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Review

Identifying the barriers to antiepileptic drug adherence among adults with epilepsy

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ABSTRACT

Purpose: To identify the barriers to antiepileptic drug (AED) adherence among adults with epilepsy (AWE). The impact of AED non-adherence on quality of life (QoL) was also examined.
Method: Systematic design (SR) study. A search strategy was undertaken with no time limits, for articles published in English, in MEDLINE, CINANL, PsycINFO, EMBASE, Cochrane databases and grey literature sources. Eligibility criteria included participants with epilepsy over 18 years, who were prescribed AEDs. Adherence had to be defined and adherence assessment measurements identified. A screening process was undertaken to select eligible studies. Eight studies met the inclusion criteria and were included in a quantitative synthesis. Quality of evidence was conducted using the EBL critical appraisal checklist and assessing risk of bias within individual studies.
Results: Across the included studies a high prevalence of non-adherence was identified. AED non-adherence was associated with specific beliefs about medications, being depressed or anxious, poor medication self-administration management, uncontrolled recent seizures, frequent medication dosage times, poor physician-patient relationship and perceived social support. Additionally, AED non-adherence impacted negatively on QoL as a result of poor seizure control.
Conclusion: Although included studies were of good quality, risk of biases reduced the generalisability of results. Findings suggested that comprehensive adherence assessments should routinely be performed. Recommendations for future research include the use of longitudinal research designs and a follow up SR to include the 16–18-year-old population.

1. Introduction

Approximately 50 million people globally have epilepsy making it the most common neurological disease [1]. AEDs are considered the mainstay of treatment [2] and can result in 70% of patients achieving seizure freedom once an effective regime is followed [3]. "Medication adherence" is the extent to which individuals take their medications as prescribed with respect to dosage and dosage intervals [4]. The term "adherence" reflects contemporary patient-centered healthcare systems in which patients and prescribers collaborate on treatment plans, rather than patients simply "complying" with instructions [5].

From the current literature, AED non-adherences rates among adults with epilepsy (AWE), range from 29 to 39% [6]. Therefore, the effectiveness of AED regimes is compromised leading to higher incidences of fractures, injuries and automobile accidents [7]. Retrospective research has demonstrated the impact of non-adherence on healthcare utilisation and costs as a result of increased emergency department attendances and inpatient admissions [6,8].

Consequently, AED non-adherence is associated with adverse clinical outcomes and increased mortality rates [7]. Patients may be being incorrectly classified as having refractory epilepsy [9]. Additionally, non-adherent AWE are known to have increased risks of convulsive status epilepticus [10]. However, the most serious consequence of AED non-adherence is the increased risk of sudden unexplained death in epilepsy patients [11]. Therefore, identifying the barriers to AED adherence is viewed as imperative to enabling practitioners develop appropriate strategies to improve adherence rates [6].

It was evident that undertaking this SR was timely, as there has been a surge in researchers, investigating the reasons for AED

Abbreviations: AED, antiepileptic drug; AWE, adults with epilepsy; ESMS, epilepsy self-management scale; MMAS, Morisky medication adherence scale; MPR, medication possession ratio; QoL, quality of life; SR, systematic review.

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non-adherence, with robust studies been published globally. While individual studies have identified specific barriers to AED adherence, contradictory findings emerged.

Well controlled epilepsy has been identified as leading to non-adherence [12] which contradicted other research which associated experiencing fewer seizures with more adherent behaviour [13]. Some argue it's the fear of and the occurrence of medication side-effects such as cognitive difficulty or weight gain that leads to reduced AED adherence [14]. However, others found adherence was dependent on treatment effectiveness rather than occurrence of side-effects [15]. It is also suggested that monotherapy increases adherence rates [13]. In contrast, adherence rates have been reported to be higher among AWE on polytherapy due to stronger medication necessity beliefs [16].

Variances between research findings on this subject have been attributed to population, geographical and methodological differences between studies [17]. Furthermore, while most definitions presume adherence is a stable patient characteristic, evidence suggests it's a much more dynamic process [18]. Each of these factors have led to a lack of clarity on this subject and hindered the development of substantive conclusions.

The primary outcome measure of this SR was to determine AED adherence and non-adherence rates among AWE and thereupon identify the specific barriers that contribute to AEDnon-adherence. The secondary outcome measures were the impact on quality of life (QoL) for AWE that was attributed to AED non-adherence.

