, medication education, activation, monitoring for symptoms and side effects, and medication adherence.

**Patient Education**

In six of 10 articles, education is described as a central role of the nurse. In four studies, it was not specified or apparently not a formal part of the intervention. Deen et al. (2011) described a telephone patient medication education and activation strategy as well as scripted responses to treatment barriers and reasons for non-adherence (e.g., concerns about addiction, specific side effects). Edlund et al. (2008) described education by phone, which included information about depression such as causes, common symptoms, treatments available, and reasons patients should seek treatment. Unützer et al. (2002) used a 20-minute educational videotape and a booklet about late-life depression during the initial visit with nurse care managers. Dobsha et al. (2006) used telephone calls to deliver education 1 to 2 weeks after enrollment (information included ways to explore barriers, emphasize adherence, and encourage communication with clinicians about depression), and supplemental unspecified educational materials were mailed. Participants were invited to attend a 2-hour group depression education discussion led by the nurse care manager or a depression education class offered by a member of the mental health team. The nurse management intervention reported by Fortney et al. (2007) was detailed and included education via scripted telephone encounters with patients. The entire training program and intervention materials are described in the manual Comprehensive Guide to Care Management Version 2.0 (available online at https://www.netdss.net/CMMManual.pdf). Stuart et al. (2003) tested the relative effectiveness of three approaches and were less detailed about study educational materials but did report use of education that was specifically designed as an orientation for participants in the IVR program.

Several studies did not mention or provide details on how education was part of the intervention (Dietrich et al., 2004; Jacobs, 2005; Simon et al., 2006). However, in the case of Simon et al. (2006), crisis management and scripted motivational interviewing were used and may have included educational components.

Less frequently mentioned aspects of the nurse role were patient counseling, feedback to the treatment team and treating physician, and patient referral. There were variants that could be considered psychotherapeutic beyond medication and depression education and adherence problem-solving strategies. These strategies activated, motivated, or supported the patient. In the study by Jacobs (2005) of split versus integrative treatment, APNs conducted psychotherapy as well as medication prescription and monitoring. Simon et al. (2006) referred to crisis management and scripted motivational interviewing techniques that are frequently seen in psychotherapy practices.

Feedback given by nurses on pa-
tient or treatment progress to treating physicians, PCPs, or the team as a whole was reported in several studies (Dietrich et al., 2004; Dobscha et al., 2006; Fortney et al., 2007; Simon et al., 2006, 2011; Unützer et al., 2002). Finally, facilitation of referrals was mentioned in three of the study reports. Unützer et al. (2002), Dobscha et al. (2006), and Simon et al. (2006) reported that nurses facilitated mental health agency referrals. Additionally, Unützer et al. (2002) reported nurses to have referred patients for health and social services as clinically indicated.

Despite clarity in intervention themes, there were significant reporting deficits in the descriptive details of nurses’ activities in ADM adherence programs. In some cases, it was difficult to discern what proportion of the care management was conducted by nurses.

LIMITATIONS

Studies included in the review show some deficits. An important concern is the inconsistency and weaknesses of some measures of adherence. The most frequently used measure, patient self-report, might not be valid if used alone. Optimal recall period required might invalidate results if patients are asked to recall beyond two 24-hour periods. However, use of the self-report Morisky Medication Adherence Scale demonstrated concordance with pharmacy fill data among older adults with hypertension (Krousel-Wood et al., 2009). Some measures of adherence make it impossible to distinguish between a provider-ordered prescription change or discontinuation for good reason and ADM stopped by the patient without provider consultation.

As with all time-bound literature reviews, the findings of the review reflect the period reviewed. Investigator bias was addressed through independent coauthor analysis and resolution of differences. The sample of studies reviewed was small and limits generalizability. There is a small amount of research that addresses a lack of confidence among nurses to manage depressed patients, but in the majority of the studies, RNs were either specially educated in mental health or they were part of a multidisciplinary team that included a psychiatrist. Only one study did not mention the education of the RN.

IMPLICATIONS FOR NURSING

Suboptimal treatment of depression in primary care settings threatens the significant value of the many ADMs available. Patients with depression often lack adherence to their ADMs, resulting in suboptimal treatment. In the busy primary care practice, RNs emerge as key participants in depression care management. The aim of this systematic literature review was to summarize the results of clinical trials using nurses in ADM adherence programs and describe the specific components of the nurse’s role in care management.

