

## Self-reported attitudes about medication in Lebanese people with epilepsy

**Lara Mroueh<sup>a,b,c,\*</sup>, Farid Boumediene<sup>a,b</sup>, Jeremy Jost<sup>a,b,d</sup>, Voa Ratsimbazafy<sup>a,b,d</sup>, Pierre-Marie Preux<sup>a,b</sup>, Pascale Salameh<sup>c</sup>, Amal Al-Hajje<sup>c</sup>.**

<sup>a</sup> INSERM, U1094, Tropical Neuroepidemiology, Limoges, France

<sup>b</sup> Univ. Limoges, UMR 1094, Tropical Neuroepidemiology, Institute of Epidemiology and Tropical Neurology, GEIST, 87000 Limoges, France

<sup>c</sup> Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University, Hadath, Beirut, Lebanon

<sup>d</sup> CHU Limoges, Department of Pharmacy, 87000 Limoges, France.

\*Corresponding author

E-mail address: [laramroueh@outlook.com](mailto:laramroueh@outlook.com)

Number words/Abstract: 314

Number words/Article: 3627

Figure 1: Percentages of 4-MMAS answers and adherence score

Table 1: Description of the study population

Table 2: Description of health status and history of epilepsy

Table 3: Comparison of people with epilepsy with positive and negative attitudes towards medication

Table 4: Final results of regression using the status of attitudes as the dependent variable

Table 5: Final results of regression using the seizure control as the dependent variable

## Abstract

Background: Epilepsy is a common worldwide neurological disorder. For people with epilepsy, adherence and attitudes towards medication is a crucial step to improve efficacy of prescribed treatment and to prevent seizures.

Objectives: The first aim of this study was to evaluate attitudes towards antiepileptic medications in Lebanese population. Secondary aims were to assess factors affecting attitudes and associated with epilepsy control.

Material and Methods: A cross-sectional study was conducted in out-patients neurology clinics located in Beirut-Lebanon. Data was collected using a structured questionnaire. Self-report of medication taking behaviors were assessed using the abbreviated (4-items) Morisky Medication Adherence Scale (MMAS-4). Epilepsy was considered as controlled if the patient had no seizures in the last 6 months.

Results: Among 250 people with epilepsy (PWE) recruited in this study, male-to-female ratio was 0.87 (116/134), and 50.8% were married. Mean duration of epilepsy was  $13.7 \pm 12.8$  years. Valproate was the most common antiepileptic drug used followed by levetiracetam and carbamazepine. About 60.8% of the population presented partial epilepsy. Uncontrolled epilepsy was present in more than half of participants (55.2%), with only 32.4% had positive attitudes to their medication. Positive attitudes towards antiepileptic increased in people who found their treatment was efficacious (OR=4.9; 95%CI 1.2-20.0;  $p=0.03$ ), who had controlled epilepsy (OR=3.4; 95%CI 1.6-7.1;  $p=0.001$ ), and who were diagnosed as people with epilepsy between the age of 12-20 years (OR=3.1; 95%CI 1.1-8.4;  $p=0.03$ ). Oppositely, these attitudes decreased in participants who felt their treatment as an economic burden (OR=0.2; 95%CI 0.1-0.4;  $p<0.001$ ), and in depressive people (OR=0.4; 95%CI 0.2-0.9;  $p=0.04$ ). Controlled epilepsy was higher in people who contacted a neurologist if seizure occurred, in people with positive attitudes, and after a long duration of disease, but it decreased if patient didn't follow neurologist's instructions in fasting period.

Conclusions: Lebanese PWE were less likely to have positive attitudes towards medication, which may lead to poor epilepsy control. Depression and economic burden were the major factors decreased these attitudes. Identifying factors affecting attitudes to medication and leading to controlled epilepsy may help clinicians to elaborate educational programs to optimize medication adherence.

Keywords: Epilepsy; Attitudes; Behaviors; Antiepileptic drug; Lebanon.

## 65 1. INTRODUCTION

66 Epilepsy is a neurological chronic disorder that affects almost 70 million people of all ages  
67 worldwide, of whom 85% live in developing countries [1]. According to the International League  
68 Against Epilepsy (ILAE), epilepsy is a brain disease defined by at least two unprovoked (or  
69 reflex) seizures occurring more than 24 hours apart [2]. Epilepsy treatment gap is defined as  
70 frequency of people with active epilepsy who need treatment but don't receive it [3,4], exceeded  
71 75% in most low-income countries and in rural regions [5,6].

72 Antiepileptic drugs (AED) are essential to control epilepsy, and are able to reduce seizures  
73 frequency in almost 67% of people with epilepsy (PWE) [7]. Despite a large number of AED  
74 present to date, low adherence and negative attitudes lead to failure of treatment. Studies showed  
75 that non-adherence to antiepileptic medication was associated with poor seizure control [8].

76 Many studies showed that worse attitudes and non-adherence proportions among PWE were  
77 similar to other chronic diseases and ranged between 30% and 50% [9–13]. Lack of adherence to  
78 AED might lead to therapeutic failure, poor quality of life, and increase in the risk of seizures  
79 recurrence [8,14,15]. Patients' non-adherent having negative attitudes towards drugs present  
80 uncontrolled epilepsy, and are at higher risk of status epilepticus (prolonged seizures) [16]. As a  
81 result, number of hospital admissions, healthcare costs, rate of morbidity and mortality increase  
82 [17–22]. Furthermore, the risk of sudden unexpected death in epilepsy (SUDEP) is higher in non-  
83 adherent PWE [23].

84 Based on these consequences, identifying the barriers to patient's attitudes towards AED is  
85 considered essential for clinicians to develop strategies in order to improve attitudes to medication  
86 in PWE [11]. Some known factors are unmodifiable by a neurologist in treatment strategy, such as  
87 age of disease onset, epilepsy etiology (symptomatic, idiopathic, and cryptogenic), and location of

88 epileptogenic zone (partial or generalized) [10]. The other modifiable factors are socio-economic  
89 factors, health care factors, comorbidities, cultural beliefs about epilepsy, frequency of seizures,  
90 treatment management, adverse events of AED, type/ frequency of medication use, cost of  
91 treatment and forgetfulness [23,24]. These factors can be controlled, and health care providers  
92 should resolve these problems to improve patient's attitudes to treatment.

93 A literature review showed that multiple factors that influence medication adherence worldwide.  
94 But, very few published studies evaluated attitudes to medication among PWE in Arab countries.  
95 Two countries (Saudi Arabia and Palestine) have evaluated adherence to AED [10,25]. More  
96 studies are necessary to detect these factors among Arabic people who present some specific  
97 habits, attitudes and cultures [10].

98 For this purpose, this study aims firstly to evaluate attitudes towards antiepileptic medications in  
99 Lebanese population, and secondary to assess factors affecting attitudes and associated with  
100 epilepsy control.

