

The Role of Pharmacists' Interventions in Increasing Medication Adherence of Patients With Epilepsy: A Scoping Review

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Objectives: Epilepsy is a chronic disease that requires long-term treatment and intervention from health workers. Medication adherence is a factor that influences the success of therapy for patients with epilepsy. Therefore, this study aimed to analyze the role of pharmacists in improving the clinical outcomes of epilepsy patients, focusing on medication adherence.

Methods: A scoping literature search was conducted through the ScienceDirect, PubMed, and Google Scholar databases. The literature search included all original articles published in English until August 2023 for which the full text was available. This scoping review was carried out by a team consisting of pharmacists and neurologists following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews and the Joanna Briggs Institute guidelines, including 5 steps: identifying research questions, finding relevant articles, selecting articles, presenting data, and compiling the results.

Results: The literature search yielded 10 studies that discussed pharmacist interventions for patients with epilepsy. Five articles described educational interventions involving drug-related counseling with pharmacists. Two articles focused on similar pharmacist interventions through patient education, both verbal and written. Three articles discussed an epilepsy review service, a multidisciplinary intervention program involving pharmacists and other health workers, and a mixed intervention combining education and training with therapy-based behavioral interventions.

Conclusions: Pharmacist interventions have been shown to be effective in improving medication adherence in patients with epilepsy. Furthermore, these interventions play a crucial role in improving other therapeutic outcomes, including patients' knowledge of self-management, perceptions of illness, the efficacy of antiepileptic drugs in controlling seizures, and overall quality of life.

Key words: Pharmacy, Epilepsy, Seizures, Intervention, Adherence

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INTRODUCTION

Epilepsy is a neurological disorder characterized by the occurrence of unprovoked seizures [1]. These seizures are recurrent and result from excessive and abnormal neuronal activity in the brain, which can be caused by various factors including head trauma, stroke, or metabolic disorders [2]. According to data from the World Health Organization, it is estimated that 50 million people worldwide have epilepsy, and 70% of them

could be seizure-free with proper diagnosis and treatment [3]. However, the prevalence of treatment failure is still significant, as demonstrated by the results of the Standard and New Antiepileptic Drugs trial, which reported a 29% rate of antiepileptic medication failure among patients with generalized tonic-clonic seizures [4]. Additionally, about 63% of individuals receiving epilepsy treatment show favorable seizure control in response to the prescribed therapy, while 37% experience treatment failure with poor seizure control [5]. To date, poor drug adherence remains a major cause of uncontrolled therapy in patients with epilepsy. Adherence to medication involves patient behavior in taking medication according to the prescriber's (doctor's) instructions [6,7]. Non-adherence to medication regimens is a potential risk for the recurrence of epilepsy and is closely linked to a higher incidence of hospitalization and increased financial burdens [8-10].

Epilepsy treatment is complex and may require multiple antiepileptic drugs, special diets, and neurostimulation [11]. Additionally, the use of antiepileptic drugs often leads to side effects and drug-drug interactions [12,13], which can result in poor patient adherence, especially among those with limited knowledge about the disease and its treatment [14]. Given these challenges, the role of pharmacists is crucial in providing education and counseling [15]. Pharmacists have demonstrated their ability to enhance medication adherence among epilepsy patients [16]. According to a systematic review by Reis et al. [17], pharmacists can positively impact epilepsy patients by increasing adherence to antiepileptic drugs, enhancing knowledge about epilepsy, and improving patients' quality of life. One strategy of the American Epilepsy Society for managing epilepsy is to integrate pharmacists who can collaborate with other health workers to improve access to health services [18]. However, there is limited information on how pharmacists specifically contribute to increasing patients' adherence to medication. Therefore, this literature review aims to examine the contribution of pharmacists to improving the clinical outcomes of epilepsy patients, focusing particularly on medication adherence.

