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Medication Adherence and Lifestyle Burden in Adults with Generalized Epilepsy Receiving Monotherapy or Polytherapy

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Abstract

Objective: Medication adherence is a major determinant of seizure control in epilepsy. This study aimed to compare adherence between patients receiving antiseizure medication monotherapy and polytherapy, identify item-level non-adherence behaviors that differ between groups, and evaluate whether a structured lifestyle checklist provides additional explanatory value beyond treatment complexity.

Methods: This cross-sectional outpatient study included 200 adults with generalized epilepsy, comprising 100 patients treated with monotherapy and 100 treated with polytherapy. Adherence was assessed using a reverse-coded 8-item Morisky Medication Adherence Scale (MMAS-8), with higher total scores indicating worse adherence. The dataset also included age, monthly seizure frequency, adverse-effect status, daily drug count, and an 8-item lifestyle checklist. Group comparisons, Spearman correlation analyses, and two multivariable linear regression models with HC3 robust standard errors were used.

Results: Polytherapy was associated with worse reverse-coded adherence compared with monotherapy [median 3.0 (interquartile range 2.0-3.0) vs. 2.0 (1.0-2.0); $p<0.001$]. The most prominent item-level differences were forgetting medication while away from home (35% vs. 8%, $p<0.001$) and difficulty remembering medication (34% vs. 8%, $p<0.001$). Lifestyle burden was higher in the polytherapy group and was correlated with worse adherence (Spearman $r=0.666$, $p<0.001$). In the extended model, polytherapy [$\beta=0.487$, 95% confidence interval (CI) 0.244-0.730, $p<0.001$] and lifestyle checklist total score ($\beta=0.434$ per point, 95% CI 0.338-0.531, $p<0.001$) were independently associated with poorer adherence.

Conclusion: Polytherapy and greater lifestyle burden were associated with poorer self-reported medication adherence. Because the MMAS-8 has not been specifically validated in a Turkish epilepsy population and the 8-item lifestyle checklist has not undergone formal psychometric validation, these findings should be interpreted cautiously and regarded as exploratory and hypothesis-generating.

Keywords: Epilepsy, antiseizure medication, adherence, MMAS-8, polytherapy, lifestyle

INTRODUCTION

Medication adherence is one of the most important determinants of seizure control in epilepsy and, in routine care, one of the most vulnerable determinants. Breakthrough seizures, emergency visits, injuries, loss of independence, and avoidable health care utilization may follow missed doses or inconsistent medication-taking behavior. The clinical challenge is that non-adherence rarely presents openly. Instead, it often appears as a lack of efficacy, which may prompt the clinician to follow a familiar sequence: dose escalation, addition of another antiseizure medication, or adjustment of dosing frequency.

Our initial clinical observation was that this reflex pathway does not always address the underlying reason for persistent seizures. In outpatient neurology practice, some patients report seizure recurrence following periods of sleep deprivation, stress, intensive screen exposure, excessive caffeine intake, irregular meals, dehydration, alcohol exposure, or repeated disruption of daily routines. Others experience difficulties with adherence when away from home or when increasingly complex medication schedules must be integrated into work, caregiving, school, or transportation demands. When these domains are not systematically explored, the next therapeutic step may become pharmacologic escalation rather than an evaluation of whether the current treatment plan is practically sustainable.

The existing literature on epilepsy adherence supports the clinical relevance of treatment burden, although findings remain heterogeneous. Sweileh et al. used the 8-item Morisky Medication Adherence Scale (MMAS-8) in adults with epilepsy and demonstrated that poorer self-reported adherence is associated with lower treatment satisfaction and worse seizure control.[1] Dayapoğlu et al.[2] showed that low adherence may coexist with negative beliefs about medication, while Narducci et al.[3] emphasized the broader contribution of mood

symptoms, resilience, and quality-of-life domains to medication-taking behavior. Collectively, these studies suggest that adherence is not solely a pharmacologic variable but a behavioral outcome arising from the interaction of regimen design, cognition, beliefs, psychological distress, and routine stability.