101

## 102 **2. MATERIAL AND METHODS**

### 103 **2.1. Study design**

104 A cross-sectional study was conducted in outpatient neurologic clinics of three tertiary care  
105 hospitals, two medical centers and ten private neurologic clinics located in Beirut-Lebanon. Beirut  
106 is the capital and largest city of Lebanon. Greater Beirut is generally considered as a growth of  
107 Beirut city and its peripheral areas (suburbs). These areas are urbanized and considered densely  
108 populated

109 This survey was carried out over a period of 6 months from February 1<sup>st</sup>, 2018 to July 30<sup>th</sup>, 2018.  
110 The clinics included in this study are visited by PWE from different Lebanese regions. The list of  
111 neurologists was obtained from Lebanese Order of Physicians.  
112 The estimated sample size was 217 patients (with a 95% confidence interval (CI), and a 5%  
113 precision error [26]) based on a previous published study using Morisky scale and reporting that  
114 only 17% of Lebanese patients with chronic diseases were adherent to their treatment [27].  
115 Lebanese outpatients above 18 years of age, diagnosed with epilepsy by a neurologist, and taking  
116 at least one AED for at least one month were included in the study.  
117 Participants who had mental retardation or intellectual disability, who were newly diagnosed with  
118 epilepsy (adherence of patient who didn't take AED for at least 4 weeks can't be evaluated),  
119 presented non-epileptic psychogenic seizures, who were taking AED for neuropathic pain, and  
120 pregnant women were not included. Also, participants who didn't give written consent to  
121 participate in the study were not included.

122

## 123 **2.2. Data collection**

124 Data was collected using a structured questionnaire prepared at first in English, and then presented  
125 in Arabic, the local language, to facilitate comprehension for patients.  
126 It was translated into Arabic Language by two independent translators. A back translation to  
127 English was done by another bilingual translator, who was not included in developing the initial  
128 version. The original Arabic version and the back translated English version were compared to  
129 resolve any inconsistency. A pilot study was done with 20 PWE to identify any problem in  
130 comprehension. These participants were not included in the final sample of the study.

131 The questionnaire was divided into six sections. Demographic data, natural history of  
132 epilepsy/etiology, and treatment were parts used from standardized questionnaire for investigation  
133 of epilepsy in tropical countries [28].

134 - Socio-demographic characteristics: age, gender, height and weight, region of residence,  
135 education level, occupation, marital status, number of workers/family, presence of medical  
136 insurance.

137 - History of epilepsy: duration of epilepsy, age of disease onset, family history, seizures in last 5  
138 years, seizure control, seizure type, and etiology.

139 - Treatment: type of AED, number of AED, number of pills/day, frequency of administration,  
140 reason for discontinuing treatment, appearance of side effects and its type (such as tiredness,  
141 nervousness, headache, skin's problem, hair loss, weight gain/loss, blurred vision, upset stomach,  
142 difficulty in concentrating, depression, disturbed sleep)[29], and measure serum level of AED.

143 - Health status: presence of comorbidities (any chronic disease other than epilepsy), and  
144 medication history.

145 - Self-report of medication taking behaviors were assessed using the abbreviated (4-items)  
146 Morisky Medication Adherence Scale (MMAS-4).

147 - General behaviors and attitudes towards medication: in absence/occurrence of seizures, in  
148 fasting/busy periods, if side effects appear, if no money/health coverage, if any neighbor's patient  
149 advices to stop medication, if participant forget to take medication, frequency of neurology visits,  
150 follow healthcare provider instruction, efficacy of treatment approved by participant, and if a  
151 treatment was an economic burden. These variables were not considered by MMAS-4. Data  
152 collection was done by a bilingual, Arabic native investigator using a face to face interview with  
153 PWE. All PWE attending neurology clinics and fulfilling inclusion criteria were included in this

154 study. The interviewer checked the patient's file to confirm diagnosis and inclusion criteria before  
155 taking written informed consent. Data concerning history of epilepsy, medication and health status  
156 was extracted from patient's file. The questionnaire was completed for all patients by a unique  
157 investigator during a 15 minutes face to face interview, during the patient's visit to the  
158 neurologist's clinic. The same questions were asked in the same manner and tone in Arabic to all  
159 patients to facilitate direct understanding.

160

### 161 **2.3. Definition of dependent variables**

162 In this study, seizure control was defined as studies done in Brazil and UK [30,31]. Epilepsy was  
163 arbitrarily classified as controlled if the patient had no seizures in the last 6 months and  
164 uncontrolled if he/she had at least one seizure in the last 6 months.

165 The MMAS-4 is a standardized validated questionnaire, used in this study to evaluate and reflect  
166 general health behaviors toward AED therapy. This structured self-report consists of 4 items with  
167 four "yes/no" questions [32,33].

168 Based on previous studies [10,30,34], each item is coded 0 if the answer is "Yes" and 1 if "No". A  
169 score can range from 0 to 4. Patients who had a score = 4 were considered adherent having  
170 positive attitudes towards AED and who had a score <4 were considered non-adherent having  
171 negative attitudes. The adherent state was considered for a patient responding "No" to all 4  
172 questions and this reflects positive attitudes. However, if one response was "Yes", a patient was  
173 considered non-adherent with negative attitudes. Cronbach's alpha was measured to evaluate  
174 reliability of the translated Arabic scale in this study. It was 0.705, which indicates a high level of  
175 internal consistency for a scale in this sample.

176

## **2.4. Data analysis**

Statistical analysis was done with the Statistical Package for the Social Sciences (SPSS) software, version 20. Descriptive analysis was used to describe qualitative (by frequency and percentage) and quantitative (by mean and standard deviation) variables. Comparative analysis was carried using Pearson's chi-square test or Fisher's exact test to report significant differences for qualitative variables between PWE with positive and negative attitudes. Student's t-test was used to compare the means between positive and negative attitudes groups. Variables having p-value  $<0.2$  were included in the multivariate model. Backward logistic regression was done to determine predictors affecting attitudes to treatment and controlled epilepsy. The variable "Attitudes towards AED" was dichotomized into a dependent variable as "Positive/ Negative", and seizure control into "Controlled/ Uncontrolled". Statistical tests were considered significant with a p-value  $<0.05$  and a confidence interval of 95%.

## **3. RESULTS**

### **3.1. Socio-demographic and clinical characteristics**

Two hundred fifty patients were recruited, with an average age of 40.2 ( $\pm 14.8$ ) ranging from 18 to 85 years. More than half of PWE (53.6%) were females and lived in Beirut (62.0%). The majority of the participants were unemployed (52.4%). Around quarter of this population (24.8%) have never been to school (Table 1).

Of all the participants, 56.8% had comorbidities, where hypertension and heart problems (cardiac insufficiency/ arrhythmia/ atrial fibrillation) were the most common (24.0%) followed by depression and anxiety (12.8%). Seventy-six patients (30.4%) had a family history of epilepsy. The mean duration of epilepsy was 13.7 years ( $\pm 12.8$ ). More than half of PWE (55.2%) had an



200 uncontrolled epilepsy. The majority of population (61.6%) presented partial epilepsy, with  
201 symptomatic etiology in 57.6% of cases. Monotherapy was prescribed in 60% of PWE; Valproic  
202 acid (50.0%), levetiracetam (26.4%), and carbamazepine (23.6%) were the most common AED  
203 prescribed. More than half of participants (58.0%) didn't take their medication daily, due to  
204 several reasons, including forgetfulness (37.9%), medication cost (13.1%), unavailability of drugs  
205 (13.1%), or absence of seizures (13.1%). Side effects of AED affected 57.2% of PWE (Table 2).

206

### 207 **3.2. Attitudes towards antiepileptic drugs**

208 More than half of the patients (56.0%) said they forgot to take their AED. Thereby, within the  
209 remaining some patients were classified non-adherent having negative attitudes because they had  
210 stopped taking medication if they felt better (30.4%) or worse (20.4%). However, only 32.4% of  
211 the study population were considered having positive attitudes to antiepileptic medication based  
212 on the sum of MMAS-4 score (Figure 1).

