

# Differences in knowledge about epilepsy and antiepileptic drugs among pharmacy-dispensing workers in Cambodia and in Lao PDR

Noudy Sengxeu, Farid Boumédiène, Somchit Vorachit, Phetvongsinh Chivorakoun, Vimalay Souvong, Chanthanom Manithip, Samleng Chan, Sina Ros, Kimly Chea, Chanraksmey Aon, et al.

#### ▶ To cite this version:

Noudy Sengxeu, Farid Boumédiène, Somchit Vorachit, Phetvongsinh Chivorakoun, Vimalay Souvong, et al.. Differences in knowledge about epilepsy and antiepileptic drugs among pharmacy-dispensing workers in Cambodia and in Lao PDR. Epilepsy & Behavior, 2019, pp.106834. 10.1016/j.yebeh.2019.106834. hal-02426605

### HAL Id: hal-02426605 https://unilim.hal.science/hal-02426605

Submitted on 21 Jul 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



# Differences in knowledge about epilepsy and antiepileptic drugs among pharmacy-dispensing workers in Cambodia and in Lao PDR

Auteurs lists:

**SENGXEU Noudy** - (1) INSERM, Univ. Limoges, CHU Limoges, UMR\_S 1094, Tropical Neuroepidemiology, Institute of Neuroepidemiology and Tropical Neurology, Limoges, France, - (2) Faculty of pharmacy, University of health sciences, Vientiane, Lao PDR,

**BOUMEDIENE Farid** - (1) INSERM, Univ. Limoges, CHU Limoges, UMR\_S 1094, Tropical Neuroepidemiology, Institute of Neuroepidemiology and Tropical Neurology, Limoges, France,

**SOMCHIT Vorachit** - (3) Lao Association for Patient with epilepsy, Vientiane, Lao PDR,

**CHIVORAKOUN Phetvongsinh** - (3) Lao Association for Patient with epilepsy, Vientiane, Lao PDR,

**SOUVONG Vimalay -** (3) Lao Association for Patient with epilepsy, Vientiane, Lao PDR,

**MANITHIP Chanthanom** - (2) Faculty of pharmacy, University of health sciences, Vientiane, Lao PDR

**CHAN Samleng** – (4) Cambodian Society of Neurology, Calmette Hospital, Phnom Penh, Cambodia,

**ROS Sina** – (4) Cambodian Society of Neurology, Calmette Hospital, Phnom Penh, Cambodia,

**CHEA Kimly** – (5) Faculty of medicine, University of health sciences, Phnom Penh, Cambodia,

**AON Chanraksmey** - (4) Cambodian Society of Neurology, Calmette Hospital, Phnom Penh, Cambodia,

**PREUX Pierre-Marie** - (1) INSERM, Univ. Limoges, CHU Limoges, UMR\_S 1094, Tropical Neuroepidemiology, Institute of Neuroepidemiology and Tropical Neurology, Limoges, France,

**RATSIMBAZAFY Voa** - (1) INSERM, Univ. Limoges, CHU Limoges, UMR\_S 1094, Tropical Neuroepidemiology, Institute of Neuroepidemiology and Tropical Neurology, Limoges, France, - (6) CHU Limoges, Department of Pharmacy, F-87000 Limoges, France

**DUFAT Hanh** - (7) Natural Products, Analysis and Synthesis, CiTCoM (Cibles Thérapeutiques et Conception de Médicaments)-UMR 8038 CNRS/Université Paris Descartes, Faculty of Pharmacy of Paris, University of Paris Descartes USPC, Paris, France.

**JOST Jeremy** - (1) INSERM, Univ. Limoges, CHU Limoges, UMR\_S 1094, Tropical Neuroepidemiology, Institute of Neuroepidemiology and Tropical Neurology, Limoges, France, (6) CHU Limoges, Department of Pharmacy, F-87000 Limoges, France

#### Abstract

Epilepsy is the most common neurological disorder encountered in primary care in Southeast Asia. People with epilepsy require long-term therapy management. Non-adherence to antiepileptic drugs (AEDs) has been identified as a major factor in suboptimal control of epilepsy. Pharmacies offer patients a first-line point of contact with the healthcare system. Many pharmacies operate with limited or non-qualified human resources that can lead to insufficient knowledge, inappropriate supply of medicines and insufficient counseling.

**Objective:** The aim of this study was to evaluate the qualification and knowledge concerning epilepsy and antiepileptic drugs among pharmacy-dispensing workers who sell drugs to people with epilepsy.

**Method:** A cross-sectional qualitative study was conducted in public and private pharmacies, in both urban and rural areas of Cambodia and Lao PDR. The knowledge was collected through a questionnaire.

**Results:** A total of 180 respondents from 123 outlets in the two countries were included in this study. A proportion of 40.8% (31) of respondents in Cambodia and 38.5% (40) in Lao PDR were pharmacists, followed by sellers who did not received any healthcare training with a proportion of 18.4% (14) in Cambodia compared to 20.2% (21) in Lao PDR. Head trauma was cited as the main cause of epilepsy by 72.4% (55) in Cambodia and 27.2% (28) in Lao PDR (p<0.001). Epilepsy was considered as a contagious disease by 6.6% (5) of respondents in Cambodia compared to 18.4% (19) in Lao PDR (p=0.03). Eighty-seven percent (66) of respondents in Cambodia knew at least one long-term antiepileptic drug, *versus* 67.3% (70) in Lao PDR (p=0.003). Phenobarbital was mentioned in more than 90.0% of cases in both countries. In overall, 15.4% (21) thought that if seizures are controlled for some months, people with epilepsy could stop taking their antiepileptic drugs. Only one respondent from Lao PDR was aware of drug-drug interaction between antiepileptic drugs and oral contraception.

**Conclusion:** An educational intervention should be implemented to improve the knowledge of epilepsy and AEDs for pharmacy-dispensing workers. This could include advice for all pharmacy-dispensing workers in order to improve AED management and follow-up of therapeutic adherence.