METHODS

This scoping review was conducted by a team of pharmacists and neurologists in accordance with the Joanna Briggs Institute (JBI) guidelines [19] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Ex-

tension for Scoping Reviews [20]. The framework for the scoping review, based on the JBI guidelines, comprises 5 stages: identifying research questions, locating relevant articles, selecting articles, presenting data, and summarizing the findings [19]. The study selection process adhered to a flowchart adapted from the PRISMA statement [20].

Identify Research Questions

The research question was as follows: how can pharmacists contribute to improving medication adherence in epilepsy patients?

Find Relevant Research

We conducted a scoping literature search using the databases ScienceDirect, PubMed, and Google Scholar. The search employed a Boolean combination of terms: ("pharmacist" or "pharmacy") AND ("intervention") AND ("epilepsy" or "epileptic") AND ("adherence" or "compliance"). This search included all original articles published in English up to August 23, 2023, with full texts available. Four authors—IE, ZI, NMY, and IS—implemented a two-step procedure to select relevant articles. Initially, after eliminating duplicates, each author independently reviewed the titles and abstracts of articles that discussed interventions conducted by pharmacists for epilepsy patients, without restricting the type of intervention or study.

Research Article Selection

The next step was to read full-text articles that meet the inclusion criteria: (1) interventions conducted by pharmacists or in collaboration with other multidisciplinary health practitioners, (2) studies published in English, (3) no restrictions on the types of interventions provided in the full-text articles, (4) the therapeutic parameters observed included adherence, with or without secondary outcomes such as knowledge, seizure control, or quality of life (Figure 1).

Data Presentation

Four authors (IE, ZI, NMY, IS) were responsible for data extraction and presentation from the included studies. The tables record information such as authors, publication year, country, study design, pharmacist interventions, participants involved, outcome parameters, and study results. The data are presented through a qualitative analysis based on the existing data in each article (Table 1) [7,21-29]. Additional details about

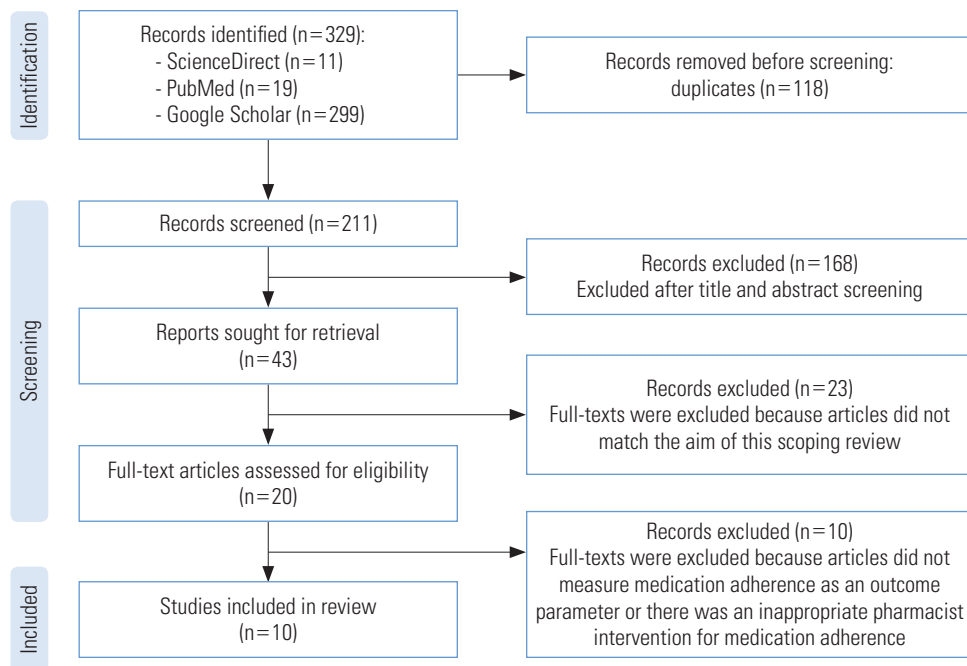


Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of article selection.

the type and description of interventions can be found in Table 2 [7,21,22,24,26,27,30-32].

