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Psychosocial interventions to improve adherence in depressed and anxious older adults prescribed antidepressant pharmacotherapy: a scoping review

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Abstract: Medication nonadherence in depressed and anxious older adults is prevalent and associated with non-response to antidepressant pharmacotherapy. Evidence-based options to improve medication adherence are limited in this population. To review the state of the literature on the types and efficacy of psychosocial interventions for improving antidepressant pharmacotherapy adherence in depressed and anxious older adults. We conducted a scoping review according to PRISMA-ScR guidelines. PubMed/Medline and article references starting in 1980 up to 28 February 2023 were reviewed. Of the 710 records screened, 4 psychosocial interventions were included in the review. All studies included depressed older adults, and none included anxious older adults. Samples included racial and ethnic minorities and were primarily women. The psychosocial interventions consisted mainly of psychoeducation with usual care as the control comparison. Measures of antidepressant adherence included selfreported adherence or pill counting. Three of the four randomized controlled trials improved medication adherence rates and reduced depression symptom burden. Effective interventions exist for improving antidepressant medication adherence in depressed older adults. Improved adherence can reduce depression symptom burden. The lack of interventions for anxious older adults highlights the need to develop and deliver interventions for anxious older adults prescribed antidepressant pharmacotherapy.

Keywords: aging, behavior change, geriatrics, mental health, randomized controlled trial

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Introduction

Medication adherence is defined as the process by which patients take their medication(s) according to the prescribed dose, timing, frequency, and direction.¹ It involves multiple factors such as getting prescriptions filled, remembering to take medication on time, and understanding the directions. According to the American Medical Association, patients are adherent when they take at least 80% of their medication(s) as prescribed.² Medication non-adherence includes the non-initiation of treatment, suboptimal implementation of the treatment plan (e.g. missed doses and/or infrequent administration), or early discontinuation of treatment.¹ Among older adults (e.g. 65+ years), nonadherence across multiple medication classes is associated with poor health outcomes, including higher health care costs, increased hospital admissions, and increased morbidity and mortality.³

It is well-documented that nonadherence to antidepressant medication is common among older adults (13–37% of primary care patients) and associated with nonresponse to pharmacotherapy.⁴ Key risk factors for antidepressant nonadherence include psychological and cognitive barriers such as perceived stigma, fears about antidepressants, low health literacy, and impaired executive function.^{5–7} Other risk factors include medication cost, side effects, and

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polypharmacy. Our group recently published that low perceived symptom severity and early response to pharmacotherapy are also associated with worse adherence.⁸

Given that many of these risk factors are modifiable (e.g. misconceptions about antidepressants, lack of an explicit strategy to improve adherence that is discussed during the clinic visit) a variety of interventions have been developed to improve antidepressant medication adherence in older adults. For example, numerous studies have assessed barriers to medication nonadherence9 and the effectiveness of interventions to improve medication adherence across the lifespan.^{10,11} While reviews of medication adherence have been published,¹⁰ no review has focused exclusively on treatment programs or interventions aimed at improving antidepressant adherence in older adults. To address this gap in the literature with the goal of improving clinical care, we conducted a scoping review to answer the following research question: In older adults with depression and/or anxiety, what is the state of the science of existing psychosocial interventions on antidepressant medication adherence? Psychosocial interventions are interpersonal or informational activities or strategies that target behavioral, cognitive, emotional, and/or social factors for improving medication adherence. Given the high prevalence and poor health outcomes of medication nonadherence in late-life, we focus on older adults. We also focus on depressed and/or anxious adults because these conditions are both common and frequently comorbid in late-life and often treated with antidepressants.¹² For each study that met criteria for inclusion in this scoping review, we characterize the psychosocial intervention tested and summarize the medication adherence rates and changes in depressive or anxiety symptoms. Standard principles and procedures as outlined in the PRISMA-ScR Statement were followed.13

Methods

Data sources and strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR) guideline was followed, according to their published checklist. We searched PubMed/Medline databases from 1980 to 2023 using a search strategy following the PRESS 2015 guidelines (e.g. translation of the research question; Boolean and proximity operators; subject headings; text word searching; spelling, syntax, and line numbers; limits and filters; and sources).14 The search was conducted by JMK, who is certified in Responsible Literature Searching (see Supplemental File 1). The search strategy consisted of controlled vocabulary using Boolean operators and natural language terms representing the concepts of (1) older adults, (2) depression and anxiety, (3) psychosocial interventions, and (4) antidepressant medication adherence. An English language limit was applied to search results. In addition to the electronic search, reference lists from the identified articles were reviewed for additional studies. Search results were downloaded into Microsoft Excel and duplicate records were removed.