**Key word:** knowledge; epilepsy; antiepileptic drugs; pharmacy-dispensing workers; Cambodia; Lao PDR.

#### 1. Introduction

settings in Southeast Asia [1]. Treatment for this condition is frequently managed by primary care physicians and nurses due to the lack of specialty care services and neurologists [1, 2]. People with epilepsy (PWE) require long-term antiepileptic drug (AED) therapy. The goal of medication is to balance process between seizure control and tolerance [3]. The firstgeneration AEDs (sodium valproate, carbamazepine, phenytoin and phenobarbital) are documented as the main AEDs available in Southeast Asia [4]. They have several side effects, drug-drug interactions (DDI) such as decreasing efficacy or increasing side effects of comedications [5]. Women with epilepsy are a specific population that needs counseling and comprehensive information about issues related to contraception and the potential teratogenicity of epilepsy and AEDs [6]. These unmanaged drug-related adverse events are well known to be one of the leading causes of treatment discontinuation by patients themselves [7]. Furthermore, studies have demonstrated that PWE do not receive enough information about epilepsy and its treatment [8, 9]. Non-adherence to AEDs has been identified as a major factor in the suboptimal control of epilepsy. However, treatment failure due to DDI or avoidable side effects and lack of information is often underestimated. Pharmacies, public and private, offer to patients a first-line point of contact with the healthcare system. Pharmacists and/or pharmacy-dispensing workers remain some of the most accessible healthcare professionals. They are an important way of providing medicines, counseling, knowledge and advice on the safe and effective use of drugs [10-12]. A study has demonstrated the positive benefits for patients of pharmacist AED therapy management, including a significant improvement in adherence through therapeutic patient education. These interventions have shown a decrease in health expenses by significantly reducing avoidable hospital admissions [13]. In a study aimed at assessing perceptions of community pharmacist's and their potential role, PWE have expressed their interest in having their pharmacist become more involved in their health care and communicate more with their

Epilepsy is the most common neurological disorder encountered in primary care

doctor, especially with regard to DDI and adverse reactions [14]. Despite the important role of pharmacists, knowledge gaps in AED therapy among pharmacists were reported [15]. Likewise, pharmacists or pharmacy-dispensing workers were poorly cited as a source of medication information [7].

In Southeast Asia, Cambodia and the Lao People's Democratic Republic (Lao PDR) are resource-limited settings and have a prevalence of epilepsy of 5.8 and 7.7/1000 respectively [16-18]. In these countries, the epilepsy treatment gap (defined as the number of people with a condition or disease who need treatment for it but who do not get it [19]) was estimated to be 65.8% in Cambodia and 90.0% in Lao PDR [20-22]. Epilepsy is included in the mental health programs of these two countries. The initial national program for mental health was established in 2000 in Cambodia and in 2007 in Lao PDR. This program provides community mental health outreach and training of physicians and nurses in the public sector. However, pharmacists and other health professionals who dispense AEDs to PWE were not included in the program [22-24].

Many pharmacies in these countries operate with limited or non-qualified human resources that can lead to insufficient knowledge, inappropriate supply of medicines and insufficient counseling [25]. In general, studies on dispensing practices in pharmacies in both Cambodia and Lao PDR have reported that the provision of drug use information was inadequate. Patients had little opportunity to obtain adequate information about their treatment: a quarter of patients do not know how to take their drugs [26]. In addition, a lack of properly packaged and labeled drugs was documented. The inadequate information provided in pharmacies may be due to a lack knowledge among pharmacists or pharmacy-dispensing workers [26, 27]. Furthermore, poor knowledge of epilepsy and AEDs among nurses and physicians was documented in Lao PDR [28]. To the best of our knowledge, no study has been performed concerning epilepsy knowledge among any type of healthcare professionals in Cambodia. The aim of this study was to describe and compare the qualification and knowledge concerning epilepsy and AEDs among pharmacy-dispensing workers in Cambodia and Lao PDR.

#### 2. Methodology

#### 2.1. Identification of health facilities in Cambodia and Lao PDR

Healthcare facilities in Cambodia and Lao PDR are organized in two sectors: public and private. In the public sector, there are four levels of organization: central/national hospitals, provincial hospitals, district hospitals and health centers. Health centers are often staffed by medical assistants, nurses and/or midwifes with low to mid-level qualifications and non-physician staff. The private sector is composed of private hospitals, clinics and pharmacies. In both countries, most of the private facilities are owned by public health staff having a dual practice. There is no clear definition to distinguish private 'clinics' and private 'hospitals'. The use of the name 'hospital' is preferred, probably for marketing purposes. These private facilities are mostly located in the capital city [23, 24]. Private pharmacies are classified in three categories for both Cambodia and Lao PDR, according to the qualification of the license:

- Level I: managed by the pharmacist (5 years of university education);
- Level II: run by a pharmacist assistant (3 years of university education);
- Level III: run by any healthcare professional, mostly nurses or midwifes.

In Lao PDR, only level I and II are authorized to sell antiepileptic drugs. Conversely, in Cambodia, all registered private pharmacies are authorized to sell all registered pharmaceutical drugs including AEDs [11, 28].

#### 2.2. Survey setting and sampling strategy

A cross-sectional descriptive study was conducted from February to July 2018 in Lao PDR and Cambodia. The estimated population of Lao PDR was 6.5 million (2015 Population Census) and 13 million for Cambodia (2008 Population Census). Three provinces in each country were selected: i) capital province, ii) the second biggest province after the capital, iii) a province that shares a border with a neighboring country. According to those criteria, six provinces were included in the study (figure 1). Then, in each province, the district with the

highest population density was selected as the urban district and the district that had the lowest population density was selected as the rural one.

The urban district had a wide variety of health-care providers, including all levels of public health facilities (central hospital, provincial hospital, district hospital and health centers), private hospitals, clinics and pharmacies. In the rural district, only the district hospital, health centers, pharmacies and a few clinics were present.

**Type of outlet included:** In this study, we included the provincial hospitals, district hospitals and pharmacies in the selected area. All types of pharmacy (level I, II, III) in each district were included. In Lao PDR, level III pharmacies are not allowed to sell AEDs, but they were included as almost all the pharmacies in rural areas were level III.

**Type of outlet not included:** Central/national hospitals, private hospitals and clinics were not included because we did not obtain authorization from the Ministry of Health. Primary health centers were not included in our study because they only dispense first aid drugs [29].

