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Antiepileptic drug adherence and persistence in children with epilepsy attending a large tertiary care children's hospital

Yon-Kyong Lee [1], Young-Mi Ah [1], Yun Jung Choi [1], Yoon Sook Cho [2], Ki Joong Kim [3], Ju-Yeun Lee [1]

[1] College of Pharmacy, Institute of Pharmaceutical Science and Technology, Hanyang University, Gyeonggi-do,
[2] Department of Pharmacy, Seoul National University Hospital, Seoul,
[3] Division of Pediatric Neurology Department of Pediatrics, Seoul National University Children's Hospital, Seoul, South Korea

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ABSTRACT – We aimed to evaluate antiepileptic drug treatment persistence and adherence in paediatric epilepsy patients and investigate the association between medication-taking behaviours and clinical outcome.
Methods. Medical and prescription records of newly treated paediatric epilepsy patients, aged 1-18 years who initiated antiepileptic drug monotherapy in a tertiary teaching hospital, were retrospectively reviewed. The rates of overall treatment, non-persistence, a treatment gap >60 days, and adherence, as measured by a medication possession ratio ≥0.8, were assessed. The relationship between non-adherence and clinical outcome, defined as an emergency department visit or hospitalisation due to seizure-related reasons, was analysed.
Results. A total of 1,172 patients met the inclusion criteria. The proportion of patients who were both persistent and adherent at one year was 70.14% and decreased to 56.83% at two years. Patients who started an antiepileptic drug at one year of age, took older generation antiepileptic drugs as the initial treatment, and those diagnosed with localized seizures were less likely to be adherent to and persistent with overall antiepileptic drug treatment. Patients who were non-adherent to antiepileptic drug treatment were at an increased risk of hospitalisation or emergency department visits for seizure-related reasons (adjusted HR 2.10, 95% CI 1.25-3.55).
Conclusions. This large population study shows that 70% of paediatric epilepsy patients were persistent with and adherent to antiepileptic drugs after one year of treatment and confirms that non-adherence to antiepileptic drug treatment is an important factor in seizure-related clinical outcome.

Key words: persistence, adherence, antiepileptic drug, children, breakthrough seizures, emergency, newly diagnosed epilepsy

Correspondence:
Ju-Yeun Lee
College of Pharmacy,
Institute of Pharmaceutical Science and Technology, Hanyang University,
55 Hanyangdaehak-ro, Sangnok-gu,
Ansan Gyeonggi-do 15588, South Korea
<jypharm@hanyang.ac.kr>

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Epilepsy, a disease of the brain characterised by recurrent unprovoked seizures, is among the most common and serious, but treatable, neurological disorders in childhood (Fisher *et al*., 2014). The World Health Organization (WHO) estimates that 4-10 of every 1,000 people in the general population have epilepsy (WHO, 2016). The prevalence of treated epilepsy in Korea has been estimated to be 2.41 in every 1,000 people, with a higher prevalence in children (Lee *et al*., 2012).

Antiepileptic drug (AED) therapy is the primary treatment for epilepsy. By controlling seizures, AEDs can substantially impact a patient's health-related quality of life. Although AEDs may not cure the condition, patients may remain seizure-free with an appropriate regimen, and those who are seizure-free for two or more years with AED treatment can be withdrawn from therapy. Up to 70% of newly diagnosed patients with epilepsy were observed to become seizure-free when the most effective AED regimen was followed (Sander, 2004).

Two major components of medication-taking behaviour are persistence and adherence. Persistence is a measure of treatment continuity, the length of time from the day of treatment start to its discontinuation. Adherence reflects the extent to which patients conform to their prescriptions during the time they are persistent with treatment (Cramer *et al*., 2008). Proper medication-taking behaviour is vital to controlling seizures and is correlated with clinical outcome in epilepsy patients. Hovinga *et al*. showed that non-adherence to AEDs in adults was associated with reduced seizure control and a lowered quality of life (Hovinga *et al*., 2008). Furthermore, poor adherence has been linked to an increased risk of mortality, higher incidence of emergency department visits, hospital admission, and increased healthcare costs in the adult epilepsy population (Davis *et al*., 2008; Faught *et al*., 2008). Modi *et al*. prospectively collected adherence and seizure data and showed that short-term and long-term non-adherence was a significant predictor of seizure events in 109 and 124 children with newly diagnosed epilepsy, respectively (Modi *et al*., 2014a; 2014b).

