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Original Article

Medication Adherence and Associated Factors in Older Adults at a Tertiary Outpatient Clinic in Thailand

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SUMMARY

Background: Adherence to medication is an essential part of achieving health outcomes in the elderly. However, there is a paucity of data regarding medication adherence and associated factors in Thailand, especially in tertiary settings where patients have more complicated medication regimens.
Methods: This was a cross-sectional study conducted from May 2019 to May 2020. We examined older patients at the outpatient clinic of an internal medicine department at a tertiary care hospital in Thailand. Eligible patients included age ≥ 60 years, had at least one chronic disease that requires long-term medication, and had to follow-up regularly for at least three months before participating in this study. Exclusion criteria were patients with mental, visual, aural, or severe limb impairment that interfered with communication or self-management of medication. Demographic characteristics were collected, and the 8-item Morisky Medication Adherence Scale (MMAS-8) was used to measure medication adherence.
Results: A total of 250 participants were included, of whom 24.2%, 39.2%, and 36.4% practiced good, moderate, and poor medication adherence, respectively. Multivariate regression analysis showed poor medication adherence was associated with adverse drug reactions (ADR, adjusted odds ratio [AOR] 4.8), concurrent use of over-the-counter (OTC) drugs (AOR 2.02), and high Thai Geriatric Depression Scale (TGDS) scores (AOR 1.44).
Conclusion: Self-reported nonadherence to medication is prevalent in geriatric outpatients with chronic diseases. Factors associated with poor medication adherence were identified. Targeted intervention is recommended to improve compliance included thoroughly taking history of ADR, review all current prescriptions and OTC drugs, and depression screening.

1. Introduction

Medication adherence is described by the World Health Organization as "the degree to which the person's behavior corresponds with the agreed recommendations from a health care provider"[1] and can play an important role in controlling diseases. This is especially true for patients with chronic illnesses, as they require continuous treatment over a long period.[2] Apart from iatrogenesis, poor medication adherence can lead to numerous adverse health outcomes including poor prognosis, diminished therapeutic benefits, overtreatment, greater healthcare utilization, increased hospitalization, higher rates of 30-day readmission, and higher rates of falls in the elderly.[3–5,6] Older adults often have chronic diseases that require multiple medications, as well as atypical presentation or non-specific presenting symptoms.[7] Polypharmacy and complex medication regimens are thus more common in older adults, putting them at greater risk of nonadherence than younger patients.

In previous studies, medication adherence has ranged from 19 to 100% depending on the study design, clinical setting, measurement tools used, and patients' cultural backgrounds.[8–11] For example, a study in older patients at a tertiary care hospital in Bangalore found the rate of medication adherence to be only 19.12%[8] and another in a rural healthcare center in India reported that about a third (32.7%) of participants were non-adherent.[9] One study in chronic heart failure patients (average age of 63.1 years) at a tertiary care hospital, Thailand reported high, moderate, and poor medication adherence of 38.3%, 50% and 11.7%.[11] However, a study in Chinese older adults in a community in Hong Kong found the rate of adherence to be 90.8%.[10] According to the recommendation of World Health Organization and Miller et al., factors associated with poor medication adherence can be classified into patient factors, medication factors, healthcare provider factors, healthcare system factors, and socioeconomic factors.[3] For older patients, there are specific factors that may be associated with non-adherence including 1) increased susceptibility to drug-related complications due to pharmacodynamic and pharmacokinetic changes, 2) multiple diseases that require polypharmacy and cause functional limitations, 3) increased risk of drug interactions, and 4) receiving healthcare services across multiple providers, complicating their pharmaceutical regimen.[12]

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There have been few studies regarding medication adherence and associated factors in Thailand, especially in tertiary settings where patients often have severe and complex chronic conditions. There is only one study in a chronic heart failure clinic of a tertiary care hospital as mentioned earlier.[11] It is thus crucial to assess the extent of medication adherence in this population. Better understanding of the factors associated with poor adherence will help ensure that patients get the full therapeutic benefits from treatment. The objectives of this study were to assess medication adherence using the 8-item Morisky Medication Adherence Scale in geriatric patients with chronic illnesses at a tertiary care hospital and to determine any associated factors.