Outlets sampling: This study was performed as an ancillary study of a project aimed at assessing the quality of AEDs in Southeast Asia and the number of outlets was calculated based on this objective. The sampling methodology was adapted from that one used in another project performed in sub-Saharan Africa and published in 2018 [30]. These outlets were considered first to collect AEDs samples and then to evaluated qualification and knowledge about epilepsy and antiepileptic drugs among pharmacy-dispensing workers (health professionals or non-health professionals). A required number of participants or pharmacy-dispensing workers was not calculated as this was a comprehensive sampling of all pharmacy-dispensing workers present at the sampled outlets during the period of the AEDs collection.

#### 2.3. Questionnaire

The survey instrument was developed by authors in the English language and translated into the local languages by the first author, native of Lao PDR, and one medical doctor native of Cambodia. Then the questionnaire was back translated into English for accuracy. The questionnaire was pre-tested in Vang Vieng district (160 km north of Vientiane, the capital).

The study team interviewed 4 pharmacy-dispensing workers from the district hospital and 6 pharmacy-dispensing workers from different private pharmacies to assess understanding and ease of use before making general use of the questionnaire.

The questionnaire contained 24-items (supplementary Table S1) and was structured into three sections: (i) professional background and experience with epilepsy, (ii) knowledge of epilepsy (cause, symptoms, diagnosis, etc.), (iii) knowledge of AEDs (DDI, side effects). The questionnaire contained mostly closed-ended questions (yes/no/do not know, and multiple-choice questions).

In each district, the investigators first met with the district authorities to obtain lists of existing registered outlets. A simple randomization was performed with table randomization, and the outlets selected were visited by the investigators and one of the district authority's workers. All pharmacy-dispensing workers presented in the outlets selected were asked to answer the questionnaires at their workplace. After agreeing to participate and signing a consent form, they completed the paper version of the questionnaire. All pharmacy-dispensing workers at the time of the visit were asked to complete the questionnaire in separate rooms. Investigators stayed with them at all times to answer any questions they had regarding the questionnaire and to check completion when they finished. It took between 20 and 30 minutes to complete the questionnaire.

#### 2.4. Data analysis

Statistical analyses were performed using SPSS version 23.0. The comparative analysis of qualitative variables from Cambodia versus Lao PDR was performed using the Chi-2 tests and Fisher exact tests, while one-way ANOVA was performed for quantitative variables. The significant threshold for all analyses was set at 0.05. To predict the variables associated with an increase chance of having knowledge of at least one long-term AED, a logistic regression was performed separately for Cambodia and Lao PDR. Only variables with a p-value <0.25 after univariate analysis were entered into a multivariate logistic regression model using the backward stepwise exclusion method.

#### 3. Results

## 3.1. Sociodemographic and experience with epilepsy among pharmacy-dispensing workers

A total of 180 respondents from 123 outlets in both countries were included in this study (42.0% from Cambodia and 58.0% from Lao PDR). The sampling flowchart of outlets and the number of outlets declining to participate was indicated in Figure 2. Overall, more than half (65.0%) of respondents were located in urban areas and were in the private sector. A proportion of 40.8% (31) of respondents in Cambodia and 38.5% (40) in Lao PDR were pharmacists, followed by sellers who did not received any healthcare training with a proportion of 18.4% (14) in Cambodia compared to 20.2% (21) in Lao PDR. All sellers without healthcare qualifications were found in private pharmacies only in both countries. In Lao PDR, 18.2% (19) of the respondents included were from level III pharmacies. Overall, respondents had been dispensing medicines for 1 to 42 years. A proportion of 42.0% (75) of respondents reported that they had PWE come to ask for or purchase AEDs in their facility. Details of specific experiences with epilepsy are shown in Table 1.

#### 3.2. Sources of information relating to epilepsy

Of all respondents, only one (0.6%) from Lao PDR was not aware of epilepsy. Overall, the significant difference between Cambodia and Lao PDR concerning the sources of information on epilepsy was education at schools and universities (64.5% vs. 47.6%, p=0.024), and mass media or scientific leaflets (44.7% vs.14.6%, p<0.001). Overall, however, only 1.9% (2) of respondents from Lao PDR had received continuous training on epilepsy after the university (table 2).

#### 3.3. Knowledge of epilepsy and diagnosis

Epilepsy was considered to be a contagious disease by 6.6% (5) of respondents in Cambodia compared to 18.4% (19) in Lao PDR (p=0.03) (table 2). Furthermore, 69.7% (53) and 17.5% (18) of respondents, respectively, said that epilepsy could be treated (p<0.001). Head trauma was cited as the main causes of epilepsy by 72.4% (55) in Cambodia and 27.2% (28) in Lao PDR (p<0.001), cysticercosis was mentioned by 17.1% (13) *vs.* 4.9% (5) (p=0.01), respectively. Unknown origin was mostly cited by respondents in Lao PDR compared to Cambodia (19.4% (6) vs. 7.9% (20), p=0.03). A proportion of 71.1% (54) in Cambodia said that there was only one type of epileptic seizure (tonic-clonic seizure), while 46.6% (48) said this in Lao PDR (p=0.001). Overall, 41.3% (74) of respondents reported that they did not know how to diagnose epilepsy. Among respondents who knew, electroencephalogram (EEG) was mentioned in 42.1% (32) in Cambodia and 9.7% (10) in Lao PDR (p<0.001).

#### 3.4. Knowledge of antiepileptic drugs

Eighty-seven percent (66) of respondents in Cambodia were aware of at least one long-term AED, while they were 67.3% (70) in Lao PDR (p=0.003). Phenobarbital was mentioned by more than 90.0% in both countries. Conversely, three others major AEDs (carbamazepine, phenytoin, sodium valproate) were cited in Cambodia more than in Lao PDR (57.6% (38) vs. 32.9% (23), p=0.006; 42.4% (28) vs. 18.6% (13), p=0.003, 21.2% (14) vs. 5.7% (4), p=0.01 respectively). More than 40.0% of respondents in both countries knew that PWE have to take AEDs depending on type of their seizure. Overall, 58.1% (79) of respondents said that PWE who started AEDs have to take them for their whole life. From our observation, 15.4% (21) thought that if seizures are controlled for some months, PWE could stop AEDs, and 20.0% (27) advised women with epilepsy to stop taking AEDs if they become pregnant. Only one respondent from Lao PDR was aware of the fact that enzyme-inducing antiepileptic drugs may reduce the effectiveness of contraceptives. We found that 37.5% (51) did not know any side effect of AEDs (table 3).