Results Compilation

A series of discussions among all reviewers was conducted to refine the best approach for reviewing, summarizing, and presenting the literature findings in a consistent format. The results are organized and summarized based on their relevance to the overall research question.

Ethics Statement

As this was a scoping review, data extraction was conducted solely from published articles. Therefore, no institutional review board approval was needed.

RESULTS

A comprehensive search of the ScienceDirect, PubMed, and Google Scholar databases yielded a total of 329 entries identified as potentially relevant for the study. After screening to remove duplicates and examining the abstracts of articles used in this scoping review, 43 articles were obtained. Upon reviewing the full-text, we excluded 33 articles due to objectives that did not match and because they did not measure medication adherence as an outcome parameter. The adherence measure-

ments used in the reviewed articles included not only questionnaires but also blood drug levels (Figure 1).

This scoping review examines all publications that involve interventions by pharmacists or pharmacy students in treating patients with epilepsy. The contributions of pharmacists identified in the studies include providing counseling (verbal, written, and online consultations), as well as setting schedules and reminders for medication adherence [7,22,25,27-29]. Additionally, pharmacists may distribute informational leaflets to patients as part of their clinical practice [24]. Educational interventions through counseling are often paired with strategies to improve adherence to drug regimens, such as modifying drug schedules to simplify medication intake [22]. Pharmacist interventions also encompass education through personal consultations, which cover understanding the disease (patient's condition), drug use (adherence, benefits, administration methods, preparation, drug interactions, procedures for reporting side effects, seizures, and how to contact a clinician if issues arise during treatment) [23,25]. As health professionals, pharmacists collaborate with other healthcare providers in multidisciplinary programs to offer insights into epilepsy medications and therapies for comorbid conditions (Table 1) [26]. Moreover, collaboration between pharmacists and other multidisciplinary professionals is not limited to healthcare workers but can also include educators. Research by Yilmazel

Table 1. Characteristics of the included studies

No	Study (country of origin of the study)	Study design	Pharmacist intervention	Participants involved	Outcome parameter measurements	Results of the study
1	Fogg et al., 2012 [21] (UK)	One-arm interventional study	PLEC Participants in the clinic received a 30-min consultation with a practice-based pharmacist. The pharmacist allows patients with epilepsy to ask questions about their medication	A total of 106 patients participated; Of these, 82 received PLEC, but only 50 patients completed the intervention thoroughly	Self-reported medication adherence using the MARS Epilepsy-related quality of life using the QOLIE-10 General psychological well-being via the GHQ-12, a 12-item questionnaire	Medication adherence increased significantly ($p=0.030$); Quality of life (QOLIE score post-PLEC) improved significantly ($p=0.049$); The total GHQ-12 score also improved significantly ($p=0.009$, Wilcoxon matched pairs)
2	Tang et al., 2014 [22] (China)	RCT with 2 groups: group I (control) received an educational intervention, and group II received both educational and behavioral interventions	Education and behavioral interventions Education intervention (written and oral instruction); A pharmacist provided patient education and counseling in accordance with the criteria of the American Society of Health-System Pharmacists The cue-dose training therapy-based behavioral intervention included a modified drug schedule	A total of 109 patients with epilepsy were randomized into 2 groups	Adherence using the MMAS-4 Frequency of seizures Understanding of AED information (the 5 items tested in the questionnaire were the name of the AED, dosage, length of AED use, how to deal with adverse drug responses, and missed pills) (31-item) QOLIE-31	There was a statistically significant difference between the baseline and follow-up levels of adherence ($p<0.001$), as well as seizures ($p<0.001$) Knowledge score ($p<0.00$) However, no statistically significant difference ($p>0.05$) existed between the intervention and control groups Adherence increased ($p=0.827$) Control of seizures ($p=0.988$) Knowledge improvement ($p=0.231$) Overall quality of life ($p=0.947$)
3	AlAjmi et al., 2017 [7] (Kingdom of Saudi Arabia)	Quasi-experimental study with 2 groups (control and intervention)	An educational interview with a pharmacist (30-min structured verbal face-to-face interview) Education on the medical aspects of epilepsy, as well as information on AEDs; Education materials such as instructional pharmacy interviews, brochures, or pill organizers were used to deliver information on the medical features of epilepsy in the first portion and information on antiepileptic drugs	After 6 wk, only 29 patients in the control group and 27 patients in the intervention group had completed the adherence measurement	Medication adherence using MMAS-8	The intervention group had statistically significant differences between before and after the intervention ($p<0.001$) The medication adherence score in the control group did not show a statistically significant difference after the second visit ($p=0.792$) At baseline, there was no statistically significant difference between the intervention and control groups in adherence scores, but a difference after the intervention was significant ($p=0.024$)
4	Li et al., 2018 [23] (Malaysia)	Quasi-experimental groups	ERS The ERS quality indicator uses QUIET, which has 3 components: a review of the epileptic condition, and individualized epilepsy counseling	The no. of respondents was 203, but 156 patients completed the study until the final follow-up	ERS quality (QUIET) Seizure frequency	There was an increase in counseling (89.3%), drug-related reviews such as side effects (77.9%), and drug interactions (82.1%) There was a statistically significant decrease in the number of seizures at the end of follow-up ($p<0.001$)

