

**Predictors of Quality of Life in Adults with Epilepsy:  
A Systematic Review Comparing Studies from High- and Low/Middle-Income  
Countries**

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MLNNWA002

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**COMPULSORY DECLARATION**

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### Abstract

Epilepsy is the most prevalent of the non-communicable diseases that have a neurological origin. Of the approximately 50 million people worldwide who are affected, more than 80% of cases are found in low- and middle-income countries (LMICs) such as South Africa. Diminished quality of life (QoL) is common in people with epilepsy (PWE). Broadly speaking, QoL is defined as one's general wellbeing as perceived through subjective experiences and position in life. Several individual factors affect how PWE perceive their general wellbeing; these factors, which include the person's sociodemographic profile, epilepsy-related clinical characteristics, psychiatric comorbidities, and other psychosocial influences, therefore play important roles in determining their QoL. The current study aimed to undertake a systematic review that provided an updated integration and evaluation of knowledge on the predictors of QoL in adults with epilepsy. The review also aimed to describe how the influence of these predictors might differ in LMICs as compared to high-income countries (HICs). A total of 100 original research articles met the inclusion criteria for the systematic review (43 from HIC and 57 from LMICs). The results of the study showed that globally and specifically in HICs, an interaction of seizure-related factors and psychiatric comorbidities were the main predictors of QoL. In LMICs, however, the influence of sociodemographic factors was also profoundly significant, particularly level of education. Given that the burden of epilepsy is more profound in LMICs than in HICs, it is thus crucial that clinicians and researchers are aware of how the influence of these predictors might differ from one geographic region to another – such awareness will allow the design or adjustment of interventions to optimize them for use in different countries.

*Keywords:* quality of life, epilepsy, predictors, LMICs, HICs, PWE

## **Chapter 1:**

### **Introduction and Literature Review**

Epilepsy is the most prevalent of the non-communicable diseases that have a neurological origin. This medical condition is characterized by recurrent seizures that occur as a result of frequent disorderly electrical activity in the brain (Scheffer et al., 2018). Of the approximately 50 million people worldwide who are affected, more than 80% of cases are found in low- and middle-income countries (LMICs) such as South Africa (Ngugi et al., 2010).

Diminished quality of life (QoL) is common in people with epilepsy (PWE). Broadly speaking, QoL is defined as one's general wellbeing as perceived through subjective experiences and position in life (World Health Organization, 1998). Numerous tools have been developed to measure QoL in PWE. The Quality of Life in Epilepsy (QOLIE; Devinsky et al., 1995), World Health Organization Quality of Life (WHOQOL; World Health Organization, 1998) and the Short Form Health Survey (SF-36; Ware Jr & Gandek, 1998) are some of the most commonly used measures. Although these measures are strictly quantitative in nature, they enable clinicians and researchers to have an indication of the factors that may be affecting the QoL of PWE. Of note here too is that all of these instruments evaluate QoL via holistic assessment of physical health, psychological state, and social functioning.

Epilepsy impacts negatively on all these domains of functioning, albeit to varying degrees in different PWE (Andersson et al., 2020; Bradley et al., 2016; Braga, 2021; Caplan, 2019; Forthoffer et al., 2020; Gutter et al., 2019; Henning et al., 2019; Kılınç et al., 2018; Lopez & Xu, 2021; Michaelis et al., 2020; Noe, 2019; Pandey et al., 2020; Tao et al., 2021). Although it is easily assumed that impaired QoL results from deteriorating social functioning, other contributing factors might include clinical factors such as age at onset and existing psychiatric comorbidities (Park & Lee, 2020; Salpekar & Mula, 2019).

Hence, it seems clear that several individual factors (including the person's sociodemographic profile, epilepsy-related clinical characteristics, psychiatric comorbidities, and other psychosocial influences) affect how PWE perceive their general wellbeing and, thus, that these factors help determine their QoL.

Understanding these factors and the ways in which they affect QoL is crucial in managing the condition and in developing interventions to enhance overall health and wellbeing in PWE. Therefore, the aim of this systematic review was to provide an updated integration and evaluation of knowledge on the predictors of QoL in adults with

epilepsy. The review furthermore aimed to describe how the influence of these predictors might differ from LMICs to high-income countries (HICs).

### **Characteristics of Epilepsy**

According to an official report by International League Against Epilepsy (Fisher et al., 2014), epilepsy is defined by any the following:

- I. “Two unprovoked seizures that occur less than 24 hours apart
- II. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
- III. An epilepsy syndrome diagnosis” (p.477).

An *epilepsy syndrome diagnosis* can be classified at three levels: epilepsy type, seizure type, and syndrome. Depending on their cause, seizures can be focal, generalized, or have an unknown origin. Causes can include structural impairments, genetic defects, infections, and immune system or metabolic dysfunction (Espinosa-Jovel et al., 2018). Although causes of seizures can be identified, in up to half of cases the aetiology is unknown.

The type of epilepsy an individual presents with can also be classified according to whether seizure localization is generalized, focal, a combination of the two, or unknown. *Generalized seizures* affect both hemispheres of the brain simultaneously, which results in symptoms being experienced bilaterally (Fisher et al., 2017). These seizures can be classified as being of either a motor or non-motor (absence) type. Motor seizures are characterized by symptoms such as jerking movements or muscle stiffness, and hence they have the following sub-classification scheme: clonic (accompanied by jerking movements), tonic (accompanied by muscle rigidity), atonic (accompanied by muscle weakness), or myoclonic (accompanied by brief muscle twitching). Absence seizures, in contrast, are characterized by a lack of motor symptoms and brief periods of blanking out. Note, however, that in some cases absence seizures can co-occur with brief muscle twitching in a specific part of the body (e.g., the eyelids; Beghi, 2020).

Focal seizures, which are so called because they have a specific locus of onset and tend to affect only one hemisphere of the brain, occur more commonly than generalized seizures (Marashly, 2021). Focal seizures can, however, also be classified as being of either a motor or non-motor type. Of note here is that some motor symptoms (e.g., automatisms such as chewing) and some non-motor symptoms (e.g., changes in body temperature) are commonly associated with focal seizures (Fisher et al., 2017). Focal seizures are further divided into two types (those with intact awareness or those with impaired awareness) based

on whether or not the patient experiences alterations in their awareness during a seizure. In the unique case of focal to bilateral tonic-clonic seizures, the onset of the seizure is focal and then it spreads bilaterally affecting both sides of the brain in a manner similar to a generalized seizure (Fisher et al., 2017).

Making an accurate diagnosis of an epilepsy syndrome is often a complex task due to the myriad of causes that can bring about seizures, as well as their distinct electroclinical presentations and outcomes (Scheffer et al., 2017). Diagnosis is further complicated by the sometimes-overlapping clusters of clinical features often associated with each syndrome and by the fact that age at onset can affect how the epilepsy presents—syndromes may present differently depending on whether they are childhood- or adult-onset (Howell et al., 2021; Stöberg et al., 2020; Vorderwülbecke et al., 2022).

Hence, a thorough clinical investigation is a crucial part of the diagnostic process. This clinical investigation often requires neuroimaging (e.g., EEG), a comprehensive clinical interview and medical history-taking, as well as an extensive neurological examination and neuropsychological assessment (Scheffer et al., 2018).

Proper epilepsy management is largely dependent on reaching an accurate diagnosis as well as considering the influence of comorbidities, such as depression or anxiety. The success of management interventions also varies depending on the geographical region in which the patient resides. There are differences in terms of availability of epilepsy specialists, access to medications, and the prevalence of endemic illnesses that can lead to epilepsy syndromes (Thijs et al., 2019). For instance, in areas such as rural Tanzania where neurocysticercosis (NCC) is endemic, 30% of epilepsy cases are associated with that infection (Millogo et al., 2019).

### **Epidemiology and Treatment Gaps**

As mentioned earlier, epilepsy affects approximately 50 million people worldwide, with about 80% of those affected residing in LMICs<sup>1</sup> (Ngugi et al., 2010). Globally, approximately 2.4 million people are diagnosed with epilepsy each year. Annually, between 30 and 50 per 100 000 people are diagnosed with epilepsy in HICs; in LMICs, this figure could be twice as high. This differential may be accounted for by a number of possible reasons. For instance, in LMICs there is higher incidence of birth-related injuries and traumatic brain injuries, limited medical infrastructure, heightened risk of endemic diseases (e.g., NCC), as well as relative inaccessibility of adequate healthcare (Beghi, 2020).

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<sup>1</sup> LMICs and HICs were defined based on the [World Bank country classifications](#).

Although most PWE reside in LMICs, epilepsy care in those countries lags far behind that in HICs. This is partly due to large treatment gaps in epilepsy care in LMICs, where in this case the term *treatment gap* refers to the proportion of PWE who need treatment but do not receive it (Kwon et al., 2022). A pertinent systematic review reported a significant global disparity in epilepsy care between LMICs and HICs (Meyer et al., 2010). A total of 74 studies, emerging from 38 different countries, were included in the final review sample. Sixteen emerged from low-income countries (e.g., Uganda), 13 from middle-income countries (e.g., South Africa), and 9 from HICs (e.g., France). Findings indicated that the treatment gap was highest in low-income countries (over 75%), and that most middle-income countries also had a significant treatment gap (over 50%). In contrast, many HICs had very low treatment gaps (less than 10%). Additionally, there was significant within-country variation in treatment gaps when studies included estimates from both rural and urban settings: The gap was considerably higher in rural than urban settings.

According to Singh and Trevick (2016), the main cause of this treatment gap is the lack of epilepsy specialists in LMICs. For instance, they found that on average European countries have 33 epilepsy-focused neurologists per 10 million people whereas on average African countries have only 6 such neurologists per 10 million people. Furthermore, these African neurologists represent nearly all of those in their professional specialization in their countries, whereas the neurologists specialising in epilepsy care in European countries only represent 6.8% of their total number of neurologists.

A further note here is that even within LMICs there are treatment gaps. As noted above, rural clinical settings are typically far less well equipped than urban and suburban clinical settings. In South Africa, for instance, the facilities that are best equipped to provide epilepsy care (i.e., those that form part of the country's private healthcare system) are concentrated in urban settings and are far removed from rural areas, and the majority of South Africa's neurologists and other epilepsy specialists work in private healthcare facilities (Wagner et al., 2020). In contrast, the country's public healthcare system administers overcrowded and poorly equipped facilities in both urban and rural areas. Moreover, expenditure for public hospitals is constrained and remains a challenge for South Africa's health budget (Tunzi & Simo-Kengne, 2020).

Although the South African public healthcare system serves most of the country's population, it is ill-equipped to handle epilepsy patients. For example, patients are more likely to receive older anti-seizure medicines (ASMs) as this dispensation is more cost

effective. However, patients are more likely to experience more intense side-effects when treated with these drugs as compared to newer ASMs (Perucca et al., 2020).

This pattern of treatment gaps has also been observed in India, where a treatment gap of 40–90% is seen in rural areas as compared to 22–50% in urban and suburban areas (Meyer et al., 2010).

Global disparities in terms of accessing treatment are not only present due to financial limitations in providing care; lack of education about the condition, as well as other social factors, are also implicated. Several studies have noted that beliefs, taboos, and stigma can account for the treatment gaps observed in LMICs, particularly in rural settings (Anguzu et al., 2021; Giuliano et al., 2019; Molla et al., 2020; Molla et al., 2021; Tedrus et al., 2017). Moreover, poor understanding of the disease and its social, cognitive, and psychological impact may hinder patients from seeking care.