Unfortunately, reported adherence to medication in paediatric epilepsy is low. Non-adherence to AEDs is estimated to range from 28% to 59% with different methods (Asadi-Pooya, 2005; Modi *et al*., 2011a, 2011b; Liu *et al*., 2013; Shah *et al*., 2013; Gabr and Shams, 2015; Lie *et al*., 2015; Shetty *et al*., 2015). Aylward *et al*. reported that non-persistence at one year was 26.6% in children with epilepsy (Aylward *et al*., 2015). Age, seizure type, depressive mood, duration of illness, age of mother, number of administered drugs, seizure frequency, socioeconomic status, and some family factors have been suggested to be related to medication-taking behaviour in the paediatric population in previous studies (Liu *et al*., 2013; Shah *et al*., 2013; Aylward *et al*., 2015; Gabr and Shams, 2015; Loiselle *et al*., 2015; Shetty *et al*., 2015).

Medication-taking behaviours in prior studies were examined in small cohorts, and assessed using patient self-reporting, questionnaires, drug level monitoring, or electronic monitoring caps (Asadi-Pooya, 2005; Modi *et al*., 2011a, 2011b, 2014b; Liu *et al*., 2013; Shah *et al*., 2013; Gabr and Shams, 2015; Lie *et al*., 2015), which potentially affects patient medication-taking behaviour. These results do not reflect the long-term medication-taking behaviour in the real-world setting. On the other hand, retrospective analysis using prescription data could reflect patient medication-taking behaviour in the real-world setting, as there is no influential intervention at the time of taking medication. Despite the shortfall that measuring adherence based on prescription data may only indicate medication acquisition instead of medication consuming pattern (Andrade *et al*., 2006), retrospective analysis using prescription data is one of the most widely adopted methods as it enables assessment in a large population over a long period of time (Steiner and Prochazka, 1997). The long-term follow-up has significant consequences since epilepsy is a disease state which requires long-term medication, and poor adherence is reported to contribute to negative clinical outcome.

Long-term persistence with AEDs in real-world paediatric populations using claims data has been evaluated in limited studies (Shetty *et al*., 2015), and there are no published studies in which emergency department (ED) visits or hospital admissions were examined in the context of AED adherence outcomes in the paediatric population.

This study aimed to evaluate medication-taking behaviours associated with persistence and adherence and identify predictive factors in relation to clinical outcome in a large number of paediatric patients attending a tertiary care hospital.

Methods

Study design and patient selection

This study was a retrospective cohort study using medical records and prescription data retrieved from the electronic database of the Children's Hospital of Seoul National University Hospital (SNUH). SNUH Children's Hospital is a prominent 285-bed hospital treating 500 ambulatory paediatric patients a day.

Newly treated paediatric epilepsy patients, aged 1-18 years who initiated AED monotherapy from 1st January 2008 to 30th June 2011, were included.

Diagnostic codes for epilepsy or seizures from the tenth version of the International Classification of Diseases and Related Health Problems (ICD-10), G40*(epilepsy) and G41*(status epilepticus), were used to identify patients with epilepsy in the present study. The study was limited to newly treated AED users by excluding patients who were prescribed any AED within the year prior to the date of first AED prescription (index date). Only patients who started AED treatment with monotherapy were included in order to minimize the possibility of including transferred patients who had undergone long-term treatment in another hospital.

Patients who were prescribed AEDs for the treatment of diseases other than epilepsy, patients hospitalised for more than seven days within the first year of AED initiation (to exclude severely ill patients due to other causes), and patients who had received fewer than two outpatient prescriptions (making the calculation of adherence impossible) were excluded from the analysis. The number of patients who received AED prescription only once may therefore be considered as primary non-adherent, and were also identified and excluded from the study.