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Table 1. Continued from the previous page

No	Study (country of origin of the study)	Study design	Pharmacist intervention	Participants involved	Outcome parameter measurements	Results of the study
5	Jinil et al., 2018 [24] (India)	One-arm interventional study	<p>Patient counseling Counseling for pediatric Patients' caregivers use leaflets about epilepsy and its treatment</p>	66 subjects completed the second visit	Medication adherence using MMAS-4	The no. of patients who had high adherence increased after giving counseling interventions with leaflet designs (from 0.00 to 36.36%)
6	Ma et al., 2019 [25] (China)	Quasi-experimental study with 2 groups (control and intervention)	<p>Patients/families are served by a pharmacy and receive educational interventions The pharmacy service and verbal instruction information supplied to patients/families included the following: (1) Understanding of the epilepsy illness condition; (2) AED treatment (treatment rationale, benefits, drug adherence, and treatment duration); (3) Medication administration (dosing, when to take a dose, storing the medication, and what to do if a dose is missed); (4) Drug interactions or drug-food interactions; (5) Medication side effects and what to do if you experience them; (6) How to properly discontinue or switch medications; (7) Drug concentrations in the laboratory are monitored; (8) How to contact clinicians</p>	<p>There were 1031 patients from the intervention hospital, and 1902 valproic acid samples were taken There were 1134 patients from the control hospital, and 2441 valproic acid samples were taken</p>	Medication adherence using the Simplified Medication Adherence Questionnaire	Adherence to medications increased from 56.0% to 73.9%
7	Zheng et al., 2019 [26] (China)	RCT with 2 groups: group I (control) received usual care, and group II received usual care with an additional 12-mo multidisciplinary program	<p>The epilepsy specialist nurse, psychiatrist, and pharmacist give the information about epilepsy The intervention's (multidisciplinary program) content included knowledge of epilepsy (the condition itself, its comorbidities, therapies, medication use, and pregnancy-related difficulties), daily self-management skills, and pertinent psychosocial information from a specialist epilepsy nurse, psychiatrist, pharmacist, and members of the multidisciplinary management program; (1) personal interviews; (2) online counseling</p>	184 patients with epilepsy from a tertiary hospital in eastern China (92 in the control group and 92 in the intervention group)	<p>Medication adherence using MMAS-8 Standard of living (OOLIE-31) The BDI measured the severity of depression Anxiety (according to the BAI) Frequency of seizures</p>	<p>Medication adherence ($p=0.006$) A higher overall OOLIE-31 score ($p=0.001$) There were fewer patients with severe depression ($p=0.013$) Anxiety ($p=0.002$) in the intervention group, more patients with moderate-to-high AED use After 12-mo, there was a statistically significant increase in the proportion of patients in the control and intervention groups who had low seizure frequency ($p=0.001$)</p>