2. Material and methods

2.1. Participants and setting

This was a cross-sectional sub-study of the project entitled "Prevalence of medication nonadherence and adverse health outcomes of older patients." It was conducted in older patients with chronic illnesses at an outpatient clinic of the Srinagarind Medical School Internal Medicine Department (Thailand) from May 2019 to May 2020. The clinic is a tertiary care referral center at a university hospital located in the Northeastern part of Thailand to which patients are sent from other departments and other community hospitals. The inclusion criteria were age ≥ 60 years (the definition of older adults in Thailand) and at least one chronic disease that requires long-term medication. The patients had to follow-up regularly for at least three months prior enrolling in this study. Patients with mental, visual, aural, or severe limb impairment that interfered with communication or self-management of medication were excluded from the study. The eligible patients were 258 cases where 8 cases were withdrawn due to unwillingness to participate in this study. Therefore, completed data were collected in 250 patients. Study flow is shown in Figure 1.

2.2. Instrument

2.2.1. 8-item Morisky Medication Adherence Scale (MMAS-8)

The MMAS, developed by Donald E. Morisky, is a generic self-report scale assessing medication-taking behavior.[13] While the original scale consisted of only four items, a revised eight-item version was developed with improved psychometric properties to address the complex barriers to medication adherence.[14] Each item of the MMAS measures a specific behavior and is not a determinant of adherence behavior. Response choices are yes/no for items 1–7 and a 5-point Likert response for the last item. Scores obtained from this scale range from 0 to 8, where higher scores indicate higher adherence. Scores of 8, 6 to less than 8, and less than 6 were classified as high, medium, and low adherence, respectively.[14] The Thai version of the MMAS-8 has been validated with a Cronbach's alfa coefficient of 0.71 and intraclass correlation coefficient of 0.8319.[15]

2.2.2. Frailty syndrome

Frailty syndrome was diagnosed using the 5-item FRAIL scale when the patients met at least 3 in 5 of the phenotypic criteria which included 1) fatigue (feeling exhausted most of the time), 2) resistance (limitations climbing 1 flight of stairs), 3) ambulation (inability to walk alone > 100 meters), 4) illness (5–11 of the following diseases: hypertension, diabetes mellitus, cancer, chronic lung disease, heart attack, congesting heart failure, angina, asthma, arthritis, stroke, kidney disease), and 5) loss of weight (unplanned weight loss > 5% over a past year). One point was given for each item (a total of 0 = best and 5 = worst).[16–18]

2.2.3. Rowland Universal Dementia Assessment Scale (RUDAS)

The Rowland Universal Dementia Assessment Scale (RUDAS) is a six-item cognitive test which was developed and validated by Rowland et al. in Australia. This screening tool measures a variety of cognitive domains including memory, praxis, visuoconstruction, language, and visuospatial domain. It is easy to administer and has various items addressing frontal lobe function.[19,20] The Thai version of the RUDAS has a total possible score of 30. A score of 23 or 24 may indicate dementia in patients with a sixth-grade or lower education (71.4% sensitivity and 76.9% specificity), and of 24 or 25 may do so in those with seventh-grade education or above (77% sensitivity and 70% specificity).[21,22]

2.2.4. Thai Geriatric Depression Scale-15 (TGDS-15)

The 15-item Thai Geriatric Depression Scale is a shortened version of the original Geriatric Depression Scale (GDS). It consists of 30 items aimed at ascertaining respondents' feelings, behaviors, and ideas concerning depression over the previous week. The TGDS-15 is less time-consuming and has better diagnostic properties for screening major depression among older patients than the original GDS. At a cut-off point of ≥ 5 in outpatient settings, the sensitivity and specificity are 0.92 and 0.87, respectively.[23]

2.3. Procedure

A convenience sample of the potential patients were asked to enroll in the study by a team of researchers that was composed of 3 physicians. They had meeting regularly before and between collecting the patient information. If the problems occurred, discussion was made with final conclusion. The ones who were willing to participate would then sign the informed consent. Demographic patient information was collected by trained clinical researchers. The demographic data consisted of age, gender, educational level, marital status, family size, self-rated health status and life satisfaction, and comorbid illnesses. Data regarding medication use consisted of medication history, number of daily medications, daily frequency medication administration, history of adverse drug reactions (ADR) (defined as an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product over