The patient medical records and prescription data were followed for at least three years from the date of first AED prescription. Approval from the Institutional Review Board at SNUH was obtained prior to collecting and analysing the data (Approval Number: H-1305-633-492).

Antiepileptic drug treatment persistence and adherence

Overall, AED treatment persistence over the three years after AED initiation was calculated. A patient was considered "persistent" until observation of a sixty-day prescription gap in days supplied with medication. In other words, patients did not have any AED prescription for more than sixty days after termination of any previous medication were categorized as "non-persistent" (*i.e.* discontinued therapy).

As there may have been various reasons for discontinuation of any AED therapy, clinic visit records were tracked in order to identify whether discontinuation was due to a clinical decision. We classified the reasons for treatment discontinuation into two categories: physician-initiated AED discontinuation and patient-initiated AED discontinuation. No further AED prescription by physicians during patient follow-up visits was considered physician-initiated AED discontinuation and absence of further follow-up visits to a clinic was considered as patient-initiated AED discontinuation. If a patient had no record of clinic visits within the study period or came back after a treatment gap of more than one year, their treatment was also categorised as patient-initiated AED discontinuation.

Treatment adherence was estimated according to the prescription record at one, two, and three years after the index date. Adherence was measured using the medication possession ratio (MPR), one of the most widely used measures of adherence (Andrade *et al*., 2006; Raebel *et al*., 2013). MPR was defined as the number of total days covered by all AED prescriptions over the number of days between start and end date of medication supply, according to the last prescription. Calculated MPRs $\geq$1.0 were truncated to 1.0. Patients with an MPR lower than 0.8 were marked as non-adherent. A cut-off point of 0.8 was set based on the threshold that has been widely used in previous studies, including an adherence study in an adult epileptic population (Faught, 2012). Although use of the cut-off point has not been validated in the paediatric epilepsy population, the threshold of 0.8 has been used in 75% of all previous adherence or persistence evaluation studies (Andrade *et al*., 2006).

Demographic and clinical variables

Patient age at treatment initiation, sex, residential area, initial AED, and seizure type were extracted and collected from medical records to identify factors affecting medication-taking behaviour. As recommended by the National Institute of Child Health and Human Development Pediatric Terminology released in July 2011 (Williams *et al*., 2012), patients were categorized into four age groups: 12-24 months (toddler), 2-5 years (early childhood), 6-11 years (middle childhood), and 12-18 years (adolescence). AEDs prescribed for the study population were categorised as older generation AEDs (*i.e.* carbamazepine, ethosuximide, phenobarbital, phenytoin, and valproate) and newer generation AEDs (*i.e.* gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, topiramate, vigabatrin, and zonisamide). Clonazepam was excluded because of its rare use as a monotherapy for epilepsy, as it is more often used for non-epileptic purposes. Epilepsy type was grouped into generalized seizure, localized seizure, and others. Residential area was categorized into city or rural area according to the administrative district, based on the address. The proportion of patients with AED change (addition or switch) over the first six months and over the first year were calculated, respectively.

Clinical outcome evaluation

Clinical outcome was evaluated in patients over the two years following the first year of treatment. This evaluation excluded patients who were lost to

follow-up before the end of the first year. Although the most accurate measure of clinical outcome is seizure frequency, this type of data is difficult to obtain retrospectively due to incomplete documentation in medical records. As a surrogate measure, cases of ED visits or hospitalisation due to seizure-related reasons were assessed as clinical outcomes (Goodman *et al.,* 2012; Shcherbakova *et al.,* 2014). We confirmed that the ED visits or hospitalisation were related to seizures, based on the medical records. For the patients who discontinued AED treatment and never returned to the clinic, the number of days between the date of AED initiation and the last clinic visit was considered as the duration of persistence; data were censored on the date corresponding to the last clinic visit when performing Cox proportional hazard regression in the assessment of clinical outcome.

Statistical analysis

Persistence over a three-year period was presented using Kaplan-Meier curves. Factors affecting medication-taking behaviours (persistence and adherence over two years) were determined using logistic regression analysis. We performed multivariate Cox proportional hazards regression analysis to assess the effect of medication-taking behaviours on clinical outcome incidence with an adjustment for patient age, sex, diagnosis, residence, and initial drug class. All analyses were performed using SAS version 9.4 statistical software (SAS Institute, Inc., Cary, NC).