Intervention studies support a similar perspective. A Cochrane review by Al-Aqeel et al.[4] concluded that reminder-based and mixed behavioral interventions may improve adherence in epilepsy, although the evidence remains limited and methodologically diverse. Jung et al.[5] reported improved satisfaction and adherence after switching selected patients from immediate-release to once-daily extended-release levetiracetam, reinforcing the concept that treatment simplification may be as important as pharmacologic potency in real-world settings. At the same time, epilepsy care may benefit from a broader chronic disease framework. For conditions such as diabetes and hypertension, contemporary guidelines emphasize lifestyle optimization, patient education, medication review, and regimen simplification as core components of disease control rather than optional considerations.[6-8] A similar perspective may be relevant to epilepsy, where seizure threshold is sensitive to sleep deprivation and, in some patients, to excessive stimulant intake.[9,10]

Preliminary analyses of the present dataset demonstrated that polytherapy was associated with worse reverse-coded adherence scores, and that the most discriminating item-level problems were related to memory-dependent behaviors rather than intentional discontinuation. Building on these findings, the study incorporated a structured lifestyle checklist to move beyond clinical assumptions toward measurable variables. This approach enabled evaluation of a more clinically relevant model: not only whether polytherapy is associated with poorer adherence, but also whether lifestyle burden coexists with treatment complexity and independently contributes to adherence outcomes.

Accordingly, the aims of the present study were fourfold: (1) to compare self-reported adherence between monotherapy and polytherapy groups; (2) to identify specific Morisky scale items associated with the greatest difficulties; (3) to compare lifestyle burden between groups and determine which domains differ; and (4) to assess whether lifestyle burden is associated with adherence after adjustment for age, seizure frequency, adverse effects, and daily drug count.

METHODS

This cross-sectional observational study was conducted among adult patients with generalized epilepsy who were diagnosed according to the International League Against Epilepsy (ILAE) criteria and were consecutively recruited from the high-volume outpatient neurology clinic in the Department of Neurology at Adıyaman University Training and Research Hospital.

MAIN POINTS

- Polytherapy was associated with poorer self-reported medication adherence than monotherapy.
- Memory-dependent adherence problems accounted for the primary item-level differences between the treatment groups.
- Burden on the lifestyle checklist was associated with worse adherence, but the findings from this non-validated checklist should be considered exploratory.

The analytic sample comprised 200 consecutive patients, including 100 treated with monotherapy and 100 treated with polytherapy. Data collection was performed between May 1, 2022, and August 1, 2022; analysis was conducted between August 1, 2022, and October 1, 2022.

Inclusion criteria were: age ≥18 years, diagnosis of generalized epilepsy based on ILAE criteria, and treatment with stable antiseizure medication (monotherapy or polytherapy) for at least 6 months. Exclusion criteria included a diagnosis of schizophrenia, bipolar disorder, or intellectual disability; an inability to reliably complete the questionnaire; recent changes in antiseizure medication regimen within the last 3 months; and incomplete or unreliable data. All data were collected through face-to-face structured interviews.

The study protocol was approved by the Adıyaman University Non-Interventional Clinical Research Ethics Committee (approval no: 2022/4-5; date: April 20, 2022), and all participants provided informed consent prior to inclusion.

The dataset included responses to 8 adherence items derived from the Morisky medication adherence framework,[11] together with the total adherence score, age, monthly seizure frequency, adverse-effect status, and daily drug count. In the current dataset, adherence items were reverse-coded, so that a value of 1 indicated problematic medication-taking behavior and higher total scores indicated worse adherence. All analyses and interpretations were performed accordingly. Item-level analyses treated each binary item as indicating the presence or absence of a problematic adherence behavior.

A structured 8-item lifestyle checklist was administered. The checklist was developed to record clinically relevant, lifestyle-related exposures described in the epilepsy literature, including sleep, stimulant intake, meal regularity, hydration, stress, screen exposure, and non-drug triggers.[9,10,12,13]

The checklist recorded whether, during the previous month, the patient reported any of the following: recurrent sleep reduction (fewer than 6 hours of sleep at least twice per week); fragmented night sleep; more than one hour of screen exposure before bedtime; marked daily stress or anxiety; consumption of more than two caffeinated drinks per day; skipped meals or irregular eating; perceived inadequate hydration; and exposure to non-drug seizure triggers (e.g., bright light, intense screen exposure, alcohol, or extreme fatigue). The checklist total score was calculated as the sum of endorsed items, with higher values representing a greater burden of lifestyle-related risk factors.