213

### 214 **3.3. Comparative analysis between PWE with positive and negative attitudes towards** 215 **medication**

216 Regarding disease history, uncontrolled epilepsy was found in 44.4% of PWE with positive  
217 attitudes to AED compared to 60.4% of PWE with negative attitudes ( $p=0.02$ ). Forgetfulness was  
218 the main reason for stopping medication in 32.5% of PWE with negative attitudes compare to no  
219 PWE having positive attitudes group. Experience of side effects was higher among PWE having  
220 negative attitudes (65.1%) than others (40.7%) ( $p<0.001$ ). Measure of the serum level of AED was  
221 done by 76.8% of PWE having positive attitudes compare to. 31.3% of PWE with negative

attitudes ( $p<0.001$ ). Depression was significantly higher ( $p=0.04$ ) among PWE with negative attitudes (27.8%) than in those who had positive attitudes (16%).

As for the patient's behaviors, 17.2% of PWE with negative attitudes forgot to take medicine compare to 7.4% of PWE with positive attitudes in a busy period. A proportion of 38.5% of PWE having negative attitudes could not buy treatment compared to 23.5% of PWE having positive attitudes due to a lack of money or no health coverage. In fasting period, 44.4% of PWE with positive attitudes increased time between 2 doses ( $>12h$ ) compare to 26% of others. Also, increasing dose when seizure occurs ( $p=0.02$ ), stopping medication in seizure-free period or when side effects appear ( $p<0.001$ ), and skipping doses in fasting period ( $p=0.003$ ) were factors which significantly differed between 2 groups of PWE with positive and negative attitudes (Table 3).

### **3.4. Factors affecting attitudes towards antiepileptic medications**

This study showed that seven factors predict patient's attitudes. Efficacy of treatment was an important predictor ( $OR=4.9$ ; 95%CI 1.2-20.0;  $p=0.03$ ). Controlled epilepsy also increased the odds of having positive attitudes ( $OR=3.4$ ; 95%CI 1.6-7.1;  $p=0.001$ ). Onset of epilepsy at age between 12-20 years was a factor leading to increased positive attitudes, compared to onset at age  $<12$  years ( $OR=3.1$ ; 95%CI 1.1-8.4;  $p=0.03$ ).

While, patient's positive attitudes decreased in participants who thought that their treatment was an economic burden ( $OR=0.2$ ; 95%CI 0.1-0.4;  $p<0.001$ ), depressive PWE ( $OR=0.4$ ; 95%CI 0.2-0.9;  $p=0.04$ ), who visited their neurologist clinics every year ( $OR=0.2$ ; 95%CI 0.04-0.5;  $p=0.002$ ) or every few years (only when a seizure occurs) ( $OR=0.2$ ; 95%CI 0.1-0.7;  $p=0.01$ ), and in older people ( $OR=0.97$ ; 95%CI 0.94-0.99;  $p=0.02$ ) (Table 4).

### 3.5. Factors affecting controlled epilepsy

In this study, controlled epilepsy was higher in people who contact a specialist if seizure occurs (OR=2.9; 95%CI 1.3-6.5; p=0.01), in PWE who had positive attitudes towards AED (OR=1.9; 95%CI 1.1-3.4; p=0.03), and after a long duration of disease (OR=1.04; 95%CI 1.02-1.07; p<0.001). However, risk of controlled seizures decreased if patient didn't follow neurologist's instructions in fasting period (OR=0.5; 95%CI 0.3-0.9; p=0.03) (Table 5).

## 4. DISCUSSION

Only 32.4% of PWE presented positive attitudes to AED, similar to a study from Ethiopia [9], but lower than findings in other countries such as Palestine (36.0%) [25], England (41.0%) [35], Lao (57.6%) [36], and Saudi Arabia (61.7%) [10]. This variation between countries could be due to different habits, behaviors, cultures between populations [10].

Four indirect methods are used to measure medication adherence in the outpatient setting [37]: Self report, electronic medication monitoring, pharmacy refill rates and pill counts.

Electronic medication-measurement systems are expensive and rarely available in the outpatient setting. Pharmacy refill rates is not applicable because drugs (AED included) in Lebanon are delivered without prescription and do not require a renewal of prescription at every purchase. Also, it was difficult to count number of pills and to compare with the total number of pills received by a patient because the patient was seen only once, and did not carry his pills during his neurologist's visit. So we chose MMAS-4, a simple and economical self-reporting method.

A study conducted in essential hypertension established the concurrent and predictive validity of MMAS-4 regarding blood pressure measurements recorded throughout a 3-year follow-up period

267 [32]. This self-reporting method is used for different chronic diseases, epilepsy included, in  
268 several countries and populations [9,10,25,30,35,36].

269 However, a comparison with studies using other methods to evaluate adherence shows that a low  
270 percentage of adherence was more present in studies using subjective methods such as MMAS. In  
271 studies using MMAS to estimate adherence in PWE, percentage of adherence ranged between  
272 20% and 55% [30,35,36,38]. However, objective measures such as a medication possession ratio,  
273 which definition and estimation differ between studies, show that adherence varied between 50%  
274 and 65% [12,17,19,39,40]. In addition, a therapeutic drug concentration monitoring in prospective  
275 studies show that adherence to medication was around 60% [41,42].

276

277 This study identified three key factors that increase positive attitudes in PWE. These attitudes  
278 were present in people who had good perception toward AED, and who were correctly motivated  
279 [43]. The PWE who were satisfied and felt that treatment was effective had more positive attitudes  
280 in this population.

281 Controlled epilepsy is a factor leading to increased positive attitudes in this study. When epilepsy  
282 is controlled, adherence and positive health behaviors to AED increased. This is in agreement with  
283 other studies [15,30].

284 Attitudes to medication were also associated with age of epilepsy onset. People diagnosed as  
285 epileptic at adolescence (12-20 years) had more positive attitudes than those diagnosed during  
286 childhood (<12 years). Adolescents were more able to follow instructions of neurologists, and  
287 learn more about their disease and treatment. In pediatric patients, parents have a critical role to  
288 improve adherence. However, they may tend to be fearful and stressed, this may negatively affect  
289 attitudes to AED [44].

290 Oppositely, positive attitudes to medication decreased by four factors. Positive attitudes were  
291 lower in PWE who felt that their treatment was an economic burden, similar to another study  
292 conducted in Ethiopia [45]. Cost of medications was found to be a big burden due to absence of  
293 health coverage for some Lebanese people

294 Depressive PWE were less adherent with negative attitudes to AED. Another study showed also a  
295 significant correlation between medication adherence and depressive status [46].

296 PWE who visit neurologist clinic only every year or every few years had less positive attitudes.  
297 Patient education about the disease and treatment is essential to resolve patient distress and  
298 improve patient's attitudes to medication [15,47].

299 Positive attitudes towards antiepileptic medications decreased in older age. In Ethiopia, older  
300 PWE were less adherent with negative attitudes [9], in agreement with another study done in  
301 China that reported the same association [8]. Older people present physical difficulties and  
302 cognitive problems making it difficult to follow healthcare provider's instructions [48]. However,  
303 presence of other comorbidities, complexity of treatment regimen, and multiple daily dosing  
304 decreased also adherence [44].

305 The reasons for discontinuation of treatment in this study included forgetfulness, high medication  
306 cost, adverse effects, unavailability of drugs, inefficacy of treatment and absence of seizures.