#### 3.5. Variables to predict knowledge on the treatment of epilepsy

Approximately 13% (10) of respondents in Cambodia did not know any long-term AEDs compared to 32.7% (34) of respondents in Lao PDR. After a control of confounding in the final multivariate logistic regression analysis for Cambodia, no significant associated factor was found. For Lao PDR, three factors were found to be significantly associated with an increased chance of knowing at least one AED molecule. These factors were: working in the public sector compared to the private sector (aOR = 6.24, 95%, CI = [2.06–18.87]), seeing an epileptic seizure (aOR = 2.70, 95%, CI = [1.02–7.09]), and having patients with epilepsy come to purchase AEDs at their workplace, (aOR = 7.35, 95%, CI = [2.49–21.69]).

#### 4. Discussion

Kwan & Brodie reported in 2000 that nearly 60% of PWE could achieve seizure control by adhering to prescribed AEDs, but poor adherence to AEDs was reported in approximately one-third of PWE [31-33]. PWE frequently purchase their AEDs at pharmacies. In this way, pharmacy-dispensing workers play an essential role in providing information on the appropriate use of AEDs and on identifying and managing side effects when dispensing AEDs to PWE. These are important factors that contribute to improving adherence to the medication regimen [34]. Our results in both Cambodia and Lao PDR demonstrated that pharmacists, who are educated and supposed to be well-trained about medications, accounted for less than a half of pharmacy-dispensing workers. One in five pharmacy-dispensing workers were sellers without any medical or pharmaceutical training. In Cambodia, the number of unqualified pharmacy-dispensing workers found in our study was less than in a previous study published in 2004 (89.6%); this reduction may be due to restrictions in pharmacy regulations in Cambodia [11]. In Lao PDR, however, our results were consistent with a previous study performed in 2001, reporting a proportion of 24.5% of non-healthcare qualified pharmacy-dispensing workers [35]. In addition, inadequate qualification among pharmacy-dispensing workers combines with the shortage of medical books that has been reported over the past 20 years in Lao PDR [28]. This point could lead to inadequate information on medical education and incorrect practices among pharmacydispensing workers not only for PWE, but for all patients.

In this study, we pointed out many gaps in the pharmacy-dispensing worker's knowledge of epilepsy (mainly related to AEDs). This finding was in accordance with a study showing insufficient knowledge about epilepsy among different types of healthcare professionals such as physical educators, nutritionists and physiotherapists [36]. This knowledge gap can lead to inadequate counseling for PWE, which is consistent with findings in other studies that reported suboptimal performances at pharmacies, including a lack of drug information and counselling for PWE in Cambodia [11]. For Lao PDR, no specific study was performed on counseling by pharmacy-dispensing workers for PWE, but when we compare recent studies on the quality of antenatal care services [37] and knowledge of sexually transmitted infections [38] among healthcare providers which reported limited knowledge, poor services and insufficient counseling, these are consistent with our findings. This insufficient knowledge of epilepsy in both Cambodia and Lao PDR are probably a consequence of a lack of training on epilepsy and AEDs – only half of them received epilepsy training at school or university, and a minority received post-graduate training on epilepsy. Misunderstanding of epilepsy (there is only one type of seizure, epilepsy is a communicable disease and is untreatable) in both Cambodia and Lao PDR was higher than two previous studies among Cameroonian medical students and health-care professionals in Saudi Arabia [39, 40], but lower than for student nurses in Cameroon [41].

We observed in our study that pharmacy-dispensing workers in Cambodia have a better knowledge of epilepsy than those in Lao PDR, perhaps due to differences in curricula and the time allocated to the study of epilepsy. Another explanation could be the fact that one-quarter of respondents from Lao PDR worked at level III pharmacies that were not supposed to sell AEDs. Nevertheless, this was a pragmatic study assessing the situation in real conditions. Knowledge of epilepsy and AEDs among pharmacy-dispensing workers in Lao PDR was low, but the improvement of knowledge was highlighted when compared to the

previous study performed in 2003 among physicians and nurses [28]. The ability to mention at least one long-term AEDs and knowing that discontinuing AEDs could be dangerous was improved. This was probably due to the annual training program and information about this disease that has become easily accessible by internet or mass media [29, 42, 43]. Conversely, no previous studies on knowledge of epilepsy and AEDs among healthcare workers had been performed in Cambodia.

Inadequate knowledge of AEDs was observed in both Cambodia and Lao PDR. Among pharmacy-dispensing workers who knew about the treatment of epilepsy in our study, phenobarbital was the most cited in both countries, similar to a study in Zambia [44], probably be due to the availability of this molecule in developing countries [45, 46]. Furthermore, only 36% were aware of the need to adhere to AED regimens during pregnancy. This result is lower than studies conducted in Palestine with 58.1% [47] and Israel with 93% [48]. The reduction of the effectiveness of contraceptives due to the enzyme-inducing features of most of the major AEDs was unknown in almost all pharmacy-dispensing workers in our study, whereas in other studies, more than 70% of pharmacists and healthcare professionals were aware of this DDI [47, 49, 50]. In Cambodia and Lao PDR, about three out of five pharmacy-dispensing workers know limited number of side effects associated with AEDs. This constituted a discrepancy when compared to previous studies in Palestine [47] and Israel [48]. This discrepancy may be due to the fact that all of the respondents in these previous studies were pharmacists and had better knowledge of large number of various negative effects of AEDs.

#### 5. Strengths and limitations

The major limitation of our study was that we could not investigate the central hospital in Cambodia. To be able to compare Cambodia versus Lao PDR, the central hospital in these two countries was not considered in the analysis. We recognize that the over-representation of private pharmacies in the sample may have generated a selection bias with regard to the situation of all drug-dispensing outlets in these countries. This was the first study to assess

these aspects in these countries, and private pharmacies remain the main type of outlets in the supply chain. The main strength of this first study is that we assessed knowledge among pharmacists and all pharmacy-dispensing workers in real-life situations in Cambodia and Lao PDR. Respondents were not allowed to consult or look for answers in any resources when answering the survey questions.

