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# An evaluation of pharmacist knowledge on treatment with antiepileptic drugs

Yifat Roth [a], Miri Y. Neufeld [b], Ilan Blatt [c], Shiri Guy-Alfandary [d], Sivan Rasaby [e], Dana Ekstein [f,**], Sara Eyal [a,*]

[a] Division of Clinical Pharmacy, School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel
[b] EEG and Epilepsy Unit, Department of Neurology, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Department of Neurology, Sheba Medical Center, Tel Hashomer, Israel
[d] Clinical Pharmacy Unit, Maccabi HMO, Modiin, Israel
[e] Shalvata Medical Center, Clalit Health Services, Hod Hasharon, Israel
[f] Department of Neurology, the Agnes Ginges Center of Neurogenetics, Hadassah-Hebrew University Medical Center, Ein Kerem, Jerusalem, 91120, Israel

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ABSTRACT

*Purpose:* As pharmacists play an important role in managing antiepileptic drug (AED) therapy, they should be aware of different aspects of the treatment. Our aim was to evaluate pharmacists' knowledge of the pharmacological treatment of epilepsy, and their recommendations under hypothetical situations, through a written questionnaire.

*Methods:* The questionnaire included 22 questions divided into three sections: demographic data (eight questions), knowledge of specific aspects of AED therapy (true/false; four questions), and actions taken in theoretical situations involving AED therapy (multiple choice; ten questions). The questionnaire was distributed to pharmacists practicing in Israel and working in pharmacies and/or participating in professional meetings and continued education programs.

*Results:* One hundred and twenty one pharmacists completed the questionnaire (response rate 19%). The mean overall score was 48 ± 15% correct answers. Most pharmacists were aware of the need to continue AED treatment during pregnancy, the risk of generic switches, and the need to call the physician for loss of seizure control (92%, 89% and 81% of responders, respectively). Twelve percent identified correctly all three situations in which the clinicians should be contacted urgently, and 27% did not identify any of them. The total score was related to the academic degree (PharmD vs. other) and to the duration since training completion.

*Conclusion:* Pharmacists were knowledgeable regarding some aspects of care of people with epilepsy. However, our study, as in previous studies among health care professionals, identified some gaps in knowledge. These findings indicate the need for better education of pharmacists regarding epilepsy and its treatment.



## 1. Introduction

Antiepileptic drugs (AEDs) are the essence of epilepsy treatment, and 70-80% of adults with new onset epilepsy may become seizure free with optimal AED therapy [1,2]. However, up to half of the patients treated with AEDs experience adverse effects [2,3] and 20–30% are drug resistant [4,5]. In addition, sometimes more than one AED is required in order to control seizures, and patients may be treated for concomitant diseases. This may lead to drug–drug interactions [6,7]. The medical treatment of people with epilepsy (PWE) is even further complicated by the fact that certain subpopulations, such as women of childbearing age and patients of Asian origin, present very specific considerations [8,9]. Accordingly, a survey among PWE attending a tertiary referral epilepsy outpatient clinic indicated that patients know more about epilepsy in general than about their own condition [10]. All of these issues may have a substantial influence on the control of seizures and on patients' quality of life, and therefore should be well recognized by healthcare providers.

* Corresponding author at: Institute for Drug Research, Room 613, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem, Ein Kerem, Jerusalem, 91120, Israel. Tel.: +972 2 675 8667; fax: +972 2 675 7246.
** Corresponding author. Tel.: +972 2 6777741; fax: +972 2 6777624.
*E-mail addresses:* yifat.harif@mail.huji.ac.il (Y. Roth), mirin@tlvmc.gov.il (M.Y. Neufeld), Ilan.Blatt@sheba.health.gov.il (I. Blatt), guy_s@mac.org.il (S. Guy-Alfandary), sivan.rasaby@mail.huji.ac.il (S. Rasaby), dekstein@hadassah.org.il (D. Ekstein), sarae@ekmd.huji.ac.il (S. Eyal).

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Pharmacists play a key role in the therapeutic management of PWE. Pharmacists have the opportunity to prevent drug-related untoward occurrences, by representing the last barrier between the patient and the drug. They can verify that the dose is reasonable; warn prescribing physicians regarding potential drug–drug interactions; and give patients essential drug information, such as information regarding possible drug-related adverse events [11–13]. Moreover, a survey among PWE indicated that patients most commonly consult their pharmacist with regard to drug interactions and adverse effect information [13]. This clearly indicates the need for pharmacists to be knowledgeable regarding epilepsy and its treatment. However, previous research indicated that pharmacists' acquaintance with specific areas of AED prescription and utilization, i.e., women's health [14] and generic drug substitution [15], is lacking. These findings are along the same line of evidence with data showing that even neurologists treating epilepsy patients are not continuously updated with regard to AED treatment [16].