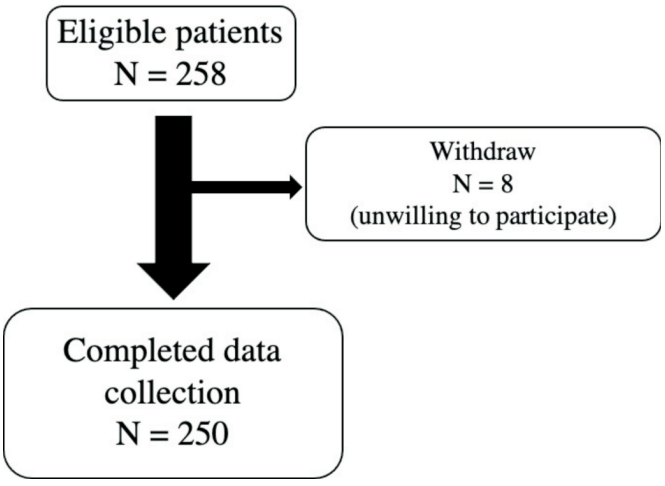

Figure 1. Study flow.

the past),[24] use of over-the-counter medication (defined as herbal medicines, dietary supplements, or nonprescribed drugs bought during last two years without prescriptions), knowledge about medication indications and side effects, and information received regarding medication. Frailty syndrome was diagnosed using the FRAIL scale (score 3–5). The RUDAS was used to diagnose cognitive impairment, and the TGDS-15 was used to assess degree of depression. Medication adherence was evaluated using the MMAS-8. All information was collected by self-reported questionnaires except for the RUDAS that was administered to the patients by the trained researchers. However, if the patients did not understand the self-reported questionnaires, the trained researchers would help them to answer the questionnaires.

2.4. Sample size calculation

Sample size calculation was based on the primary objective of this study, which was to estimate the proportion of older patients with poor medication adherence at the outpatient clinic. An estimated prevalence of 19.12% was derived from a previous study with a similar population.[25] A formula for estimating a population proportion with specified absolute precision was used to calculate this. We determined that a sample size of at least 238 participants would be sufficient to achieve the required significance level of 0.05. We thus enrolled a total of 250 participants.

2.5. Statistical analysis

Descriptive statistics for demographic data were presented as median and inter-quartile range since the distribution of these data was not normal. Factors associated with poor medication adherence were assessed using univariate and multivariate regressions analysis. In terms of univariate analysis, crude odds ratios (OR) and 95% confidence intervals (CI) were used to consider the strength of association. Factors with p-values of < 0.20 were then entered into a multiple logistic regression model. p-values of < 0.05 were considered to indicate statistically significant differences, and adjusted odds ratios (AOR) and 95% CI were used to determine the strength of association. All data analysis was carried out using STATA version 10.0 (StataCorp, College Station, Texas).

Ethical approval was provided by the Khon Kaen University Faculty of Medicine Ethics Committee as instituted by the Helsinki Declaration (approval number HE621115).

3. Results

3.1. Patient characteristics and medication adherence

Two hundred fifty older patients were enrolled in this study, the demographic characteristics of whom are shown in Table 1. The median age was 69 years and the majority (40%) of patients had six years of education. Approximately 80% were married. Hypertension was the most common comorbid illness (77.6%) followed by diabetes mellitus (49.2%). Only about one-fifth had good medication adherence (Figure 2).

3.2. Predictors of poor medication adherence

Table 2 shows factors associated with poor medication adherence (MMAS-8 < 6) based on univariate and multivariate regression analyses. According to univariate analysis, age, education, family size, number of daily medications, frequency of medication administration, history of ADR, concurrent use of OTC drugs, understanding of drug indications, understanding of side effects, having received information about their medication, self-rated good health, life satisfaction, frailty, and comorbidity with DM, HT, or TGDS had p-values < 0.2. After checking for multicollinearity, those factors were

Table 1
Demographic data of the studied population.