In summary, LMICs are constrained in providing adequate care and management of PWE, placing these patients in a disadvantageous position relative to their counterparts in HICs.

### **Sociodemographic Influences on Quality of Life in PWE**

Several studies have found associations between sociodemographic factors and QoL in PWE (see, e.g., Andersson et al., 2020; Chen et al., 2016; Kováts et al., 2017; Lopez & Xu, 2021). These sociodemographic factors include marital status, gender, and level of education. However, there is conflicting evidence regarding the direction of these associations (Yang et al., 2020). For instance, in terms of marital status, some studies report that married PWE have better QoL than those that are unmarried (Ayanda & Sulyman, 2020a; Tefera et al., 2020a; Zhong et al., 2021). The findings from these studies emphasize the importance of social support provided by that marriage. In contrast, however, are studies reporting that being married is strongly associated with lower QoL in PWE (Ashwin et al., 2013).

Zhong et al. (2021) found gender to be strongly associated with QoL in PWE, with women reporting significantly lower levels of QoL in comparison to men. This gender difference in QoL has been replicated in several epilepsy studies, with the attribution for disparities attributed variously to increased seizure worry in women (Srikanth et al., 2021), concerns about motherhood and reproductive issues relating to epilepsy and its treatment (Grant et al., 2013), and social factors such as lack of support and isolation (Lee et al., 2021). Of note, however, is that numerous studies report no such gender differences in the QoL of PWE (Bala et al., 2016; Elliott & Mares, 2012; Kaddumukasa et al., 2019; Lee et al., 2021).

A related strand of this research reports that level of education may also be a predictor of QoL in PWE. Several studies have found that higher levels of education are associated with better QoL (Kinyanjui et al., 2013; Saadi et al., 2016; Tefera et al., 2020). One plausible reason for this association is that being educated increases awareness of the disease, which can potentially lead to better compliance with treatment and the use of healthier coping mechanisms (Atakli et al., 2016). Furthermore, lower levels of education may be significantly associated with higher levels of stigma, and hence with poorer QoL (Giuliano et al., 2019).

### **Influence of Epilepsy-Related Clinical Factors on Quality of Life in PWE**

The literature on how seizures impact negatively on the lives of PWE is well established (Campos-Fernández et al., 2020; Maschio et al., 2017; O'Rourke & O'Brien, 2017; Rassart et al., 2020). However, because epilepsy can be characterized by either generalized or focal seizures, and because these variations of the condition have unique clinical features and affect different brain networks, patients with different types of seizures can differ in terms of how their QoL is affected. Moreover, some types of epilepsy are intractable and require surgery. Medically intractable epilepsy is chronic, disruptive, and disabling (Fletcher et al., 2015). Due to these intricacies, it is often difficult to decipher which of these clinical factors are influencing the affected person's QoL, and just as difficult to disentangle the individual contributions of each influencing factor.

Age at epilepsy onset, seizure frequency and severity, and the effects of anti-seizure medicines (ASMs) are some of the most impactful clinical factors in intractable epilepsy. Several studies indicate that patients with an earlier age of onset (and hence longer duration of epilepsy) are more likely to report poorer QoL (Baranowski, 2018; Edefonti et al., 2011; Tombini et al., 2021). However, numerous similar studies have found the effect of age of onset or other age-related factors to be insignificant in determining QoL, particularly when controlling for other sociodemographic factors (Yang et al., 2020).

Studies also suggest that as the duration of the disease increases, the effects of epilepsy-related clinical factors (such as seizure severity) become more pronounced and therefore begin to affect QoL more significantly (Ayanda & Sulyman, 2020; Pauli et al., 2012; Wang et al., 2017). For instance, Chen et al. (2018) showed that increased duration of temporal lobe epilepsy (TLE) was strongly associated with self-reported emotional and behavioural distress, which in turn were significantly associated with poorer QoL. These findings are similar to those of Puri et al. (2018), who found that longer duration of epilepsy was strongly correlated with markers of poor QoL such as diminished cognitive abilities and impaired social functioning.

Of note is that a small group of studies indicates that *shorter* disease duration and *later* age of onset are associated with poorer QoL (Alonso-Vanegas et al., 2013; Taylor et al., 2011a; Wang et al., 2017). To account for these findings it is essential to note that, within the PWE population, adults are often more prone than children to developing psychiatric comorbidities and that these psychiatric comorbidities are associated with poorer QoL (Witt et al., 2014). Furthermore, shorter disease duration places one at a disadvantage due to immediate adjustments that must be made to activities of daily living and to coping mechanisms.

Patients with high levels of seizure severity and frequency often experience significant disruptions of their daily functioning, along with increased seizure worry and high levels of anxiety due to anticipation of recurrent seizures (Micoulaud-Franchi et al., 2017). Hence, it is unsurprising that numerous studies report on a negative relationship between seizure frequency and QoL (Hu et al., 2020; Nair et al., 2020; Oliveira et al., 2021). The significance of this relationship arises largely from the fact that seizures tend to disrupt many different activities of everyday functioning, from self-care to driving and employment retention (Alexander et al., 2018; Viteva, 2013).

Seizure severity can predict QoL independently of seizure frequency (Adebayo et al., 2014; Akosile et al., 2021; Fawale et al., 2014; Hamid et al., 2013; Kaddumukasa et al., 2019; Viteva, 2014). For instance, Vickery et al. (2000) found, in sample of patients with intractable partial epilepsy, modest associations between seizure severity and QoL and, independently, significant correlations between seizure frequency and QoL. However, it is important to note that these findings might have been influenced by sampling bias: only patients with intractable epilepsy were recruited.

Although the administration of ASMs can be beneficial in cases of intractable epilepsy because they reduce seizure severity, some of these drugs (particularly the older forms) have a number of unfavourable side-effects that can impact negatively on the patient's sleep, behaviour, and cognition (Njamnshi et al., 2019; Quon et al., 2020). For instance, a review on the current clinical practices in epilepsy care by Burakgazi and French (2016) showed that the common side effects observed in PWE on Topiramate included drowsiness and word-finding difficulties. Similarly, Njamnshi et al. (2019) conducted a community-based case-control study comparing sleep quality between PWE and healthy controls. This study found that obstructive sleep apnoea was the most prevalent sleep disorder in PWE. Additionally, using Phenobarbital and/or Carbamazepine was associated with sleep disturbance in PWE. Therefore, apart from the use of older ASMs, the drug interactions of

ASMs used in polytherapy may exacerbate the presence of these adverse effects (Perucca et al., 2020; Zaccara & Perucca, 2014). Thus, this AED factor may be particularly important to consider in LMICs, where there is relatively limited availability of newer forms of these drugs (Saadi et al., 2016).

### **Impact of Psychiatric Comorbidities on Quality of Life in PWE**

The prevalence of psychiatric comorbidities in PWE tends to be higher than that in healthy controls (Ertem et al., 2017a). This relatively high prevalence is of concern because numerous studies suggest that psychiatric illness has a negative effect on the QoL of PWE (Ettinger et al., 2014; Hamid et al., 2013; Izci et al., 2016; Pulsipher et al., 2006). This effect exists in both intractable epilepsies and in cases where the epilepsy has been surgically treated and seizure freedom has been achieved.

The negative effects of psychiatric comorbidities on QoL in PWE is, by and large, attributed to the psychological and economic costs that come with treating and managing these illnesses while coping with epilepsy (Helmstaedter & Witt, 2012). These costs include the burden of attending more medical appointments and the expenses associated with acquiring additional medications (Chen et al., 2018; Pulsipher et al., 2006; Ridsdale et al., 2017). In LMICs, an additional burden often involves a curtailed ability to access appropriate psychiatric treatment (Birbeck, 2010; Cameron et al., 2012; Espinosa-Jovel et al., 2016; Espinosa-Jovel et al., 2018; Saadi, Patenaude, & Mateen, 2016).

Depression and anxiety are the most commonly occurring psychiatric comorbidities in PWE (Forthoffer et al., 2021; Fox et al., 2021; Gandy et al., 2021; Gruenbaum et al., 2021; Grzegorzewska et al., 2021; Lu et al., 2021; Mangaard et al., 2021). Taylor et al.'s (2011) systematic review found that these affective disorders were significant predictors of diminished QoL in epilepsy. Several studies published since that review have confirmed that depression, in particular, is a significant contributor to poor QoL in this clinical population and have described a number of factors that might contribute to the development and progression of depression in PWE (Chung et al., 2012; Faught, 2012; Hamid et al., 2013; Shallcross et al., 2015). One of these factors is non-adherence to ASMs, which frequently leads to worsening health outcomes (e.g., poor seizure control) and which has been linked directly to depressive symptoms (Alsaadi et al., 2017; Bala et al., 2016; H. F. Chen et al., 2016; Luoni et al., 2011; Milovanović et al., 2014; Ridsdale et al., 2017; Şenol et al., 2007). Another factor is the manner in which PWE perceive epilepsy and the stigma attached to it – there have been associations found between depressive symptoms and stigma, with those who

report experiencing higher levels of stigma being more likely to develop depressive symptoms (Ridsdale et al., 2017).

Epilepsy-associated stigma tends to be more prevalent in LMICs, particularly in rural communities where a general lack of understanding of the illness might prevail (Espinosa-Jovel et al., 2018; Saadi, Patenaude, & Mateen, 2016; Shallcross et al., 2015; Tefera et al., 2020). For instance, in some rurally-based cultures, epilepsy may be seen as a punishment or as the consequence of witchcraft (Fletcher et al., 2015). In these contexts, PWE experience significant levels of stigma, which can contribute to the development of depression and ultimately result in diminished QoL.

### **Impact of Other Psychosocial Factors on Quality of Life in PWE**

Numerous studies indicate that psychosocial factors such as stigma, employment status, driving ability, and degree of social support affect QoL in PWE (Alsaadi et al., 2017; Chung et al., 2012; Keikelame et al., 2017). As noted in the previous section, research on the effects of stigma on QoL in epilepsy is well established – especially because this social phenomenon is common in several cultures (Atadzhanov et al., 2010; Boling et al., 2018; Bruno et al., 2012; Chung et al., 2012; Ridsdale et al., 2017; Saadi et al., 2016; WHO, 2018). In the case of PWE, stigma is characterized by rejection and social exclusion as a result of experiencing or anticipating adverse social judgement based on the patient's medical status (Espinosa-Jovel et al., 2018).

A few studies have suggested distinguishing between *felt stigma* and *enacted stigma*. The former is characterized by self-stigmatization or internal stigma (i.e., the individual's own feelings of shame or embarrassment regarding their condition), whereas the latter is stigma imposed by others (Scambler & Hopkins, 1990). Numerous studies have found that felt stigma is more common in PWE who live in HICs, whereas enacted stigma is more common among LMIC-dwelling PWE (Atadzhanov et al., 2010; Baskind & Birbeck, 2005; Brigo et al., 2015). One possible means to account for this difference is that LMICs tend to be characterized by more limited opportunities for education, higher levels of unemployment, and higher treatment gaps. These factors have all been found to play a crucial role in the influence of enacted stigma on QoL in PWE (Wilmschurst et al., 2014).

PWE are more also at high risk of being unemployed or of losing their jobs because their neurological condition disrupts their ability to work at an optimal level (Alexander et al., 2018). Similarly, the presence of seizures also plays a significant role in their ability to drive as it poses a significant risk on the road (Elsharkawy, May, Thorbecke, & Ebner, 2009; E.

