J Med Biosci Vol. 5 No. 1 January - June 2023;63-73 DOI: 10.14456/jmbs.2023.XX

Original article

Antidepressant adherence and associated factors in Thai elderly with depressive disorders: a cross-sectional study

Thapanee Jaipinta[1], Sookjaroen Tangwongchai[2, 3, *]

[1]Program in Mental Health, Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Cognitive Impairment and Dementia Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Abstract

Background: Antidepressant adherence is an essential factor influencing clinical responses in depressive disorders. Most Thai depressive patients had poor antidepressant adherence, but the study specific to the elderly, who are vulnerable and unique, is still lacking.

Objective: To investigate antidepressant adherence and associated factors among Thai elderly with depressive disorders.

Methods: A cross-sectional study was conducted at King Chulalongkorn Memorial Hospital. Patients aged at least 60 years old, who were diagnosed with depressive disorder and received at least one antidepressant prescription, were included in the study. Subjects' personal and medical data were obtained from the questionnaire and medical records. Antidepressant adherence was assessed through the Medication Taking Behavior measure for Thai patients (MTB-Thai). Multiple logistic regression was used to examine the association between various factors and having suboptimal adherence.

Results: This study included 119 subjects, in which 16.0%, 16.8%, and 67.2% had low, moderate, and high adherence to antidepressants, respectively. Logistic regression analysis revealed moderate to severe depression, single/divorced/separated marital status, and receiving a treatment regimen that the additional instruction to split tablet of psychotropic medication significantly increased the risk for low-moderate antidepressant adherence with the adjusted Odd ratio of 6.04 (95% confidence interval [CI] = 1.08, 33.76), 2.95 (95% CI = 1.24, 7.03), and 2.56 (95%CI = 1.09, 6.03), respectively.

Conclusion: The present study identifies only one in six of Thai elderly with depressive disorder reported suboptimal antidepressant adherence. It is recommended to closely monitor the antidepressant nonadherence in the elderly with risk factors and intervene to improve their adherence.

Keywords: Aged, antidepressive agents**,** depressive disorder, medication adherence.

***Correspondence to:** **Sookjareon Tangwongchai,** Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
E-mail: sookjaroen@gmail.com
Received: May 31, 2022
Revised: June 8, 2022
Accepted: July 27, 2022

An aging society has become a global phenomenon as the number of people aged 60 and over continues rising worldwide and disproportioning to a younger generation. According to World Health Organization, the number of people aged 60 and older was 1 billion in 2019 and is expected to reach 2.1 billion by 2050.[1] In Thailand, there are currently 12.3 million older people, accounting for approximately one-fifth of the total population; additionally, Bangkok is the province with the largest elderly population.[2]

The adjustment processes associated with life transitions in old age result in a higher risk of illness and disease than at any other age[3], which may lead to stress or depression. Depression is one of the most common geriatric psychiatric disorders. Also, it is a significant risk factor for disability and mortality in elderly patients worldwide.[4] According to age, the elderly had the highest depression prevalence and disability-adjusted life years (DALYs).[5] The average expected prevalence of depression among the elderly was 31.7%.[4] Depression could lead to poor quality of life, social isolation, self-harms, or suicide.[6] Thirty percent of Thai elderly has experienced at least one episode of severe depression as a result of a poor quality of life.[7] In addition, the suicide rate among older depressed patients is double that of young depressed patients.[8]

The treatment of elderly with depressive disorders is crucial since it can resolve numerous problems due to depressive disorder. The goal of treatment is not only symptom remission but also the long-term prevention of recurrent episodes, the return to full functioning, and the improvement of quality of life.[9] However, patients must adhere to antidepressants for an extended period to gain these benefits. Previous research revealed that elderly with depressive disorders had a strong tendency of recurrence, with the recurrence rates of 50.0% - 90.0% during the first few years. A recurrent depressive episode is a significant risk factor for chronic diseases, cognitive impairment, and dementia. Furthermore, older patients with geriatric depression had a significantly poorer clinical response and a lower rate of full recovery than younger patients.[8]

Medication adherence is 'the extent to which a person's behavior-taking medication, following a diet, and/or executing lifestyle changes, corresponds with an agreed recommendation from a health care provider.[10] Currently, medication adherence is crucial to determine the efficacy and safety of treatment. In previous international studies, the rate of nonadherence to medication was up to 60.0% of patients with depressive disorders, and the figure can be as high as 75.0% among older individuals.[11, 12] One study in Thailand has shown that the prevalence of medication nonadherence was 77.0% in patients with depressive disorder.[13] The medication nonadherence had various consequences. It affects not just the patients' health and well-being but also caregivers and society. Numerous studies investigated antidepressant adherence and associated factors in order to develop clinical recommendations for improving medication adherence among depressed patients, including the elderly. These factors can be categorized into five domains: socioeconomic domain, health care team/health system domain, condition domain, therapy domain, and patient domain.[10]