#### 6. Conclusion

An educational intervention should be implemented to improve the knowledge of epilepsy and AEDs among pharmacy-dispensing workers. This could include the ability to provide advice for all pharmacy-dispensing workers in order to improve AED management (reducing DDI and managing side effects) and follow-up for therapeutic adherence, which could be divided into three dimensions: acceptance, compliance with the recommendation and persistence of this compliance. Due to the fact that pharmacy-dispensing workers have regular contacts and are easily accessible for PWE, the compliance and acceptance dimensions could be supported and enhanced, especially since all advice delivered by pharmacy-dispensing workers is free to PWE when AEDs are dispensed. We suggest that communication and collaboration between healthcare professionals such as pharmacydispensing workers and physicians could provide a beneficial improvement to care management for PWE. This collaboration could improve care in a variety of ways, including medication management, patient counselling and therapeutic education [51]. As result of this study, professional educational programs (initial formation and continuing education), and patients' information should be developed. In addition, the professional activities should comply with the pharmacy regulation, in particular which regard to authorized personnel.

#### **Ethical approval**

Ethical approval for this study was obtained from the National Ethics Committee for Health Research, Ministry of Health of Cambodia (reference No.12/NECHR) and Lao PDR (reference No.077/NECHR). Written informed consent was systematically obtained from all participants prior to the interview and all answers were kept confidential.

### **Funding**

None of the authors has any conflicts of interest to disclose. This work was supported by the Foundation Pierre Fabre [2018]. The funder was not involved in the study design, data collection and analysis, decision to publish, or writing the manuscript.

#### **Conflicts of interest statement**

None of the authors has any conflicts of interest to disclose.

#### Reference

- [1] World Health Organization. Atlas: country resources for neurological disorders, www.who.int/mental\_health/neurology/epidemiology/en; 2004 [Accessed 21 November 2018].
- [2] Trinka E, Kwan P, Lee B, Dash A. Epilepsy in Asia: Disease burden, management barriers, and challenges. Epilepsia 2018;60 Suppl 1: 7-21.
- [3] Cascino GD. Epilepsy: contemporary perspectives on evaluation and treatment. In: Mayo Clin Proc: Elsevier; 1994. p. 1199-1211.
- [4] Mac TL, Tran DS, Quet F, Odermatt P, Preux PM, Tan CT. Epidemiology, aetiology, and clinical management of epilepsy in Asia: a systematic review. Lancet Neurol 2007;6: 533-43.
- [5] Diaz RA, Sancho J, Serratosa J. Antiepileptic drug interactions. Neurologist 2008;14: S55-65.
- [6] May TW, Pfafflin M, Coban I, Schmitz B. [Fears, knowledge, and need of counseling for women with epilepsy. Results of an outpatient study]. Nervenarzt 2009;80: 174-83.
- [7] Liu L, Yiu C-H, Yen D-J, Chou M-H, Lin M-F. Medication education for patients with epilepsy in Taiwan. Seizure 2003;12: 473-477.
- [8] Couldridge L, Kendall S, March A. A systematic overviewa decade of research'. The information and counselling needs of people with epilepsy. Seizure 2001;10: 605-614.
- [9] Jain P, Patterson V, Morrow J. What people with epilepsy want from a hospital clinic. Seizure 1993;2: 75-78.
- [10] McAuley JW, Mott DA, Schommer JC, Moore JL, Reeves AL. Assessing the needs of pharmacists and physicians in caring for patients with epilepsy. J Am Pharm Assoc (Wash) 1999;39: 499-504.
- [11] Yang D, Plianbangchang P, Visavarungroj N, Rujivipat S. Quality of Pharmaceutical Items Available from Drugstores in Phnom Penh, Cambodia. Southeast Asian J Trop Med Public Health 2004; 35:741-747.
- [12] Bunting BA, Cranor CW. The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication therapy management program for asthma. J Am Pharm Assoc (2003) 2006;46: 133-147.
- [13] Koshy S. Role of pharmacists in the management of patients with epilepsy. Int J Pharm Pract 2012;20: 65-68.
- [14] McAuley JW, Miller MA, Klatte E, Shneker BF. Patients with epilepsy's perception on community pharmacist's current and potential role in their care. Epilepsy Behav 2009;14: 141-145.
- [15] Shawahna R, Atrash A, Jebril A, Khalaf A, Shaheen E, Tahboosh H. Pharmacists' knowledge of issues in pharmacotherapy of epilepsy using antiepileptic drugs: A cross-sectional study in Palestinian pharmacy practice. Epilepsy Behav 2017;67: 39-44.
- [16] Chongsuvivatwong V, Phua KH, Yap MT, Pocock NS, Hashim JH, Chhem R, Wilopo SA, Lopez AD. Health and health-care systems in southeast Asia: diversity and transitions. Lancet 2011;377: 429-437.
- [17] Preux PM, Chea K, Chamroeun H, Bhalla D, Vannareth M, Huc P, Samleng C, Cayreyre M, Gerard D, Dumas M, Oum S. First-ever, door-to-door cross-sectional representative study in Prey Veng province (Cambodia). Epilepsia 2011;52: 1382-7.
- [18] Tran DS, Odermatt P, Le TO, Huc P, Druet-Cabanac M, Barennes H, Strobel M, Preux PM. Prevalence of epilepsy in a rural district of central Lao PDR. Neuroepidemiology 2006;26: 199-206.
- [19] Kale R. The treatment gap. Epilepsia 2002;43: 31-33.
- [20] Meinardi H, Scott R, Reis R, On Behalf Of The Ilae Commission on the Developing World JS. The treatment gap in epilepsy: the current situation and ways forward. Epilepsia 2001;42: 136-149.
- [21] Chisholm D, WHO-CHOICE. Cost-effectiveness of first-line antiepileptic drug treatments in the developing world: a population-level analysis. Epilepsia 2005;46: 751-759.