The primary outcome was the reverse-coded adherence total score. Secondary analyses included frequencies of individual adherence items, the lifestyle checklist total score, and frequencies of individual lifestyle items.

Statistical Analysis

Age was summarized as mean ± standard deviation and compared using Welch's t-test. Non-normally distributed continuous variables were summarized as medians (interquartile ranges) and compared using the Mann-Whitney U test. Categorical variables

were compared using the chi-square test or Fisher's exact test, as appropriate. Spearman's correlation coefficient was used to assess the relationship between lifestyle burden and adherence. Two multivariable linear regression models with HC3 robust standard errors were fitted: the first included treatment group, age, monthly seizure frequency, adverse-effect status, and daily drug count; the second additionally included lifestyle checklist total score. Statistical significance was set at $p<0.05$. Statistical analyses were performed using Python (Python Software Foundation, Wilmington, DE, USA) with the pandas, SciPy, and statsmodels libraries.

RESULTS

The groups were similar in age, monthly seizure frequency, and prevalence of adverse effects, while the daily drug count was higher in the polytherapy group (Table 1). Reverse-coded MMAS-8 total scores were higher in the polytherapy group ($p<0.001$; Figure 1).

At the item level, the clearest between-group differences were observed for forgetting medication when away from home and difficulty remembering medication (both $p<0.001$; Table 2). Intentional discontinuation behaviors did not differ meaningfully between groups.

The Lifestyle checklist total score was higher in the polytherapy group ($p<0.001$). Excess caffeine intake, skipped or irregular meals, and exposure to non-drug triggers differed significantly between groups (Table 3). Lifestyle burden was correlated with poorer adherence both in the full cohort (Spearman $r=0.666$, $p<0.001$; Figure 2) and within each treatment group.

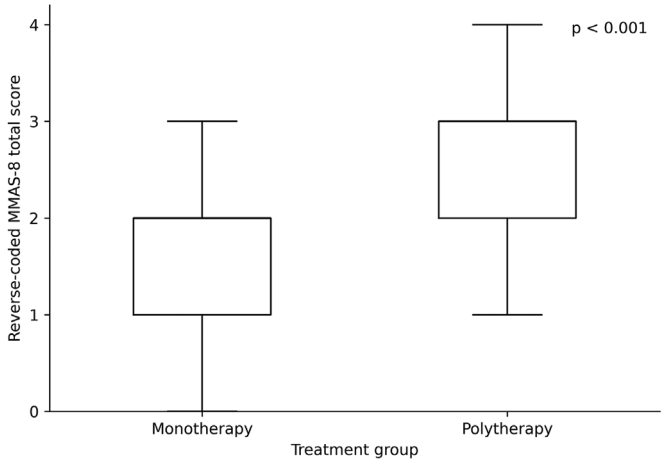


Figure 1. Reverse-coded MMAS-8 total score by treatment group. Higher scores indicate worse adherence. The polytherapy group showed an upward shift in the score distribution relative to the monotherapy group
MMAS-8: 8-item Morisky Medication Adherence Scale

In Model 1, polytherapy remained associated with worse adherence [$\beta=0.844$, 95% confidence interval (CI) 0.554-1.134, $p<0.001$]. After lifestyle burden was added (Model 2), both polytherapy ($\beta=0.487$, 95% CI 0.244-0.730, $p<0.001$) and the lifestyle checklist total score ($\beta=0.434$ per point, 95% CI 0.338-0.531, $p<0.001$) were associated with worse adherence; the model R^2 increased from 0.244 to 0.495 (Table 4).