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No	Study (country of origin of the study)	Study design	Pharmacist intervention	Participants involved	Outcome parameter measurements	Results of the study
8	Chandrasekhar et al., 2020 [27] (India)	One-arm interventional study	Patient counseling The counseling intervention included an educational interview involving a 30-min structured verbal face-to-face interview	100 epileptic inpatients at a South Indian tertiary care hospital's neurology department	Medication adherence using the MMAS-4 Believing in medication use belief survey (contained 10 questions, with a 5-point Likert scale used to record the response to each statement strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree)	According to the study, the total improvement in medication adherence and patient understanding was statistically significant following the intervention; High adherence was found in 62% of participants, medium adherence in 20%, and low adherence in 18% Medication belief assessment showed statistically significant results ($p \leq 0.05$)
9	Jarad et al., 2022 [28] (Jordan)	RCT with 2 groups: intervention group (received the standard medical care and pharmacist-led educational interview) and control group (only received the standard medical care)	Pharmacist-led clinical education As an intervention group, clinical pharmacist-led education was used In addition to routine medical care, the first group had a 30-min educational conversation with the parent/caregiver led by a clinical pharmacist; The control group was given only standard medication care	At the time of the follow-up, 71 patients (36 in the intervention group and 35 in the control group) were included in the statistical analysis	Adherence to medication using the MMAS-8 Safety using the Perceptual Evaluation of Speech Quality Score Parent/caregiver satisfaction with AED information was assessed using the Soccer Injury Movement Screen Score The Paediatric Quality of Life Epilepsy Module Score was used to assess quality of life in pediatric patients with epilepsy	At the follow-up, there was a significant difference in medication adherence between the 2 groups ($p < 0.001$) There was no significant difference between groups in terms of effectiveness ($p > 0.05$) or safety ($p = 0.08$) at follow-up Higher information satisfaction ($p < 0.001$) The intervention group had higher quality of life ($p = 0.05$)
10	Tamilselvan et al., 2022 [29] (India)	One-arm interventional study	Patient counseling (no detailed explanation of the form and counseling material provided)	The total no. of respondents was 150, but only 109 patients completed the study by the end of the follow-up period	Medication adherence was evaluated using the MMAS-8 Quality of life using the QOLIE-31 (version 1.0) questionnaire	Improvement in medication adherence from the mean of MMAS-8 score (standard deviation) in the first and end of follow-up was 4.50 (1.80) and 5.23 (1.29) The educational group exhibited a positive correlation with all the subscales of QOLIE-31

PLEC, pharmacist-led epilepsy consultations; MARS, Medication Adherence Rating Scale; QOLIE, quality of life in epilepsy; GHQ, General Health Questionnaire; RCT, randomized controlled trial; MMAS, Morisky Medication Adherence Scale; AED, antiepileptic drug; ERS, Epilepsy Review Service; QUIET, Quality Indicator in Epilepsy Treatment; BDI, Beck Depression Inventory.