307 Forgetfulness was the main reason for non-adherence and discontinuing treatment in this study.  
308 This was reported also in other studies [8,9,49,50], which found that forgetfulness was the key  
309 reason for being non-adherent. Most people may forget to take medication when they are busy at  
310 work, away from their home or while travelling. High cost of drugs was significantly associated  
311 with decreased adherence, similar to a study done in China [8]. PWE who experienced adverse  
312 effects of AED had negative attitudes. A common cause for stopping antiepileptic treatment, and

313 limiting adherence without consulting neurologist was adverse effects [8,51]. PWE who stop  
314 taking their medication when the drug is not available had negative attitudes than those who  
315 didn't. Thus, the inability to obtain treatment in this population leads to decreased adherence and  
316 positive attitudes to medication. The Lebanese government should provide and preserve the  
317 required drugs in the public sector at any time in a better manner. Participants who had negative  
318 beliefs about their treatment were significantly non-adherent to AED. This negative perception  
319 was probably due to treatment failure and recurrence of seizures. These results were similar to  
320 another study conducted in UK [12].

321

322 Controlled epilepsy was positively associated with adherence and positive attitudes to AED. A  
323 reciprocal significant association was found between patient's attitudes and controlled epilepsy,  
324 where low medication adherence and negative attitudes showed to be also a cause for uncontrolled  
325 epilepsy, similar to results in other studies [14,52,53]. Precisely, PWE who stop treatment are  
326 more likely to have uncontrolled epilepsy. This suggests that evaluation of adherence can predict  
327 epilepsy outcome.

328 Duration of epilepsy was a factor affecting controlled epilepsy. PWE who were diagnosed as  
329 epileptics since long time were more likely to have controlled epilepsy. Seizures may take longer  
330 time to become controlled. Long duration leads to adaptation for this disease, and then improved  
331 adherence. In Nigeria, PWE were more likely to have controlled epilepsy when they are in older  
332 age [54].

333 However, controlled epilepsy decreased if patient didn't follow neurologist's instructions in  
334 fasting period. Some research was carried out on PWE during the fasting month. During this  
335 period, only two meals are consumed per day, separated by a fasting time of 11 to 18 hours

336 depending on season [55]. A study done in Turkey showed that some of PWE had more seizures  
337 during fasting month. This increase was probably due to changes in the way epilepsy medicine  
338 were taken, sleep patterns being disturbed, and going for a long time without food [55]. For this,  
339 PWE should follow neurologist's instructions in fasting period such as adapting posology and  
340 prescribing extended-release drugs taken once a day.

341

342 This study was the first to evaluate attitudes to antiepileptic medications in Lebanese PWE, and  
343 one among few studies done in the Arab world which has its specific culture and behaviors.  
344 However, due to a lack of studies in Arab countries, we didn't have enough data to compare our  
345 findings.

346 With a cross-sectional design, it is impossible to establish causal relationship. Some recall bias  
347 may be present due to the fact that self-report was the method used to evaluate behaviors towards  
348 medication. Self-report is the most practical method in the outpatient setting, but it tends to  
349 overestimate responses compared to the objective methods. In addition to this, the overestimation  
350 of acceptable responses may be due to the fact that the questionnaire was completed by the  
351 investigator and not privately by the patient. This study evaluated medication problems related to  
352 treatment acceptance and patient's attitudes towards medications; all people accepted to take AED  
353 but a low level of positive attitudes was found.

354 Participants were recruited from neurology clinics due to necessity of accurate diagnosis, but  
355 selection bias may be present. However, to reduce selection bias, and to be more representative,  
356 PWE were recruited from different health structures (private clinics, clinics in hospitals, and  
357 clinics in medical centers). Those health structures allow people from all economic stages to  
358 access neurologists' consultation. Since PWE were recruited from neurologists' clinics, a high

level of adherence was expected; however, low adherence was found. This approves diversity of  
PWE recruited and reduces the risk of recruitment bias.

A longitudinal prospective study will be necessary to focused on people who discontinue their  
medication after a long-time treatment. Persistence of adherence during a follow-up period could  
be evaluated in future studies.

## **5. CONCLUSIONS**

Lebanese PWE were less likely to have positive attitudes towards antiepileptic medications,  
which may lead to poor epilepsy control. The positive attitudes of PWE are cornerstone to  
improve epilepsy treatment, prevent recurrence of seizures, reduce the risk of hospitalization and  
improve quality of life. Diagnoses followed by pharmacological treatment are not enough in  
epilepsy management. Thus, evaluation of patient's attitudes is essential in clinical practice, and  
should be a base in treatment management to predict epilepsy control.

Depression, economic burden and visiting neurologist's clinic every year or every few years  
predicted negative attitudes towards antiepileptic medications in our study. Non-respect of  
recommendations to neurologist leads in turn to uncontrolled epilepsy. Depressive people should  
be managed effectively by a specialist. Prescribing generic drugs with affordable costs and  
having access to a better social security systems in Lebanon are needed to provide medication to  
patients with no health insurance and thereby limit the economic burden felt by PWE. Contact  
neurologist and follow his recommendations in case of seizure occurrence or during fasting  
periods were necessary to control epilepsy.

Educating PWE and their families about disease and treatment management, adapting simple  
medication regimens by neurologists (such as monotherapies to reduce number of pills, and



382 extended-release drugs to reduce frequency of dosing), ensuring a good relationship between  
383 PWE and healthcare professionals, and attending regularly to appointments, are important for  
384 attaining good adherence to treatment. In fact, using easy reminders to take medications (pill  
385 reminder boxes, calendars, alarms, watches with beeper alarms, caregivers reminder) is important  
386 to optimize medication adherence and enhance positive attitudes for PWE. Educational programs  
387 about the disease and treatment are also necessary for attaining good attitudes towards medications  
388 for PWE.

389

#### 390 **CONFLICT OF INTEREST**

391 There is no conflict of interest.

392

#### 393 **FUNDING**

394 This research did not receive any specific grant from funding agencies in the public, commercial,  
395 or not-for-profit sectors.