So far, there is only one previous study in Thailand that examined drug adherence in elderly with depressive disorders, which showed the average scores of drug adherence behavior, but the prevalence of suboptimal antidepressant adherence was not stated.[14] Moreover, the associations of certain factors, such as marital status, the severity of depression, and the amount of prescribed medication, with antidepressant adherence are still inconclusive.[8, 11, 12, 14] Furthermore, some factors, such as social support and trust between patients and healthcare workers, that were associated with poor adherence in other countries cannot be generalized to Thai patients due to the difference in health systems. Additionally, since the invention of a new tool called 'Medication Taking Behavior measure for Thai patients (MTB-Thai),' antidepressant adherence can be measured more comprehensively.[14, 15] The present study aimed to examine antidepressant adherence and associated factors among Thai elderly patients with depressive disorders.

Materials and methods

Sampling and procedure

This cross-sectional study was conducted at the Psychiatric Outpatient Department of King Chulalongkorn Memorial Hospital, Thailand, from August to December 2021. The study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB no. 340/64).

The participants were older adults with aged at least 60 years old, had been previously diagnosed for depressive disorders with the International Statistical

Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes as F32 (depressive episode), F33 (recurrent depressive disorder), F34 (persistent mood/ affective disorders), F38 (other mood/affective disorders), or F39 (unspecified mood/affective disorders), received at least one antidepressant prescription and had a stable medication regiment within the past two weeks, as well as not be demented based on the Thai Mental Status Examination (TMSE) score below 24. Patients diagnosed with schizophrenia or other psychotic disorders, bipolar disorders, dementia, or serious physical illness were excluded.

Subjects who fulfilled the inclusion and exclusion criteria were consecutive recruited. The sample size was calculated using an estimating single proportion based on a reported prevalence of 41.0% of antidepressant adherence in one Thai psychiatric institute.[13] This would require a sample size of approximately 93 to attain a 10.0% margin of error and a 95% confidence interval (CI).

Instruments and measures

Participants' personal data was obtained from self-report questionnaire for demographic and psychosociographic data. The authors also collected data from the patient's medical record; included diagnosis of depressive disorders, comorbidities, and current medication.

Antidepressant adherence was evaluated using the Medication Taking Behavior measure for Thai patients (MTB-Thai) questionnaire,[15] In brief, the MTB-Thai questionnaire consists of six items that evaluate antidepressant adherence in the preceding two weeks with the response choices on a 4-point Likert scale. The overall score ranges from 0 to 24, which can be categorized as low (< 22), moderate (22 – 23), and high (24) antidepressant adherence. This questionnaire has good internal consistency and test-retest reliability with the Cronbach's alpha coefficients (α) of 0.76, intraclass correlation coefficients (ICC) of 0.83.

The severity of depression was determined with the Thai Geriatric Depression Scale (TGDS).[16] It is a 30-item self-administered questionnaire. The total TGDS score ranges from 0 to 30, which can be further divided into four categories: normal (0 - 12), mild depression (13 - 18), moderate depression (19 - 24), and severe depression (25 - 30). The TGDS shows a high internal consistency with the Kuder–Richardson 21 method (KR-21) of 0.93.

Social support was estimated using the Social Support Questionnaire (SSQ)[17] which consists of 16 items from three dimensions of social support, including emotional support, informational support, and tangible support. The overall SSQ score ranges from 16 to 80 and is classified as low (< 58), moderate (58 - 74), and high (> 74) level of social support. Each component of SSQ has a good internal consistency.

The patient-physician relationship questionnaire[18] evaluated the patients' trust in their physicians. It was developed using a trusted domain from the primary care assessment survey. It consists of 8 items and is cut off into three trust levels as low (8 - 18 score), moderate (19 - 29 score), and high (30 - 40 score) with acceptable internal consistency.

The complexity of the medication regimen was evaluated by using the Medication Regimen Complexity Index (MRCI)[19] and obtained from the medical records. MRCI has 65-items with high inter-rater reliability (ICC = 0.997) that evaluated three domains, including dosage form, dosing frequency, and additional instruction concerning the administration method of the medication. Each item might have a different score calculated based on its complexity (0.5 - 12.5 scores per item). A higher total score indicates a more complex treatment regimen.

Statistical analysis

Descriptive data were analyzed and reported for descriptive statistic in forms of frequency and percentages for categorical variables and median with interquartile range (IQR) or mean with standard deviation (SD) for continuous variables based on normality test. Comparing the difference between proportions was performed using Pearson's Chi-square test or Fisher's exact test as appropriate. Spearman's rank correlation was used to investigate the association between two continuous variables.