Table 2. Summary of pharmacist interventions to improve medication adherence in epilepsy patients

Type of intervention	Pharmacist contribution	Description of the intervention
Education intervention	Pharmacist counseling about epilepsy uses leaflets (written instructions), personal interviews (face-to-face consultation), and online counseling [7,21,24,26,27]	An educational intervention can be provided by pharmacists or other health workers such as doctors; An educational intervention including explanations of medication use, discussions of the importance of adherence, and information about the effects of non-adherence and problems related to medication management can increase adherence to medication use [30]
Psycho-behavioral/ behavioral intervention	Pharmacists can use drug reminders (use pill organizers) [7] Cue dose training therapy to remind patients about their drug schedule [22]	A behavioral intervention or skills-based psychological intervention is another intervention that is carried out to change behavior and requires practice and understanding so that it can produce various physiologic changes [31]; Psycho-behavioral interventions, based on the theory of psychotherapy, include behavioral, cognitive behavioral, and mind-body treatments; Behavioral interventions and self-management may improve the quality of life and health-related emotional well-being of adults and adolescents with epilepsy [31]
Mixed/combo intervention	An education intervention has been combined with a behavioral intervention in a modified medication schedule, which was presented in the form of a table that illustrated the daily medication therapy of participants with pictures of antiepileptic drugs, along with cues to take their medication [22]	Pharmacists combine patient education (written or oral instructions) with a behavioral intervention [32]

[33] indicates that there is generally low awareness of epilepsy, negative attitudes towards the condition, and limited health literacy among teachers and students. This highlights an opportunity for pharmacists to partner with teachers to enhance epilepsy awareness through activities such as workshops, panels, and health education training on epilepsy.

DISCUSSION

Epilepsy is a chronic condition that requires long-term treatment. The administration of antiepileptic drugs typically starts with a monotherapy at the lowest possible dose, which may be increased to achieve effective levels while minimizing side effects. If seizures continue, a combination of antiepileptic drugs may be required [34]. In this context, pharmacists play a crucial role by reviewing patient medications, conducting drug reconciliations, analyzing adverse events, and implementing interventions to enhance treatment outcomes [35]. According to ten reviewed studies, pharmacist interventions are designed to improve drug adherence through either direct or face-to-face counseling, or via digital services [26]. Direct counseling involves providing patients with detailed information about epilepsy symptoms, seizure triggers, antiepileptic drugs, medication adherence, and the effectiveness of these drugs in controlling seizures [7,21,24,27,29]. Additionally, printed leaflets containing information about epilepsy treatment can be distributed to the patient's caregiver [24]. Moreover, Tang et al. [22] implemented an educational intervention that combined

direct face-to-face counseling with a behavioral strategy by providing a medication-taking schedule. This intervention included a modified medication schedule presented in a table format, which illustrated the daily therapy regimen with pictures of the antiepileptic drugs and cues to remind patients to take their medication. This approach helps patients better understand their treatment regimen and prevents them from missing doses. Lastly, Zheng et al. [26] explored the effects of comprehensive counseling provided by multidisciplinary health worker teams.

According to the reviewed studies, interventions conducted by pharmacists have played a crucial role in improving patient health outcomes, particularly in enhancing medication adherence. Research conducted by AlAjmi et al. [7], Fogg et al. [21], Chandrasekhar et al. [27], Jarad et al. [28], and Tamilselvan et al. [29] demonstrates that educational interventions, either through direct verbal counseling or structured 30-minute face-to-face interviews, can significantly increase adherence to medication regimens and strengthen patients' belief in their treatment (Table 1). Additionally, studies by AlAjmi et al. [7] and Jarad et al. [28] indicated a significant difference in drug adherence between control and intervention groups. Another effective counseling method, providing leaflets, has proven particularly beneficial for caregivers of pediatric epilepsy patients [24]. In the realm of pharmaceutical care, counseling is crucial for enhancing the quality of life among epilepsy patients [36]. The goal of educational interventions is to bolster patient knowledge about the disease and treatment, as well

as to alter patient beliefs or perceptions about their treatment, as assessed by a questionnaire. Such education helps reduce patients' fear of the stigma associated with seizures and enhances their ability to self-manage epilepsy [36]. Educational interventions can be administered by pharmacists or other healthcare professionals, such as doctors. Li et al. [23] developed a program known as the Epilepsy Review Service, which provided comprehensive information about the disease, including the types of seizures, their duration, triggers, and potential side effects. The service also included a therapeutic drug monitoring service, which served as a reference for dose adjustments by prescribing doctors and helps prevent drug toxicity.