Results

Demographic characteristics

Of the initially identified 1,502 patients who were prescribed an AED during the study period, patients prescribed an AED for treatment of another disease (*n*=6; 0.40%), patients who were hospitalised for more than seven days within the first year of treatment initiation (*n*=163; 10.85%), and patients who received fewer than two outpatient prescriptions (*n*=161; 10.72%) were excluded from this analysis. The final study population included a total of 1,172 patients.

The characteristics of patient demographics and clinical variables are shown in *table 1*. The mean age at treatment initiation for included patients was 9.06±4.85 years. More than half of the cohort was male. The majority of patients were prescribed a newer generation AED at treatment initiation (69.03%; *n*=809).

A quarter of patients (25.1%) and 30.8% of patients switched or had additional AEDs over the first six months and over the first year, respectively.

Table 1. Patient demographics and treatment characteristics (>n=1172).

Variables	*n* (%)
Age (years)	
1 (toddler)	51 (4.35)
2-5 (early childhood)	208 (17.75)
6-11 (middle childhood)	486 (41.47)
12-18 (adolescent)	427 (36.43)
Sex	
Male	666 (56.83)
Female	506 (43.17)
Residential area	
City	1046 (89.25)
Rural area	126 (10.75)
Parents' educational status (*n*=204)	
≥High school	194 (16.5)
≤Middle school	10 (0.9)
Not available	968 (82.6)
Seizure type	
Localized	495 (42.24)
Generalized	251 (21.42)
Others	426 (36.35)
Initial antiepileptic drug generation	
Older AED	363 (30.97)
Newer AED	809 (69.03)
Initial antiepileptic drug	
Oxcarbazepine	432 (36.86)
Valproate	311 (26.54)
Lamotrigine	162 (13.82)
Topiramate	152 (12.97)
Levetiracetam	52 (4.44)
Vigabatrin	10 (0.85)
Carbamazepine	25 (2.13)
Phenobarbital	9 (0.77)
Diphenylhydantoin	12 (1.02)
Ethosuximide	6 (0.51)
Zonisamide	1 (0.09)

AED: antiepileptic drug

Treatment persistence and adherence

Over the first year, 830 patients (70.82%) were persistent with therapy. These patients continued to have their AED prescriptions issued without a gap of more than 60 days between prescriptions, and the cumulative persistence rate decreased to 57.00% and 40.02% over two and three years, respectively, as shown in *figure 1*. The cumulative discontinuation rate of AED therapy due to clinical reasons increased from 2.22% over one year to 14.76% over three years. The annual rate of treatment discontinuation for clinical reasons was similar over the second year (2.17%) and increased to 18.56% at the third year, but non-persistence or

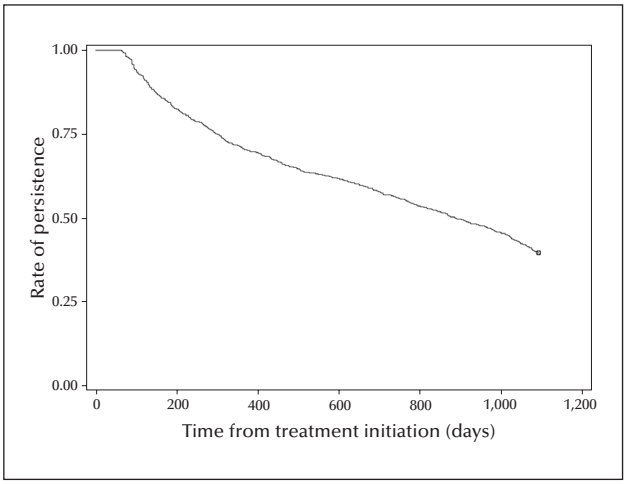


Figure 1. Kaplan-Meier curve for AED treatment persistence over three years.

discontinuation due to patient will peaked in the first year (26.96%) and gradually decreased over the subsequent two years (11.23%), as shown in *figure 2*. A total of 1,074 (91.64%), 1,043 (88.99%), and 1,023 patients (87.29%) were adherent based on a calculated MPR of at least 80%, at one, two, and three years after treatment initiation, respectively. The proportion of patients who were persistent with an MPR ≥80% at one year was 70.14%, and this decreased to 56.83% at two years (*figure 3*).