Binary logistic regression analysis was used to analyze the associations between related factors and antidepressant adherence. The significant level was set at a two-sided *P* - value of less than 0.05. SPSS Statistics version 28.0 was used to perform all statistical analyses.

Results

Sample characteristics

The study enrolled 119 subjects. The demographic, psychosociographic, comorbidity and medication variables for the study sample are shown in Table 1.

The majority of the study subjects were female, married, Buddhist, retired, and had moderate social support. The mean (± SD) number of all comorbidities and physical comorbidities was 3.9 ± 2.9 and 3.8 ± 2.8, respectively. Most of the patient had dyslipidemia (56.3%), hypertension (49.6%) and diabetes mellitus (29.4%). The majority of ICD-10 diagnostic codes assigned to patients were F32-depressive episode. The mean (± SD) duration of treatment for depression was 8.9 ± 7.1 years. The median number of psychotropic medications was two. Polypharmacy, consisting of ≥ 4 drug items, was identified in 15.1% of the patients. Monotherapy was the most frequently prescribed antidepressant pattern while the most frequently prescribed antidepressant class was selective serotonin reuptake inhibitors (SSRIs) including sertraline, escitalopram, and fluoxetine. The participants demonstrated a high level of patient trust and respect for the physician.

Table 1. Subjects' characteristics (n = 119).

Characteristics	N (%)
Female	86 (72.3)
Age (years); Mean ± SD	67.1 ± 5.7
Marital status	
Married	62 (52.1)
Widowed	19 (16.0)
Single	18 (15.1)
Divorced	14 (11.8)
Separated	6 (5.0)
Education	
Elementary or lower education	29 (24.4)
Secondary education	31 (26.1)
Higher secondary education	59 (49.6)
Monthly incomes (Baht)	
Mean ± SD	17,074.6 ± 20,125.7
Median (Interquartile range)	10,000 (700 – 25,000)
History of alcohol use	
Previous users	54 (45.4)
Current users	19 (15.9)
History of Tobacco use	3 (2.5)
History of Cannabis use	5 (4.2)
Needed caregivers for daily life management	5 (4.2)
Needed caregivers for medication management	9 (7.6)
Social support[a] (SSQ scores)	
Mean ± SD	64.9 ± 11.5
Median (Interquartile range)	67 (58 - 74)
Low social support (SSQ score < 58)	28 (23.5)
Moderate social support (SSQ score = 58 - 74)	64 (53.8)
High social support (SSQ score > 74)	27 (22.7)
Diagnosis of depressive disorder	
Depressive episode F32 (F32, F32.0, F32.1, F32.2, F32.3, F2.9)	102 (85.7)
Recurrent depressive disorder F33.4	4 (3.4)
Dysthymia F34.1	13 (10.9)
Severity of depression[b] (TGDS scores)	
Mean ± SD	5.7 ± 6.5
Median (Interquartile range)	3 (1 - 8)
Normal (TGDS score = 0 - 12)	101 (84.9)
Mild depression (TGDS score = 13 - 18)	9 (7.5)
Moderate depression (TGDS score = 19 - 24)	7 (5.9)
Severe depression (TGDS score = 25 - 30)	2 (1.7)

Table 1. (Con) Subjects' characteristics (n = 119).

Characteristics	N (%)
Number of physical comorbidities; Mean ± SD	3.8 ± 2.8
Psychiatric comorbidities[c]	11 (9.2)
Number of drug use; Median (Interquartile range)	
Total drugs	8 (5 - 11)
Drugs of physical comorbidity	5 (3 - 9)
Antidepressants	1 (1 - 2)
Drugs of psychiatric comorbidity	1 (0 - 2)
Pattern of antidepressant prescription	
Monotherapy	77 (64.7)
Combination therapy	42 (35.3)
Patient's trust for physician[d] (scores)	
Mean ± SD	37.5 ± 3.6
Median (Interquartile range)	39 (37 - 40)
Low trust (8 - 18 score)	0 (0.0)
Moderate trust (19 - 29 score)	7 (5.9)
High trust (30 - 40 score)	112 (94.1)
Antidepressant adherence[e] (MTB-Thai scores)	
Mean ± SD	23.0 ± 2.0
Median (Interquartile range)	24 (23 - 24)
Low adherence	19 (16.0)
Moderate adherence	20 (16.8)
High adherence	80 (67.2)
Medication Regimen Complexity Index of psychotropic medication (scores)	
Mean ± SD	7.8 ± 3.3
Median (Interquartile range)	7 (5.5 - 9.0)

[a] Social support was quantified using the Social Support Questionnaire (SSQ)
[b] Severity of depression was determined using the Thai Geriatric Depression Scale (TGDS)
[c] Psychiatric comorbidities including anxiety disorders and mild neurocognitive disorders
[d] Patient's trust for physician quantified using the patient-physician relationship questionnaire
[e] Antidepressant adherence was evaluated using the Medication Taking Behavior measure for Thai patients (MTB-Thai)