The aim of this study was to evaluate pharmacists' knowledge regarding the use of AEDs, and their recommendations based on this knowledge, through a written questionnaire. We were also interested in identifying the impact of demographic variables on pharmacists' knowledge. The survey included pharmacists with various levels of formal education and experience.

## 2. Methods

### 2.1. Ethics approval

The study protocol was approved and a waiver of consent granted by the Institutional Review Board at the Hadassah-Hebrew University Medical Center, Protocol No. 0486-13-HMO. The questionnaire was filled anonymously and data were saved without identifying details.

### 2.2. Participants

Participants in the study were licensed pharmacists, certified by the Israeli Ministry of Health, who understand and speak Hebrew and who were willing to answer a 22-item questionnaire. Pharmacists who already completed the questionnaire in another setting, pharmacist assistants, undergraduate students and trainees who were not licensed at the time of the study were excluded. Enrollment began on December 2013 and ended on June 2014.

### 2.3. The questionnaire

The questionnaire (supplementary information) included three types of questions: A. Questions aimed to collect demographic data; B. A true/false format of questions assessing AED-related knowledge ($n = 4$); C. A single-response, multiple-choice format of questions listing pharmacists' possible actions in theoretical situations involving AED therapy ($n = 10$). Parts B and C included questions regarding emergency situations ($n = 3$), women's health ($n = 3$) and drug–drug interactions ($n = 5$), along with miscellaneous topics (generic switches, lamotrigine's initial dose, and interpretation of valproic acid blood concentration; $n = 3$). Two questions were included in similar studies that had taken place in the United States [14,15,17]. Parts B and C questions were followed by sections entitled "comments", each including two empty lines.

The initial version of the questionnaire was composed by three of the authors of this work (YR, DE, SE) and was changed to the final form after revision for content validity and clarity by two epileptologists (MYN and IB, former and current presidents of the Israeli Chapter of the International League Against Epilepsy – ILAE) and two PharmD currently practicing pharmacists (SG and SR). For validating that the subjects do not provide arbitrary answers, one difficult true/false question (urinary retention is an adverse effect that may require the use of a catheter in patients that are taking rufinamide – correct answer: false – this being an adverse event of retigabine) was presented in part B of the questionnaire and was not included in the final analysis. As expected, only 21 participants (10%) gave a correct answer to this question and 98 (81%) noted that they did not know the correct answer. Following comments from the participants, the two answers suggesting not dispensing the drugs and calling the physician in response to each of the three emergency situations in part B (three questions in total) were both considered correct (see supplementary information).

### 2.4. Data collection

Following permission granted from the relevant administrative personnel in charge, the questionnaire was presented to pharmacists in one of the following four settings: (1) Pharmacists working in drugstores of Super-Pharm, the largest drugstore chain in Israel, were approached in 9 out of 12 stores in Jerusalem during working hours. The questionnaire forms were collected 2–7 days later; (2) Maccabi Health Maintenance Organization's (HMO) pharmacists were approached, during a training course unrelated to epilepsy or AEDs. Pharmacists were allowed 15 min to complete the questionnaire; (3) The forms were distributed to pharmacists participating in one of two semiannual meetings of the Pharmaceutical Society of Israel (PSI). The entire meeting day was allotted to completing the questionnaire; (4) The forms were distributed to pharmacists participating in the PharmD Program of the Hebrew University School of Pharmacy. Fifteen minutes were allotted to complete the questionnaire.

Pharmacists were not supposed to consult any information resources when they were taking the quiz, and those who answered the quiz in small classes (pharmacists participating in the PharmD program or Maccabi's pharmacists) were not able to do so. We could not validate that the other pharmacists did not use information resources. No financial incentives were offered to encourage participation. However, a document containing detailed answers to the study questions was prepared and distributed among members of the organizations participating in the study.