Factors affecting medication-taking behaviours

Based on multivariate logistic regression analysis, the odds of being adherent and persistent over two years were significantly lower in toddlers (OR 0.26, 95% CI 0.13-0.53) than in adolescents. Yet, the early and middle childhood group did not show a significant difference compared to adolescents. Patients who initially started treatment with a newer AED, relative to older AED initiators (OR 1.89, 95% CI 1.43-2.50), and patients diagnosed with a generalized seizure type (OR 1.45, 95% CI 1.04-2.02), relative to localized seizure types, were more likely to be adherent and persistent. Change of AED medications within six months of treatment initiation did not affect adherence or persistence over two years (*table 2*).

Outcome evaluation

Out of a total number of 1,172 patients, 196 (16.72%) were lost to follow-up within one year of treatment initiation, leaving 976 patients to be included in the

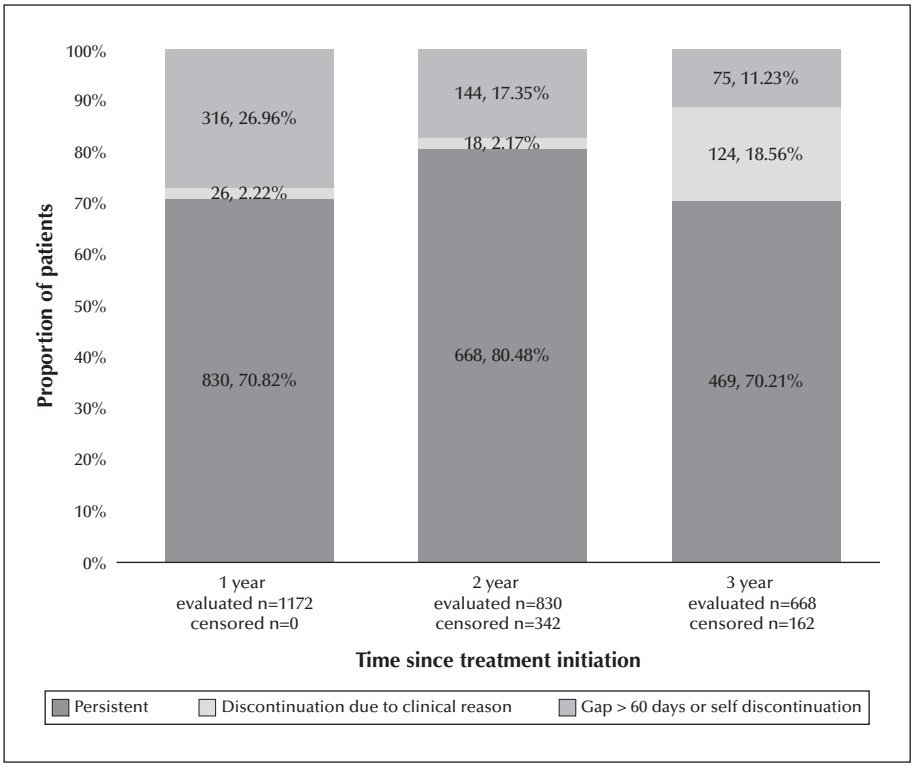
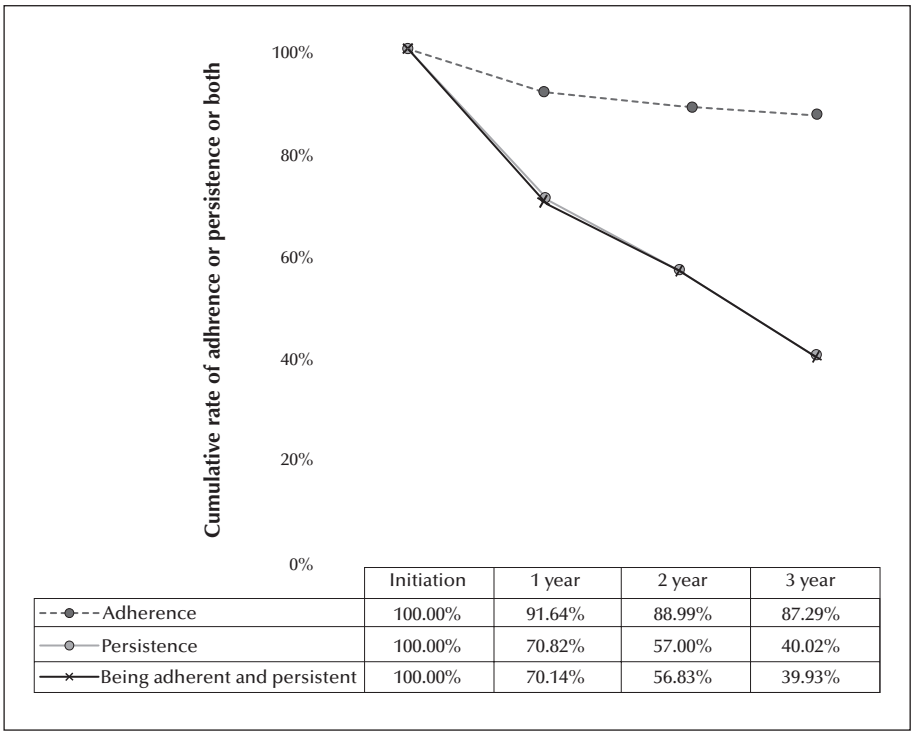