Variables	N = 250
Age (years), med (IQR 1,3)	69 (64,75)
Male, n (%)	116 (46.4)
Years of education, n (%)	
< 6	100 (40)
7–12	71 (28.4)
> 12	79 (31.6)
Marital status, n (%)	
Single	6 (2.4)
Married	195 (78)
Divorced	10 (4)
Widow(er)	19 (15.6)
Family size, n (%)	
1	19 (7.6)
< 3	74 (29.6)
3–5	126 (50.4)
6–8	27 (10.8)
> 8	4 (1.6)
History of drug use (years); med (IQR 1,3)	4 (3,4)
No. of medications per day, med (IQR 1,3)	5 (3,7)
Daily frequency medication administration, med (IQR 1,3)	2 (2,3)
ADR, n (%)	68 (27.2)
Concurrent use of OTC drugs, med (IQR 1,3)	111 (44.4)
Understanding of drug I/D, med (IQR 1,3)	238 (95.2)
Understanding of drug S/E, med (IQR 1,3)	72 (28.8)
Received information about their medications, med (IQR 1,3)	243 (97.2)
Self-rated good health, med (IQR 1,3)	120 (48)
Life satisfaction, med (IQR 1,3)	240 (96)
Frailty, med (IQR 1,3)	8 (3.2)
Comorbid conditions, med (IQR 1,3)	
DM	123 (49.2)
HTN	194 (77.6)
CVA/TIA	28 (11.2(
CKD	53 (21.2)
Arthritis	26 (10.4)
RUDAS, med (IQR 1,3)	26 (24,28)
TGDS, med (IQR 1,3)	1 (1,3)

Note: med, median; IQR, inter-quartile range; n, number of patients; No., number; ADR, adverse drug reaction; OTC drug, over-the-counter drug; I/D, indication; S/E, side effect, frail using the FRAIL scales ≥ 3; DM, diabetes mellitus; HTN, hypertension; CVA, cerebrovascular disease; TIA, transient ischemic attack; CKD, chronic kidney disease; RUDAS, Rowland Universal Dementia Assessment Scale; TGDS, Thai Geriatric Depression Scales.

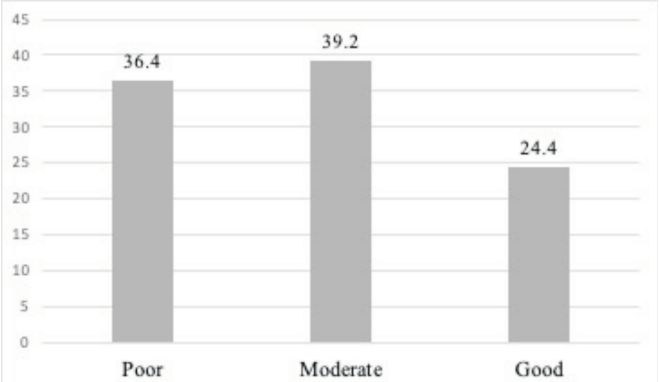

Figure 2. Medication adherence among older patients with chronic illnesses at the outpatient clinic according to the MMAS-8 (%).

Table 2
Factors associated with poor medication adherence according to univariate and multivariate logistic regression analyses.