Viteva, 2013a). The impact of these psychosocial factors is likely to be more significant in LMICs due to social, geographic, and economic barriers to care, as well as limited resources or personnel available for the effective management of epilepsy (Wilmshurst et al., 2014).

## **Chapter 2:**

### **Rationale, Aims, and Significance**

Epilepsy is a chronic and disabling condition. The burden of this neurological disorder is particularly high in low- and middle-income countries that are characterized by populations with relatively limited access to health care, medication, and resources; profound treatment gaps; high rates of poverty; and high levels of epilepsy-associated stigma (Saadi et al., 2016). Globally, sociodemographic factors (e.g., marital status), clinical factors (e.g., seizure severity), psychiatric comorbidities (e.g., depression), and psychosocial factors (e.g., employment status) have been identified as significant predictors of quality of life in persons with epilepsy. Understanding how these factors (individually and in interaction) affect QoL in PWE is important in treating and managing the condition, and in ensuring that its personal, familial, and socioeconomic burden is minimized. Moreover, it is crucial for clinicians and researchers to consider these factors when developing interventions to improve QoL in PWE.

Although the burden of epilepsy is most significant in LMICs, relatively few studies investigate the impact of this neurological condition on the QoL of PWE in those countries. For instance, of the 86 studies included by Taylor et al. (2011) in their systematic review of factors predicting diminished QoL in PWE, only 25 emerged from LMICs. Moreover, the authors did not consider whether, or to what extent, the country or geographic region in which individual studies were conducted might have affected their findings. Hence, although they concluded that seizure severity and frequency and particular psychiatric comorbidities (e.g., depression) were definitely associated with lower levels of QoL, and that evidence for the influence of sociodemographic factors was inconclusive, they did not consider that PWE in LMICs are more likely than those in HICs to experience (a) limited access to health care, medication, and resources; (b) profound treatment gaps; (c) higher rates of poverty; and (d) higher levels of epilepsy-associated stigma (Saadi et al., 2016). Thus, it is essential to distinguish between high-income countries and LMICs in terms of factors predicting QoL as data from the former may not be applicable to the latter (e.g., factors that are more prominent influences on the QoL of PWE in LMICs may not be as prominent in HICs).

### **Aims of the Research**

The systematic review presented here aimed to summarize, integrate, and evaluate current knowledge on the predictors (sociodemographic, clinical, psychiatric, psychosocial) of QoL in PWE. To a certain extent, then, the current work represents an update on the review published more than a decade ago by Taylor et al. (2011). However, this study also aimed to extend the scope of that review by explicitly acknowledging that the impact of these

predictors is likely to be affected by the social, cultural, and economic context in which epilepsy is experienced (Hamid et al., 2013b). Hence, a critical aspect of the novelty of this study is that it compares the influence of these predictors in LMICs against that in HICs, and then attempts to identify the best predictors of QoL in PWE who live in LMICs.

### **Anticipated Significance of the Research**

The results of this study will allow clinicians and researchers to gain a better understanding of the factors that predict QoL in PWE (especially for those living in LMICs). Understanding how sociodemographic profiles, epilepsy-related clinical characteristics, psychiatric comorbidities, and other psychosocial influences affect QoL is crucial in the management of the condition and in developing interventions to enhance overall health and wellbeing in PWE. Given that the burden of epilepsy is more profound in LMICs than in HICs, it is also crucial that clinicians and researchers are aware of how the influence of these predictors might differ from one geographic region to another – such awareness will allow the design or adjustment of interventions to optimize them for use in different countries.

### **Chapter 3:**

#### **Method**

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher, Liberati, & Tetzlaff, 2009). The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42021239705).

#### **Search Strategy**

The search process began on February 1, 2021 and was completed on April 15, 2021. I conducted literature searches in the following electronic academic databases: EBSCOhost (AfricaWide, PsycINFO, CINAHL), Scopus (including Medline), JSTOR, and PubMed. Table 1 shows the search terms used for each database, as well as the total number of articles identified within each database and the overall total of unique articles identified at this stage of the search process.

After completing these searches of the above-named electronic databases, I perused the reference lists of relevant systematic reviews (Lu et al., 2021; Meyer et al., 2010; Stevanovic et al., 2011a; Taylor et al., 2011b) to see whether they contained additional articles, not identified by the previous searches, relevant to the current purposes. That perusal identified no additional articles – most of the works cited by these systematic reviews were already included in the wide pool under consideration.

**Table 1.** Search Terms for Each Database and Number of Articles Identified by Each Search

| Database  | Keywords                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Number of Articles Found | Duplicates | Total |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|------------|-------|
| EBSCOhost | <i>“epilepsy” AND (“quality of life” OR “health related quality of life” OR QOLIE) AND adults*</i>                                                                                                                                                                                                                                                                                                                                                                                                  | 207                      |            |       |
| Scopus    | <i>“epilepsy” AND (“quality of life” OR “health related quality of life” OR QOLIE) AND adults*</i>                                                                                                                                                                                                                                                                                                                                                                                                  | 3336                     |            |       |
| JSTOR     | <i>“epilepsy” AND (“quality of life” OR “health related quality of life” OR QOLIE) AND adults*</i>                                                                                                                                                                                                                                                                                                                                                                                                  | 1112                     |            |       |
| PubMed    | (quality of life: <i>"quality of life"</i> [MeSH Terms] OR ( <i>"quality"</i> [All Fields] AND <i>"life"</i> [All Fields]) OR <i>"quality of life"</i> [All Fields]) (adults: <i>"adult"</i> [MeSH Terms] OR <i>"adult"</i> [All Fields] OR <i>"adults"</i> [All Fields] OR <i>"adult's"</i> [All Fields]) (epilepsy: <i>"epilepsie"</i> [All Fields] OR <i>"epilepsy"</i> [MeSH Terms] OR <i>"epilepsy"</i> [All Fields] OR <i>"epilepsies"</i> [All Fields] OR <i>"epilepsy's"</i> [All Fields ]) | 2455                     |            |       |
|           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 7110                     | 2868       | 4242  |

*Note.* The only restriction placed on each search was that the retrieved article had to have been published in English. Note that there were no year restrictions placed on any of these searches.

## **Inclusion/Exclusion Criteria**

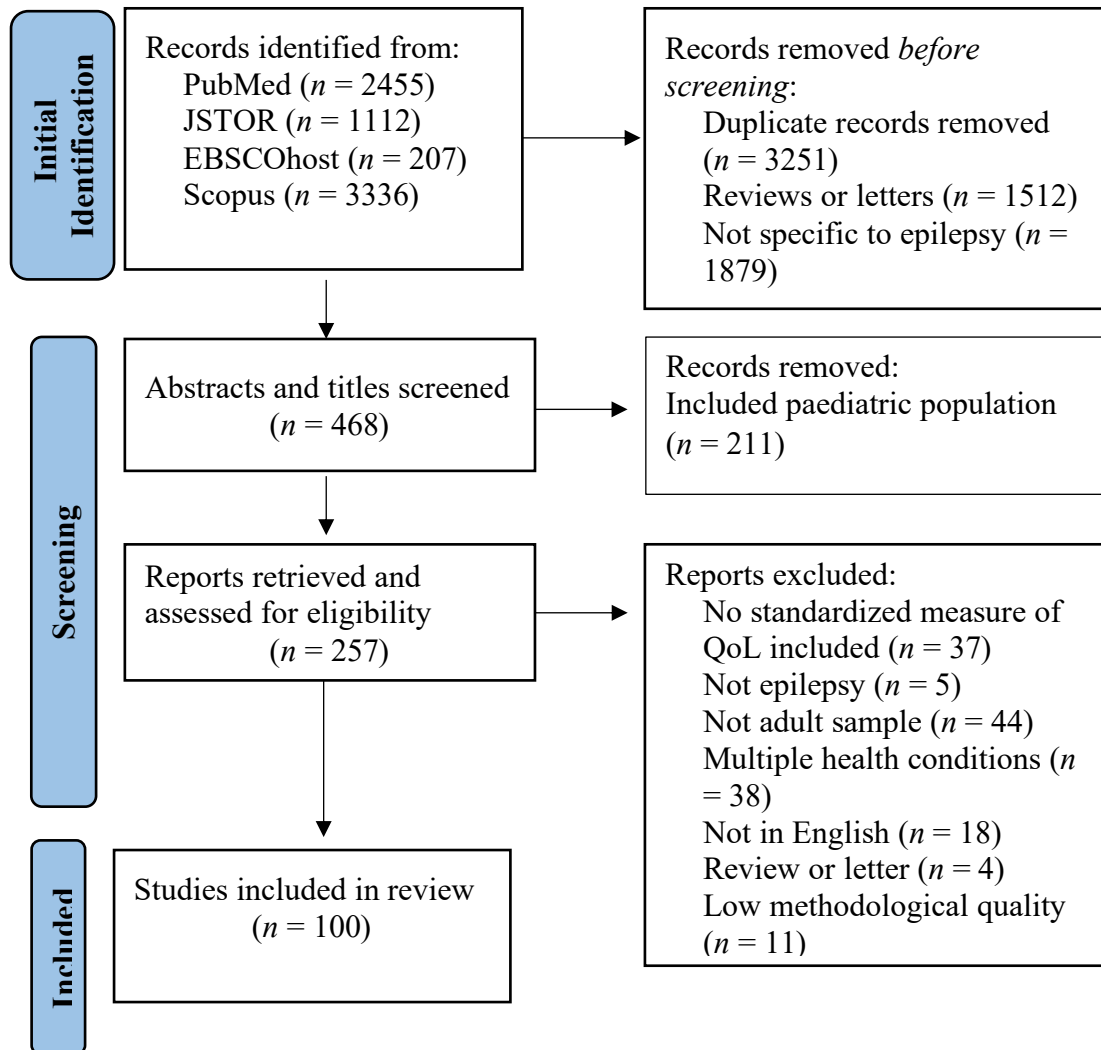
Two researchers (the author and another postgraduate student in psychology) independently screened and reviewed the titles, abstracts and, later, the full texts of possibly eligible studies. In the case of any discrepancies, a resolution was reached through discussion. In accordance with the aims of the systematic review, studies focusing on the four classes of predictors were taken into consideration: sociodemographic factors, epilepsy-related clinical factors, psychiatric comorbidities and psychosocial factors. The full texts of all the articles that were potentially relevant were obtained and examined independently by the two reviewers based on the set of inclusion/exclusion criteria listed below.

Articles were ultimately included in the review if they (1) had been published in English, (2) assessed QoL in adults (people 18 years and older), (3) used at least one validated or standardized measure of QoL (general or epilepsy-specific), and (4) presented findings for the relationship between overall QoL and a factor from the classes of predictors mentioned above (e.g., seizure frequency, depression, employment status, stigma, cognition).

Articles were excluded from this review if they (a) assessed QoL in a different clinical population (i.e., not in PWE), (b) included in their sample multiple health conditions (e.g., cancer and epilepsy), (c) presented no original data (e.g., reviewed previously published studies or engaged in correspondence about previously published studies), or (d) were of low methodological quality (see below for more detail regarding this criterion).

Figure 1 below is a flowchart illustrating the data collection flow.

**Figure 1.** *PRISMA Flowchart: Process of Identifying Studies to be Included in the Systematic Review*



Note. QoL = quality of life.