Antidepressant adherence

Antidepressant adherence presented by antidepressant taking behavior, was measured using the Medication Taking Behavior measure for Thai patients (MTB-Thai). The mean (± SD) and median MTB-Thai score was 23.0 ± 2.0 and 24 (IQR 23 - 24), respectively. The MTB-Thai scores were classified as high, moderate, or low adherence. (67.2%, 16.8% and 16.0%, respectively). Almost all subjects never missed to take their prescriptions, took them at non-prescribed times, discontinued taking them, or adjusted their dosage regimens (Table 2). Certain subjects discontinued antidepressant medication due to concerns about possible drug interactions with COVID-19 vaccines (3.4%).

Chi-square and Fisher's exact test demonstrated that the following factors were significantly associated with antidepressant adherence: marital status, social support, depression severity, number of drug use in antidepressants with psychiatric comorbidity drugs, and pattern of antidepressant prescription (Table 3). Because the complexity of depressive disorder with psychiatric comorbidity regimen and patient's trust for physician did not correlate statistically significantly with antidepressant adherence ($r = -0.156$, $P = 0.091$ and $r = -0.005$, $P = 0.961$, respectively). We analyzed detail items of them using Chi-square and Fisher's exact test and the result showed that two factors were significantly associated with antidepressant adherence; the additional instruction to split tablet of psychotropic medication and the trust in physician justifications for treatment (Table 3).

According to Spearman's rank correlation, social support, as measured by the SSQ scores, was positively correlated with adherence, as measured by the MTB-Thai scores ($r = 0.237$, $P < 0.01$), whereas

depression severity, as measured by the TGDS score, and number of antidepressant use, was negatively correlated with MTB-Thai scores (r = - 0.293, $P < 0.01$ and r = - 0.233, $P < 0.05$, respectively).

The logistic regression analysis was performed and found that moderate to severe depression, single/divorced/separated marital status, and the additional instruction to split tablet of psychotropic medication were found to be significantly associated with low-moderate antidepressant adherence in the forward stepwise model as shown in Table 4.

Table 2. Antidepressant taking behavior of elderly with depressive disorders (n = 119).

Antidepressant taking behavior	≥ 5 times n (%)	3 - 4 times n (%)	1 - 2 times n (%)	Never n (%)
Forget to take medicines	3 (2.5)	2 (1.7)	12 (10.1)	102 (85.7)
Not taking medicines as times prescribed	5 (4.2)	3 (2.5)	11 (9.2)	100 (84.1)
Stop taking medicines because of ADR	6 (5.0)	0 (0.0)	0 (0.0)	113 (95.0)
Stop taking medicines because of getting better	4 (3.4)	0 (0.0)	1 (0.8)	114 (95.8)
Stop taking medicines for other reason	2 (1.7)	1 (0.8)	1 (0.8)	115 (96.7)
Adjust dosage regimens	6 (5.0)	0 (0.0)	7 (5.9)	106 (89.1)

ADR = adverse drug reaction

Table 3. Association between variable factors of elderly with depressive disorders and antidepressant adherence by Chi-square and Fisher's exact test (n = 119).

Variable factors	Antidepressant adherence		*P* - value
	High n (%)	Low-Moderate n (%)	
Marital status			0.006**
Married and widowed	61 (76.3)	20 (51.3)	
Single/Divorced/ Separated	19 (23.7)	19 (48.7)	
Social support			0.007**
Moderate-High social support	67 (83.8)	24 (61.5)	
Low social support	13 (16.2)	15 (38.5)	
Depression severity			0.006**,p
Normal to mild depression	78 (97.5)	32 (82.1)	
Moderate to severe depression	2 (2.5)	7 (17.9)	
Number of drug use in antidepressants with psychiatric comorbidity drugs			0.025*
<4	72 (90.0)	29 (74.4)	
≥4	8 (10.0)	10 (25.6)	
Pattern of antidepressant prescription			0.032*
Monotherapy	57 (71.3)	20 (51.3)	
Combination therapy	23 (28.7)	19 (48.7)	
Additional instruction to split tablet of psychotropic medication			0.011*
No	58 (72.5)	19 (48.7)	
Yes	22 (27.5)	20 (51.3)	
Trust in physician justifications for treatment			0.025*
Absolutely trust	72 (90.0)	29 (74.4)	
Not trust/ Not sure/Trust	8 (10.0)	10 (25.6)	

*$P < 0.05$, ** $P < 0.01$, p = Fisher's exact test

Table 4. Factors associated with low-moderate of antidepressant adherence in elderly with depressive disorders by binary logistic regression (n = 119).