Factors	Univariate			Multivariate		
	Crude OR	(95% CI)	p-value	Adjusted OR	95% CI	p-value
Age	0.96	(0.92–0.99)	0.04	0.96	(0.92–1.01)	0.12
Male	1.21	(0.72–2.03)	0.47			
Years of education						
< 6	1	-	-	1	-	-
7–12	1.71	(0.90–3.22)	0.09	1.91	(0.853–4.37)	0.13
> 12	1.51	(0.81–2.81)	0.19	1.87	(0.8–4.39)	0.15
Marital status						
Single	1	-	-			
Married	0.58	(0.12–2.97)	0.52			
Divorce	1	(0.13–7.57)	1.00			
Widow	0.39	(0.06–2.25)	0.29			
Family size						
Alone	1	-	-	1	-	-
< 3	0.43	(0.16–1.20)	0.11	0.41	(0.12–1.43)	0.16
3–5	0.47	(0.18–1.23)	0.12	0.85	(0.26–2.78)	0.79
6–8	0.72	(0.22–2.33)	0.59	0.92	(0.21,3.96)	0.91
> 8	0.9	(0.10–7.78)	0.92	0.93	(0.08–11.42)	0.95
Experience of drug use (years)	0.98	(0.72–1.32)	0.89			
No. of medication a day	1.11	(1.01–1.23)	0.03	1.12	(0.97–1.29)	0.12
Frequency of taking medication a day	1.29	(0.94–1.78)	0.12	1.14	(0.74–1.76)	0.55
Experience of ADR	4.38	(2.43–7.90)	0.00	4.80	(2.39–9.62)	0.00*
Concurrent use of OTC drug	1.83	(1.08–3.07)	0.02	2.02	(1.07–3.82)	0.03*
Known I/D drug use	0.39	(0.12–1.27)	0.12	0.39	(0.09–1.7)	0.21
Known S/E of drug use	1.75	(1.00,3.06)	0.05	1.61	(0.77–3.36)	0.21
Received information about drug	0.09	(0.01–0.76)	0.03	0.67	(0.24–1.89)	0.45
Self-rated good health	0.67	(0.40–1.13)	0.13	0.93	(0.48–1.79)	0.82
Satisfy life	1.79	(0.50–6.36)	0.37	0.28	(0.05–1.75)	0.17
Being frail	3.02	(0.71–12.95)	0.14	2.15	(0.31–15.08)	0.44
Comorbid						
DM	1.25	(0.31.65–1.17)	0.4			
HT	0.64	(0.35–1.17)	0.15	0.52	(0.24–1.22)	0.10
CVA/TIA	1.6	(0.72–3.53)	0.25			
CKD	1.08	(0.57–2.01)	0.82			
Arthritis	1.32	(0.58–3.01)	0.51			
RUDAS	1.13	(0.59–2.16)	0.70	0.96	(0.87–1.05)	0.38
TGDS	1.46	(1.15–1.50)	0.00	1.44	(1.21–1.70)	0.00*

Note: OR, odds ratio; ADR, adverse drug reaction; OTC drug, over-the-counter drug; I/D, indication; S/E, side effect, frail using the FRAIL scales ≥ 3; DM, diabetes mellitus; HTN, hypertension; CVA, cerebrovascular disease; TIA, transient ischemic attack; CKD, chronic kidney disease; RUDAS, Rowland Universal Dementia Assessment Scale; TGDS, Thai Geriatric Depression Scale.

entered into the model for multivariate analysis, according to which history of ADR, use of OTC medications, and increased TGDS were associated with poor adherence ($p < 0.05$).

4. Discussion

Adherence to medication is fundamental in achieving clinical outcomes and improving the health of older adults.[26] This study examined medication adherence mainly in the young-old population. We found that the rate of good adherence was rather low (24.4%), while that of poor adherence was relatively high (36.4%) compared with previous studies that reported good medication adherence ranged from 19–100% as mentioned earlier in the introduction part.[8–11,25,27] A study in geriatric patients (majority 60–70 years of age, as in our study) at a tertiary care hospital in Bangalore using the 20-item MMAS, for example, found that 45.41% had good medication adherence, and 35.35% and 19.12% had moderate and poor compliance, respectively.[25] Another study in Hong Kong's New Territories found that 65.1% of hypertensive outpatients (mean age 65.7 years) practiced good compliance (MMAS-8 > 6), and 32.6% had poor compliance.[8] Another study at the outpatient clinic of a primary care hospital in the Northeastern part of Thailand using the MMAS-8 reported that 33.8%, 40.8%, and 25.4% of older adults with chronic diseases had high, moderate, and poor compliance, respectively,[27] and one study of chronic heart failure clinic of a tertiary care hospital in the Northern part of Thailand (average age of participants of 63.1 years) found level of medication adherence using the MMAS-8 of high, moderate and poor compliance was 38.3%, 50.0%, and 11.7%, respectively.[11] Possible reasons for these differences are variations in measurement methods, studied populations, and cultural factors. The study in Bangalore, for example, used a modified version of the MMAS, which consisted of 20 items, as opposed to the 8-item version used in our study.[25] In addition, cultural factors, such as beliefs surrounding medication, concerns regarding daily medications, perceptions regarding health and chronic illnesses, self-care practices, and social support, may also have been factors.[8,28] The finding of this study represented the level of medication adherence of urban older adults with chronic medical illnesses of a tertiary care hospital in the Northeastern part of Thailand where the complexities of illnesses, disease severity, and cultural background are different from the existing reports.[8–11,25,27] However, a single tool to measure medication adherence is insufficient, further studies which using more than one validated tool for measurement of medication adherence is recommended.