In general, these studies reported positive findings in ADM adherence enhancement using nurses as care managers. Some of these studies demonstrated lower symptom severity (Simon et al., 2011) or better response and remittance (Fortney et al., 2007) and/or decrease in symptoms and functional impairment (Unützer et al., 2002). Studies showing positive adherence levels using nurses also reported higher patient satisfaction with health care.

Although explorations of the effect of nurses’ roles on ADM adherence enhancement have begun, current research findings are not sufficient to support the conclusion that treatment programs using RNs as case/care managers are significantly better than other approaches. Future research that replicates these studies and clearly describes the roles of care managers and nurse practitioners is needed. Further, applications of a sound theoretical framework to support nursing role activities proposed will add credibility to the available evidence about efficacious ADM adherence enhancement programs. Adding to the complexity of this task is the fact that primary care settings are heterogeneous, thus limiting the applicability of findings about a single program useful to all. Still, we are left with the probability that nurse care management systems might significantly improve ADM adherence, which would help ameliorate a major concern in treating the rising number of patients reporting clinical depression in primary care settings.

REFERENCES


nurses. Archives of Psychiatric Nursing, 19, 256-263.


Dr. Heise is Associate Professor, and Dr. van Servellen is Visiting Professor, College of Nursing, Brigham Young University, Provo, Utah. Dr. van Servellen is also Professor Emerita, School of Nursing, University of California, Los Angeles, California.

The authors have disclosed no potential conflicts of interest, financial or otherwise.

Address correspondence to Barbara A. Heise, PhD, APRN, BC, CNE, Associate Professor, Brigham Young University, College of Nursing, 562 SWKT, Provo, UT 84602; e-mail: barbara-heise@byu.edu.

Received: July 8, 2013
Accepted: September 20, 2013
Posted: December 4, 2013
doi:10.3928/00279635-20131126-08
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Author (Year) [Country]</th>
<th>Study Design</th>
<th>Intervention: Nurse Role</th>
<th>Population/Sample Characteristics</th>
<th>Measures of Adherence</th>
<th>Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaborative Care: A Chronic Care Model for Depression</td>
<td>Deen et al. (2011) [USA]</td>
<td>RT</td>
<td>Nurse Case Managers</td>
<td>Seven community VA community-based Outpatient Clinics 395 patients screened with PHQ9 suitable for primary care treatment with score of PHQ9 of ≥ 12 Intervention group n = 177 Usual care n = 218</td>
<td>Measure specifically designed for the study as patients responses to how frequently they took ADM in previous month and if took dosage prescribed. A score of ≥ 80% of dosages in month is deemed adherent.</td>
<td>Adherence: Intervention predicted higher treatment adherence (OR = 2.11, 95% CI = 1.02 – 4.36, p = 0.04). Satisfaction with Health Care: Intervention status significantly predicted higher satisfaction. Patient-Centeredness of Care: Intervention status significantly predicted higher ratings of patient-centered care.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Author (Year)</td>
<td>Study Design</td>
<td>Intervention: Nurse Role</td>
<td>Population/Sample Characteristics</td>
<td>Measures of Adherence</td>
<td>Study Outcomes</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>------------------------</td>
<td>--------------</td>
<td>-------------------------------------------</td>
<td>-----------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **On-line Care Management Messaging Follow-up Program** | Simon et al., (2011) [USA] | RCT          | On-line Trained Psychiatric Nurse Care Managers | 208 patients starting ADMs in Outpatient Clinics. Intervention group n = 106 Usual care n = 102 | Prescription refill data assessing total days dispensed and receipt of second AD indicating medication switch or combination. | **Adherence:** Intervention patients showed higher rates of adherence at 3 months; 81% continued care more than 3 months vs. 61% of usual care group (p = 0.001).  
**Symptom Severity:** Lower SCL scores after 5 months.  
**Satisfaction with Treatment:** Greater satisfaction with treatment. |
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Author (Year) [Country]</th>
<th>Study Design</th>
<th>Intervention: Nurse Role</th>
<th>Population/Sample Characteristics</th>
<th>Measures of Adherence</th>
<th>Study Outcomes</th>
</tr>
</thead>
</table>
| Depression Treatment Intervention to Reduce Negative Beliefs and Attitudes about ADMs | Edlund et al. (2008) [USA] | RCT          | Depression Care Manager  | 395 primary care patients in VA healthcare system, receiving annual primary care depression screen (PHQ-9 score of ≥ 12)  
Intervention group n = 177  
Usual care n = 218 | Self-report whether ≥ 80% dosages taken in prior month. | Adherence:  
Beliefs not associated with adherence. At baseline, 73% of the sample believed they had depression. 66% believed ADMs would be helpful, but 65% believed could handle depression symptoms on own.  
Beliefs about ADMs:  
Intervention had few effects on beliefs and were not in expected direction.  
Clinical Response:  
Beliefs not associated with taking medication or clinical response. |
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Author (Year) [Country]</th>
<th>Study Design</th>
<th>Intervention: Nurse Role</th>
<th>Population/Sample Characteristics</th>
<th>Measures of Adherence</th>
<th>Study Outcomes</th>
</tr>
</thead>
</table>
| *Telemedicine Based Collaborative Care Model* | Fortney et al. (2007) [USA] | Randomized Intervention Trial | Case Managers            | 395 primary care patients with PHQ9 depression severity scores ≥ 12 followed for 12 months.     | Patient self-report and pharmacy data, ≥ 80% prescriptions taken as prescribed in previous month at 6 and 12 months. | **Adherence:** Intervention patients more likely to be adherent at both 6 (OR = 2.11; 95% CI = 1.02 - 4.36; p = .04) and 12 months (OR = 2.72; 95% CI = 1.36 – 5.44; p = < .01).  
**Respond/Remit:** Intervention patients more likely to respond by 6 months and remit by 12 months. |