### Risk of Bias

To limit the risk of bias, the same two reviewers examined the methodological quality of the 111 studies that remained potentially eligible for inclusion in the systematic review after initial identification, screening, and application of the eligibility criteria listed above.

This examination of methodological quality was facilitated by the use of a 17-item checklist (see Appendix A) that is based on the theoretical and methodological considerations described by Altman (2008). There is precedent for using this checklist in previous systematic reviews assessing QoL in PWE (Baranowski, 2018; Stevanovic et al., 2011). The checklist has also been used systematic reviews of QoL in other health conditions (Den Oudsten et al., 2007; Kuijpers et al., 2004; Mols et al., 2005).

The reviewers independently scored the methodological quality of the potentially eligible articles. Once more, disagreements were resolved by discussion. Studies received a point for each of the 17 items on which they met the criteria for good methodological quality. Ultimately, the studies were classified as follows: (1) *high quality* studies were those that received 12 or more points, (2) *moderate quality* studies were those that received between 8 and 11 points, and (3) *low quality* studies were those that received 7 or fewer points. Studies classified as being of low methodological quality ( $n = 11$ ) were excluded from the pool of reviewed articles (see Figure 1).

### **Data Extraction and Analysis**

As Figure 1 shows, a total of 100 original research articles ultimately met the criteria for inclusion in the systematic review. These articles were stored on the PubMed database; Mendeley software was also used to store information about this final sample of articles.

I extracted the following data from each article: year of publication, authors, title of study, country in which the study was conducted, demographics of the sample, sample size, method(s) of data analysis, measure(s) of QoL used, measure(s) of depression or anxiety used, measure(s) of perceived stigma used, methodological quality score, type of study design (cross-sectional or longitudinal) and results. The extracted data were stored on an MSExcel database. A second researcher (the same person who had been involved in screening and methodological evaluation) conducted an independent review and check of all the extracted information. Where there was disagreement, consultation meetings were held so that consensus could be reached. The extracted data for all the studies included in the final systematic review can be found in Table 2.

Due to the heterogenous nature of the studies (e.g., differences in measures used to assess QoL, differences in psychiatric screening tools) a metanalysis was not conducted. Instead, I conducted a narrative synthesis that sought to summarize, integrate, and evaluate current knowledge on the predictors (sociodemographic, clinical, psychiatric, psychosocial) of QoL in PWE. Furthermore, considering how the impact of these predictors is likely to be affected by the social, cultural, and economic context in which epilepsy is experienced, a critical aspect of this synthesis was to also compare the influence of these predictors in LMICs against that in HICs and to thereby assist in identifying the best predictors of QoL in PWE who live in LMICs.

**Table 2.** *Extracted Information from All the Articles Included in the Final Systematic Review.*

| Year | Author          | Title                                                                                                                                                | Country                | Demographics                                                                                                        | Sample size | Data analysis method                     | QoL measure      | Depression/Anxiety | Stigma | Quality Score | Study Design    | Results                                                                                                                                                                                                                                                                                                                                      |
|------|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------------------------------|-------------|------------------------------------------|------------------|--------------------|--------|---------------|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1997 | van Hout et al. | Relationship Between Seizure Frequency and Costs and Quality of Life of Outpatients with Partial Epilepsy in France, Germany, and the United Kingdom | France, Germany and UK | outpatients, 18-65, stable partial epilepsy.                                                                        | 300         | Spearman's rank correlation coefficients | FSQ (translated) | NA                 | NA     | 10            | cross-sectional | QOL as measured by the FSQ declined as the frequency of seizures increased. All subscales, other than sexual relationships, showed a significant decrease in quality. % employed dropped ( $p=0.027$ ) with increased seizure group. Time lost and patient costs increased with group. ( $r$ 0.37 and 0.31 respectively) $p<0.001$ for both. |
| 1999 | Leidy et al.    | Seizure frequency and the health-related quality of life of adults with epilepsy                                                                     | USA                    | nonsurgical adults with epilepsy                                                                                    | 139         | Bivariate and multivariate modelling     | SF-36            | NA                 | NA     | 12            | cross-sectional | In the multivariate model, seizure frequency was a significant inverse predictor of HRQL across all domains ( $p<0.01$ to $0.001$ ). Men reported poorer physical function than women ( $p<0.05$ ), and patients with a comorbid condition had poorer HRQL in the areas of pain ( $p<0.05$ ) and general health perception ( $p<0.01$ )      |
| 2000 | Markand et al.  | Health-Related Epilepsy Quality of Life Outcome in Medically Refractory Treated with Anterior Temporal Lobectomy                                     | USA                    | patients with medically refractory complex partial seizures who completed a presurgical evaluation for possible ATL | 90          | repeated measures ANOVA model            | QOLIE-89         | NA                 | NA     | 15            | longitudinal    | Overall QOL and 10 of the sub measures had a significant effect. 5 of these were group*time interactions while the others were just group effects. It should be noted that the 4 main effects of group (Health perception, overall score, seizure worry and attention were already significant at baseline).                                 |

|      |                   |                                                                                                                                            |                 |                                                                     |     |                                         |                                       |       |    |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------|---------------------------------------------------------------------|-----|-----------------------------------------|---------------------------------------|-------|----|----|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2002 | Engelberts et al. | Cognition and health-related quality of life in a well-defined subgroup of patients with partial epilepsy                                  | Netherlands     | outpatients with partial epilepsy, matched with healthy controls    | 112 | linear regression                       | Self-reported HRQOL                   | NA    | NA | 10 | cross-sectional | Patients scored lower on measures of attention ( $P = 0.03$ ), learning ( $P = 0.02$ ) and speed of information processing ( $P = 0.00$ ).                                                                                                                                                                                                                                                                                                                                                   |
| 2002 | Au et al.         | Predicting the quality of life in Hong Kong Chinese adults with epilepsy                                                                   | Hong Kong/China | outpatients, adults                                                 | 67  | Correlation and hierarchical regression | QOLIE-89                              | HADS  | NA | 9  | cross-sectional | Overall effect of both biomedical and psychosocial variables (after controlling for biomedical). Individually, anxiety was the only significant predictor within either of the blocks of variables, with locus of control approaching significance.                                                                                                                                                                                                                                          |
| 2003 | Djibuti et al.    | Influence of clinical, demographic, and socioeconomic variables on quality of life in patients with epilepsy: findings from Georgian study | Georgia         | adult epileptic outpatients being treated in the epilepsy programme | 115 | linear regression                       | QOLIE-31                              | NA    | NA | 12 | cross-sectional | Seizure frequency predicted poor quality of life overall and on all subscales. Education predicted better quality of life on cognitive and social functioning, overall quality of life and total score. Duration of epilepsy predicted better social functioning and seizure worry scores, while age was associated with poorer cognitive function, QOL and energy.                                                                                                                          |
| 2003 | Cramer et al.     | The influence of comorbid depression on quality of life for people with epilepsy                                                           | USA             | Adults with epilepsy                                                | 501 | ANOVA and hierarchical regression       | QOLIE-89 and Sheehan Disability Scale | CES-D | NA | 13 | cross-sectional | Significant correlations were found between QOLIE-89 subscales and scores for depression ( $-0.723$ ), seizure severity ( $-0.372$ ), and bothersomeness ( $-0.542$ ), as well as SDS disability ( $0.645$ ) (all $P < 0.0001$ ), but not for age, gender, or duration of epilepsy. Hierarchical regression showed that people with major depression had significantly poorer HRQOL than those with no depression, when controlling for seizure type and recency ( $F = 167.4, P < 0.0001$ ) |

|      |                  |                                                                                                                               |             |                                                |     |                                   |          |                                                               |    |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------|------------------|-------------------------------------------------------------------------------------------------------------------------------|-------------|------------------------------------------------|-----|-----------------------------------|----------|---------------------------------------------------------------|----|----|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2003 | Choi-Kwon et al. | Factors affecting the quality of life in patients with epilepsy in Seoul, South Korea                                         | South Korea | Outpatients with epilepsy                      | 168 | ANOVA and hierarchical regression | QOLIE-31 | HADS                                                          | NA | 13 |                 | Factors affecting the QOL were: age ( $P < 0.01$ ), education in years ( $P < 0.01$ ), employment status ( $P < 0.05$ ), employment type ( $P < 0.05$ ), current economic status ( $P < 0.05$ ), seizure frequency ( $P < 0.01$ ), the number of anti-seizure medicines ( $P < 0.01$ ), family life/social life dissatisfaction ( $P < 0.01$ , respectively), social support ( $P < 0.01$ ), the symptoms of anxiety and depression ( $P < 0.01$ , respectively) and ADL dysfunction ( $P < 0.01$ ). In linear regression, the symptom of anxiety was the most important factor in explaining lower QOL in patients with epilepsy, while depression ( $P < 0.01$ ), social life dissatisfaction ( $P < 0.01$ ), ADL dysfunction ( $P < 0.05$ ) and seizure frequency ( $P < 0.05$ ) were also significant factors. |
| 2004 | Argyriou et al.  | Psychosocial effects and evaluation of the health-related quality of life in patients suffering from well-controlled epilepsy | Greece      | Outpatients with epilepsy and healthy controls | 100 | linear regression                 | SF-36    | Questionnaire based on Hamilton and Mandr's depression scales | NA | 9  | cross-sectional | Healthy controls had better physical and social functioning as well as vitality.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

|      |                  |                                                                             |         |                                                                                       |     |                       |       |    |    |    |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------|------------------|-----------------------------------------------------------------------------|---------|---------------------------------------------------------------------------------------|-----|-----------------------|-------|----|----|----|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2004 | Sillanpää et al. | Perceived Impact of Childhood-onset Epilepsy on Quality of Life as an Adult | Finland | Children younger than 16 (at start of study) up to 45 by the end. + matched controls. | 182 | ANOVA and chi squared | SF-36 | NA | NA | 12 | longitudinal | No significant differences were found between subjects and controls on any of the eight subscales or in the total SF-36 scores. If we examine the scores within subgroups of subjects, only two statistically significant differences appear between the index patients and controls. The 61 subjects in remission without medication reported significantly more physical pain than did controls (p < 0.05). In addition, the 13 subjects in remission but still taking regular AED therapy reported more limitations in usual role activities because of emotional problems. |
|------|------------------|-----------------------------------------------------------------------------|---------|---------------------------------------------------------------------------------------|-----|-----------------------|-------|----|----|----|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|      |                |                                                                                                                                      |                              |                                          |                       |                   |                       |     |                                         |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|------|----------------|--------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------------------------------------|-----------------------|-------------------|-----------------------|-----|-----------------------------------------|----|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2004 | Nubukpo et al. | Psychosocial issues in people with epilepsy in Togo and Benin (West Africa)<br>II: quality of life measured using the QOLIE-31 scale | Togo and Benin (West Africa) | Adults with Epilepsy and controls        | 496 plus 496 controls | ANOVA and T-tests | QOLIE-31 (Translated) | NA  | NA                                      | 10 | cross-sectional | In Togo, controls had a significantly (P < 0.0001) better quality of life ( $80.3 \pm 7.4$ ) than Adults with Epilepsy ( $49.5 \pm 14.4$ ) referring to the QOLIE-31 Overall score. The findings were similar in Benin among Adults with Epilepsy ( $52.1 \pm 33.4$ ) and controls ( $72.2 \pm 12.7$ ). On the different subscales of QOLIE-31, comparison of Adults with Epilepsy and controls also revealed significant differences. With respect to Social Functioning, Adults with Epilepsy scored lower than controls (P < 0.0001); Adults with Epilepsy scored worse in Cognitive Functioning and Emotional Functioning than controls (P < 0.0001). Assessment of Overall quality of life was better in controls than in Adults with Epilepsy (P < 0.0001). Most Adults with Epilepsy interviewed did not feel healthy (item 31), compared with controls (P < 0.0001). Adults with Epilepsy felt significantly (P < 0.0001) more tired and lacking in energy than controls |
| 2004 | Aydemir et al. | Changes in quality of life and self-perspective related to surgery in patients with temporal lobe epilepsy                           | Turkey                       | Adults with Epilepsy pre vs post-surgery | 41                    | T-tests           | SF-36                 | BDI | stigma and impact of epilepsy inventory | 9  | cross-sectional | Seizure frequency and comorbidity had significant effects on QOL where amount of ASMs and QOL were negatively related ( $r = -0.318$ , $P < 0.05$ ).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |

|      |                       |                                                                                                                                               |        |                                              |                   |                                                                    |                    |                          |    |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|--------|----------------------------------------------|-------------------|--------------------------------------------------------------------|--------------------|--------------------------|----|----|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2004 | Liou et al.           | Health related quality of life in adult patients with epilepsy compared with a general reference population in Taiwan                         | Taiwan | Adults with Epilepsy                         | 296 +296 controls | ANOVA linear regression                                            | Taiwan WHOQOL-BREF | NA                       | NA | 12 | cross-sectional | There was a significant trend of improved scores for fewer seizure occurrences among patients. Healthy subjects showed significantly higher scores than patients with epilepsy for overall health and in physical, psychological and social domains. more frequent seizures predicted worse environmental, physical psychological and social functioning.                                                                                                                               |
| 2005 | Cankurtaran et al.    | Psychiatric morbidity, quality of life, and disability in mesial temporal lobe epilepsy patients before and after anterior temporal lobectomy | Turkey | patients with medically refractory MTLE      | 22                | non-parametric t-test (mann-whitney U), Friedman variance analysis | WHOQOL-BREF        | HDRS, HARS               | NA | 11 | longitudinal    | There was no significant difference in the mean scores on the WHOQOL-BREF domains and in the responses to the first question regarding the general evaluation of quality of life before and after surgery. For the second question on the level of satisfaction with respect to health, the difference between the three ratings was statistically significant ( $\chi^2 = 12.5, P = 0.002$ ). This result indicates that patients were more satisfied with their health after surgery. |
| 2005 | Alanis-Guevara et al. | Sleep disturbances, socioeconomic status, and seizure control as main predictors of quality of life in epilepsy                               | Mexico | Adults with Epilepsy                         | 401               | linear regression                                                  | QOLIE-31           | psychiatric consultation | NA | 9  | cross-sectional | The variables that most strongly predicted a lower QOLIE-31 total score after multiple regression were sleep disorders ( $P < 0.001$ ), socioeconomic status ( $P < 0.001$ ), female gender ( $P = 0.002$ ), and high seizure frequency ( $P = 0.001$ ). In this study, neither depression nor time of evolution of epilepsy had significant influence on QOLIE-31 scores.                                                                                                              |
| 2006 | Szaflarski et al.     | Quality of life in medication-resistant epilepsy: the effects of patient's age, age at seizure onset, and disease duration                    | USA    | patients with medication-resistant epilepsy. | 101               | linear regression                                                  | QOLIE-89)          | POMS                     | NA | 11 | cross-sectional | Depression and Adverse effects predicted poorer QOL.                                                                                                                                                                                                                                                                                                                                                                                                                                    |

|      |                  |                                                                                                                                       |          |                                     |     |                   |                       |           |    |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------|------------------|---------------------------------------------------------------------------------------------------------------------------------------|----------|-------------------------------------|-----|-------------------|-----------------------|-----------|----|----|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2006 | Meldolesi et al. | Factors associated with generic and disease-specific quality of life in temporal lobe epilepsy                                        | Italy    | adults with drug resistant epilepsy | 106 | linear regression | QOLIE-31 + WHOQOL-100 | BDI, STAI | NA | 11 | cross-sectional | Anxiety and depression were strongest predictors of low QOL. Epilepsy only predicted some domains.                                                                                                                                                                                                                                                                                                                           |
| 2006 | Mikati et al.    | Normalization of quality of life three years after temporal lobectomy: a controlled study                                             | Lebanon  | Temporal lobectomy patients         | 57  | ANOVA test        | ESI-55                | NA        | NA | 10 | cross-sectional | QOL was significantly better in the surgery group in the well-being, functioning, and role-limitation domains. QOL was non-significantly different in the surgery and healthy control groups for other domains and scales. The non-surgery group scored significantly lower than healthy controls in the functioning and role-limitation domains.                                                                            |
| 2006 | Saburi et al.    | Perceived family reactions and quality of life of adults with epilepsy                                                                | Zimbabwe | Adults with epilepsy                | 66  | Correlation       | QOLIE-89              | NA        | NA | 8  | cross-sectional | Quality of life was not adversely affected in the physiologic, self-concept, and interdependence modes but was affected in the role-function mode. Family reactions were positively correlated with the quality of life ( $r = .39$ , $p = < .01$ ). The effect of the independent variable, perceived family reactions ( $R^2 = .15345$ , $F = 11.60132$ , $p = < .01$ ), explained 15% of the variance in quality of life. |
| 2007 | Senol et al.     | Influence of fatigue, depression, and demographic, socioeconomic, and clinical variables on quality of life of patients with epilepsy | Turkey   | Adults with Epilepsy                | 103 | linear regression | QOLIE-89              | BDI       | NA | 8  | cross-sectional | Seizure frequency, fatigue, and depression best predictors of quality of life in patients with epilepsy. One or more seizures per month, severe fatigue, and depression are associated with lower quality of life in some but not all domains.                                                                                                                                                                               |

|      |                   |                                                                                    |         |                                                             |     |                                     |          |      |    |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|------|-------------------|------------------------------------------------------------------------------------|---------|-------------------------------------------------------------|-----|-------------------------------------|----------|------|----|----|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2007 | Mosaku et al.     | Quality of life and associated factors among adults with epilepsy in Nigeria       | Nigeria | Adults with Epilepsy                                        | 51  | linear regression                   | QOLIE-10 | HADS | NA | 8  | cross-sectional | lower QOL predicted by female sex ( $p < 0.05$ ), seizure frequency ( $p < 0.01$ ), using more than 1 anti-seizure medicines (ASMs) ( $p < 0.01$ ), GHQ-30 score ( $p < 0.01$ ), high anxiety score ( $p < 0.001$ ), and high depression score ( $p < 0.01$ ). linear regression showed that depressive symptoms were the single most important factor explaining low QOL.                                                                                                                                                                                                                                                                                                                                 |
| 2007 | Harden et al.     | The effect of seizure severity on quality of life in epilepsy                      | USA     | Women from the baseline phase of a clinical treatment trial | 118 | correlation and regression          | QOLIE-31 | BDI  | NA | 8  | cross-sectional | Severity of seizure correlated with Seizure Worry ( $r = 0.265$ , $P = .004$ ) and Social Functioning ( $r = 0.280$ , $P = 0.002$ ). Two additional domains were significantly correlated: Overall Quality of Life ( $r = 0.210$ , $P = 0.023$ ) and Cognitive ( $r = 0.209$ , $P = 0.024$ ). When the potentially confounding effect of depression, measured by the Beck Depression Inventory, was controlled for, the regression of seizure severity with QOLIE-31 Seizure Worry remained significant ( $P = 0.006$ , $R^2 = 0.153$ ), as did the regression with QOLIE-31 Social Functioning ( $P = 0.002$ , $R^2 = 0.184$ ) and the regression with QOLIE-31 Cognitive ( $P = 0.037$ , $R^2 = 0.30$ ). |
| 2009 | Tanriverdi et al. | Quality of life after extratemporal epilepsy surgery: a prospective clinical study | Canada  | post op epilepsy patients                                   | 23  | Nonparametric "Mann-Whitney U"-test | QOLIE-10 | NA   | NA | 14 | longitudinal    | Results indicated that HRQOL and psychosocial functioning in the epilepsy group was significantly impaired relative to normal controls. A greater perception of stigma and more frequent seizures was also strongly related to poor quality of life and reduced psychosocial function.                                                                                                                                                                                                                                                                                                                                                                                                                     |

|      |                   |                                                                                              |           |                                                                                                                      |                  |                            |                 |    |              |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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| 2008 | McLaughlin et al. | Stigma, seizure frequency and quality of life: the impact of epilepsy in late adulthood      | Australia | Older adults with epilepsy compared with a similar, age-matched control group                                        | 64               | linear regression          | QOLIE-31        | NA | Stigma scale | 10 | cross-sectional | This study found that seniors with epilepsy do not have poorer HRQOL compared with general epilepsy populations. However, when compared with general populations without epilepsy, seniors with epilepsy report a significantly lower HRQOL across all domains.                                                                                                                                                                                                                                                                     |
| 2008 | Laccheo et al.    | Assessment of quality of life among the elderly with epilepsy                                | USA       | Elderly population (60 years or older)                                                                               | 23               | T test and weighted scores | QOLIE-31, SF-36 | NA | NA           | 9  | cross-sectional | The mean HRQOL for surgery patients was higher in five of the 17 Quality of Life in Epilepsy Inventory 89 dimensions and worse in none. Among patients with more than 7 years of follow-up, HRQOL was better in three dimensions and worse in none. Among patients with 7 years of follow-up or less, HRQOL was better in two dimensions and worse in the language dimension of the QOLIE-89.                                                                                                                                       |
| 2008 | Stavem et al.     | Long-term seizures and quality of life after epilepsy surgery compared with matched controls | Norway    | Patients who underwent epilepsy surgery and matched medically treated nonsurgical controls with intractable epilepsy | 70 matched pairs | T test for paired samples  | QOLIE-89        | NA | NA           | 13 | cross-sectional | Independent factors affecting QoL were: seizure frequency (Overall QoL $P = 0.0001$ , Seizure worry and Emotional well-being $P < 0.0001$ , Energy/fatigue and Social functioning $P = 0.01$ ); duration of the disease (Overall QoL and Energy/fatigue $P = 0.01$ , Seizure worry $P = 0.008$ , Cognitive functioning $P < 0.0001$ ); polytherapy only for the Emotional well-being $P < 0.0001$ ; and use of benzodiazepines (Overall QoL, Energy/fatigue, Social functioning $P = 0.002$ , Cognitive functioning $P < 0.0001$ ). |