### 2.5. Data analysis

The final score was expressed as the percentage of correct answers of each pharmacist. The option "I don't know" was considered a separate category, and included in the estimation of the score per question as a wrong answer. Responders were grouped into one of two categories of duration since graduation from training (five years or less and longer than five years) and of countries in which the BScPharm degree was obtained (Israel, other). Descriptive statistics were obtained for the various variables. Response patterns were evaluated using the two-tailed Mann–Whitney test, the Kruskal–Wallis test, and the Pearson correlation (GraphPad Instat 3, La Jolla, CA, USA), as appropriate. The results are reported as mean ± standard deviation (SD), unless otherwise indicated. A $p$-value $\leq 0.05$ was considered significant.

## 3. Results

A total of 121 pharmacists completed the questionnaire. These included 17 pharmacists out of the 59 pharmacists working in 2014 in the nine approached Super-Pharm stores in Jerusalem (29%), all 29 pharmacists who participated in Maccabi HMO's training class, 65 out of the 535 participants of the PSI conferences (5.4% of participants), and 10 PharmD students who attended a

research seminar and had not completed the questionnaire elsewhere (100% of eligible participants). The total response rate was 19%.

The compiled demographic data are presented in Table 1. Most responders were women (72%) and studied pharmacy in Israel (84%). Thirty seven percent completed only a BSc in pharmacy. The remainder of pharmacists participating in this study had additional degrees, including one quarter of all participants who completed a PharmD degree. The majority (63%) estimated that they encounter ten or less PWE each month, and only one fifth underwent AED-related training during the year preceding the survey.

The total mean score was 48 ± 15% (Fig. 1). Overall, the true/false questions were relatively easier to address, compared with the multiple choice questions (76 ± 22% vs. 45 ± 17%, respectively; $p < 0.01$). Pharmacists obtained the highest correct scores on the true/false statements inquiring about the use of AEDs during pregnancy and the outcome of generic switches (93% and 89%, respectively). Only 13 ± 38% were familiar with the prescription issues related to valproic acid–lamotrigine interaction. The scores of the different topics were similar. Statistical analysis to assess variation among the topics was not conducted due to the small number of questions representing each topic. Across all questions and all study participants, the option "I don't know (f)" was selected in 5.0% of cases.

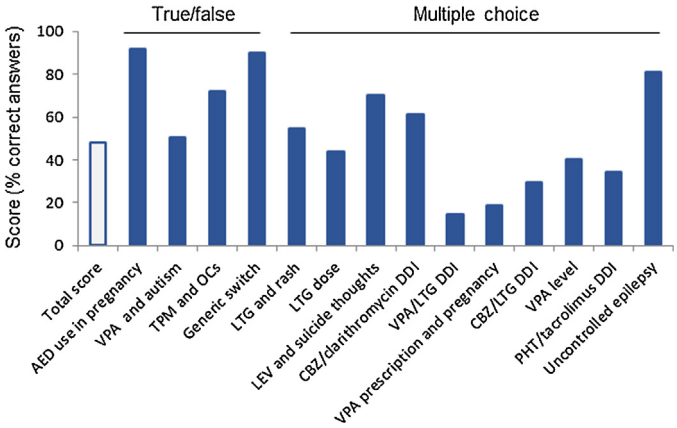


**Fig. 1.** Total scores across all responders. CBZ, carbamazepine; DDI, drug–drug interaction; LEV, levetiracetam; LTG, lamotrigine; OCs, oral contraceptives; PHT, phenytoin; PWE, people with epilepsy; TPM, topiramate; VPA, valproic acid.

**Table 1**
Characteristics of study participants.

| Parameter | No. (%) |
|---|---|
| **Total participants** | 121 |
| **Age (years) [mean ± SD, (range)]** | 35.2 ± 9.1 (24–67) |
| **Sex** | |
| Men | 33 (28%) |
| Women | 86 (72%) |
| Not indicated | 2 |
| **Country of academic studies** | |
| Israel | 102 (84%) |
| Other[a] | 19 (16%) |
| **Highest academic degree**[b] | |
| BSc or equivalent | 39 (37%) |
| MSc or equivalent | 26 (25%) |
| PhD | 6 (6%) |
| PharmD | 27 (26%) |
| Other[c] | 6 (6%) |
| Not indicated | 17 |
| **Duration since graduation (years)** | |
| 0–2 | 24 (20%) |
| 3–5 | 28 (24%) |
| 6–10 | 26 (22%) |
| 11–20 | 28 (24%) |
| >20 | 13 (11%) |
| Not responded | 2 |
| **Occupation** | |
| Community/retail pharmacy, full time | 46 (38%) |
| Community/retail pharmacy, part time | 32 (26%) |
| Hospital, full time[d] | 19 (16%) |
| Other[e] | 24 (20%) |
| **Estimated number of PWE/month** | |
| 0 | 23 (21%) |
| 1–5 | 29 (26%) |
| 6–10 | 18 (16%) |
| 11–20 | 21 (19%) |
| >20 | 20 (18%) |
| Not indicated | 10 |
| **AED training over the past year** | |
| None | 95 (79%) |
| Academic | 7 (6%) |
| PSI | 5 (4%) |
| Other[f] | 13 (11%) |
| Not indicated | 1 |
| **Setting** | |
| PSI | 65 (54%) |
| Maccabi HMO | 29 (24%) |
| Super-Pharm | 17 (14%) |
| PharmD seminar | 10 (8%) |