Eligibility screening

Inclusion criteria for this review were: (1) intervention studies aimed at improving adherence with a minimum of two data points (randomized controlled trials, demonstration studies, pilot feasibility studies, and open-label studies); (2) study samples aged 50 years and older (including those with results for those 50 and older presented separately from all ages); (3) depressed or anxious older adults who were prescribed antidepressant pharmacotherapy; and (4) an assessment of medication adherence. Articles were excluded if: (1) the study did not report medication adherence; (2) they were non-English articles; or (3) the article was not original research. Figure 1 summarizes the literature search process.

The titles and abstracts of potentially relevant articles were screened independently by two authors. After the screening of titles and abstracts, the full texts of studies fulfilling the inclusion criteria were again screened by two authors working independently. Any disagreements concerning eligibility (at any level of review) were resolved through discussion. A third reviewer was available for conflict resolution.

Data extraction and analysis

To advance to the next level of review all articles were required to be written in English, and both reviewers had to agree on all of the following entry criteria for data extraction:(1) Does the population include adults aged 50 and older; (2) Does the population focus on depressed or anxious adults (major depression, minor depression, depression with comorbid anxiety, or any depression/anxious

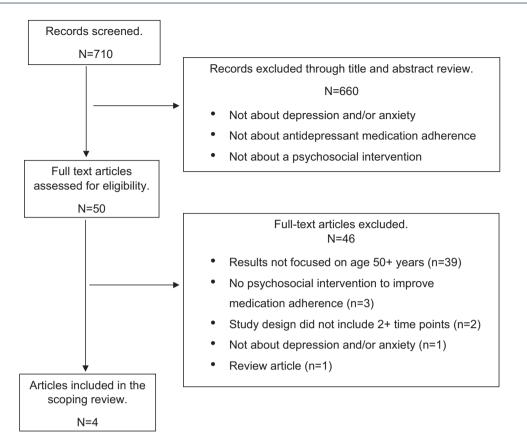


Figure 1. Study selection flow chart.

synonym); (3) Are the study participants prescribed antidepressant pharmacotherapy; (4) Does the article describe a psychosocial intervention aimed at improving adherence; (5) Does the article contain a minimum of two time points (e.g. baseline and post-intervention); (6) Does the article describe measures of medication adherence.

Data were extracted from the final set of articles by two reviewers (SS and MG). Data was charted on a shared Excel document. Extracted data included the author names and dates of publication, geographic location(s) of trial, number of participants, mean age, trial design, description of psychosocial intervention, description of control group, follow-up time points, measurement of medication adherence, change in adherence, measurement of depression and anxiety, and change in depression and anxiety. Any disagreements in data extraction were resolved by discussion between the reviewers. Results are presented descriptively for individual studies that report means and standard deviations for outcome variables. A narrative synthesis was used to summarize and explain the findings of the included studies. As per the guideline recommendations for a scoping review, we did not conduct quality assessment or appraisal.^{13,15,16}

Results

Identification and selection of the literature

After the removal of duplicates, a total of 710 articles were obtained from our search of PubMed/ Medline and cross-checking references. After screening the titles and abstracts of these publications, 660 articles were excluded. Reasons for exclusion are shown in Figure 1. Most were excluded because the article did not focus on depression or anxiety, did not focus on antidepressant medication adherence, or did not involve an intervention treatment. Fifty full-text articles were assessed for eligibility, with the exclusion of 46 articles. Reasons for exclusion: not age >50(n=39), not a psychosocial intervention to improve medication adherence (n=3), study design did not include 2+ time points (n=2), not about depression and/or anxiety (n=1); and not an original study (n=1). A total of four articles

were included. Information presented in Table 1 includes the sample sizes, age of study participants, types of psychosocial interventions tested, and main findings. All the studies were randomized controlled trials (RCT) published between 2010 and 2020; one was a pilot RCT.¹⁷ Three of the studies were conducted in the United States and one was conducted in Korea.¹⁸

Study sampling – generalizability of findings

All studies used non-probability sampling techniques. One study was conducted with a sample of older adults with Medicaid coverage; the other studies were conducted with samples of adults recruited from geriatric/primary care^{6,17} and outpatients in general medical and geriatric subspecialty units.¹⁹ All studies included depressed older adults. Three studies included adults who met DSM-IV criteria for depression at the time of enrollment,^{6,17,18} and one study included older adults who scored ≥ 10 on the staff-administered Patient Health Questionnaire-9.¹⁹ No study included anxious older adults.