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| 2008 | Piperidu et al. | Association of demographic, clinical and treatment variables with quality of life of patients with epilepsy in Greece     | Greece | Outpatients with epilepsy                                                | 223 | Hierarchical linear regression                       | QOLIE-31 | NA         | NA | 13 | cross-sectional | All participants showed significantly improved QOL in both short- and long-term follow-ups compared to preoperative status regardless of seizure status ( $p < 0.001$ ). Seizure-free patients showed better QOL than those of patients who continued to have seizure during postoperative period. Furthermore, improved QOL was correlated with seizure status and shorter duration of epilepsy ( $p = 0.001$ )          |
| 2009 | Canuet et al.   | Factors associated with impaired quality of life in younger and older adults with epilepsy                                | Japan  | Older adults with epilepsy against the same parameters in younger adults | 146 | Multivariate linear regression analyses              | QOLIE-31 | BDI        | NA | 13 | cross-sectional | Best QoL predictors were BDI-II and seizure frequency, with BDI-II providing more than 3 times the impact of seizure frequency. BDI-II also substantively predicted most QOLIE-31 domains. Additionally, epilepsy duration positively correlated with overall QoL only among older adults.                                                                                                                                |
| 2009 | Kwan et al.     | Association of subjective anxiety, depression, and sleep disturbance with quality-of-life ratings in adults with epilepsy | China  | Adults with epilepsy                                                     | 247 | Univariate and multivariate linear regression models | QOLIE-31 | HADS, HARS | NA | 11 | cross-sectional | By multivariate analysis, in order of degree of contribution, HADS anxiety subscale score, MOS Sleep Scale Sleep Problems Index score, HADS depression subscale score, number of current anti-seizure medicines used, and seizure freedom in the past 4 weeks, significantly correlated with QOLIE-31 overall score, accounting for 65.2% of the variance. Complex interrelationships were present between these factors. |

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| 2009 | Ekaterina I Viteva I, Zahari I Zahariev | Depressivity, anxiety and quality of life in patients with refractory epilepsy | Bulgaria | Patients with refractory epilepsy             | 94  | Correlational analysis             | QOLIE-89         | BDI-II, HADS                | NA  | 8 | cross-sectional | The QOLIE-89 showed a low overall assessment of the quality of life in 54 patients (57.45% of the sample). We found: 1. A strong correlation between depressivity and the low overall assessment of quality of life as well as the assessment in the subscales for limitations due to physical problems, emotional wellbeing, attention/concentration, and memory. 2. A strong correlation between the increase of severity of depressivity and decrease of the overall assessment of quality of life. 3. A weak correlation between anxiety and the low overall assessment of QOL as well as the assessment in all subscales. |
| 2009 | Hessen et al.                           | Health concerns predicts poor quality of life in well-controlled epilepsy      | Norway   | Seizure-free epilepsy patients on monotherapy | 158 | Univariate regression analysis     | QOLIE-89         | Norwegian Edition of MMPI-2 | NA  | 9 | cross-sectional | Univariate regression analysis revealed significant association between subnormal QOLIE-89 score and patients with substantial health concerns, patients unemployed/on disability benefit and patients with depression. However, linear regression showed that a pathological score on the MMPI-2 Health Concerns scale was the only significant predictor of poor quality of life (OR = 10.76, p = 0.007).                                                                                                                                                                                                                    |
| 2009 | Kumari et al.                           | Stigma and quality of life in individuals with epilepsy: a preliminary report  | India    | Adults with epilepsy                          | 45  | Spearman's correlation coefficient | WHOQOL, QOLIE-89 | GHQ-12                      | SSE | 8 | cross-sectional | The perception of stigma was strongly associated with epilepsy, but there was no difference between the treated and untreated groups with epilepsy. Also, stigma and quality of life were negatively correlated.                                                                                                                                                                                                                                                                                                                                                                                                               |

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| 2009 | Mula et al.       | Manic/hypomanic symptoms and quality of life measures in patients with epilepsy                      | Italy + Germany | Adult outpatients with epilepsy                | 117 | Total and subscales scores of QOLIE-31      | QOLIE-31 | MINI | NA | 9  | cross-sectional | Among 117 evaluated patients, 17 fulfilled DSM-IV criteria for manic/hypomanic episodes. Patients with MHS, as compared to those without, showed lower scores in emotional well-being, energy and fatigue, medication effects, social function and total QOLIE score. However, there was no between-groups difference in educational achievements, employment status, living situation, comorbid psychiatric disorders, history of suicide or abuse of illicit drugs.                                                                                                                                                                                                                                                             |
| 2009 | Elsharkawy et al. | Long-term outcome and determinants of quality of life after temporal lobe epilepsy surgery in adults | Germany         | Temporal lobe epilepsy (TLE) surgery in adults | 222 | Univariate analyses + Multivariate analyses | QOLIE-31 | NA   | NA | 12 | cross-sectional | Multivariate analyses (stepwise regression analyses) revealed that especially the time since the last seizure and the severity of AED side effects had a strong impact on QOL. However, aura at last follow-up, psychiatric treatment and employment were seen in the multivariate analyses as significant predictors of some QOL subscales as well. Most subscales of QOL showed a steep, non-linear increase within the first years of seizure freedom and remained relatively stable except for cognitive function which showed continuous improvement parallel to seizure freedom. For patients who were seizure free since surgery, side effects of AED and/or psychiatric treatment were the strongest determinants of QOL. |
| 2009 | Tiamkao et al.    | Seizure attacks while driving: quality of life in persons with epilepsy                              | Thailand        | Driving in persons with epilepsy               | 245 | Student t-test                              | SF-36    | NA   | NA | 9  | cross-sectional | Adults with Epilepsy having a seizure attack while driving had a significantly lower QOL in four of the eight categories compared with patients who had not. Adults with Epilepsy who had a seizure-related accident had a significantly lower mean value in the vitality category than those who did not.                                                                                                                                                                                                                                                                                                                                                                                                                        |

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| 2009 | Ramon Edmund o D Bautista 1, E Tannahill Glen | Seizure severity is associated with quality of life independent of seizure frequency                                                                       | USA    | Adults with epilepsy | 142 | univariate analysis + multiple linear regression | QOLIE-10   | NA    | NA                  | 10 | cross-sectional | On univariate analysis, increased seizure severity and seizure frequency were significantly associated with poorer QOLIE-10 scores. The correlation between seizure severity and frequency was insignificant. On multiple linear regression, both seizure severity and frequency were independently associated with QOLIE-10 scores.                                                            |
| 2009 | Giray et al.                                  | Health-related quality of life of patients with epilepsy in Turkey                                                                                         | Turkey | Adults with epilepsy | 221 | Linear regression analysis                       | WHOQOL-100 | NA    | NA                  | 12 | cross-sectional | The analysis of variance showed that the partial epilepsy subgroup had significantly lower averages for all the quality-of-life subfields except for the social relationship dimension. On regression analysis, being married, having a generalized type of seizure and being treated with fewer medications were all related to higher scores on the HRQOL.                                    |
| 2010 | Whatley et al.                                | Examining the relationships of depressive symptoms, stigma, social support and regimen-specific support on quality of life in adult patients with epilepsy | USA    | Adults with epilepsy | 147 | Hierarchical multiple linear regression model    | QOLIE-31   | CES-D | Parent Stigma Scale | 9  | cross-sectional | The results of correlational analyses revealed statistically significant negative correlations between depressive symptoms, stigma and sometimes regimen-specific support and QOL and statistically significant positive correlations between social support and QOL. A hierarchical multiple linear regression model revealed that depressive symptoms accounted for the most variance in QOL. |

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| 2010 | Inês Cunha 1, Jorge Oliveira | Quality of life after surgery for temporal lobe epilepsy: a 5-year follow-up                                                                      | Portugal  | Adults with epilepsy       | 32 | repeated-measures ANOVA | QOLIE-31 | SCL-90 | NA | 10 | longitudinal    | Participants were compared before and after receiving temporal lobe surgery. They concluded that improvement in overall, cognitive and social function scores were statistically significant throughout the study. Seizure worry score ceased to be significant at the fifth year. Previous psychopathology was a negative influence on social and seizure worry score. Compared to left lobectomies, right lobectomies showed significant better results in overall scores at six months and one year follow-up. |
| 2010 | McLaughlin et al.            | The impact of depression, seizure variables and locus of control on health related quality of life in a community dwelling sample of older adults | Australia | Older adults with epilepsy | 64 | linear regression       | QOLIE-31 | CIDI   | NA | 10 | cross-sectional | Depression, dysthymia and more frequent seizures were important predictors of HRQOL, accounting for 63% of the variance, with dysthymia the strongest individual predictor of impaired HRQOL.                                                                                                                                                                                                                                                                                                                     |

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| 2011 | Choi I et al.   | Factors contributing to concerns of persons living with epilepsy                                                                                | South Korea | Adults with Epilepsy | 178 | Stepwise linear regression analysis | QOLIE-10 | HADS | Stigma scale | 8 | cross-sectional | Across all patients, both AKA levels (median: 80.0, range: 0–170) and overall HRQOL (median 51.5; range 15–97) were moderate. Awareness was significantly correlated only with Seizure Worry ( $r_s = + 0.29$ , $p < 0.05$ ), whereas Knowledge was not significantly linked to any domain. However, Attitudes was significantly correlated with all domains ( $r_s = + 0.35$ to $+ 0.47$ , $p < 0.01$ ) except Medication Effects and Seizure Worry. Patients with good AKA levels (Total Score $\geq$ median) experienced significantly better Overall Quality of Life and Cognitive Functioning ( $p < 0.05$ ). Findings showed that AKA may play an important role in influencing patients' HRQOL, suggesting that epilepsy treatment efforts should also focus on enhancing AKA through epilepsy awareness to improve health outcomes. |
| 2011 | Edefonti et al. | Health-related quality of life in adults with epilepsy: the effect of age, age at onset and duration of epilepsy in a multicentre Italian study | Italy       | Adults with epilepsy | 815 | Regression analyses                 | Epi-QoL  | NA   | NA           | 9 | cross-sectional | The effect of depression on QOL in epilepsy is strong, accounting for approximately half of the variance when compared with formal QOL measures.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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| 2011 | Gülpek et al.                          | Psychiatric comorbidity, quality of life and social support in epileptic patients                                                                       | Turkey   | Adults with Epilepsy | 50E + 50C | MANCOVA                                            | WHOQOL-BREF    | SCID-I, BDI, BAS | NA        | 10 | cross-sectional | It emerges that, if no other known correlates of the overall Epi-QoL score are considered, age and duration of epilepsy can be expected to have a significant consistent negative association, and age at onset a positive association of limited significance (i.e. significant in one model only), with HRQOL in epilepsy. However, none of the age-related variables showed a significant effect on the overall Epi-QoL score, after adjusting for a selected set of confounders including demographic and clinical factors, and, in particular, the seizure frequency in the preceding 12 months. |
| 2011 | Gordon-Perue et al.                    | Quality of life of patients with epilepsy living in Kingston, Jamaica                                                                                   | Jamaica  | Adults with Epilepsy | 101       | Regression model                                   | QOLIE-31       | NA               | NA        | 11 | cross-sectional | Psychological and physical subscale scores of WHOQOL-BREF were significantly lower in epileptic patients. In the epileptic group, a multi-variate analysis of covariance demonstrated that depression was a significant covariate for physical and psychological domains, anxiety was a significant covariate for psychological domain, social support was a significant covariate for social and environmental domains, and age of epilepsy onset was a significant covariate for physical domain of QOL.                                                                                            |
| 2010 | Pei Lin Lua 1, Widiasmoro Selamat Neni | Awareness, knowledge, and attitudes with respect to epilepsy: an investigation in relation to health-related quality of life within a Malaysian setting | Malaysia | Adults with Epilepsy | 60        | Spearman's coefficient and the Mann-Whitney U test | Malay QOLIE-30 | NA               | Malay AKA | 11 | cross-sectional | Predictors of quality of life included number of anti-seizure medicines ( $P=0.039$ ), epilepsy duration ( $P<0.05$ ), and functional status ( $P<0.001$ ). Neither seizure frequency nor socioeconomic status predicted QOLIE-31 scores.                                                                                                                                                                                                                                                                                                                                                             |