2. Methods

2.1. Search strategy and study selection

A systematic search for original research published in peer-reviewed journals in the MEDLINE, CINANL, PsycINFO, EMBASE, and Cochrane databases without time limits was conducted. Eligibility criteria included: AWE over 18 years who were prescribed AEDs with a main focus being the identification of either inhibitors or enablers to AED adherence in AWE. Adherence had to be defined with the measurement used identified. Studies that used participants with learning disabilities, memory impairment or any severe co-morbidities were excluded to avoid introducing confounding factors. Only English language publications were considered due to lack of translation resources.

Search words/terms utilized both MeSH and non-MeSH: such as epilepsy or epilep* or anticonvulsant* or antiepilep* medication* or antiepilep* drug* or anti-epilep* medication* or anti-epilep* drug* (non-MeSH) OR Medication Adherence (MeSH) OR adher* (non-MeSH) OR compliance or comply or complies or compliant (non-MeSH) OR Compliance (MeSH) OR concord*(non-MeSH) OR barrier* or inhibit* or enable* or influenc* or influential or obstacle* or hinder* hindrance (non-MeSH). Variances existed across the databases regarding how MeSH terms and language and age limits could be applied.

Within grey literature the Open grey, Lenus, and Rian databases were searched. Additionally, "Epilepsia" "Seizure" and "Epilepsy & Behavior" journals were hand searched during dates not held within the MEDLINE database. Two review authors (GOR & JJOB) independently assessed titles and, where available, abstracts of the studies were identified by the search strategy against the eligibility criteria for inclusion in the review. In total, 1916 records were screened. A flow chart summary of the literature search is outlined in Fig. 1. Eight records met the inclusion criteria [19–26]. A list of excluded articles can be found as Supplementary material (S1).

2.2. Quality of evidence assessment and data collection

Critical appraisal of the evidence from each included study was undertaken using the EBL critical appraisal checklist [27]. Overall validity of a study required (Yes/Total) is $\geq$75% or ((No + Unclear)/Total) is $\leq$25%. The results are outlined in Table 1.

Apart from two studies [24,25], six studies had robust sample sizes. The use of participants with private health insurance [20] refractory epilepsy [21] computer literacy skills [23] poor seizure control and "underserved" healthcare access [25] very good seizure control [19,26] limited findings generalisability. The introduction of confounding factors was reduced in six studies [19–22,25,26] with stringent eligibility criteria. However, two studies [23,24] did not outline any exclusion criteria for the AWE samples. In Hovinga et al. [23] the epilepsy diagnosis was self-reported, reducing internal validity. Three studies [22,23,25] failed to outline their sequence generation process, making judgement unclear. Only one study [20] used random selection processes.

Only five studies, reported their response rates with varying results: 55% [19,26], 22.1% [20], 28% [23], and 72% [24]. Two studies provided research incentives to participants [20,23] which may lead to demographic bias [28]. The use of postal surveys in four studies [19,20,24,26] may have increased response bias due to the non-participation of individuals with literacy difficulties [17]. One study [23] provided insufficient information to allow replication. This study did not disclose the questions posed to their physician sample [23].

Three studies reported receiving both ethical approval and obtaining informed consent [20,21,25]. While four studies [19,22,24,26] obtained ethical approval, no reference was made to consenting. Only one study [23] reported upholding anonymity. Two studies failed to report on any ethical aspects of their work [23,25] hindering judgement.

Chapman et al. [19] was judged at high risk of attrition bias as scores were prorated where fewer than half of item scores were missing from the beliefs about medicines questionnaire [29] and perceived sensitivity to medicines scale [30] responses along with missing data in clinical and demographical information within individual items. In Ettinger et al. study [20], 465 patients were

Table 1
Critical appraisal of included studies.

Study	Population	Data collection	Study design	Reporting results	Overall validity
Chapman et al.[19]	50%	100%	100%	100%	86%
Ettinger et al.[20]	67%	100%	100%	83%	86%
Ferrari et al.[21]	67%	100%	100%	67%	82%
Guo et al.[22]	83%	80%	100%	100%	91%
Hovinga et al.[23]	33%	80%	60%	83%	64%
Jones et al.[24]	33%	100%	100%	83%	77%
Shallcross et al.[25]	50%	100%	100%	83%	81%
Smithson et al.[26]	50%	100%	100%	50%	73%