- [22] Barennes H, Tran D-S, Latthaphasavang V, Preux PM, Odermatt P. Epilepsy in Lao PDR: From research to treatment intervention. NEUROL ASIA 2008;13: 27-31.
- [23] Pacific WHOROftW. The Kingdom of Cambodia health system review. Manila: WHO Regional Office for the Western Pacific 2015; Health systems in transition vol.5, no.2.
- [24] Pacific WHOROftW. The Lao People's Democratic Republic health system review. Manila: WHO Regional Office for the Western Pacific 2014; Health System in Transition; Vol.4 No.1.
- [25] Smith F. The quality of private pharmacy services in low and middle-income countries: a systematic review. Pharm World Sci 2009;31: 351-61.
- [26] Keohavong B, Syhakhang L, Sengaloundeth S, Nishimura A, Ito K. Rational use of drugs: prescribing and dispensing practices at public health facilities in Lao PDR. Pharmacoepidemiol Drug Saf 2006;15: 344-347.
- [27] Chareonkul C, Khun VL, Boonshuyar C. Rational drug use in Cambodia: study of three pilot health centers in Kampong Thom Province. Southeast Asian J Trop Med Public Health 2002;33: 418-24.
- [28] Harimanana A, Chivorakul P, Souvong V, Preux PM, Barennes H. Is insufficient knowledge of epilepsy the reason for low levels of healthcare in the Lao PDR? BMC Health Serv Res 2013;13: 41.
- [29] Barennes H, Sengkhamyong K, Sambany EM, Koffi PN, Chivorakul P, Empis G, Clavel S, Somphavong S, Wangkou N, Rajaonarivo C, Harimanana A. Children's access to treatment for epilepsy: experience from the Lao People's Democratic Republic. Arch Dis Child 2011;96: 309-13.
- [30] Jost J, Ratsimbazafy V, Nguyen TT, Nguyen TL, Dufat H, Dugay A, Ba A, Sivadier G, Mafilaza Y, Jousse C, Traikia M, Leremboure M, Auditeau E, Raharivelo A, Ngoungou E, Kariuki SM. Quality of antiepileptic drugs in sub-Saharan Africa: A study in Gabon, Kenya, and Madagascar. Epilepsia 2018;59: 1351-1361.
- [31] May TW, Berkenfeld R, Dennig D, Scheid B, Hausfeld H, Walther S, Specht U. Patients' perspectives on management and barriers of regular antiepileptic drug intake. Epilepsy Behav 2018;79: 162-168.
- [32] Lin CY, Chen H, Pakpour AH. Correlation between adherence to antiepileptic drugs and quality of life in patients with epilepsy: A longitudinal study. Epilepsy Behav 2016;63: 103-108.
- [33] Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342: 314-9.
- [34] Chen C, Lee DS, Hie SL. The impact of pharmacist's counseling on pediatric patients' caregiver's knowledge on epilepsy and its treatment in a tertiary hospital. Int J Clin Pharm 2013;35: 829-34.
- [35] Stenson B, Syhakhang L, Eriksson B, Tomson G. Real world pharmacy: assessing the quality of private pharmacy practice in the Lao People's Democratic Republic. Soc Sci Med 2001;52: 393-404.
- [36] Vancini RL, Benedito-Silva AA, Sousa BS, Gomes da Silva S, Souza-Vancini MI, Vancini-Campanharo CR, Cabral FR, de Lima C, Barbosa de Lira CA. Knowledge about epilepsy among health professionals: a cross-sectional survey in São Paulo, Brazil. BMJ Open 2012;2: e000919.
- [37] Phommachanh S, Essink DR, Wright EP, Broerse JEW, Mayxay M. Do health care providers give sufficient information and good counseling during ante-natal care in Lao PDR?: an observational study. BMC Health Serv Res 2019;19: 449.
- [38] Phrasisombath K, Thomsen S, Hagberg J, Sychareun V, Faxelid E. Knowledge about sexually transmitted infections (STIs) and attitudes toward female sex workers with STI symptoms among health care providers in Laos. Asia Pac J Public Health 2012;24: 940-52.
- [39] Alaqeel A, Alebdi F, Sabbagh AJ. Epilepsy: What do health-care professionals in Riyadh know? Epilepsy Behav 2013;29: 234-7.
- [40] Njamnshi AK, Angwafor SA, Baumann F, Angwafo FF, 3rd, Jallon P, Muna WF. Knowledge, attitudes, and practice of Cameroonian medical students and graduating physicians with respect to epilepsy. Epilepsia 2009;50: 1296-9.

- [41] Njamnshi AK, Tabah EN, Bissek AC, Yepnjio FN, Angwafor SA, Dema F, Fonsah JY, Tatah G, Njih IN, Njamnshi VL, Angwafo FF, 3rd, Muna WF. Knowledge, attitudes and practices with respect to epilepsy among student nurses and laboratory assistants in the South West Region of Cameroon. Epilepsy Behav 2010;17: 381-8.
- [42] Tran DS, Zen J, Strobel M, Odermatt P, Preux PM, Huc P, Delneuville L, Barennes H. The challenge of epilepsy control in deprived settings: low compliance and high fatality rates during a community-based phenobarbital program in rural Laos. Epilepsia 2008;49: 539-40.
- [43] Chivorakoun P, Harimanana A, Clavel S, Jousseaume S, Barennes H. [Epilepsy in Lao Popular Democratic Republic: difficult procurement of a first-line antiepileptic contributes to widening the treatment gap]. Rev Neurol (Paris) 2012;168: 221-9.
- [44] Chomba EN, Haworth A, Atadzhanov M, Mbewe E, Birbeck GL. Zambian health care workers' knowledge, attitudes, beliefs, and practices regarding epilepsy. Epilepsy Behav 2007;10: 111-9.
- [45] Cameron A, Bansal A, Dua T, Hill SR, Moshe SL, Mantel-Teeuwisse AK, Saxena S. Mapping the availability, price, and affordability of antiepileptic drugs in 46 countries. Epilepsia 2012;53: 962-9.
- [46] Odermatt P, Ly S, Simmala C, Angerth T, Phongsamouth V, Mac TL, Ratsimbazafy V, Gaulier JM, Strobel M, Preux PM. Availability and costs of antiepileptic drugs and quality of phenobarbital in Vientiane municipality, Lao PDR. Neuroepidemiology 2007;28: 169-74.
- [47] Shawahna R, Atrash A, Jebril A, Khalaf A, Shaheen E, Tahboosh H. Evaluation of pharmacists' knowledge of women's issues in epilepsy: A cross-sectional study in Palestinian pharmacy practice. Seizure 2017;46: 1-6.
- [48] Roth Y, Neufeld MY, Blatt I, Guy-Alfandary S, Rasaby S, Ekstein D, Eyal S. An evaluation of pharmacist knowledge on treatment with antiepileptic drugs. Seizure 2016;34: 60-5.
- [49] McAuley JW, Casey J, Long L. An evaluation of pharmacists' knowledge of women's issues in epilepsy. Epilepsy Behav 2009;14: 243-6.
- [50] Long L, Montouris G. Knowledge of women's issues and epilepsy (KOWIE-II): a survey of health care professionals. Epilepsy Behav 2005;6: 90-3.
- [51] Kelly DV, Bishop L, Young S, Hawboldt J, Phillips L, Keough TM. Pharmacist and physician views on collaborative practice: Findings from the community pharmaceutical care project. CPJ / RPC 2013;146: 218-226.