Factors	β	Adjusted Odds Ratio	95% CI of adjusted OR		*P* - value
			Lower	Upper	
Moderate to severe depression	1.80	6.04	1.08	33.76	0.041*
Single/Divorced/Separated marital status	1.08	2.95	1.24	7.03	0.014*
Additional instruction to split tablet of psychotropic medication	0.94	2.56	1.09	6.03	0.031*

*$P < 0.05$

Discussion

Medication adherence is the key factor that influence clinical responses in diseases,including depressive disorders, which are typically treated with antidepressants as first-line therapy.[9, 20] Report from Prukkanone B, *et al*. indicated that the majority of Thai patients with major depression have low adherence to antidepressant therapy.[13] However, no study has identified a prevalence of low antidepressant adherence among Thai elderly with depressive disorders, who are vulnerable and have unique characteristics. Based on data from a self-reported questionnaire, this study found that low and moderate antidepressant adherence among Thai elderly with depressive disorders was 16.0% and 16.8%, respectively. Previous studies in the last 20 years indicated that the nonadherence rate among depressed elderly ranged from 40.0% to 75.0%[12], with a tendency for this percentage to decrease in subsequent studies. The present study found that the majority of Thai elderly with depressive disorders had high antidepressant adherence of 67.2 %, which corresponded to the average drug adherence behavior score in elderly with depressive disorders in Nakhon Ratchasima province with a high score that nearly achieved full score.[14] Furthermore, our study's antidepressant adherence is consistent with that of other studies, which shown that the majority of depressive elderly adhered to their medication. The prevalence of moderate to high and low antidepressant adherence was 77.0% and 23.0% among older Chinese patients with major depression.[8] A national study in the United States found that antidepressant adherence among older adults with dementia and major depressive disorder ranged from 64.0% to 74.0%.[21, 22]

The current study discovered that antidepressant adherence among Thai elderly was higher than in previous studies of elderly in other countries and Thai young adult patients with depressive disorders. Nevertheless, there are major differences between our study and prior researches, including age-specific characteristics and treatments settings. Numerous studies have indicated that elderly with depression had significantly higher antidepressant adherence than younger patients.[23 - 26] Despite concerns about the detrimental effects of depression treatment, such as drug dependence, adverse drug events, and drug interactions, the elderly prioritized medication and sought it more than other age groups.[8, 27] This is due to awareness of the disease severity, self-value, necessity of treatment, and a positive attitude toward therapy.[23, 25, 26, 28] In addition, older adults had a high prevalence of comorbidities, with an average of 3.8 per subject in our study. Experience with diseases and disease management, understanding of the disadvantages of stopping treatment, and having a routine habit of consistently taking medications may influence antidepressant adherence in the elderly.[26] Previous research found an association between religious activity engagement, depression improvement, and treatment-seeking behavior, including medication use.[12] Since Thai elderly was high level of religious activity practice, there might be a correlation between them and good adherence to depression medication. [29]

Our research was conducted in a tertiary care hospital, where mental health professionals were available, would relate to high antidepressant adherence. Other studies have found an association between patients receiving psychiatric care or achieving appropriate care and a significantly greater likelihood of antidepressant adherence.[26, 30] This may be because psychiatric professionals generally receive more training in engaging the patients and motivational interviewing than other health professionals and have

the ability to build therapeutic relationships, especially in terms of communication and empathy with depressed patients. They can recommend or adjust antidepressant regimens for individuals based on efficacy and safety, as agreed upon by the health provider and the patient. Furthermore, some patients receiving therapy in tertiary care hospitals were referred to a psychiatrist because they may have had severe depression or treatment-resistant depression, which may have enhanced their motivation and insight into the benefits of antidepressant adherence.[26, 31, 32]

It is generally acknowledged that medication adherence in depressed elderly may be related to various factors.[12, 33] In this study, moderate to severe depression, single/divorced/separated marital status, and additional instruction to break or crush tablet were statistically associated with lower antidepressant adherence in multiple logistic regression analysis. The association between the severity of depression and antidepressant adherence was also observed in another study, which found that patients who received antidepressant for the treatment of depression may discontinue or not adhere to their medication due to clinical non-improvement.[11] In contrast, patients whose depressive symptoms improved had a decreased likelihood of discontinuing antidepressant therapy.[34] Consequently, the severity of depression is comparable to an indicator of treatment efficacy. The research found that a perception of medication inefficacy was a common reason for treatment discontinuation in elderly with depressive disorders.[11] Furthermore, patients with more severe symptoms of depression are more likely to have a negative attitude of therapy. Nevertheless, patients with milder depressive symptoms will have more positive attitudes, including attitudes toward therapy[35], beliefs about antidepressants, and understanding of the importance of continuing depression medication in order to encourage antidepressant adherence.[8, 12, 36] Additionally, functional impairment in severe depression, including the physical inability to self-administer medicines, may directly lead to the reduction or absence of some behaviors, including antidepressant use.