396

#### 397 **REFERENCES**

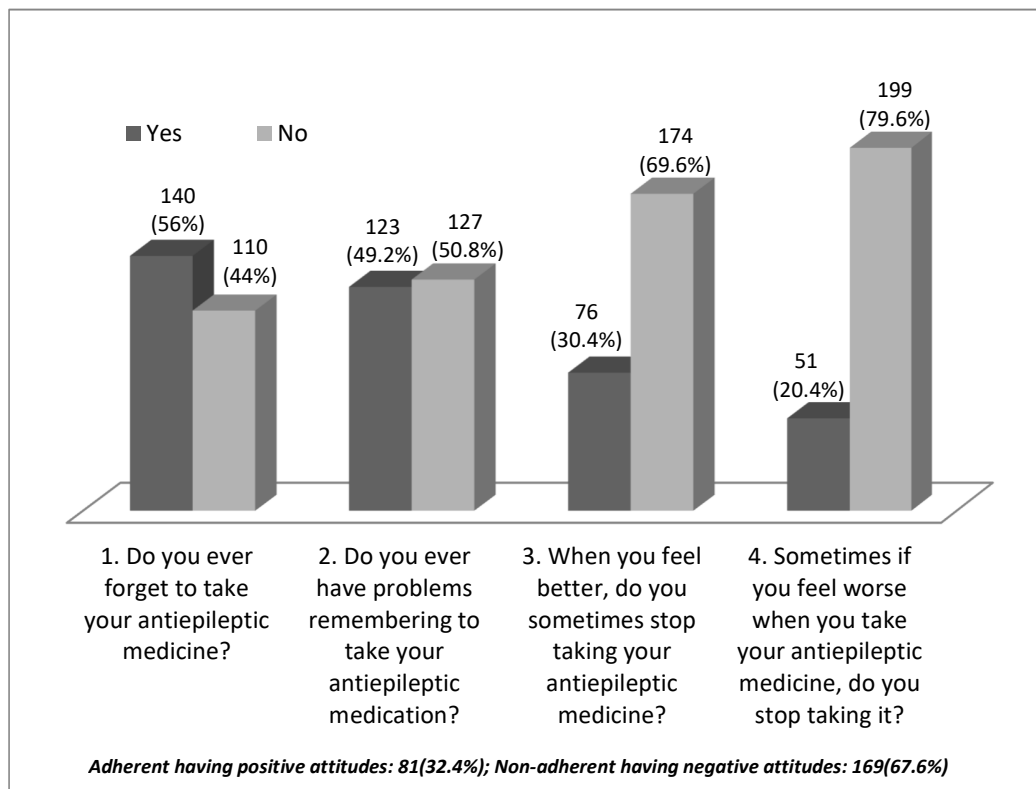
- 398 [1] Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden  
399 of active and life-time epilepsy: a meta-analytic approach. *Epilepsia* 2010;51:883–90.  
400 doi:10.1111/j.1528-1167.2009.02481.x.
- 401 [2] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE  
402 official report: a practical clinical definition of epilepsy. *Epilepsia* 2014;55:475–82.  
403 doi:10.1111/epi.12550.
- 404 [3] Kale R. Global Campaign against Epilepsy: the treatment gap. *Epilepsia* 2002;43:31–3.
- 405 [4] Meinardi H, Scott RA, Reis R, Sander JW, ILAE Commission on the Developing World.  
406 The treatment gap in epilepsy: the current situation and ways forward. *Epilepsia*  
407 2001;42:136–49.
- 408 [5] Meyer A-C, Dua T, Ma J, Saxena S, Birbeck G. Global disparities in the epilepsy treatment  
409 gap: a systematic review. *Bull World Health Organ* 2010;88:260–6.  
410 doi:10.2471/BLT.09.064147.

- [6] Mbuba CK, Ngugi AK, Newton CR, Carter JA. The epilepsy treatment gap in developing countries: a systematic review of the magnitude, causes, and intervention strategies. *Epilepsia* 2008;49:1491–503. doi:10.1111/j.1528-1167.2008.01693.x.
- [7] Elger CE, Schmidt D. Modern management of epilepsy: a practical approach. *Epilepsy Behav* 2008;12:501–39. doi:10.1016/j.yebeh.2008.01.003.
- [8] Liu J, Liu Z, Ding H, Yang X. Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *Epileptic Disord* 2013;15:289–94. doi:10.1684/epd.2013.0588.
- [9] Hasiso TY, Desse TA. Adherence to Treatment and Factors Affecting Adherence of Epileptic Patients at Yirgalem General Hospital, Southern Ethiopia: A Prospective Cross-Sectional Study. *PloS One* 2016;11:e0163040. doi:10.1371/journal.pone.0163040.
- [10] Gabr WM, Shams MEE. Adherence to medication among outpatient adolescents with epilepsy. *Saudi Pharm J* 2015;23:33–40. doi:10.1016/j.jsps.2014.05.003.
- [11] Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. *Epilepsia* 2008;49:446–54.
- [12] Chapman SCE, Horne R, Chater A, Hukins D, Smithson WH. Patients' perspectives on antiepileptic medication: relationships between beliefs about medicines and adherence among patients with epilepsy in UK primary care. *Epilepsy Behav* 2014;31:312–20. doi:10.1016/j.yebeh.2013.10.016.
- [13] Getnet A, Woldeyohannes SM, Bekana L, Mekonen T, Fekadu W, Menberu M, et al. Antiepileptic Drug Nonadherence and Its Predictors among People with Epilepsy. *Behav Neurol* 2016;2016:3189108. doi:10.1155/2016/3189108.
- [14] Kaddumukasa M, Kaddumukasa M, Matovu S, Katabira E. The frequency and precipitating factors for breakthrough seizures among patients with epilepsy in Uganda. *BMC Neurol* 2013;13:182. doi:10.1186/1471-2377-13-182.
- [15] Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: survey of patients with epilepsy and physicians. *Epilepsy Behav* 2008;13:316–22. doi:10.1016/j.yebeh.2008.03.009.
- [16] Skinner HJ, Dubon-Murcia SA, Thompson AR, Medina MT, Edwards JC, Nicholas JS, et al. Adult convulsive status epilepticus in the developing country of Honduras. *Seizure* 2010;19:363–7. doi:10.1016/j.seizure.2010.05.007.
- [17] Ettinger AB, Manjunath R, Candrilli SD, Davis KL. Prevalence and cost of nonadherence to antiepileptic drugs in elderly patients with epilepsy. *Epilepsy Behav* 2009;14:324–9. doi:10.1016/j.yebeh.2008.10.021.
- [18] Neligan A, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. *Brain J Neurol* 2011;134:388–95. doi:10.1093/brain/awq378.
- [19] Faught E, Duh MS, Weiner JR, Guérin A, Cunnington MC. Nonadherence to antiepileptic drugs and increased mortality: findings from the RANSOM Study. *Neurology* 2008;71:1572–8. doi:10.1212/01.wnl.0000319693.10338.b9.
- [20] Cramer JA, Wang ZJ, Chang E, Powers A, Copher R, Cherepanov D, et al. Healthcare utilization and costs in adults with stable and uncontrolled epilepsy. *Epilepsy Behav* 2014;31:356–62. doi:10.1016/j.yebeh.2013.09.046.
- [21] Molugulu N, Gubbiyappa KS, Vasudeva Murthy CR, Lumae L, Mruthyunjaya AT. Evaluation of self-reported medication adherence and its associated factors among epilepsy