Figure 1: Study areas in Cambodia and Lao PDR

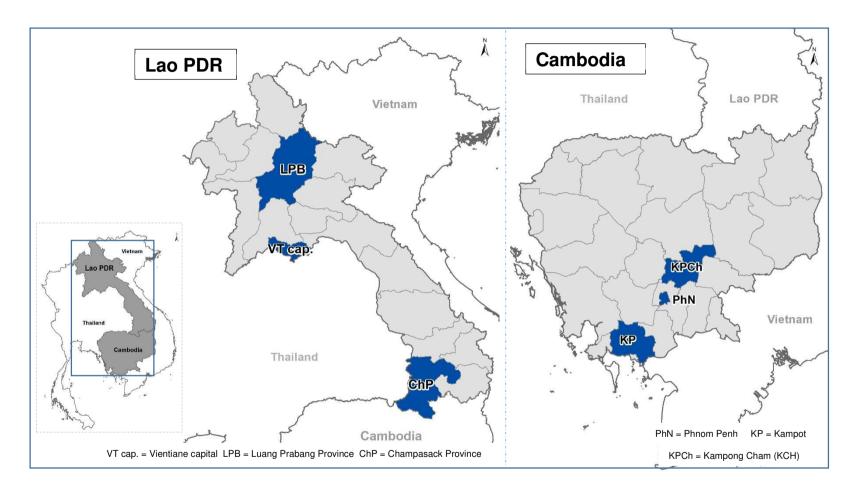


Figure 2: Study sampling flowchart for Cambodia and Lao PDR

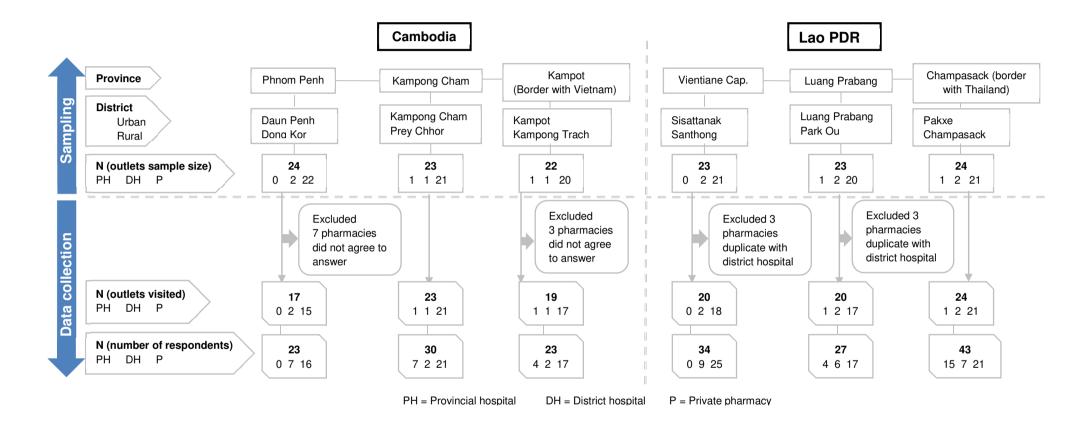


Table 1: Sociodemographics of the respondents

		Total	Cambodia	Lao PDR	Р
		N= 180	n= 76	n= 104	
Study zone					
: Urban area	:	117 (65.0%)	45 (59.2%)	72 (69.2%)	0.206
Rural area		63 (35.0%)	31 (40.8%)	32 (30.8%)	0.206
Health sector					
Public pharmacy		63 (35.0%)	22 (28.9%)	41 (39.4%)	0.158
Private pharmacy		117 (65.0%)	54 (71.1%)	63 (60.6%)	0.130
Qualification			į	į	
Pharmacist	į	71 (39.4%)	31 (40.8%)	40 (38.5%)	0.760
Seller (non-health worker)	- 1	35 (19.4%)	14 (18.4%)	21 (20.2%)	0.850
Physician	:	34 (18.9%)	2 (2.6%)	32 (30.8%)	< 0.001
Nurse	į	19 (10.6%)	18 (23.7%)	1 (1.0%)	< 0.001
Other*	į	21 (11.7%)	11 (14.5%)	10 (9.6%)	0.353
Age					
Mean (±SD)	!	39.9 (±12.5)	39.2 (±13.2)	40.2 (±12.1)	0.391
Professional experience in dispensing drugs	_			_	
Mean	i	14.1 (±11.2)	12.4 (±11.6)	15.3 (±10.7)	0.081
Specific experience with Epilepsy (answer yes)					
Does anyone in your family or anyone you know have epilepsy	į	36 (20.0%)	21 (27.6%)	15 (14.4%)	0.038
Have you ever seen anyone having an epileptic seizure	į	109 (60.6%)	42 (55.3%)	67 (64.4%)	0.221
Have you ever worked on Epilepsy	į	11 (6.1%)	3 (3.9%)	8 (7.7%)	0.360
Mean (std. deviation) years of following PWE		3.6 (±3.0)	4.0 (±3.5)	3.5 (±3.1)	0.822
Have you ever had patients with Epilepsy come to purchase an AED at your		75 (41.7%)	28 (36.8%)	47 (45.2%)	0.287
workplace	į	75 (41.776)	20 (00.0%)	47 (45.270)	0.207
Mean (times per month)	:	3.4 (±3.1)	2.9 (±2.3)	3.6 (±3.5)	0.366