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| 2011 | Zhao et al. | Quality of life and related factors in adult patients with epilepsy in China         | China | Adults with epilepsy | 303 | Multi regression analysis | QOLIE-89 | NA        | NA | 11 | cross-sectional | QOLIE-89 total scores of married patients ( $57.1 \pm 15.3$ ) were lower than those of unmarried patients ( $70.9 \pm 15.7$ ) ( $P < 0.001$ ). Correlation analysis revealed that QOLIE-89 total score was negatively correlated with age, course of disease, seizure severity, antiepileptic drug, type of seizure, and seizure frequency ( $r = -0.334, -0.281, -0.424, -0.117, -0.145$ , and $-0.274$ respectively, $P < 0.01$ ), and was positively correlated with educational level and economic status ( $r = 0.245$ and $0.328$ respectively, $P < 0.01$ ). Multiregression analysis revealed that five factors entered the regression equation: age ( $\beta = -0.545$ , $P = 0.001$ ), course of disease ( $\beta = -0.311$ , $P = 0.001$ ), seizure severity ( $\beta = -10.014$ , $P = 0.001$ ), educational level ( $\beta = 3.274$ , $P = 0.002$ ), and economic status ( $\beta = 6.431$ , $P = 0.001$ ). |
| 2011 | Yue et al.  | Determinants of quality of life in people with epilepsy and their gender differences | China | PWE                  | 247 | Regressive analyses       | QOLIE-31 | HAMD, SAS | NA | 11 | cross-sectional | Among all patients, regressive analyses showed that AEP score was the strongest predictor of the QOLIE-31 overall score, accounting for 10.4% of the variance. The next strongest predictors were the number of currently used anti-seizure medicines (ASMs) (3.6%), the HAMD score (2.5%), and the SAS score (1.2%). Importantly, there were gender differences in these predictors of QOL. The strongest predictors of the QOLIE-31 overall score in women were the AEP score and the number of ASMs. In contrast, the strongest predictors in men were the SAS score, the AEP score and the frequency of seizures.                                                                                                                                                                                                                                                                                                    |

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| 2011 | Jehi et al.    | Quality of life in 1931 adult patients with epilepsy: seizures do not tell the whole story | USA      | Adults with epilepsy                                                   | 1931 | Multivariate regression             | QOLIE-10      | PHQ-9      | NA | 12 | cross-sectional | Following multivariate modelling, the two most clinically significant QOL predictors were seizure severity (mean QOLIE-10 score=28.8 if LSSS>40 vs 19.2 otherwise) and depression (mean QOLIE-10 score=31.7 if PHQ-9 $\geq$ 10 vs 19.3 otherwise).                                                                                          |
| 2014 | Mohamed et al. | Quality of life of patients with epilepsy in Malaysia                                      | Malaysia | PWE                                                                    | 120  | Multivariate regression             | QOLIE-31      | HADS, MINI | NA | 11 | cross-sectional | After accounting for mood, sex, and number of anti-seizure medicines, the seizure-free group reported better cognitive and physical function and overall QOL, experienced less seizure worry, and had better self-perception. Mood was the most consistently predictive covariate, and was independently predictive of many aspects of QOL. |
| 2012 | Elliott et al. | Quality of life in young adults who underwent resective surgery for epilepsy in childhood  | Canada   | Young adults who underwent resective surgery for epilepsy in childhood | 98   | ANCOVA                              | QOLIE-31, SHE | POMS       | NA | 11 | cross-sectional | Approximately 36% (adjusted R(2)=0.36; R coefficient=0.66) of the QOLIE-31 overall score variance was explained by the history of initial precipitant injury, family history of epilepsy, disease duration, age of epilepsy onset, seizure frequency and presence of psychiatric axis-II diagnosis.                                         |
| 2012 | Pauli et al.   | Predictors of quality of life in patients with refractory mesial temporal lobe epilepsy    | Brazil   | Patients with refractory mesial temporal lobe epilepsy                 | 81   | Multiple linear regression analysis | QOLIE-31      | NA         | NA | 11 | cross-sectional | There were six factors found that associated with QOL by univariate analysis. They were undertaken surgery, older age, seizure freedom, duration of illness, good relationship with family, and mild/absence of depression. However the multivariate analysis shows that only surgery was predictive to improve QoL.                        |

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| 2012 | Burane Kanchanatawan 1, Rasrin Kasalak | Quality of life in Thai intractable epileptic patients with and without surgery               | Thailand | Thai intractable epileptic patients with and without surgery | 120 | Stepwise multiple regression | WHOQOL-BREF-26 | HRSD         | NA | 10 | cross-sectional | Those who were single, separated or widowed (t statistic= -2.71, p<0.01), had not completed primary education (t statistic=-2.308, p<0.05), not currently going for work (t statistic=-2.748, p<0.01), had seizure in the past one year (t statistic=-4.068, p<0.01), had depressive symptoms (t statistic=-3.207, p<0.01), had higher anxiety scores (t statistic=-2.727, p<0.01), had low scores in the quality of life questionnaire. Multivariate analysis showed increasing age, education less than grade V, being unmarried, widowed or separated, lower per capita income, a high anxiety score and experiencing a seizure episode in the past one year to be significantly associated with a low score in the WHOQOL-BREF questionnaire (adjusted R <sup>2</sup> =0.378, SE 9.90). |
| 2012 | Rakesh et al.                          | Quality of life among people with epilepsy: a cross-sectional study from rural southern India | India    | PWE                                                          | 91  | Multivariate analysis        | WHOQOL-BREF    | PHQ-2, GAD-7 | NA | 9  | cross-sectional | In multivariate regression analysis, BDI depression score was the predictor of overall score and all QOLIE-31 domains, except for emotional well-being. Age could be considered as a predictor of cognitive and social functioning, medical effects, and the total QOLIE -31 score. Seizure frequency was a factor associated with all HRQOL domains, except for medication effects and emotional well-being, whereas gender, education, family status, seizure type, employment, lateralization of epileptic foci, number of anti-seizure medicines, and the reported adverse events did not significantly affect HRQOL.                                                                                                                                                                   |

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| 2013 | Viteva          | Impact of stigma on the quality of life of patients with refractory epilepsy                                         | Bulgaria | Patients with refractory epilepsy | 246 | Spearman coefficient             | QOLIE-89 | NA     | 3-item stigma scale | 9  | cross-sectional | Found perceived stigma in 43.6% of patients with refractory epilepsy, and 28.7% self-reported severe stigmatization. Only 4 (5.7%) patients with pharmaco-sensitive epilepsy reported stigmatization which was mild or moderate in all cases. Perceived stigma had a negative impact on the overall score of the QOLIE-89 (T-score 47.8), as well as on all subscales of QOLIE-89, with the exception of "change in health" and "sexual relations". Patients with refractory epilepsy reporting stigmatization most commonly had very low and low scores on the subscales "health perceptions" (82.9%), "emotional well-being" (71.5%), "memory" (63.4%) and "health discouragement" (62.5%). There was a negative correlation of all QOLIE-89 subscales with perceived stigma severity. |
| 2012 | Melikyan et al. | Health-related quality of life in Russian adults with epilepsy: the effect of socio-demographic and clinical factors | Russia   | Adults with epilepsy              | 208 | Multivariate regression analysis | QOLIE-31 | BDI    | NA                  | 11 | cross-sectional | Found a minute association between seizure severity and QOLIE-31 total score ( $r = -0.262$ , $P = 0.014$ ). Increased seizure severity predicted a worse QOLIE-31 seizure worry ( $R(2) = 0.311$ , $\beta = -0.289$ ; $P = 0.003$ ). Of the seven seizure severity items, generalization of seizures and presence of falls were items that predicted a worse QOLIE-31 seizure worry score and time to recover predicted a worse QOLIE-31 total score.                                                                                                                                                                                                                                                                                                                                   |
| 2013 | Adebayo et al.  | Seizure severity and health-related quality of life of adult Nigerian patients with epilepsy                         | Nigeria  | Adults with epilepsy              | 88  | Multiple linear regressions      | QOLIE-31 | BDI-II | NA                  | 11 | cross-sectional | Factors significantly ( $p < 0.05$ ) associated with impairment of quality of life in those living with epilepsy were a low level of education, higher seizure burden, low annual income, unemployment, unskilled employment, and living in a rural residence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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| 2013 | Kinyanjui et al.  | Quality of life among patients living with epilepsy attending the neurology clinic at Kenyatta National Hospital, Nairobi, Kenya: a comparative study | Kenya    | Adults with epilepsy | 300 | Step-wise (forward) regression analysis | WHOQOL-BREF-26 | NA | NA | 10 | cross-sectional | The regression analyses indicated the existence of psychiatric co-morbidity (total score, seizure worry, emotional well-being, energy/fatigue, social function and cognitive function) and a greater seizure frequency (total score, cognitive function and energy/fatigue) as predictive factors for lower scores in the total QOLIE-31 score and in various dimensions.                                                                                                       |
| 2013 | Tedrus et al.     | Epilepsy and quality of life: socio-demographic and clinical aspects, and psychiatric co-morbidity                                                    | Brazil   | Adults with epilepsy | 132 | Regression analyses                     | QOLIE-31       | NA | NA | 10 | cross-sectional | Respondents who had one or more seizures in the past four weeks had significantly lower mean score of QOL [63.4, 95% CI: 59.2, 67.5] than those who had no seizure [mean score 73.5, 95% CI: 69.3, 77.9] after adjusting for age, sex, treatment, duration and age at onset of epilepsy [F test =11.215, p = 0.001, R <sup>2</sup> = 0.159]. All the sub-scales of QOL showed significant moderate correlation with the frequency of seizures except for cognitive functioning. |
| 2013 | Norsa'adah et al. | The quality of life of people with epilepsy at a tertiary referral centre in Malaysia                                                                 | Malaysia | PWE                  | 106 | ANCOVA                                  | QOLIE-31       | NA | NA | 9  | cross-sectional | Older age at epilepsy onset was associated with worse emotional well-being, energy/fatigue, medication effects, and seizure worry outcomes. Higher seizure frequency and older age at time of evaluation were associated with lower cognitive function scores. Generalised seizures were associated with lower scores based on the variables: seizure worry, overall quality of life, emotional well-being, and cognitive function.                                             |

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| 2013 | Alonso-Vanegas et al. | Self-reported quality of life in pharmacoresistant temporal lobe epilepsy: correlation with clinical variables and memory evaluation | Mexico | Pharmacoresistant temporal lobe epilepsy  | 60  | Spearman coefficient       | QOLIE-31 | NA | NA    | 9  | cross-sectional | Patients with epilepsy with major depression had poorer quality life ( $36.4 \pm 1.8$ ) compared to those without depression ( $41.7 \pm 3.8$ , $P < 0.001$ ). Depression, having one seizure or more per month and having seizures within one month of interview were correlated with poorer quality of life, $P < 0.001$ . Multivariate linear regression analyses showed that depression and recent seizures predicted having poorer quality of life in patients with epilepsy.                                                                                                                                            |
| 2014 | Zou et al.            | Is antiepileptic drug withdrawal status related to quality of life in seizure-free adult patients with epilepsy?                     | China  | Seizure-free adult patients with epilepsy | 187 | Linear regression analysis | QOLIE-31 | NA | SKATE | 11 | cross-sectional | The QOLIE-31 overall score of the non-withdrawal group was lower than that of the withdrawal group ( $p < 0.01$ ). The LAEP score was the strongest predictor of the QOLIE-31 overall score of all subjects, explaining 26.9% of the variance. The second strongest predictor was the SSRS score, explaining 12.9%, and the other predictors were the NHS3 score (5.2%), education level (2.3%), age (1.5%), and marriage (1.0%). Furthermore, the strongest predictors in the non-withdrawal group were the LAEP and SSRS scores, while in the withdrawal group, the strongest predictors were stigma scores and employment. |