Interventions for epilepsy patients can also be administered by a multidisciplinary team of health workers, including pharmacists, neurologists, and nurses. These professionals are expected to deliver integrated and comprehensive information and services tailored to their specific areas of expertise [26]. Such interventions have been shown to significantly enhance medication adherence and quality of life, as measured by the 8-item Morisky Medication Adherence Scale (MMAS-8) and the 31-item Quality of Life in Epilepsy questionnaires, respectively. Moreover, Tang et al. [22] reported that educational interventions (both verbal counseling and written materials) combined with behavioral changes, such as the use of medication reminders, significantly improved medication adherence and seizure control. Patients were prompted to take their medication through the use of illustrated tables that outlined their daily therapy schedules. However, there was no significant difference in outcomes between the control group, which received only educational interventions, and the intervention group, which received both educational and behavioral interventions (Table 2). Behavioral interventions, or skill-based psychological strategies, are implemented to modify behavior. They require practice and understanding to effectively change habits and enhance quality of life [37]. Furthermore, improving patient self-management or self-efficacy in their treatment can lead to greater therapy success, foster adaptation to chronic disease treatment patterns, and directly impact the patient's quality of life [38].

Adherence to taking medication refers to the extent to which a patient follows the prescriber's instructions when using medication [6]. Research has shown that adherence to antiepileptic drug therapy can prevent seizures or even achieve seizure freedom in up to 70% of cases [39]. A study by Niriyao

et al. [40] found that epilepsy patients with low medication adherence were eleven times more likely to experience uncontrolled seizures compared to those with high medication adherence. Adherence to treatment can be measured directly or indirectly [16]. Direct methods include measuring drug levels in hair or body fluids such as blood or saliva. Indirect methods, in contrast, utilize non-biological tools, including self-reported pill counts, appointment attendance, medication refills, questionnaires, and seizure frequency [41]. Questionnaires are commonly used as indirect measures to assess drug adherence outcomes, including the MMAS-8, MMAS-4 [22,26-28], the Simplified Medication Adherence Questionnaire [25], and the Medication Adherence Report Scale [21].

This scoping review indicates that pharmacists can improve medication adherence and impact other parameters, such as seizure control and quality of life for epilepsy patients, through three types of interventions: educational, psycho-behavioral, and mixed interventions (Table 2). This aligns with findings from a review by Al-Aqeel et al. [32], which suggests that adherence can be increased through these three intervention methods. However, this scoping review has limitations, including only reviewing articles published in English and the need for a broader literature search across more databases. Another limitation is the narrow inclusion criteria related to outcome parameters, as the criteria for this review are limited to pharmaceutical interventions concerning drug use adherence (medication adherence). Future reviews could explore pharmacist interventions on epilepsy awareness, potentially involving other health workers or social workers.

CONCLUSION

Pharmacist interventions have been shown to be effective in improving medication adherence among epilepsy patients. Direct counseling, provided either through face-to-face interactions or digital services, equips patients with essential information about their condition and insights into epilepsy symptoms, seizure triggers, and antiepileptic drugs. Additionally, distributing educational materials like leaflets can be particularly helpful for caregivers of pediatric epilepsy patients. Multidisciplinary interventions that include pharmacists, neurologists, and nurses offer comprehensive care that can improve both drug adherence and the quality of life for epilepsy patients. Furthermore, behavioral interventions, such as medication reminders and skill-based psychological support, can sig-

nificantly boost medication adherence and seizure control. Overall, pharmacist interventions are crucial in optimizing therapy outcomes, which include increased knowledge of self-management, improved perception of illness, enhanced effectiveness of antiepileptic drugs in controlling seizures, and better quality of life.

NOTES

Conflict of Interest

The authors have no conflicts of interest associated with the material presented in this paper.

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Author Contributions

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