Figure 2. Annual persistence rate at one, two, and three years after AED treatment initiation.



	Initiation	1 year	2 year	3 year
Adherence	100.00%	91.64%	88.99%	87.29%
Persistence	100.00%	70.82%	57.00%	40.02%
Being adherent and persistent	100.00%	70.14%	56.83%	39.93%

Figure 3. Cummulative rate of adherence, and adherence and persistence at one, two, and three years after AED treatment initiation.

clinical outcome evaluation. Among the patients included, a total of 85 patients (8.71%) experienced a clinical complication during the two subsequent years after the first year of treatment: 32 patients (3.28%) after six months, 55 patients (5.64%) after one year, and 77 patients (7.89%) after 18 months. Seizure-related ED visits and hospital admission was reported for 46 and 54 patients at the first and second subsequent year, respectively. Among them, 15 patients had a history of both ED visits and hospital admission.

Multivariate Cox proportional hazards regression analysis revealed that treatment non-adherence at two years significantly increased the risk of hospitalisation or ED visits (adjusted HR 2.10, 95% CI 1.25-3.55).

Discussion

This study assessed antiepileptic drug adherence and persistence in paediatric epilepsy patients using prescription data from a large tertiary hospital with a specialised paediatric care hospital.

The one-year rate of non-persistence with AEDs was shown to be 29.18%, which is similar to the result from a previous study, assessed using an electronic monitoring device in 117 children newly diagnosed with epilepsy (26.6%) (Aylward *et al*., 2015). The true rate of non-persistence might be higher than that based on this study, since 10.72% of the total patients were excluded from the analysis due to lack of further follow-up. We further categorized non-persistence as discontinuation due to clinical decisions or patient choice. Only a small proportion of patients discontinued treatment due to clinical decision by the second year of treatment, but discontinuation due to clinical decisions increased during the third year. This observation is in line with the consensus that treatment can be withdrawn after more than two years of seizure-free status (Beghi *et al*., 2013).

Around 90% of patients showed MPR greater than or equal to 80% (defined as being adherent) at one year, and 87% at three years in this study. The poor persistence rate shown in this study, especially at three years, should not be directly interpreted as poor adherence because AED treatment withdrawn by the treating clinician contributed to the fall in persistence in around 19% of patients.