This study identified the characteristics of additional instruction to split tablet of psychotropic medication and its association to antidepressant adherence among Thai elderly with depressive disorders. As a result of the physiological changes associated with aging, such as decreases in visual acuity and muscle weakness[37], the majority of aged participants in our study who self-administer medications had difficulty with drug use and a lower likelihood of antidepressant adherence. This is consistent with research indicating that the risk of non-adherence increases when additional requirements do not fit into a subject's consolidated routine.[33] Therefore, healthcare professionals should avoid prescribing split tablets to older depressed patients, which is a component of the regimen's complexity in depression treatment. Previous studies found that depressed patients with multiple or complicated drug dosages, frequency of administration and types, as well as additional requirements that may not fit into the subject's consolidated routine, all had a negative association with antidepressant adherence.[12, 33] Nevertheless, the complicated regimen of psychotropic medication was unrelated with antidepressant adherence in this study. All our elderly received at least one prescribed medication in the form of oral capsules/tablets, to be taken once daily and at a specific time for the treatment of depressive disorders. In addition, due to the small sample size, there may be no statistical significance in the difference between the regimen's complexity and elderly antidepressant adherence.

We found that the pattern of antidepressant prescription in depressed elderly was a significant factor associated with poor adherence by univariate analysis. Antidepressant combination therapy had a higher proportion of low to moderate adherence in older patients than antidepressant monotherapy. This tendency could be explained by the common clinical practice of antidepressant combination therapy in patients with severe symptoms of depression or refractory to treatment.[9, 20] Moreover, the combination antidepressant therapy had more amount and frequency of drugs used, which negatively related with antidepressant adherence[33], that was consistent with the prior studies reported the relationship between more frequency of antidepressant administration and poor medication adherence.[10, 38] This study found a similar association that the elderly with low to moderate antidepressant adherence were significantly more likely to use four or more antidepressants, the definition of polypharmacy[39], than those with high antidepressant adherence. Studies on the elderly demonstrated that the patients were more likely to have antidepressant adherence problems as the number of drugs they were prescribed

increased.[10, 38] Polypharmacy can have particularly detrimental effects on the elderly, including adverse drug reactions, drug interactions, and age-related pharmacokinetic changes, such as an increased sensitivity to toxicity and medication regimen confusion. As a result, the older patients noted that concern and fear of negative drug effects could directly affect their behaviors towards continuing medicine and altering/stopping prescriptions based on priority without informing the physician.[12, 23]

Another significant risk factor for poor antidepressant adherence among elderly with depressive disorders in this study was single, divorced, or separated marital status, which reflected the poor social support and absence of family responsibilities.[10, 11] Similar, finding was reported by Bull SA, *et al*. that the married elderly with depressive disorders were less likely to discontinue the antidepressant than those with other statuses, which could be attributed to social support encouraging them to continue treatment[34], monitoring and reminding the elderly to take medication, as well as increased the patients' self-esteem and value. Consequently, social support is one of the crucial factors encouraging on beliefs about the controllability of one's health and perception in usefulness of healthy behaviors including antidepressant administration, older depressed patients who had greater social support also had greater antidepressant adherence in studies.[8, 14, 40] This was congruent with a study of Lu Y, *et al*. that older Chinese patients with major depression frequently forget to take their medication or stop taking antidepressants when they begin to feel better, which could be explained by the fact that the majority of participants did not live with their children or family.[8] Although, widowed patients whose spouse has died can cause significant stress and loss of social support in the other spouse, influencing the presence and severity of depression as well as the risk of poor antidepressant adherence,[12] but there was no statistically significant difference in antidepressant adherence between married and widowed elderly Chinese patients with major depression.[8] It may be related to the Eastern culture of living in an extended family, in which the elderly typically performed family responsibilities and received a wide range of social support not just from their spouse, but also from their children and relatives, which might compensate for the loss of a spouse.

This study has several limitations. Firstly, the cross-sectional nature of the study limited causational inferences. Future research should investigate causal relationships using longitudinal studies. The cross-sectional study design was unable to control some potential biases, including selection and confounding bias. We endeavored to define population-based eligibility criteria, analyze by binary logistic regression, and select participants with a TMSE scores above 23 in order to control for selection and confounding bias. Consequently, our results will be cautiously generalized as well as matching by confounders should be included in future research. Secondly, we selected participants who received the outpatient services in a tertiary care hospital would not be able to generalize as the representation of all health care level in Thailand. Thirdly, no formal psychotherapy session was reported. Finally, a larger sample size would be preferable for determining more significant antidepressant adherence factors.