Two studies were conducted with primarily White (>70%), non-Hispanic (>80%) samples.^{6,17} One study focused on minority English- and Spanishspeaking adults and was conducted with a Hispanic (91%) and mixed-raced sample.¹⁹ Another study was conducted with older adults living in South Korea.18 All studies included men and women; however, a majority of participants (>80%) were women which is consistent with population estimates indicating that late-life depression is more frequently reported among women.²⁰ Education (in years) varied across the four studies with an average of 4.2 years [standard deviation (SD)=4.3 years] in the Jeong et al. RCT; 7.8 years (SD = 3.9 years) in the Raue et al. RCT¹⁹; and 14.6 years (SD=3.0 years) in the Sirey et al. RCT. Less than half of all participants across all four studies were married/living with a partner.

Intervention types and controls

Two studies by Sirey *et al.* used the Treatment Initiation and Participation (TIP) program.^{6,17} TIP consisted of clinicians reviewing symptoms of depression and antidepressant treatment, followed by assessing barriers and defining personal goals that adherence could achieve. Depression and treatment education was provided and barriers to treatment were collaboratively addressed. Finally, an adherence strategy was determined. TIP was delivered during the first 6 weeks of pharmacotherapy initiation through three 30-minute in-person meetings. The control group for TIP was treatment as usual defined as pharmacotherapy as usual. Jeong et al. examined the effects of depression care management on medication adherence.¹⁸ This intervention focused on the role of a masterslevel psychologist care manager in providing proactive support. Sessions consisted of education on depression and antidepressants and behavioral encouragement techniques. All contact was completed telephonically, twice during the first month and then monthly for the remainder of the 6 months study. Calls lasted 20-30 min. The control group was usual care where psychiatrists prescribed citalopram as usual. Raue et al. investigated the effects of Shared Decision Making (SDM) on medication adherence.¹⁹ SDM was delivered by registered nurses through a 30-min in-person meetings followed by two weekly phone calls lasting between 10 and 15 min. During each session, participants received psychoeducation and discussed their experiences and preferences. Nurses also helped overcome barriers such as appointment scheduling and transportation. The control group for SDM was usual care where physicians engaged patients in depression treatment decisions as part of routine care. None of the interventions reported a specific theoretical model that guided intervention development and testing.

Measurement tools used to assess medication adherence and clinical symptoms

Measures of antidepressant medication adherence varied across the studies and included self-report questionnaires such as the Brief Medication Questionnaire,⁶ the Medication and Nonmedication Treatment Compliance Data Form,¹⁷ and The Cornell Service Use Index.¹⁹ One study also used pill counting during in-person study visits.¹⁸ The severity of depression symptoms was measured (at baseline and over time) with the clinician-administered Hamilton Rating Scale for Depression (HRSD).²¹ The HRSD was a secondary outcome in all studies.

Key findings

The main findings in three studies were similar: participants randomized to the intervention groups – $TIP^{6,17}$ and Depression Care Management¹⁸ – had higher medication adherence rates (82% and 52% respectively) from pre- to post-intervention

Study	Country	z	Mean (SD) age	Study design	Psychosocial intervention	Control group	Study duration	Measure of medication adherence	Measure of depression symptoms	Key findings
Sirey et al. ¹⁷	USA	70	76 (9)years	Randomized controlled pilot study	TIP Intervention: Participants identified and addressed barriers to adherence (misconceptions and fears) and developed a personalized adherence strategy.	TAU: Pharmacotherapy as usual	Three intervention sessions during the first 6 weeks of pharmacotherapy plus intervention sessions at 8 and 10 weeks. Assessments at baseline, 6, 12, at baseline, 6, 12, and 24 weeks later.	Medication and Nonmedication Treatment Compliance Data Form	Hamilton Rating Scale for Depression	<i>Adherence</i> : Participants in the TIP group were significantly more adherent than participants in the TAU group at all time points. 82% adherence for TIP <i>versus</i> 43% adherence for TAU (<i>F</i> 13.27, df 1, 57.2, <i>p</i> =0.001). <i>Depression</i> : Participants in TIP had a greater decrease in depression symptoms compared to participants in TAU (<i>F</i> = 10.89, df = 1, 55.1, <i>p</i> = 0.01). The change occurred during the early treatment period (during the early intervention visits weeks 1-6) and was sustained until 24weeks.
Jeong et al. ¹⁸	Korea	57	Mean (SD) not reported	Double-blind randomized controlled trial	Care Management Intervention: Proactive support by a care manager who provided information on the causes of depression and treatment options, the importance of taking antidepressants, effects of antidepressants	UC: psychiatrist prescribed Citalopram but was allowed to replace this medication with other medications if/when patients reported side effects.	6-month intervention. Assessments at baseline and 6 months later.	Pill count	Hamilton Rating Scale for Depression	Adherence: Participants in the care management intervention were more adherent than participants in the UC group. 52% adherence for care management versus 18% for UC (p = 0.074). <i>Depression</i> : Patients in the care management intervention group showed a higher remission rate than those in the usual care group (55% versus 29%, p =0.0421).