- patients in Hospital Kuala Lumpur. *J Basic Clin Pharm* 2016;7:105–9. doi:10.4103/0976-0105.189430.
- [22] Goodman MJ, Durkin M, Forlenza J, Ye X, Brixner DI. Assessing adherence-based quality measures in epilepsy. *Int J Qual Health Care* 2012;24:293–300. doi:10.1093/intqhc/mzs017.
- [23] O' Rourke G, O' Brien JJ. Identifying the barriers to antiepileptic drug adherence among adults with epilepsy. *Seizure* 2017;45:160–8. doi:10.1016/j.seizure.2016.12.006.
- [24] Rikir E, Grisar T, Sadzot B. Treatment compliance in epileptic patients. A frequent and complex problem. *Rev Med Liege* 2010;65.
- [25] Sweileh WM, Ihbesheh MS, Jarar IS, Taha ASA, Sawalha AF, Zyoud SH, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *Epilepsy Behav* 2011;21:301–5. doi:10.1016/j.yebeh.2011.04.011.
- [26] Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med* 2013;35:121–6. doi:10.4103/0253-7176.116232.
- [27] Al-Hajje A, Awada S, Rachidi S, Zein S, Bawab W, El-Hajj Z, et al. Factors affecting medication adherence in Lebanese patients with chronic diseases. *Pharm Pract* 2015;13:590. doi:10.18549/PharmPract.2015.03.590.
- [28] Preux PM. Questionnaire in a study of epilepsy in tropical countries. *Bull Soc Pathol Exot* 1990 2000;93:276–8.
- [29] Kuzmanova R, Stefanova I, Velcheva I, Stambolieva K. Translation, cross-cultural adaptation, and validation of the Bulgarian version of the Liverpool Adverse Event Profile. *Epilepsy Behav* 2014;39:88–91. doi:10.1016/j.yebeh.2014.08.124.
- [30] Ferrari CMM, de Sousa RMC, Castro LHM. Factors associated with treatment non-adherence in patients with epilepsy in Brazil. *Seizure* 2013;22:384–9. doi:10.1016/j.seizure.2013.02.006.
- [31] Smithson WH, Hukins D, Buelow JM, Allgar V, Dickson J. Adherence to medicines and self-management of epilepsy: a community-based study. *Epilepsy Behav* 2013;26:109–13. doi:10.1016/j.yebeh.2012.10.021.
- [32] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67–74.
- [33] Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens Greenwich Conn* 2008;10:348–54.
- [34] Moura LMVR, Carneiro TS, Cole AJ, Hsu J, Vickrey BG, Hoch DB. Association between addressing antiseizure drug side effects and patient-reported medication adherence in epilepsy. *Patient Prefer Adherence* 2016;10:2197–207. doi:10.2147/PPA.S119973.
- [35] Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M. Adherence to treatment in patients with epilepsy: associations with seizure control and illness beliefs. *Seizure* 2006;15:504–8. doi:10.1016/j.seizure.2006.06.003.
- [36] Harimanana A, Clavel S, Chivorakul P, Perez F, Preux P-M, Barennes H. Associated factors with adherence to antiepileptic drug in the capital city of Lao PDR. *Epilepsy Res* 2013;104:158–66. doi:10.1016/j.eplepsyres.2012.10.008.
- [37] Hawkshead J, A. Krousel-Wood M. Techniques for Measuring Medication Adherence in Hypertensive Patients in Outpatient Settings. *Dis Manag Health Outcomes* 2007;15:109–18. doi:10.2165/00115677-200715020-00006.
- [38] Ahmad N, Othaman NI, Islahudin FH. Medication adherence and quality of life in epilepsy patients. *Int J Pharm Pharm Sci* 2013;5:401–4.

- [39] Briesacher BA, Andrade SE, Fouayzi H, Chan KA. Comparison of drug adherence rates among patients with seven different medical conditions. *Pharmacotherapy* 2008;28:437–43. doi:10.1592/phco.28.4.437.
- [40] Manjunath R, Davis KL, Candrilli SD, Ettinger AB. Association of antiepileptic drug nonadherence with risk of seizures in adults with epilepsy. *Epilepsy Behav* 2009;14:372–8. doi:10.1016/j.yebeh.2008.12.006.
- [41] Carpentier N, Jonas J, Frismand S, Vignal J-P, Rikir E, Baumann C, et al. Direct evidence of nonadherence to antiepileptic medication in refractory focal epilepsy. *Epilepsia* 2013;54:e20–23. doi:10.1111/j.1528-1167.2012.03695.x.
- [42] Samsonsen C, Reimers A, Bråthen G, Helde G, Brodtkorb E. Nonadherence to treatment causing acute hospitalizations in people with epilepsy: an observational, prospective study. *Epilepsia* 2014;55:e125–128. doi:10.1111/epi.12801.
- [43] Kyngäs H. Compliance with health regimens of adolescents with epilepsy. *Seizure* 2000;9:598–604. doi:10.1053/seiz.2000.0470.
- [44] Loisel K, Rausch JR, Modi AC. Behavioral predictors of medication adherence trajectories among youth with newly diagnosed epilepsy. *Epilepsy Behav* 2015;50:103–7. doi:10.1016/j.yebeh.2015.06.040.
- [45] Getachew H, Dekema N, Awol S, Abdi A, Mohammed M. Medication adherence in epilepsy and potential risk factors associated with non adherence in tertiary care teaching hospital in southwest Ethiopia. *Gaziantep Med J* 2014;20:59. doi:10.5455/GMJ-30-45904.
- [46] Shallcross AJ, Becker DA, Singh A, Friedman D, Jurd R, French JA, et al. Psychosocial factors associated with medication adherence in ethnically and socioeconomically diverse patients with epilepsy. *Epilepsy Behav* 2015;46:242–5. doi:10.1016/j.yebeh.2015.01.034.
- [47] Lawson VL, Lyne PA, Harvey JN, Bundy CE. Understanding why people with type 1 diabetes do not attend for specialist advice: a qualitative analysis of the views of people with insulin-dependent diabetes who do not attend diabetes clinic. *J Health Psychol* 2005;10:409–23. doi:10.1177/1359105305051426.
- [48] Cooper C, Carpenter I, Katona C, Schroll M, Wagner C, Fialova D, et al. The AdHOC Study of older adults' adherence to medication in 11 countries. *Am J Geriatr Psychiatry* 2005;13:1067–76. doi:10.1176/appi.ajgp.13.12.1067.
- [49] Johnbull OS, Farounbi B, Adeleye AO, Ogunrin O, Uche AP. Evaluation of Factors Influencing Medication Adherence in Patients with Epilepsy in Rural Communities of Kaduna State, Nigeria. *Neurosci Med* 2011;02:299–305. doi:10.4236/nm.2011.24039.
- [50] Paschal AM, Rush SE, Sadler T. Factors associated with medication adherence in patients with epilepsy and recommendations for improvement. *Epilepsy Behav* 2014;31:346–50. doi:10.1016/j.yebeh.2013.10.002.
- [51] Tan X, Pharm B, Makmor-Bakry M, Pharm M, Lau C, Tajarudin F, et al. Factors affecting adherence to antiepileptic drugs therapy in Malaysia. *Neurol Asia* 2015;7.
- [52] Birru EM, Shafi M, Geta M. Drug therapy of epileptic seizures among adult epileptic outpatients of University of Gondar Referral and Teaching Hospital, Gondar, North West Ethiopia. *Neuropsychiatr Dis Treat* 2016;12:3213–9. doi:10.2147/NDT.S119030.
- [53] Nakhutina L, Gonzalez JS, Margolis SA, Spada A, Grant A. Adherence to antiepileptic drugs and beliefs about medication among predominantly ethnic minority patients with epilepsy. *Epilepsy Behav* 2011;22:584–6. doi:10.1016/j.yebeh.2011.08.007.

- 547 [54] Obiako OR, Sheikh TL, Kehinde JA, Iwuzo EU, Ekele N, Elonu CC, et al. Factors  
548 affecting epilepsy treatment outcomes in Nigeria. *Acta Neurol Scand* 2014;130:360–7.  
549 doi:10.1111/ane.12275.
- 550 [55] Gomceli YB, Kutlu G, Cavdar L, Inan LE. Does the seizure frequency increase in  
551 Ramadan? *Seizure* 2008;17:671–6. doi:10.1016/j.seizure.2008.03.008.  
552