<table>
<thead>
<tr>
<th>Intervention</th>
<th>Author (Year) [Country]</th>
<th>Study Design</th>
<th>Intervention: Nurse Role</th>
<th>Population/Sample Characteristics</th>
<th>Measures of Adherence</th>
<th>Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression Decision Support in Primary Care</td>
<td>Dobscha et al. (2006) [USA]</td>
<td>Cluster Randomized Control Trial</td>
<td>Member of Depression Decision Support Team</td>
<td>Two urban care clinics affiliated with academic medical center. Patients screened moderate to severe depression. Intervention group n = 20 Usual care n = 21</td>
<td>Depression Guideline Measure (DGM) rating degree of adherence to guidelines; number of ADM prescriptions filled using VA pharmacy records.</td>
<td>ADM Persistence:</td>
</tr>
<tr>
<td>Intervention</td>
<td>Author (Year) [Country]</td>
<td>Study Design</td>
<td>Intervention: Nurse Role</td>
<td>Population/Sample Characteristics</td>
<td>Measures of Adherence</td>
<td>Study Outcomes</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>-------------------------</td>
<td>------------------</td>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **Structured Telephone Based Care Management Program** | Simon et al. (2006) [USA] | Randomized Trial | Care Managers            | Patients from psychiatric practices diagnosed with depressive disorder in past 30 days and no ADM in last 90 days.  
Intervention group n = 103  
Usual care n = 104 | Pharmacy refills; if no more than 10 day gap between refills in 6-month period. | **Adherence:**  
Intervention patients made more medication management visits over 6 months, \( z = 2.11, p = .035 \); no significant differences in rates of adequate medication treatment.  
**Symptom Severity:**  
Intervention had no significant effect on the mean score of the SCL depression scale, on the probability of 50% improvement in depressive symptoms, or probability of patient-rated improvement. |
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Author (Year) [Country]</th>
<th>Study Design</th>
<th>Intervention: Nurse Role</th>
<th>Population/Sample Characteristics</th>
<th>Measures of Adherence</th>
<th>Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Split vs. Integrative Therapy</em></td>
<td>Jacobs (2005) [USA]</td>
<td>Quasi-experimental Design</td>
<td>Advanced Practice Nurses (Psychiatric Nurses with Prescriptive Authority)</td>
<td>Self-paying or insurance receiving therapy with either psychiatrist or APRN. Split therapy seeing psychiatrist: n = 30 Split therapy seeing APRN with prescriptive authority: n = 30 Integrated therapy seeing psychiatrist: n = 30 Integrated therapy seeing APRN with prescriptive authority: n = 30</td>
<td>Ongoing retrospective clinician documentation of prescriptions and refills for period up to 9 months.</td>
<td><strong>Adherence:</strong> No significant difference in adherence between split or integrated method or whether seen by psychiatrist or APRN. ( \chi^2 (3, N = 122) = 4.699, p = 0.001 ). <strong>Differences in Practice:</strong> Psychiatrists used more secondary class ADMs and more anti-anxiety agents than APRN. APRNs spent more time with patients using more integrated therapy than psychiatrists.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Author (Year) [Country]</td>
<td>Study Design</td>
<td>Intervention: Nurse Role</td>
<td>Population/Sample Characteristics</td>
<td>Measures of Adherence</td>
<td>Study Outcomes</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------------</td>
<td>--------------</td>
<td>--------------------------</td>
<td>-----------------------------------</td>