Table 1. Baseline characteristics, adherence, and lifestyle burden by treatment group

Variable	Monotherapy (n=100)	Polytherapy (n=100)	p-value
Age, mean ± SD	39.98±15.58	40.64±15.43	0.764
Monthly seizure frequency, median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.223
Any adverse effect, n (%)	39 (39.0)	48 (48.0)	0.254
Daily drug count, median (IQR)	2.0 (1.0-2.0)	3.0 (2.0-4.0)	<0.001
Reverse-coded MMAS-8 total, median (IQR)	2.0 (1.0-2.0)	3.0 (2.0-3.0)	<0.001
Lifestyle checklist total, median (IQR)	2.0 (2.0-3.0)	3.0 (2.0-4.0)	<0.001

IQR: Interquartile range, SD: Standard deviation, MMAS-8: 8-item Morisky Medication Adherence Scale

Table 2. Item-level MMAS-8 non-adherence patterns

MMAS-8 item	Mono n	Mono %	Poly n	Poly %	p-value
Forgetting medication in general	74	74.0	86	86.0	0.052
Treatment disruption due to forgetting	13	13.0	19	19.0	0.335
Stopping medication when feeling worse	9	9.0	11	11.0	0.814
Forgetting medication when away from home	8	8.0	35	35.0	<0.001
Missing the previous day's dose	4	4.0	3	3.0	1.000
Stopping medication when disease seems controlled	12	12.0	14	14.0	0.833
Finding daily medication burdensome	42	42.0	50	50.0	0.321
Difficulty remembering medication	8	8.0	34	34.0	<0.001

MMAS-8: 8-item Morisky Medication Adherence Scale

DISCUSSION

This study extends prior observations by showing, within an outpatient sample, that patients receiving polytherapy had worse reverse-coded adherence than those receiving monotherapy, with the most pronounced differences observed in memory-dependent behaviors.

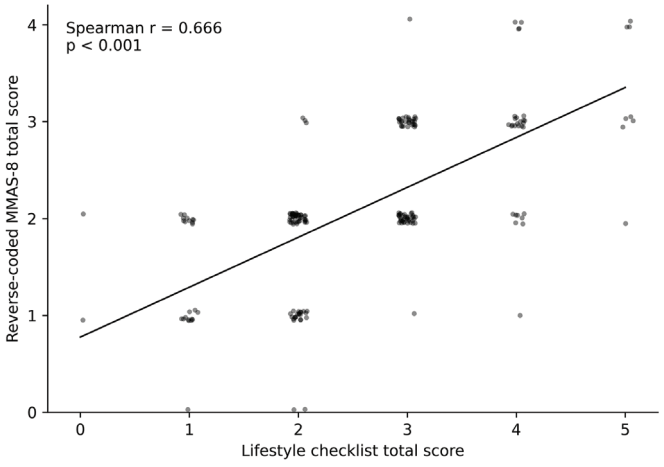


Figure 2. Association between lifestyle burden and reverse-coded adherence. Each point represents one patient. Higher lifestyle checklist totals were associated with poorer adherence in the full cohort (Spearman r=0.666, p<0.001)
MMAS-8: 8-item Morisky Medication Adherence Scale

The attenuation of the polytherapy coefficient after the inclusion of lifestyle burden suggests shared variance between treatment complexity and behavioral factors, rather than an effect attributable to drug complexity alone. This supports a more integrative outpatient model in which regimen burden and lifestyle burden may coexist.

The item-level findings were not dominated by intentional discontinuation but rather by memory-dependent behaviors, such as forgetting medication when away from home and failing to remember doses. These findings highlight the potential role of cognitive load and routine disruption in real-world adherence. Greater treatment complexity may coexist with these difficulties, but the cross-sectional design does not permit determination of directionality.

In the present cohort, excess caffeine intake, irregular eating patterns, and exposure to non-drug triggers were more frequent in the polytherapy group. These associations should not be interpreted as causal; rather, they indicate that treatment complexity and potentially destabilizing daily exposures may cluster in the same patients.