**Fig.1. Percentages of 4-MMAS answers and adherence score**

**Table 1. Description of the study population**

| Variables                                 |  | n (%) /<br>Mean $\pm$ SD <sup>1</sup> |
|---|--|---------------------------------------|
| <b>Sex</b>                                | Females  | 134 (53.6)                            |
| <b>Region of residence</b>                | Beirut   | 155 (62.0)                            |
|   | South  | 30 (12.0)                             |
|   | Mount Lebanon                                      | 21 (8.4)                              |
|   | Bekaa  | 33 (13.2)                             |
|   | North  | 7 (2.8)                               |
|   | Outside Lebanon                                    | 4 (1.6)                               |
| <b>Body mass index (BMI) <sup>2</sup></b> | Underweight (BMI<18.5 kg/m <sup>2</sup> )          | 7 (2.8)                               |
|   | Normal weight (BMI $\geq$ 18.5 kg/m <sup>2</sup> ) | 105 (42.0)                            |
|   | Overweight (BMI $\geq$ 25 kg/m <sup>2</sup> )      | 103 (41.2)                            |
|   | Obese (BMI $\geq$ 30 kg/m <sup>2</sup> )           | 35 (14.0)                             |
| <b>Education level</b>                    | Illiterate   | 62 (24.8)                             |
|   | Elementary   | 60 (24.0)                             |
|   | Intermediate                                       | 41 (16.4)                             |
|   | Secondary  | 32 (12.8)                             |
|   | University   | 55 (22.0)                             |
| <b>Occupation</b>                         | Unemployed   | 131 (52.4)                            |
|   | Employed/Self-employed                             | 97 (38.8)                             |
|   | Shepherd/ Farmer                                   | 3 (1.2)                               |
|   | Student  | 19 (7.6)                              |
| <b>Marital status</b>                     | Single lives alone                                 | 11 (4.4)                              |
|   | Single lives with family                           | 75 (30.0)                             |
|   | Married  | 127 (50.8)                            |
|   | Divorced   | 22 (8.8)                              |
|   | Widowed  | 15 (6.0)                              |
| <b>Medical Insurance</b>                  |  | 138 (55.2)                            |
| <b>Age</b>                                |  | 40.2 $\pm$ 14.8                       |
| <b>BMI</b>                                |  | 25.8 $\pm$ 6.0                        |
| <b>Number of workers/ family</b>          |  | 1.4 $\pm$ 1.1                         |

<sup>1</sup> SD: Standard deviation; <sup>2</sup> World Health Organization (WHO). Global Database on Body Mass Index

**Table 2. Description of health status and history of epilepsy**

| Variables  | Mean $\pm$ SD <sup>1</sup> / n (%) |
|--|------------------------------------|
| <b>Duration of epilepsy</b>  | 13.7 $\pm$ 12.8                    |
| <b>Age of epilepsy onset</b>   | 26.5 $\pm$ 18.8                    |
| <b>Family history of epilepsy</b>  | 76 (30.4)                          |
| <b>Presence of seizures in last 5 years</b>  | 195 (78.0)                         |
| <b>Seizure control</b>   |                                    |
| Uncontrolled (at least one seizure in last 6 months)                                     | 138 (55.2)                         |
| Controlled (no seizure in last 6 months)   | 112 (44.8)                         |
| <b>Presence of comorbidities</b>   | 142 (56.8)                         |
| <b>Type of Comorbidities</b>   |                                    |
| Hypertension / Cardiac problems (cardiac insufficiency/ arrhythmia/ atrial fibrillation) | 60 (24.0)                          |
| Dyslipidemia   | 29 (11.6)                          |
| Respiratory diseases (Asthma or COPD <sup>2</sup> )                                      | 9 (3.6)                            |
| Angina   | 7 (2.8)                            |
| Kidney disease   | 4 (1.6)                            |
| Gastrointestinal disease   | 24 (9.6)                           |
| Diabetes   | 21 (8.4)                           |
| Thyroid disease  | 19 (7.6)                           |
| Cerebrovascular Accident   | 11 (4.4)                           |
| Depression/ Anxiety  | 60 (24.0)                          |
| Psychosis/ Schizophrenia   | 32 (12.8)                          |
| Migraine   | 13 (5.2)                           |
| Cerebral Tumor   | 7 (2.8)                            |
| Other Comorbidities (Parkinson, osteoporosis, rheumatological disease...)                | 9 (3.6)                            |
| <b>Seizure type</b>  |                                    |
| Simple partial   | 50 (20.0)                          |
| Complex partial  | 73 (29.2)                          |
| Secondary generalized  | 31 (12.4)                          |
| Generalized tonic clonic   | 80 (32.0)                          |
| Generalized myoclonic  | 11 (4.4)                           |
| Generalized atonic   | 3 (1.2)                            |
| Absence  | 28 (11.2)                          |
| Others   | 1 (0.4)                            |
| <b>Epilepsy etiology</b>   |                                    |
| Idiopathic   | 20 (8.0)                           |
| Cryptogenic  | 86 (34.4)                          |
| Symptomatic  | 144 (57.6)                         |
| <b>Type of AE<sup>3</sup> medication</b>   |                                    |
| Benzodiazepines  | 36 (14.4)                          |
| Phenytoin  | 19 (7.6)                           |
| Phenobarbital  | 11 (4.4)                           |
| Carbamazepine  | 59 (23.6)                          |
| Valproate  | 125 (50.0)                         |
| Lamotrigine  | 27 (10.8)                          |
| Levetiracetam  | 66 (26.4)                          |
| Oxcarbazepine  | 12 (4.8)                           |
| Topiramate   | 22 (8.8)                           |
| Lacosamide   | 12 (4.8)                           |
| Perampanel   | 1 (0.4)                            |
| <b>AE therapy</b>  |                                    |
| Monotherapy  | 150 (60.0)                         |
| Bitherapy  | 67 (26.8)                          |
| >2 antiepileptic medications   | 33 (13.2)                          |
| <b>Taking AED daily</b>  | 105 (42.0)                         |
| <b>Main reason for stopping medication</b>   |                                    |
| Forgetfulness  | 55 (37.9)                          |
| High cost  | 19 (13.1)                          |
| Complexity of treatment regimen  | 11 (7.6)                           |
| Experience of side effects   | 12 (8.3)                           |
| Unavailability of drugs  | 19 (13.1)                          |
| Perception of inefficacy   | 10 (6.9)                           |
| Absence of seizures  | 19 (13.1)                          |
| <b>Experiencing of side effects</b>  | 143 (57.2)                         |

<sup>1</sup> SD: Standard deviation; <sup>2</sup> Chronic Obstructive Pulmonary Disease; <sup>3</sup> Antiepileptic