Results are expressed as mean ± SD (range), unless otherwise indicated.
[a] Brazil, England, France, Georgia, Hungary, Italy, Jordan, Russia.
[b] No pharmacists with a double PharmD/PhD participated in the survey. A PharmD degree was considered higher than other academic degrees, with the exception of PhD.
[c] Masters in public health (MPH).
[d] Almost all pharmacist positions in Israeli hospitals are full time. Exceptions were counted as "other".
[e] Retirement home, HMO Headquarters offices, hospital + retail pharmacy, part time at a hospital.
[f] Academic + other (not specified). PSI, Pharmaceutical Society of Israel.

A more detailed analysis of the emergency-related questions revealed that the majority of pharmacists would call the prescribing physician immediately for levetiracetam-related suicidal thoughts and for acute seizure aggravation. However, at least 25%, 13% and 7% of responders would not identify lamotrigine-induced rash, suicidal thoughts and seizure aggravation, respectively, as conditions that require immediate action (Fig. 2A–C). Although some of the other pharmacists would call the physician (16%, 13% and 7% for the first, second and third situation, respectively), they apparently would not understand the reason for doing so and would still dispense the prescribed medication. Twelve percent identified correctly all three situations in which the clinicians should be contacted urgently, and 27% did not identify any of them (Fig. 2D).

Pharmacists with a PharmD degree achieved better total scores compared to those with other advanced degrees (e.g., MSc, PhD) (60 ± 13 vs. 50 ± 14, respectively; $p < 0.05$), but not compared to BScPharm graduates. Longer time since training completion was associated with a lower total score (58 ± 13% vs. 50 ± 16% for the pharmacists who were in practice 5 years or less and those with longer time in practice, respectively; $p < 0.05$). In both cases, the differences manifested particularly with regard to questions about lamotrigine (Fig. 3 and data not shown). In contrast, the total score was not affected by the setting in which the questionnaire was distributed, gender, the country in which the BScPharm degree was obtained (Israel vs. others); whether the pharmacist worked at a community pharmacy, a hospital, or elsewhere, and whether they underwent some form of training about AEDs over the year prior to the survey ($p > 0.05$; data not shown). In addition, the total score was not associated with the number of PWE seen monthly by the pharmacist ($p > 0.05$) and did not correlate with the responders' age ($r = -0.1596$, $p > 0.05$).

Twenty six of the pharmacists included in this study added comments under the "Comments" sections of the questionnaires. Five comments related to lack of the responder's knowledge, one stated the need for more extensive education, seven referred to the availability of data sources such as drug interactions databases that