The Turkish MMAS-8 was validated in patients with hypertension rather than in those with epilepsy.[14] However, MMAS-8 has previously been used in Turkish patients with epilepsy[2] and has also undergone epilepsy-specific validation in a Chinese population.[15]

Table 3. Lifestyle checklist domains by treatment group

Lifestyle domain	Mono n	Mono %	Poly n	Poly %	p-value
Reduced sleep (<6 h at least twice weekly)	27	27.0	24	24.0	0.746
Sleep fragmentation	18	18.0	15	15.0	0.703
>1 h screen exposure before sleep	31	31.0	40	40.0	0.237
Marked daily stress/anxiety	55	55.0	60	60.0	0.567
>2 caffeinated drinks per day	19	19.0	35	35.0	0.017
Skipped meals/irregular eating	13	13.0	29	29.0	0.009
Perceived inadequate hydration	18	18.0	25	25.0	0.302
Non-drug trigger exposure	49	49.0	70	70.0	0.004

Table 4. Multivariable regression models for reverse-coded adherence total score

Predictor	Model 1 β	Model 1 95% CI	Model 1 p	Model 2 β	Model 2 95% CI	Model 2 p
Polytherapy (vs. monotherapy)	0.844	0.554 to 1.134	<0.001	0.487	0.244 to 0.730	<0.001
Lifestyle checklist total	-	-	-	0.434	0.338 to 0.531	<0.001
Age (years)	-0.001	-0.008 to 0.006	0.779	-0.001	-0.006 to 0.005	0.868
Monthly seizure frequency	0.035	-0.050 to 0.119	0.423	0.071	-0.004 to 0.145	0.065
Any adverse effect (yes)	-0.014	-0.220 to 0.192	0.897	0.005	-0.169 to 0.179	0.955
Daily drug count	-0.030	-0.165 to 0.105	0.660	-0.017	-0.125 to 0.092	0.765
Model R^2	0.244	-	-	0.495	-	-
Adjusted R^2	0.224	-	-	0.479	-	-

CI: Confidence interval

The 8-item lifestyle checklist was not a validated psychometric scale but rather a cumulative record of lifestyle-related exposures. Similar questionnaire-based epilepsy studies have assessed overlapping domains, including diet, caffeine, sleep, stress, screen exposure, and other daily behaviors.[12,13] Therefore, the checklist findings should be considered exploratory and hypothesis-generating.

These observations are consistent with evidence from adherence-enhancing interventions suggesting that simplifying treatment regimens and addressing behavioral factors may improve adherence.[4,5]

Another observation was that age, adverse effects, and daily drug count were not independently associated with adherence in the multivariable models. This finding suggests that medication-taking behavior may not be fully captured by simple measures of medication burden.

From a clinical perspective, recurrent seizures may justify a structured assessment of sleep, caffeine intake, meal regularity, hydration, daily routine, and missed doses, alongside a pharmacologic review, rather than assuming that treatment escalation is always required.

Study Limitations

This study should be interpreted in light of several limitations. It was conducted at a single center and relied on self-reported measures rather than objective adherence data, such as serum drug levels or electronic monitoring. The Turkish MMAS-8 has not been specifically validated in patients with epilepsy, and the 8-item lifestyle checklist has not undergone formal reliability or validity testing; therefore, the lifestyle-related findings, in particular, should be regarded as exploratory.

Epilepsy duration, disease severity, drug-resistant epilepsy status, and the specific antiseizure medication classes and their adverse-effect profiles were not measured in the present analysis. These factors may confound the observed associations and should be accounted for in prospective studies. Socioeconomic status and psychiatric comorbidities were not included.

Despite these limitations, the study has several strengths. Consecutive recruitment, a balanced sample, structured lifestyle assessment, item-level adherence analysis, and multivariable modeling provide a clinically relevant view of pharmacologic and behavioral factors associated with adherence.

CONCLUSION

In this cross-sectional adult epilepsy sample, polytherapy was associated with worse reverse-coded adherence compared with monotherapy, with the most prominent differences observed in memory-dependent behaviors such as forgetting medication while away from home and forgetting doses.

Lifestyle-checklist burden was also associated with poorer adherence after multivariable adjustment. These findings should not be interpreted as evidence of causality.

Because the MMAS-8 has not been specifically validated in a Turkish epilepsy population and the 8-item lifestyle checklist is a non-validated exploratory measure, the findings should be interpreted cautiously and regarded as hypothesis-generating. Prospective studies incorporating epilepsy duration, disease severity, drug-resistance status, and specific antiseizure medication classes and adverse-effect profiles are needed.

Ethics

Ethics Committee Approval: The study protocol was approved by the Adıyaman University Non-Interventional Clinical Research Ethics Committee (approval no: 2022/4-5; date: April 20, 2022).