<td>-----------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Re-engineering Systems for Primary Care Treatment of Depression</td>
<td>Dietrich et al. (2004) [USA]</td>
<td>Cluster Randomized Control Trial</td>
<td>Care Managers</td>
<td>Patients from five healthcare organizations affiliated with 10 or more primary care practices. Patients were starting or changing treatment for depression. Intervention group n = 224 Usual care n = 181</td>
<td>Patients still taking medications at 3 and 6 months.</td>
<td>ADM persistence: No significant difference in groups taking medication at 3 months (p = 0.48) and 6 months (p = 0.74). Response: Significantly more intervention patients responded to treatment at 6 months. Remit: Significantly more intervention patients remitted at 6 months. Satisfaction: Significantly more intervention patients rated their depression care as good or excellent at 6 months.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Author (Year) [Country]</td>
<td>Study Design</td>
<td>Intervention: Nurse Role</td>
<td>Population/Sample Characteristics</td>
<td>Measures of Adherence</td>
<td>Study Outcomes</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>--------------</td>
<td>--------------------------</td>
<td>-----------------------------------</td>
<td>-----------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><em>Interactive Voice Response System (IVR) to Enhance ADM Compliance</em></td>
<td>Stuart et al. (2003) [USA]</td>
<td>RCT</td>
<td>Primary Care Practice Nurses</td>
<td>Primary care patients newly prescribed ADM by primary care provider. Settings included 30 primary care practices throughout U.S. that are members of the Practice Partner Research Network (PPRNet). Three treatment strategies: randomly assigned strategies included education; education and call; or education, call, and IVR.</td>
<td>Telephone call assessments to ask if patient was taking the ADM prescribed to them.</td>
<td><strong>Adherence:</strong> There were no significant differences in patient compliance with medication among the 3 treatment strategies.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Author (Year)</td>
<td>Study Design</td>
<td>Intervention: Nurse Role</td>
<td>Population/Sample Characteristics</td>
<td>Measures of Adherence</td>
<td>Study Outcomes</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>------------------------</td>
<td>--------------</td>
<td>--------------------------</td>
<td>---------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>Collaborative Care Management Model of Late-life Depression in Primary Care Settings – Improving Mood-Promoting Access to Collaborative Treatment (IMPACT)</td>
<td>Unutzer et al. (2002) [USA]</td>
<td>RCT</td>
<td>Nurse Practitioners</td>
<td>Multisite RCT included 7 study sites representing 8 diverse health care organizations with total of 18 primary care clinics in 5 states in US. Intervention group (IMPACT) n = 906 Usual care n = 895</td>
<td>Patient self-reported use of ADMs.</td>
<td>Adherence: Intervention group significantly more likely to use ADMs or psychotherapy at 3, 6, and 12 months. Reported ADM use for 6.6 months (SD, 4.9 months) compared with 4.6 months (SD, 5.0 months) in usual care.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Symptoms and Depression Severity: Intervention greater reduction in depressive symptoms and depression severity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Satisfaction with depression care: Intervention patients expressed more satisfaction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Functional Impairment: Less impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quality of Life: Greater quality of life</td>
</tr>
</tbody>
</table>