The adherence rate measured by MPR is higher than that reported from previous studies, ranging from 42-72%, in which different measuring techniques were used. Modi *et al*. reported the initial six-month adherence to AEDs to be 42% in 124 children using electronic monitoring MEMS TrackCap (Modi *et al*., 2011b). A study by Shah *et al*. revealed a one-year overall adherence rate of 67% in 100 epileptic children by measuring AED levels in dried blood spot samples of

Table 2. Factors affecting medication-taking behaviours over two years.

	AED adherence and persistence	
Parameter	**Adjusted odds ratio**	**95% CI**
Age group (years)		
Adolescence (12-18)	1.00	
Middle childhood	0.86	0.66-0.13
Early childhood	0.91	0.64-1.30
Toddler	0.26	0.13-0.53
Sex		
Male	1.00	
Female	0.78	0.61-1.00
Initial antiepileptic drug		
Older generation antiepileptic drug	1.00	
Newer generation antiepileptic drug	1.89	1.43-2.50
Seizure type		
Localized seizure	1.00	
Generalized seizure	1.45	1.04-2.02
Others	1.11	0.85-1.47
Residential area		
City	1.00	
Rural area	0.79	0.48-1.02
AED change within 6 months		
Unchanged	1.00	
Changed	1.13	0.86-1.49

AED: antiepileptic drug; CI: confidence interval

patients (Shah *et al.*, 2013). Asadi-Pooya reported that drug compliance was satisfactory in 72.4% of 181 children and adolescents with epilepsy, as measured by self-reporting (Asadi-Pooya, 2005). A recent study by Shetty *et al.*, the only study that estimated adherence in paediatric epilepsy patients using pharmacy dispensing records, reported that only 30% of patients were more than 90% adherent to AED prescription (Shetty *et al.*, 2015). Studies that assessed adherence with MPR in adult epilepsy patients reported varied non-adherence rates between 26% and 63% (Davis *et al.*, 2008; Faught *et al.*, 2008; Manjunath *et al.*, 2009; Ettinger *et al.*, 2009; Zeber *et al.*, 2010; Shcherbakova *et al.*, 2014). The calculated MPR according to covered prescription supply can be overestimated in patients receiving only a few prescriptions and with early discontinuation of treatment. Based on the relatively high non-persistence rate, the adherence rate observed in this current study might be overestimated, suggesting that persistence should also be considered. We observed that approximately 70% of patients continued AED treatment with an MPR ≥80% at the end of the first year and this decreased to 57% at the end of the second year, relative to the time of treatment initiation. Even when accounting for overestimation, the adherence rate observed in the current study is relatively high and can be partly explained by the characteristics of the hospital setting for the study; a prominent tertiary medical centre, receiving patients from around the country. Patients who make the effort to visit this hospital may have greater awareness of the seriousness of epilepsy and the effects of treatment.

Previous studies suggest that adherence is poor in adolescents with epilepsy (Kyngas, 2000) and decreases as age increases in the paediatric epileptic population (Shetty *et al.*, 2015). This contradicts our results which indicate that low persistence and adherence was more prevalent in toddlers than adolescents. Differences in the population, including age, may partially explain this gap. Previous studies have included prevalent AED users (with a median duration of epilepsy of four years) (Shetty *et al.*, 2015), whereas this study included incident AED users. In addition, age at first AED treatment was used as a variable. There may be a difference in patients' concerns about seizure recurrence between patients who had epilepsy onset in adolescence and those with onset during their first year of life. Some researchers have suggested that age at onset of seizures is one of the risk factors for an increased relapse rate (Altunbasak *et al.*, 1999; Shinnar *et al.*, 1994), however, this remains controversial. Another factor that showed a significant correlation with medication-taking behaviour at initial treatment was the generation of AEDs. Newer generation AEDs were more highly correlated with better medication-taking behaviour. This may be, in part, due to improved adverse event profiles compared to older agents. On the contrary, in a study of adults by Bautista and Rundle-Gonzalez (2012), older generation AEDs showed slightly higher mean MPRs than newer AEDs.

Although previous studies have found that paediatric adherence or persistence to AED therapy was associated with family socio-economic status (Modi *et al.*, 2011b; Aylward *et al.*, 2015), we were not able to directly evaluate socio-economic status due to the inherent characteristics of the data source.