Informed Consent: All participants provided informed consent prior to inclusion.

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For transparency, the authors note that an artificial intelligence assisted language model (ChatGPT, OpenAI) was utilized to support text editing and language correction. This assistance was limited to linguistic refinement; all scientific content, critical analysis, and final editorial decisions were made exclusively by the authors.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.B.E., Concept: A.B.E., Design: A.B.E., Data Collection or Processing: A.B.E., Analysis or Interpretation: A.B.E., A.Z.A.T., Literature Search: A.B.E., A.Z.A.T., Writing: A.B.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Sweileh WM, Ihbesheh MS, Jarar IS, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *Epilepsy Behav.* 2011;21(3):301-305. **[Crossref]**
2. Dayapoğlu N, Turan GB, Özer Z. Evaluation of medication adherence and medication beliefs among patients with epilepsy. *Epilepsy Behav.* 2021;124:108366. **[Crossref]**
3. Narducci F, Lanzone J, Ricci L, et al. Determinants of medication adherence in people with epilepsy: a multicenter, cross-sectional survey. *Epilepsy Behav.* 2023;138:109029. **[Crossref]**
4. Al-Aqeel S, Gershuni O, Al-Sabhan J, Hiligsmann M. Strategies for improving adherence to antiepileptic drug treatment in people with epilepsy. *Cochrane Database Syst Rev.* 2020;10(10):CD008312. **[Crossref]**
5. Jung SY, Yi YY, Kang JW. Once-daily extended-release levetiracetam improves medication compliance in adolescent epilepsy patients. *Ann Child Neurol.* 2021;29(2):61-67. **[Crossref]**
6. American Diabetes Association Professional Practice Committee. Standards of care in diabetes-2025. *Diabetes Care.* 2025;48(Suppl 1). **[Crossref]**
7. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: comprehensive type 2 diabetes management algorithm - 2023 update. *Endocr Pract.* 2023;29(5):305-340. Erratum in: *Endocr Pract.* 2023;29(9):746. Erratum in: *Endocr Pract.* 2023;29(12):1025. **[Crossref]**
8. McEvoy JW, McCarthy CP, Bruno RM, et al.; ESC Scientific Document Group. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J.* 2024;45(38):3912-4018. Erratum in: *Eur Heart J.* 2025;46(14):1300. Erratum in: *Eur Heart J.* 2025;46(45):4949. **[Crossref]**

9. Dell'Aquila JT, Soti V. Sleep deprivation: a risk for epileptic seizures. *Sleep Sci.* 2022;15(2):245-249. **[Crossref]**
10. Asadi-Pooya AA, Zeraatpisheh Z, Rostaminejad M, Damabi NM. Caffeinated drinks, fruit juices, and epilepsy: a systematic review. *Acta Neurol Scand.* 2022;145(2):127-138. **[Crossref]**
11. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens (Greenwich).* 2008;10(5):348-354. Retraction in: *J Clin Hypertens (Greenwich).* 2023;25(9):889. Retraction in: *J Clin Hypertens (Greenwich).* 2023;25(9):890. **[Crossref]**
12. Saengsuwan J, Boonyaleepan S, Tiamkao S; Integrated Epilepsy Group. Diet, exercise, sleep, sexual activity, and perceived stress in people with epilepsy in NE Thailand. *Epilepsy Behav.* 2015;45:39-43. **[Crossref]**
13. Gerges SE, Badros RY, Mohamed H. The impact of sleep patterns, screen exposure and lifestyle factors on seizure frequency in epilepsy: an observational study. *Egypt J Neurol Psychiatry Neurosurg.* 2026;62:85. **[Crossref]**
14. Hacıhasanoğlu Aşılar R, Gözüm S, Çapık C, Morisky DE. Reliability and validity of the Turkish form of the eight-item Morisky medication adherence scale in hypertensive patients. *Anadolu Kardiyol Derg.* 2014;14(8):692-700. **[Crossref]**
15. Yang A, Wang B, Zhu G, et al. Validation of Chinese version of the Morisky medication adherence scale in patients with epilepsy. *Seizure.* 2014;23(4):295-299. **[Crossref]**