<sup>\*</sup> Medical student, pharmacy student, midwife, dentist, technician

Table 2 : Knowledge of epilepsy

	Total	Cambodia	Lao PDR	Р
	N= 180	n= 76	n= 104	
Do not know epilepsy	1 (0.6%)	0 (0.0%)	1 (1.0%)	1.000
Knowing epilepsy	N= 179	n= 76	n= 103	
Knowing epilepsy by (multiple answers)	:	:		
Education at school or university	98 (54.7%)	49 (64.5%)	49 (47.6%)	0.033
Heard from family, friend or another person	51 (28.5%)	21 (27.6%)	30 (29.1%)	0.868
Mass media or scientific brochures	49 (27.4%)	34 (44.7%)	15 (14.6%)	< 0.001
Training after university	2 (1.1%)	0 (0.0%)	2 (1.9%)	0.509
Epilepsy requires long-term treatment (answer yes)	148 (82.7%)	66 (86.8%)	82 (79.6%)	0.235
Can you die from epilepsy (answer yes)	118 (65.9%)	47 (61.8%)	71 (68.9%)	0.342
Epilepsy is always characterized by the same type of seizure (answer yes)	102 (57%)	54 (71.1%)	48 (46.6%)	0.001
Epilepsy is a disease that is				
Of the nervous system (answer yes)	152 (84.9%)	68 (89.5%)	84 (81.6%)	0.204
Treatable (answer yes)	71 (39.7%)	53 (69.7%)	18 (17.5%)	< 0.001
Contagious (answer yes)	24 (13.4%)		19 (18.4%)	0.026
Main causes (multiple answers)				
Genetic causes	98 (54.7%)	47 (61.8%)	51 (49.5%)	0.129
Head trauma	83 (46.4%)	55 (72.4%)	28 (27.2%)	< 0.001
Do not know	32 (17.9%)	8 (10.5%)	24 (23.3%)	0.031
Unknown origin	26 (14.5%)	6 (7.9%)	20 (19.4%)	0.033
Cysticercosis	18 (10.1%)		5 (4.9%)	0.011
Supernatural origin	5 (2.8%)		2 (1.9%)	0.652
Examinations are used to diagnose epilepsy (multiple answers)	• •	· · · · · · · · · · · · · · · · · · ·	· · · · · · · · · · · · · · · · · · ·	
Do not know	74 (41.3%)	27 (35.5%)	47 (45.6%)	0.219
Computerized tomography (CT scan) / magnetic resonance imaging (MRI)	30 (16.8%)	17 (22.4%)	13 (12.6%)	0.106
Electroencephalogram (EEG)	42 (23.5%)	32 (42.1%)	10 (9.7%)	< 0.001
Clinical sign	5 (2.8%)	3 (1.9%)	2 (1.9%)	0.652

Table 3: Knowledge of antiepileptic drugs

	Total	Cambodia n= 76	Lao PDR n= 104	Р
	n= 180			
Do not know any long-term AEDs	44 (24.4%)	10 (13.2%)	34 (32.7%)	0.003
Know at least one long-term AED	n= 136	n= 66	n= 70	
Which molecules? (multiple answers)				
Phenobarbital	126 (92.6%)	60 (90.9%)	66 (94.3%)	0.523
Carbamazepine	61 (44.9%)	38 (57.6%)	23 (32.9%)	0.006
Phenytoin	41 (30.1%)	· , •	13 (18.6%)	0.003
Valproic acid	18 (13.2%)	14 (21.2%)	4 (5.7%)	0.010
Antiepileptic drugs can be given regardless of the type of epilepsy				
Yes	30 (22.1%)		17 (24.3%)	
No	68 (50%)	36 (54.5%)	32 (45.7%)	0.585
Do not know	38 (27.9%)	17 (25.8%)	21 (30.0%)	
Epilepsy patients have to take drugs for life				
Yes	79 (58.1%)	39 (59.1%)	40 (57.1%)	
No	29 (21.3%)	13 (19.7%)	16 (22.9%)	0.902
Do not know	28 (20.6%)	14 (21.2%)	14 (20.0%)	
How to take long-term AEDs		·	·	
: Should take AEDs every day	122 (89.7%)	62 (93.9%)	60 (85.7%)	
Should take AEDs during seizures	8 (5.9%)	3 (4.5%)	5 (7.1%)	0.214
Do not know	6 (4.4%)	1 (1.5%)	5 (7.1%)	
If seizures are controlled for a few months, can people with epilepsy stop taking their antiepileptic drugs?				
; Yes	21 (15.4%)	8 (12.1%)	13 (18.6%)	
No	78 (57.4%)	34 (51.5%)	44 (62.9%)	0.060
Do not know	37 (27.2%)	24 (36.4%)	13 (18.6%)	
Should women with epilepsy stop taking their medicine if they become pregnant?				
: Yes	27 (19.9%)	15 (22.7%)	12 (17.1%)	
No	49 (36.0%)	24 (36.4%)	25 (35.7%)	0.685
Do not know	60 (44.1%)	27 (40.9%)	33 (47.1%)	
Do interactions exist between antiepileptic drugs and oral contraception?	. , ,	` .	, , ,	
: Yes	1 (0.7%)	0 (0.0%)	1 (1.4%)	
No	47 (34.6%)	30 (45.5%)	17 (24.3%)	0.025
Do not know	88 (64.7%)		52 (74.3%)	
Side effects of antiepileptic drugs		` '	, ,,	
: Phenobarbital	77 (56.6%)	36 (54.5%)	41 (58.6%)	0.730
Phenytoin	43 (31.6%)	26 (39.4%)	17 (24.3%)	0.067
Carbamazepine	42 (30.9%)	22 (33.3%)	20 (28.6%)	0.581
Do not know of any side effects of AEDs	51 (37.5%)	26 (39.4%)	25 (35.7%)	0.724

Pharmacies offer to patients a first-line point of contact with the health care system



pharmacy-dispensing workers

Qualification



**Knowledge on AEDs** 

Cambodia vs. Lao PDR

86.8% vs. 67.3%

**Know at least one AED** 

51.5% vs. 62.9%

Know that PWE can not stop to take AEDs even seizures are controlled for some months

36.4% vs. 35.7%

Know that women with epilepsy should not stop taking AEDs if they become pregnant

0.0% vs. 1.4%

Know that AEDs may reduce the effectiveness of contraceptives

39.4% vs. 35.7%

Do not know any side effects of AEDs