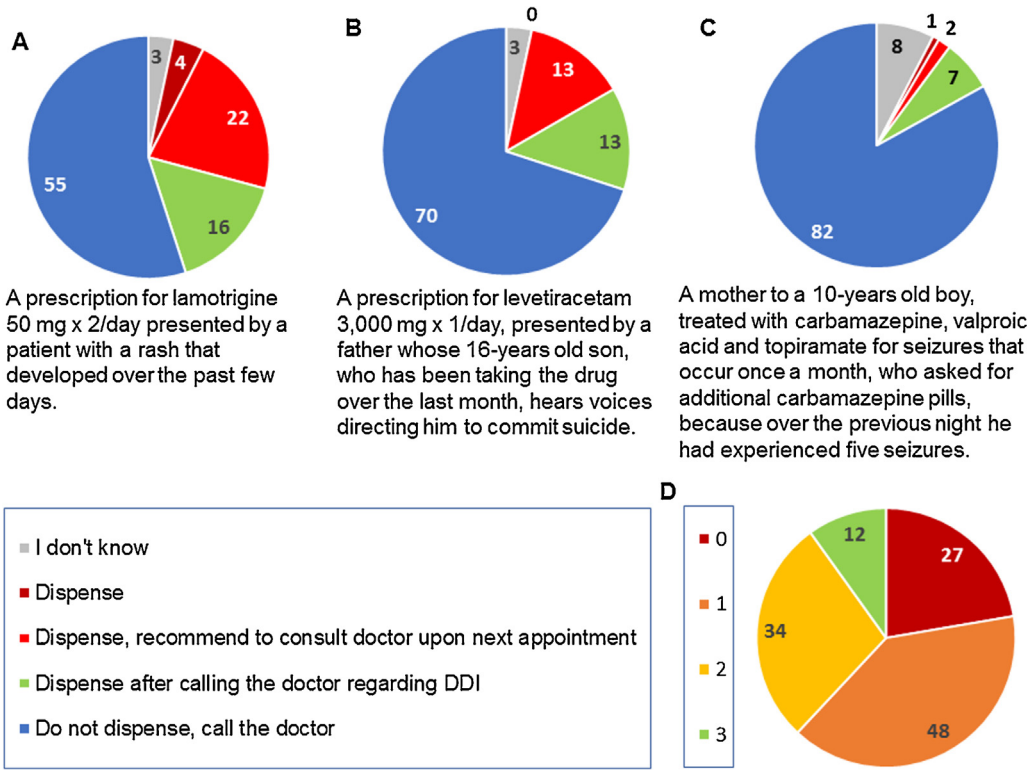


**Fig. 2.** Distibution of answers to questions about emergency situation. Three of the multiple choice questions in the questionnaire presented emergency situations. Parts A–C present the percent of pharmacists who selected each of the available responses (indicated in a box on the lower left corner). The corresponding translated question is listed below the distribution charts. Only the response "Do not dispense, call the doctor" was considered correct. (D) Percent of pharmacists who correctly identified none, one, two, or all three emergency situations. DDIs, drug–drug interactions. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

reduced the need to memorize prescription information, and the remainder of comments were related to the wording of the statements or the answers.

## 4. Discussion

Pharmacists constitute a valuable source of information for patients and prescribers [11–13]. As such, they should be familiar with various aspects of treatment with AEDs, including drug–drug interactions and women's health, and be able to consult patients. It has been shown that patients' education about epilepsy results in better seizure control, even in patients with a long history of epilepsy [18], and that PWE desire to know much more about their

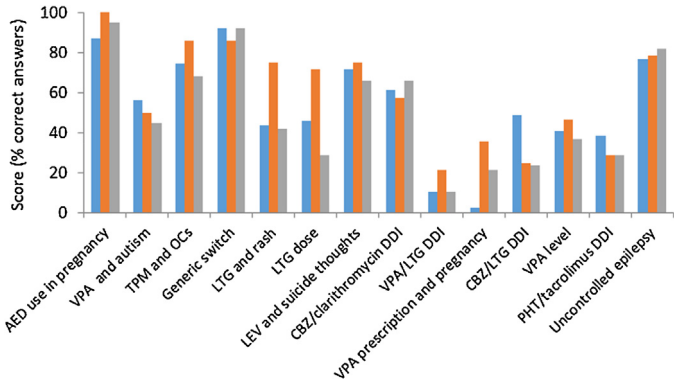


**Fig. 3.** Percent of participants responding correctly to individual questions by type of academic degree. Blue – BSc, orange – pharmD, gray – others. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

disease and medications [19]. Unfortunately, epilepsy patients' knowledge regarding their illness and its treatment is unsatisfactory [12,18]. Furthermore, pharmacists can be the first to recognize conditions in which the physician should be contacted as soon as possible. Yet, our study found significant knowledge gaps among pharmacists, including those who see PWE frequently; the mean score of surveyed pharmacists was only 48%. Several responders checked the "I don't know" option or commented that they don't know the answer, implying that they were able to admit that they have gaps of knowledge. This ability, with regard to neurologists, was previously described by Roberts et al. as the first step towards addressing changes in practice [20].