Conclusion

This is the first study that addressed the inappropriate adherence to antidepressant among Thai elderly with depressive disorders. We demonstrated that only one third of elderly Thai patients reported suboptimal adherence to antidepressant. Moderate to severe depression, single/divorced/ separated marital status, and the additional instruction to split tablet of psychotropic medication were significantly associated with low and moderateadherence.

Acknowledgements

We would like to acknowledge all the patients participated in this study and the hospital staffs assisted in data collection. Moreover, we would appreciate for permission of use for MTB-Thai from Prof. Dr. Phantipa Sakthong, the patient-physician relationship questionnaire from Dr. Napakkawat Buathong, the Social support questionnaire from Assoc. Prof. Peeraphon Lueboonthavatchai and MRCI from Faculty of Nursing, Chulalongkorn University.

Conflict of interest statement

Each of the authors has completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

Data sharing statement

The present review is based on the reference cited. Further details, opinions, and interpretation are available from the corresponding authors on reasonable request.

References

1. World Health Organization. The global network for age-friendly cities and communities: looking back over the last decade, looking forward to the next. Geneva: World Health Organization; 2018.
2. Official statistics registration systems. Population by age Pathumthani: Official statistics registration systems; 2022 [cited 2022 May,17]. Available from: https://stat.bora.dopa.go.th/stat/statnew/statMONTH/statmonth/#/displayData (in Thai).
3. National statistical office, Ministry of digital economy and society. The 2019 health and welfare survey. Bangkok: National statistical office, ministry of digital economy and society; 2020 (in Thai).
4. Zenebe Y, Akele B, W/Selassie M, Necho M. Prevalence and determinants of depression among old age: a systematic review and meta-analysis. Arch Gen Psychiatry 2021;20:55.
5. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019). DALYS (Disability-Adjusted Life Years) - depressive disorders - sex: both - age in 1990-2019 United States: Institute for Health Metrics and Evaluation; 2021 [updated April 2018; cited 2022 May,17]. Available from: http://ghdx.healthdata.org/gbd-results-tool.
6. Wannasewok K. Bipolar and related disorders and depressive disorders. In: Sitdhiraksa N, Wannasewok K, Wannarit K, Pukrittakayamee P, Apinuntavech S, Katumarn P, editors. Siriraj Psychiatry DSM-5. 3rd ed. Bangkok: Department of Psychiatry, Faculty of medicine Siriraj hospital, Mahidol university; 2016. p. 379-410. (in Thai).
7. Bunloet A. Prevalence and factors associated with depression among the elderly community residents with chronic diseases in Samliam Urban Primary Care Unit, Khon Kaen. Srinagarind Med J 2016;31:25-33.
8. Lu Y, Arthur D, Hu L, Cheng G, An F, Li Z. Beliefs about antidepressant medication and associated adherence among older Chinese patients with major depression: A cross-sectional survey. Int J Ment Health Nurs 2016;25:71-9.
9. Yatham LN, Kennedy SH. Mood Disorders: Pharmacological treatment of depression and bipolar disorders. In: Sadock BJ, Sadock VA, Ruiz P, editors. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 10 ed. Philadelphia: Lippincott Williams & Wilkins; 2017. p. 1677-701.
10. World health organization. Adherence to long-term therapies: evidence for action. Geneva: world health organization; 2003.
11. Wetherell JL, Unützer J. Adherence to treatment for geriatric depression and anxiety. CNS Spectr 2003;8: 48-59.
12. Zivin K, Kales HC. Adherence to depression treatment in older adults. Drugs Aging 2008;25:559-71.
13. Prukkanone B, Vos T, Burgess P, Chaiyakunapruk N, Bertram M. Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in Thailand. J BMC Psychiatry 2010;10:64.
14. Suemram P, Wattanapailin A, Yuttatri P, Vongsirimas N. Correlation between beliefs about depression, social support, medical co-morbidity and drug adherence behavior in elderly with major depressive disorder. JBCNM 2016;22:108-20. (in Thai).
15. Sakthong P, Sonsa-Ardjit N, Sukarnjanaset P, Munpan W, Suksanga P. Development and psychometric testing of the medication taking behavior tool in Thai patients. Int J Clin Pharm 2016;38:438-45.
16. Train the brain forum commitee. Thai Geriatric Depression Scale-TGDS. Siriraj Hosp Gaz 1994;46:1-9. (in Thai).
17. Lueboonthavatchai P, Lueboonthavatchai O. Quality of life and correlated health status and social support of schizophrenic patients' caregivers. J Med Assoc Thai 2006;89 Suppl 3:S13-9.
18. Buathong N. The association between depression and cofactors in the individual level on adherence to antiretroviral therapy of adult HIV infected patients at King Chulalongkorn Memorial Hospital [Doctor of philosophy program in community medicine]. Bangkok: Chulalongkorn University; 2008. (in Thai).
19. Tepsuriyanont S, Jirapaet V, Luangamornlert S, Praditsuwan R. Relationship between regimen complexity and medication adherence behavior in Thai elderly with hypertension. Chula Med J 2011;55: 457-72.
20. Kennedy SH, Lam RW, McIntyre RS, Tourjman SV, Bhat V, Blier P, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 3. Pharmacological treatments. Canadian J Psychiatry 2016;61:540-60.
21. Bhattacharjee S, Lee JK, Vadiei N, Patanwala AE, Malone DC, Knapp SM, et al. Extent and factors