(Continued)

Study	Country	z	Mean (SD) age	Study design	Psychosocial intervention	Control group	Study duration	Measure of medication adherence	Measure of depression symptoms	Key findings
et al. ¹⁶	USA	231	67.3 (8.4) years	Two-site randomized controlled clinical effectiveness trial	TIP Intervention: Participants identified and addressed barriers to adherence (misconceptions and fears) and developed a personalized adherence strategy.	TAU: Pharmacotherapy as usual	3 intervention sessions during the first 6 weeks of pharmacotherapy. Assessments at baseline, and 6, 12, and 24 weeks later.	Brief Medication Questionnaire	Hamilton Rating Scale for Depression	Adherence: Participants in the TIP group were five times more likely to be adherent at 6 weeks lodds ratio, 5.54; 95% CI, 2.57–11.96; χ^2 = 19.05; $p < 0.001$] and three times more likely to be adherent at both 6 and 12 weeks lodds ratio, 3.27; 95% CI, 1.73–6.17; χ^2 = 13.34; $p < .001$. Depression: Participants in the TIP group experienced a 24.9% CI: 13.9–35.9; t [337] = 4.46; adjusted $p < .0001$. Higher adherence was associated with a greater reduction in HDRS scores
	USA	202	202 72.1 (5.5) years	Randomized controlled trial	SDM Intervention: Nurses discussed patients' treatment experiences and preferences regarding treatment and addressed practical barriers to care such as transportation and/or in-house social work.	UC: Physicians engaged patients in depression treatment decisions as part of routine care.	3-week intervention. Assessments at baseline, 4, 8, and 12 weeks later.	Cornell Service Use Index	Hamilton Rating Scale for Depression	<i>Adherence</i> : There were no differences between SDM and UC in adherence to antidepressant medication. <i>Depression</i> : There were no differences between SDM and UC in the reduction of depressive symptoms.
S	hared dec	cision	making; T/	AU, treatment	SDM, shared decision making; TAU, treatment as usual; TTP, treatment a	treatment and initiation program; UC, usual care.	; UC, usual care.			

Table 1. (Continued)

compared to participants randomized to the control groups (42% and 18%). Sirey et al. also found that intervention participants were more likely to be adherent during the 6-week post-intervention follow-up period. Participants randomized to TIP and Depression Care Management also had a greater reduction in depression symptoms compared to participants in the control groups. TIP participants reported a reduction in depression symptoms early in the intervention period (1-6weeks), but this effect was not sustained over time and was like participants in the control group. Greater adherence to antidepressant pharmacotherapy in TIP was associated with a greater reduction in depression symptoms. One study showed that the psychosocial intervention and control group were not significantly different in terms of both adherence to antidepressant pharmacotherapy and the reduction of depression symptoms.19

Discussion

The purpose of this review was to summarize the current state of the science on the availability, use, and efficacy of psychosocial interventions to improve antidepressant medication in depressed and anxious older adults. All four of the identified studies were published between 2010 and 2020 which demonstrates increased attention to this challenge and supports the need for a scoping review. The results of this review are generally positive indicating that depressed older adults showed improvement in both adherence to antidepressant medication and depression symptom severity when provided with these focused interventions. To our knowledge, there is no published evidence describing interventions to improve antidepressant medication adherence in anxious older adults.