Remarkably, certain high-awareness areas were identified. Most pharmacists were aware of the risk of generic switches, and the need to call the physician for loss of seizure control (90% and 81% of pharmacists, respectively). However, although 92% of the participants acknowledged that women should continue AEDs during pregnancy, only one fifth would dispense valproic acid to a pregnant woman. Also, less than 20% of the pharmacists knew that the physician should be consulted urgently for lamotrigine-induced rash, and only 34% identified the interaction between phenytoin and tacrolimus. Of note, several responders commented that they rely on computer drug-interaction applications at work and hence the lack of knowledge should not affect their ability to consult patients with regard to drug interactions. As expected, the responders addressed better the true/false compared to multiple choice questions, both because of the more limited choice options and the relative clarity of the true/false statements that did not involve situations which could potentially be interpreted in several ways.

The duration since professional training completion and a PharmD degree were the only predictors associated with overall

score. Longer duration since graduation could be associated with the absence of updated knowledge about epilepsy and AEDs. In addition, there was a partial overlap between shorter duration since graduation and a PharmD degree. The majority of Israeli pharmacists with a PharmD degree graduated over the past four years from a single school of pharmacy, in which personalized medicine has been an important component of the curriculum. Thus, for both comparisons, the greatest gaps were detected in questions related to lamotrigine-induced Stevens-Johnson syndrome/toxic epidermal necrolysis. Interestingly, there was no relationship between larger numbers of PWE seen each month and scores. This is in contrast to previous works assessing the knowledge of health care professionals [14,21], and may be explained by reliance on computerized resources and minimal time for interacting with patients and actually consulting them. The setting in which the questionnaire was presented, and therefore the time allowed for their completion and the percentage of practicing pharmacists among the participants, did not affect the scores. Intriguingly, recent training about epilepsy or AEDs was not shown to increase performance in completing the questionnaire, although the type of training was not detailed. It is necessary to consider the optimal type of education that may efficiently improve pharmacists' knowledge and actions.

The total score of our questionnaire appears similar or slightly lower than those reported in previous studies among health professionals, which also reported severe knowledge deficits [14,15,17,20,22]. For instance, in surveys among pharmacists and neurologists or neurology residents regarding women's issues, the overall average correct scores were 60.3% [14] and 50% [20], respectively. For true/false questions that were included in previous studies, the scores of our survey were consistent with those reported before. For example, 92% of responders in our study knew that AEDs should not be stopped in women with epilepsy when they become pregnant, and 90% were aware of the issues associated with generic switches, compared to 87% of pharmacists surveyed in previously published studies, for both questions [14,15]. Among attendees of the American College of Physicians 2003 Annual Meeting, only 75% realized that pregnant women with epilepsy should remain on medication [17]. Based on the better scores obtained for the true/false compared to the multiple choice questions, it seems that the difficulty of the multiple choice part of questionnaire was at a higher level than previous questionnaires in terms of both specificity of required knowledge and the choices themselves. However, these questions have greater relevance to actual practice and they may better reflect the effect of pharmacists' knowledge on the management of PWE.

The major limitations of our study are related to potential selection bias, to the partial validation of the questionnaire, and to the potential for generalization of our results to other countries. The majority of our participants were pharmacists who attend meetings and training courses, who may be more knowledgeable than other pharmacists. Among those who attended the PSI meetings, low response rate may further increase the bias towards those who may be willing to answer the questionnaire because they felt more comfortable with their degree of knowledge. Yet, participants (including clinical pharmacists) pointed out that the questionnaire was difficult, and that the given options in the situation-related multiple choice questions did not fully reflect the possible options the pharmacist encounters at work as described above. The limited response range also reflects another limitation of the study: asking a clinical question via a multiple choice question. Furthermore, the clinical pharmacists who validated the questionnaire might not have been representative of all the pharmacists who encounter such situations in community/retail pharmacies. In addition, we assumed that the participants completing the survey on their free time (the drugstore pharmacists) did not consult others or actively search for information to answer the questions. However, no significant differences were found between the scores of participants in the various settings of the study. Although this is a local survey, performed in Israel, its scores were similar to the results presented in studies from other countries, both generally and in regard to specific questions [14,15,17,20]. Therefore, our work may be of wider relevance to the healthcare professionals involved in the management of PWE.

## 5. Conclusion

Pharmacists are in a key position to help PWE. Although they are familiar with some areas related to AED treatment, there are still gaps in knowledge. Clearly, educational interventions such as continued education courses, local interactive workshops, and practical sessions and web resources are required. These should be followed by studies assessing their effectiveness in terms of pharmacists' knowledge and patient outcome.

## Conflict of interest

None of the authors has any conflict of interest to disclose. No funding source was involved in study design; data collection, analysis and interpretation; writing the report; and decision to submit the article for publication.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.seizure.2015.11.007.

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