associated with adherence to antidepressant treatment during acute and continuation phase depression treatment among older adults with dementia and major depressive disorder. Neuropsychiatr Dis Treat 2020;16: 1433-50.
22. Bosworth HB, Voils CI, Potter GG, Steffens DC. The effects of antidepressant medication adherence as well as psychosocial and clinical factors on depression outcome among older adults. Int J Geriatr Psychiatry 2008;23:129-34.
23. Marasine NR, Sankhi S. Factors associated with antidepressant medication non-adherence. Turk J Pharm Sci 2021;18:242-9.
24. Rivero-Santana A, Perestelo-Perez L, Pérez-Ramos J, Serrano-Aguilar P, De Las Cuevas C. Sociodemographic and clinical predictors of compliance with antidepressants for depressive disorders: systematic review of observational studies. Patient Prefer Adherence 2013;7:151-69.
25. Moonchai K, Sangon S, Ninthachan P, Rungrungsiripan M. Factors associated with adherence to medication in major depressive disorder patients. Thai Res Cross Nurs J 2020;13:240-60. (in Thai).
26. Rossom RC, Shortreed S, Coleman KJ, Beck A, Waitzfelder BE, Stewart C, et al. Antidepressant adherence across diverse populations and healthcare settings. Depress Anxiety 2016;33:765-74.
27. Burnett-Zeigler I, Kim HM, Chiang C, Kavanagh J, Zivin K, Rockefeller K, et al. The association between race and gender, treatment attitudes, and antidepressant treatment adherence. Int J Geriatr Psychiatry 2014;29:169-77.
28. Sawada N, Uchida H, Suzuki T, Watanabe K, Kikuchi T, Handa T, et al. Persistence and compliance to antidepressant treatment in patients with depression: A chart review. BMC Psychiatry 2009;9:38.
29. Hengudomsub P, Watanasin D, Srisopa P, Kangchai W. Factors predicting psychological well-being of community-residing older adults. Thai Pharmaceut Health Sci J (TPHSJ) 2017;12:57-67.
30. Jang S, Cho H, Kang C, Jang S. Antidepressant adherence and its predictors in immigrants with depression: A population-based study. Medicine (Baltimore) 2020;99:e23308.
31. Johnston BJ. The role of patient experience and its influence on adherence to antidepressant treatment. J Psychosoc Nurs Ment Health Serv 2013;51:29-37.
32. Thompson L, McCabe R. The effect of clinician-patient alliance and communication on treatment adherence in mental health care: a systematic review. BMC Psychiatry 2012;12:87.
33. Solmi M, Miola A, Croatto G, Pigato G, Favaro A, Fornaro M, et al. How can we improve antidepressant adherence in the management of depression? A targeted review and 10 clinical recommendations. Braz J Psychiatry 2021;43:189-202.
34. Bull SA, Hu XH, Hunkeler EM, Lee JY, Ming EE, Markson LE, et al. Discontinuation of use and switching of antidepressants: influence of patient-physician communication. JAMA 2002;288:1403-9.
35. Zhang J, Ye C. Factors associated with loss to follow-up of outpatients with depression in general hospitals. J Int Med Res 2020;48:1-9.
36. Yeh MY, Sung SC, Yorker BC, Sun CC, Kuo YL. Predictors of adherence to an antidepressant medication regimen among patients diagnosed with depression in Taiwan. Issues Ment Health Nurs 2008; 29:701-17.
37. Page AT, Potter K, Clifford R, Etherton-Beer C. Deprescribing in older people. Maturitas 2016;91: 115-34.
38. Claxton A, de Klerk E, Parry M, Robinson JM, Schmidt ME. Patient compliance to a new enteric-coated weekly formulation of fluoxetine during continuation treatment of major depressive disorder. J Clin Psychiatry 2000; 61:928-32.
39. Muangpaisan W, Pisalsalakij D, Intalapaporn S, Chatthanawaree W. Medication nonadherence in elderly patients in a Thai geriatric clinic. Asian Biomed 2014;8:541-5.
40. Mishra SI, Gioia D, Childress S, Barnet B, Webster RL. Adherence to medication regimens among low-income patients with multiple comorbid chronic conditions. Health Soc Work 2011;36:249-58.