Across all studies, mechanisms which might account for increased medication adherence include reducing medication-specific fears, increasing perceived benefits, and increasing social support. While the SDM intervention did not increase initiation or antidepressants, it was associated with an increased uptake in psychotherapy compared to usual care in a minority population of older adults who had a stronger preference to receive psychotherapy. The authors suggest that the lack of change in antidepressant adherence rates may have been linked to the high need for social services. Furthermore, patients who receive their preferred treatment are more likely to be adherent to it.²² Some postulate that

the factors linked to adherence may be divided into different categories (modifiable, partially modifiable, and non-modifiable).23 Following this model, factors such as patient attitudes and beliefs including preferences for treatment and beliefs about the etiology of depression should be addressed in the interventions to increase adherence. Furthermore, psychoeducation and review of risk and benefits should also focus on potential side effects such as the known association of increased falls with Selective seratonin reuptake inhibitor use in older adults²⁴ as well as the potential for experiencing discontinuation syndrome,²⁵ particularly as patients commonly have concerns related to the need for long-term use of these medications which may affect adherence.

Other factors that may impact adherence include being unmarried, greater medical comorbidity, and self-reported side effects.²⁶ Furthermore, non-modifiable risk factors such as patient race and gender should be given additional considerations when thinking of adherence-specific interventions or additional support as these attributes (male gender and African American race) increase the risk for low adherence.27,28 In fact, specific patient and clinician language may influence adherence.²⁹ For example, clinician empathy and 'change talk' are associated with higher initial prescription filling and overall adherence. In addition, perceived social support seems to have a differential impact on medication adherence by race and gender such that inadequate perceived support in African-American women had the lowest adherence rates compared to white men and women.³⁰ Factors leading to non-adherence are likely to remain the same over time, therefore, implementation of strategies to increase adherence early in treatment may help maintain higher adherence rates.²⁶ Provider specialty may also impact adherence, where antidepressants started by psychiatrists were associated with higher rates of adherence. Therefore, PCPs may benefit from collaborative care models involving psychiatry and additional training in motivational interviewing to help ensure higher rates of adherence.³¹

Suggestions for future research

There are several design and methodological issues worth mentioning. First, future research should factor in the objective assessments of adherence (e.g. electronic monitoring and pill counts) which may offer a valuable supplement to traditional self-report measures among aging populations because they avoid recall bias. Second, the optimal interventional duration for intervention uptake remains unknown. For example, the non-significant trial (SDM) was only 3 weeks. However, SDM has been tested in other age groups and also found to be not an effective strategy for adherence.³² The significant interventions in our scoping review ranged from 6 weeks to 6 months with follow-up included in both RCTs by Sirev et al. Thus, for these interventions to work, the necessary intensity and duration still need to be studied. Third, future research should track and report older adults' antidepressant history. Different intervention strategies may be needed for older adults who are starting an antidepressant for the first time versus older adults who have a history of taking antidepressants and would have different reasons for reduced adherence.

Finally, clinical attention should be devoted to improving adherence in older adults with anxiety. Anxious older adults are often somatically preoccupied and may be fearful of both side effects and becoming 'addicted' to the antidepressant. Antidepressants can also, in the shortterm, feel activating and initially worsen anxiety, and patients should be educated about this usually self-limiting side effect and how to manage the experience. Other strategies to consider when working with anxious older adults include more frequent follow-up, training in motivational interviewing, and engaging family members in adherence planning and education. If the family is not supportive of their loved one's decision to receive treatment with an antidepressant, they may sabotage treatment.33

Strengths and limitations of the review

This is the first scoping review of the effects of psychosocial interventions on medication adherence in older adults. While other reviews were conducted on younger adults, this search highlights the need for additional research on the geriatric population.¹⁰ Some strengths of the paper include having RCTs which made it possible to assess the efficacy of manualized psychosocial interventions on multiple outcomes, medication adherence, and depression symptoms. Limitations of the review include the lack of availability of unpublished studies. The nature of a scoping review precludes the ability of performing a quantitative review of the data as would occur in a meta-analysis.

Conclusion

The results provide support that psychosocial interventions can improve antidepressant medication adherence and associated improvement in depression symptoms. The effective interventions included a combination of education about antidepressants, proactive support, and personalized adherence plans. More intervention development work is needed in late-life to design and implement psychosocial interventions to improve antidepressant adherence among older adults with anxiety.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication No applicable.

Author contributions

Sarah T. Stahl: Conceptualization; Formal analysis; Methodology; Visualization; Writing – original draft; Writing – review & editing.

Joelle Kincman: Formal analysis; Methodology; Software; Writing – original draft; Writing – review & editing.

Jordan F. Karp: Conceptualization; Writing – review & editing.

Marie Anne Gebara: Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

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Competing interests

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Availability of data and materials

Not applicable.

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