**Table 3. Comparison of people with epilepsy with positive and negative attitudes towards medication**

| Variables  |   | n (%)              | n (%)              | p-value |
|--|---|--------------------|--------------------|---------|
|  |   | Negative attitudes | Positive attitudes |         |
| <b>Seizure control</b>   | Controlled  | 67 (39.6)          | 45 (55.6)          | 0.02    |
|  | Uncontrolled  | 102 (60.4)         | 36 (44.4)          |         |
| <b>Age onset disease</b>   | <12 years   | 44 (26.0)          | 16 (19.8)          | 0.02    |
|  | 12-20 years   | 31 (18.3)          | 27 (33.3)          |         |
|  | 20-40 years   | 54 (32.0)          | 15 (18.5)          |         |
|  | >40 years   | 40 (23.7)          | 23 (28.4)          |         |
| <b>Measure serum level of AED if specialist prescribe this</b>   | No  | 90 (68.7)          | 13 (23.2)          | < 0.001 |
|  | Yes   | 41 (31.3)          | 43 (76.8)          |         |
| <b>When a seizure occurs</b>   | Double a dose                                       | 40 (23.7)          | 8 (9.9)            | 0.02    |
|  | Continue treatment normally                         | 64 (37.9)          | 31 (38.3)          |         |
|  | Contact a specialist                                | 65 (38.5)          | 42 (51.9)          |         |
| <b>In stable status (absence of seizures)</b>  | Stop medication                                     | 49 (29.0)          | 0                  | < 0.001 |
|  | Reduce a dose                                       | 33 (19.5)          | 2 (2.5)            |         |
|  | Continue treatment normally                         | 87 (51.5)          | 79 (97.5)          |         |
| <b>In fasting period</b>   | Not fasting   | 61 (36.1)          | 30 (37.0)          | 0.003   |
|  | Skip or reduce a dose to 2 daily doses instead of 3 | 33 (19.5)          | 11 (13.6)          |         |
|  | Increase the time between 2 doses (>12h)            | 44 (26.0)          | 36 (44.4)          |         |
|  | Take all doses together                             | 31 (18.3)          | 4 (4.9)            |         |
| <b>If side effects appear</b>  | Stop medication                                     | 47 (27.8)          | 4 (4.9)            | < 0.001 |
|  | Continue treatment normally                         | 35 (20.7)          | 13 (16.0)          |         |
|  | Contact a specialist                                | 69 (40.8)          | 62 (76.5)          |         |
|  | Contact a pharmacist                                | 18 (10.7)          | 2 (2.5)            |         |
| <b>If a patient is in busy period (at work, away from home, in outdoor dinner/ lunch or in travel), he forget his medication</b> | No  | 140 (82.8)         | 75 (92.6)          | 0.04    |
|  | Yes   | 29 (17.2)          | 6 (7.4)            |         |
| <b>If no money/ health coverage, patient buys his medication</b>   | No  | 65 (38.5)          | 19 (23.5)          | 0.02    |
|  | Yes   | 104 (61.5)         | 62 (76.5)          |         |
| <b>If a neighbor of patient advices him, he stop medication</b>  | No  | 146 (86.4)         | 77 (95.1)          | 0.04    |
|  | Yes   | 23 (13.6)          | 4 (4.9)            |         |
| <b>Frequency of neurologist clinic visits</b>  | Every month   | 24 (14.2)          | 15 (18.5)          | < 0.001 |
|  | Every 3-6 months                                    | 42 (24.9)          | 40 (49.4)          |         |
|  | Every year  | 50 (29.6)          | 14 (17.3)          |         |
|  | Every few years (when a seizure occur)              | 53 (31.4)          | 12 (14.8)          |         |
| <b>Experience of side effects</b>  | No  | 59 (34.9)          | 48 (59.3)          | < 0.001 |
|  | Yes   | 110 (65.1)         | 33 (40.7)          |         |
| <b>Following healthcare provider instructions</b>  | No  | 63 (37.3)          | 8 (9.9)            | < 0.001 |
|  | Yes   | 106 (62.7)         | 73 (90.1)          |         |
| <b>Main reason for stopping medication</b>   | Forgetfulness                                       | 55 (42.0)          | 0                  | < 0.001 |
|  | High cost   | 18 (13.7)          | 1 (7.1)            |         |
|  | Complexity of treatment regimen                     | 11 (8.4)           | 0                  |         |
|  | Experience of side effects                          | 12 (9.2)           | 0                  |         |
|  | Unavailability of drugs                             | 9 (6.9)            | 10 (71.4)          |         |
|  | Perception of inefficacy                            | 8 (6.1)            | 2 (14.3)           |         |
|  | Absence of seizures                                 | 18 (13.7)          | 1 (7.1)            |         |
| <b>Participant is satisfied and feels his treatment effective</b>  | No  | 70 (41.4)          | 3 (3.7)            | < 0.001 |
|  | Yes   | 99 (58.6)          | 78 (96.3)          |         |
| <b>Participant feels his treatment is an economic burden</b>   | No  | 66 (39.1)          | 67 (82.7)          | < 0.001 |
|  | Yes   | 103 (60.9)         | 14 (17.3)          |         |
| <b>Presence of depression/ anxiety</b>   | No  | 122 (72.2)         | 68 (84.0)          | 0.04    |
|  | Yes   | 47 (27.8)          | 13 (16.0)          |         |

*Non-significant variables:*

*Gender, Region of residence, Marital Status, Occupation, Education level, Medical insurance, Presence of comorbidities, Family history of epilepsy, Number of AE, Frequency/day, Number of drugs, Number of workers/family, Duration of disease, BMI.*

**Table 4. Final results of regression using the status of attitudes as the dependent variable**

| Variables   | Adjusted OR                    | 95% CI      | p-value          |
|---|--------------------------------|-------------|------------------|
| Age   | 0.97                           | 0.94 - 0.99 | <b>0.02</b>      |
| Presence of depression/ anxiety                           | 0.4                            | 0.2 - 0.9   | <b>0.04</b>      |
| Participant is satisfied and find his treatment effective | 4.9                            | 1.2 - 20    | <b>0.03</b>      |
| Participant feels his treatment is an economic burden     | 0.2                            | 0.1 - 0.4   | <b>&lt;0.001</b> |
| Controlled epilepsy (no seizures at least 6 months)       | 3.4                            | 1.6 - 7.1   | <b>0.001</b>     |
| Age onset disease   | <i>Reference: &lt;12 years</i> |             |                  |
| 12-20 years   | 3.1                            | 1.1 - 8.4   | <b>0.03</b>      |
| 20-40 years   | 0.5                            | 0.2 - 1.4   | 0.2              |
| >40 years   | 2.7                            | 0.9 - 8     | 0.08             |
| Frequency of neurologist clinic visits                    | <i>Reference: monthly</i>      |             |                  |
| Every 3-6 months  | 0.7                            | 0.3 - 2.1   | 0.6              |
| Every year  | 0.2                            | 0.04 - 0.5  | <b>0.002</b>     |
| Every few years (when a seizure occurs)                   | 0.2                            | 0.1 - 0.7   | <b>0.01</b>      |

OR:Odds Ratio; CI: Confidence Interval

Dependent variable: "Positive/ Negative" Attitudes.

Hosmer–Lemeshow test p-value=0.7/ Overall predicted percentage = 79.6%.

Variables excluded from the model following this order:

Family history of epilepsy, in busy period (at work, away from home, in outdoor dinner/ lunch or in travel), Following healthcare provider instructions, Gender, Number of pills/ day, if patient forget to take medication, if no money/ health coverage, if a neighbor of participant advices him to stop medication, Experience of side effects, Occurrence seizures in the last 5 years, Attitude in fasting states.

**Table 5. Final results of regression using the seizure control as the dependent variable**

| Variables  | Adjusted OR                     | 95% CI      | p-value          |             |
|--|---------------------------------|-------------|------------------|-------------|
| Attitudes status   | 1.9                             | 1.1 - 3.4   | <b>0.03</b>      |             |
| Duration of disease  | 1.04                            | 1.02 - 1.07 | <b>&lt;0.001</b> |             |
| Do not follow neurologist's instructions in fasting period | 0.5                             | 0.3 - 0.9   | <b>0.03</b>      |             |
| Attitude if seizure occurs                                 | <i>Reference: Double a dose</i> |             |                  |             |
|  | Continue medication normally    | 1.2         | 0.5 - 2.6        | 0.7         |
|  | Contact a neurologist           | 2.9         | 1.3 - 6.5        | <b>0.01</b> |

*OR:Odds Ratio; CI: Confidence Interval*

*Dependent variable: "Controlled epilepsy/ Uncontrolled epilepsy".*

*Hosmer–Lemeshow test p-value=0.6/ Overall predicted percentage = 67.6%.*

*Variables excluded from the model following this order:*

*Participant is satisfied and find his treatment effective, Following healthcare provider instructions, Gender, Number of drugs/day, Presence of tumor.*