History of ADR, concurrent use of OTC drugs, and higher TGDS scores were associated with poor medication adherence in this study. Patients who had experienced ADR were more likely to be wary of medication and disappointed with their treatment results, leading to poor compliance.[27,29] The prevalence of OTC druguse was 44.4% in this study, which is comparable to that found in a study in a hypertensive clinic in the UK (43.1%).[30] However, data with regard to OTC drug use and compliance are limited, and findings of previous studies have varied. Previous studies in which a connection has been found have suggested that it may be due to the OTC drugs reducing patients' perceived need for prescription medication.[30,31] Over-the-counter drugs also tend to have fewer side effects, are low cost (even though they are not covered by the Thailand's universal healthcare scheme), and are easier to obtain. However, some studies have found no correlation between OTC drug use and compliance, except in some subgroups.[32,33] Further studies are thus needed to clarify this potential association. We also found that depression as measured using the TGDS was related to poor compliance, a finding that is supported by several previous studies.[3,34,35] One cohort study in older adults with hypertension found that depressed patients were an estimated 1.96 times more likely to be non-adherent than non-depressed patients,[35] and meta-analysis similarly found that these patients were 1.76 times more likely to be non-adherent.[34] The supporting evidence showed that a self-report adherence like the MMAS-8 would apprehend other behaviors which may be more vulnerable to the consequences of depression.[34]

Medication adherence can improve outcomes, while poor adherence can lead to severe health and treatment consequences for certain patients.[26,32] Patients who exhibit risk factors described in this study should receive more intensive monitoring for medication adherence, and effective strategies to improve compliance should be implemented by healthcare policy makers. Physicians should thoroughly consider geriatric outpatients' history of ADR, review all of their current prescriptions and OTC drugs, and perform screening for depression. However, in a traditional clinic, physicians and nurses might not have time for regular list of all medications including herbals and other complementary drugs, the pharmacists should expand their role in the medication reconciliation process and the use of a computerized medication profile since it is normally believed to provide more accuracy than paper-based medical record. Finally, this process requires verification with the patients about their uses of the prescribed medications.[36,37] Additionally, the physicians should consider simplified prescription regimens and educate patients and their caregivers about indications and possible side effects, especially if those patients suffer from cognitive and/or physical impairment. As not all OTC medications are safe, effective monitoring and pharmacological/nonpharmacological interventions are essential.[12,30,32,35]

Several limitations of this study should be addressed. First, several collected data were self-reported which may have led to under-reporting and recall bias. For example, a history of ADR or the data on the MMAS-8; in some cases, the researchers had to clarify the questions for patients due to sensory issues. Second, this study was conducted in an internal medicine outpatient clinicat a tertiary care hospital, in which patients are more likely to have complex comorbid diseases and multiple prescriptions, making it difficult to generalize to other healthcare settings. Third, selection bias might be occurred due to a convenience sampling method that was used to enroll the participants so it could affect generalizability of the findings. Forth, according to the definition of ADR in this study, reporting bias might be occurred due to the period of recall is not part of the definition stated as different patients might refer to different periods of recall. Additionally, different people might interpret the definition given different and report ADR to different extent. Fifth, the median age of the participants was 69 years which are relatively young for older adults. The findings: therefore, could represent the results in the young-old population. Sixth, some factors which influence medication adherence did not measure in this study such as healthcare system factors (eg. lack of medication review, lack of patient education, and lack of community nursing services to pack medication), and healthcare provider factors (eg. poor communication, lack of involvement of patients, lack of confidence in physician's professionalism, lack of trust, lack of medication review, and prescription by non-specialist, and dissatisfaction with doctor visits).[3] Finally, the MMAS-8 was developed in hypertensive patients, and while hypertension was the most common disease in this study, its ability to evaluate medication adherence in patients with multiple comorbidities might be limited.

5. Conclusion

The rate of good medication adherence among the geriatric outpatients with chronic illnesses examined in this study was low. History of ADR, concurrent use of OTC medication, and higher TGDS scores were associated with poor medication adherence. Interventions to improve adherence could focus on these factors in at-risk patients including regularly assess patients' ADR status, OTC use and screen for depression. Early recognition of patients with poor adherence and the implementation of appropriate strategies are vital for improving healthcare management and reducing unfavorable outcomes.

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Completing interests

The authors have no potential conflicts of interest to declare with respect to the authorship of this manuscript.

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