One of the potential important findings of this study is that non-adherence after two years of treatment initiation is a predictor of ED visits or hospitalisation related to seizures. Patients who were non-adherent at two years were twice as likely to visit the ED or be admitted to hospital due to seizures in the second or third year following treatment initiation. The fact that seizure-related ED visits or hospitalisation does not represent seizure frequency and is only partially indicative of poor seizure control, as well as the relatively

small number of patients in this group, prevented us from drawing any conclusions. However, this finding is consistent with previous results showing that adherence to AED treatment is a good predictor of seizure control (Manjunath *et al*., 2009; Kaddumukasa *et al*., 2013; Modi *et al*., 2014a, 2014b; Samsonsen *et al*., 2014; Moura *et al*., 2015).

Most previous studies dealing with adherence or persistence in childhood epilepsy used self-reporting, questionnaires, drug-level monitoring, and electronic devices which hamper long-term evaluation in a large population and may also affect patient behaviour. To the best of our knowledge, this is the first study to evaluate both adherence and long-term persistence of AED therapy in a real-world large-sized paediatric cohort with prescription data. The findings from this study could lead to a better understanding of real-world medication-taking behaviours in childhood epilepsy.

There are, however, several imitations to our study. First, patterns in prescription data may not represent the true situation of patients. By using a prescription record, one assumes that the patient has taken all of the prescribed medication. In reality, the patients may not have obtained the prescribed medication or may not have consumed the obtained medication. This measure may therefore overestimate actual adherence. However, MPR is a validated and widely accepted parameter for computing medication adherence and a convenient tool for analysing a large patient population (Andrade *et al*., 2006; Raebel *et al*., 2013). Secondly, we evaluated data from a single centre. Although the electronic medical record data enabled us to collect various data on patient characteristics, our evaluation of adherence and persistence was limited to medication prescribed by the study institution. Patients who took AEDs prescribed from other medical facilities could not be identified using data from a single medical centre and thus were considered as non-persistent. Also, the patients lost to follow-up within one year of treatment in this centre, defined as non-persistent, were not included for analysis of clinical outcome due to a lack of data. This limitation created a bias for the remaining cohort analysed. In addition, the conclusions of this study may be limited to patient populations with similar attributes. Third, despite the fact that seizure frequency plays a critical role in assessing medication-taking behaviour and clinical outcome, surrogate endpoints, such as ED visits or hospitalisation due to seizures, were used primarily because of incomplete and inconsistent documentation, as well as the limitations associated with retrospective evaluation. Therefore, seizure-related urgent healthcare was evaluated and considered as a marker of seizure recurrence (Shcherbakova *et al*., 2014) or clinical outcome of non-adherence in the adult population (Davis *et al*., 2008; Faught *et al*., 2008; Goodman *et al*., 2012). Finally, due to the retrospective nature of this study, we were not always able to obtain reasons for discontinuation and the various patient characteristics (*e.g.* socioeconomic status) based on incomplete documentation.

Despite the limitations listed above, our study shows that 70% of paediatric epilepsy patients demonstrated AED persistence and adherence at one year after treatment initiation and further confirms that non-adherence to AED treatment is an important factor in seizure-related clinical outcome. This finding suggests that interventions for children with epilepsy in clinical practice are necessary to ensure optimal medication-taking behaviour. Furthermore, predictors identified in this study, such as epilepsy onset at 12-24 months, localized seizure type, and initial treatment with older generation AEDs, should be taken into consideration when implementing intervention strategies in order to improve adherence. □

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.
None of the authors have any conflicts of interest to disclose.

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TEST YOURSELF

(1) Treatment adherence and persistence are essential for effective seizure control in children with epilepsy. Can patients be non-persistent with AEDs at one year after treatment initiation?

(2) Can the characteristics of initially chosen AEDs (old vs. new-generation) affect persistence and adherence of overall AED treatment?

(3) Can treatment non-adherence be related to epilepsy-associated hospitalisation or visiting emergency care in children?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".