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| 2014 | Milovanović et al.             | Determinants of quality of life in people with epilepsy in Serbia                                                                      | Serbia  | PWE | 203 | Hierarchical multiple regression analysis | QOLIE-31 | BDI-II, BAI | NA  | 9  | cross-sectional | Sociodemographic factors (age, sex, education, and employment) did not significantly predict QOLIE-31 score. Significant determinants of quality of life were clinical characteristics - seizure severity and aetiology of epilepsy - accounting for 30.9% of the variance, depressive and anxiety symptoms accounting for 42.8% of the variance, and cognitive effects of anti-seizure medicines, accounting for 1.5% above other variables. |
| 2014 | Fawale et al.                  | Effects of seizure severity and seizure freedom on the health-related quality of life of an African population of people with epilepsy | Nigeria | PWE | 195 | Multiple regression analysis              | QOLIE-31 | NA          | ESS | 11 | cross-sectional | Overall, the healthy control subjects had a higher mean HRQOL score compared with the PWE put together (71.0+11.1 vs 64.2±13.6, p=.001). However, there was no difference in the mean HRQOL score between the seizure-free individuals and the healthy controls (p=.270). Seizure severity was associated with HRQOL independent of perceived stigma on a multiple regression analysis.                                                       |
| 2014 | Usha Barahmand 1, Afsar Haji 2 | The impact of intolerance of uncertainty, worry and irritability on quality of life in persons with epilepsy: irritability as mediator | Iran    | PWE | 60  | Multiple regression analysis              | QOLIE-31 | NA          | NA  | 8  | cross-sectional | Findings indicated that intolerance of uncertainty, worry and irritability have unique significant effects on quality of life.                                                                                                                                                                                                                                                                                                                |
| 2014 | Hideki Azuma, Tatsuo Akechi    | Effects of psychosocial functioning, depression, seizure frequency, and employment on quality of life in patients with epilepsy        | Japan   | PWE | 102 | Stepwise linear regression analysis       | QOLIE-31 | NDDI-E      | NA  | 10 | cross-sectional | The stepwise linear regression showed that the QOLIE-31-P overall score was explained by the effects of psychosocial functioning, depression, frequency of focal seizure, and employment, in that order, with these factors explaining 74% of the variance.                                                                                                                                                                                   |

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| 2014 | Ranjana et al. | The sociodemographic, clinical and pharmacotherapy characteristics influencing quality of life in patients with epilepsy: A cross-sectional study | India    | PWE                                         | 451 | Multiple regression analysis | QOLIE-10 | NA            | NA | 9  | cross-sectional | The univariate analysis showed factors such as lower monthly income, focal epilepsy, seizure frequency, antiepileptic drug (AED) polytherapy, conventional ASMs and frequent adverse drug reactions (ADRs) had significant negative influence on various domains of QOLIE-10 questionnaire. Multiple regression analysis showed seizure frequency as a significant predictor of most QOL domains and overall score, while ADRs as a significant predictor of all the domains. Seizure type was a predictive factor for domains like emotional well-being and overall score. |
| 2015 | Palma et al.   | Impact of epilepsy surgery on the quality of life of a low-income population through the application of the Qolice-10 scale                       | Colombia | low-income population                       | 89  | Wilcoxon non-parametric test | QOLIE-10 | NA            | NA | 10 | cross-sectional | All of the components of the QOLIE-10 scale improved significantly ( $p < 0.05$ ) after the surgical procedure, except the variable of "fear of the sudden occurrence of seizures". The variables with greatest impact after the surgical procedure were depression, work activity, and quality of life in general.                                                                                                                                                                                                                                                         |
| 2015 |                | Prevalence of depressive symptoms and their impact on quality of life in patients with drug-resistant focal epilepsy (IMDYVA study)               | Spain    | Patients with drug-resistant focal epilepsy | 515 | Multivariate modelling       | QOLIE-31 | MADRS, BDI-II | NA | 10 | cross-sectional | Depressive symptoms was observed in 62.1% [95% CI 56.1-68.1] and 64.8% [58.8-70.7] of DRE patients using MADRS and BDI-II, respectively, compared to 32.6% [27.0-38.2] and 37.2% [31.4-43.0] in the CFE group ( $p < 0.001$ ). Depressive symptoms was associated with poorer HRQOL. Multivariate modelling showed that presence of depressive symptoms on the MADRS or BDI-II had the greatest impact on mean QOLIE-31 scores.                                                                                                                                             |

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| 2015 | Tedrus et al. | Marital status of patients with epilepsy: factors and quality of life                                                                                    | Brazil | PWE                                                                     | 252 | Multiple regression analysis                                                                              | QOLIE-31 | ICD-10 | NA | 10 | cross-sectional | Logistic regression for single and married PWE revealed that singles had more abnormalities in the neurological examination ( $p = 0.029$ ) and earlier seizure onset ( $p < 0.001$ ), while for married and divorced PWE revealed the latter more psychiatric comorbidities ( $p = 0.002$ ) and longer disease duration ( $p = 0.011$ ). Regarding QOL score, linear regression showed that psychiatric comorbidity was the only factor ( $p < 0.001$ ). |
| 2015 | Chou et al.   | Long-term health-related quality of life in drug-resistant temporal lobe epilepsy after anterior temporal lobectomy                                      | Taiwan | Drug-resistant temporal lobe epilepsy after anterior temporal lobectomy | 48  | Chi-square test, Mann Whitney U test, Fisher's Exact test, Wilcoxon signed-rank test, Kruskal-Wallis test | QOLIE-89 | NA     | NA | 10 | longitudinal    | The seizure-free rate was much higher in the surgical group (53.6%) than in the medical group (5%), eight years after the initial evaluation. The follow-up QOLIE-89 score was significantly higher in the surgical group than in the medical group. Moreover, the seizure frequency inversely correlated to the QOLIE-89 score, regardless of the treatment group.                                                                                       |
| 2015 | Myers et al.  | Depression and quality of life in Spanish-speaking immigrant persons with epilepsy compared with those in English-speaking US-born persons with epilepsy | USA    | PWE                                                                     | 85  | MANCOVA                                                                                                   | QOLIE-31 | BDI-II | NA | 9  | cross-sectional | Although quality of life was diminished in both groups, Seizure Worry was worse for Hispanics after accounting for potential effects of marital status, medical insurance, use of antidepressants, seizure frequency, and number of ASMs ((1, 83), $F=7.607$ , $p=0.007$ )                                                                                                                                                                                |

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| 2015 | Pimpalkhute et al. | Assessment of quality of life in epilepsy patients receiving anti-seizure medicines in a tertiary care teaching hospital | India  | PWE                  | 60  | Unpaired t-test or one-way ANOVA           | QOLIE-31 | NA   | NA | 8  | cross-sectional | The mean (standard deviation) total score of QOLIE-31 was 64.61. A score of cognitive and medication effect were significantly better in carbamazepine group as compared to valproate group.                                                                                                                                                                                                                          |
| 2016 | Akdemir et al.     | Factors affecting the quality of life in drug-resistant epilepsy patients                                                | Turkey | PWE                  | 88  | Spearman's correlation coefficient, ANCOVA | QOLIE-89 | BDI  | NA | 8  | cross-sectional | The QoL was significantly lower in the drug-resistant patients than in the seizure-free epilepsy patients ( $p < 0.001$ ). Depression, lower education level, and unemployment were associated with lower QoL scores ( $p < 0.001$ , $p < 0.01$ , $p < 0.001$ , respectively). After adjusting for lower education level and unemployment, depression remained as an independent factor affecting QoL ( $p < 0.05$ ). |
| 2016 | Chen et al.        | Factors affecting quality of life in adults with epilepsy in Taiwan: A cross-sectional, correlational study              | Taiwan | Adults with epilepsy | 260 | Stepwise regression analysis               | QOLIE-31 | HADS | NA | 11 | cross-sectional | Stepwise regression analysis showed that seven factors were predictive for quality of life: anxiety, depression, adverse events of ASMs, social support, seizure frequency of at least once in three months, household income of NT\$ 40,001-100,000, and male gender. These factors accounted for 58.2% of the variance of quality of life.                                                                          |

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| 2016 | Bala et al.  | Differences in quality of life of women and men with drug-resistant epilepsy in Poland | Poland | PWE | 64  | Multiple regression analyses | QOLIE-31 | HRSD | NA | 9  | cross-sectional | Multiple regression analyses indicated that some distinct factors were associated with quality of life in each sex. In the group of women, there were no significant predictors of their quality of life. Among the group of men, depression intensity was the only statistically significant QoL predictor, explaining 16% of the variance (adjusted R(2)=0.16, F(6, 24)=19.7, p<0.01). Moreover, patients with depression had lowered scores in the Emotional Well-Being and Energy/Fatigue subscales, regardless of the sex.                                                                                                                                                                      |
| 2016 | Saadi et al. | Quality of life in epilepsy in Bhutan                                                  | Bhutan | PWE | 172 | Regression analyses          | QOLIE-31 | NA   | NA | 11 | cross-sectional | The QOLIE score in Bhutanese PWE was low (median 48.5, mean 48.4, standard deviation 17.3), with a statistically significantly different overall QOLIE-31 score between male and female participants. Younger age, lower educational attainment level, and increased self-perceived stigma were each observed to have an independent, negative association with QOLIE (p<0.05), while a patient's wealth quintile, sex, seizure frequency, seizure type and number of anti-seizure medicines were not. Education appeared to be most strongly associated with QOL at the high school and college levels. Of the seven subscales, the seizure worry score had the lowest scores (mean 33.1, SD 24.0). |

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| 2016 | Gu et al.         | Influence of Occupational Status on the Quality of Life of Chinese Adult Patients with Epilepsy | China    | Adult outpatients with epilepsy     | 819 | T test for paired samples  | QOLIE-31 | NA           | NA | 9 | cross-sectional | The QOLIE-31 score in the employed group was significantly higher than that in the unemployed group. The QOLIE-31 score of students was higher than those of farmers and workers. The students and farmers showed significant differences in QOLIE-31 score, cognition, emotional well-being, overall quality of life, energy/fatigue, and social function. In contrast, no significant difference was noted in seizure worry and medication effects across the three different kinds of occupation.                                                                                                                                                                                        |
| 2016 | Jovel et al.      | Factors associated with quality of life in a low-income population with epilepsy                | Colombia | Low-income population with epilepsy | 220 | Regression model           | QOLIE-10 | NDDI-E       | NA | 8 | cross-sectional | The variables included in the regression model that significantly affected QoL were depression ( $p<0.001$ ), severe daytime sleepiness ( $p=0.030$ ), structural/metabolic etiology of epilepsy ( $p=0.021$ ), drug resistant epilepsy ( $p=0.015$ ), and epilepsy with undetermined antiepileptic drug response ( $p=0.007$ ).                                                                                                                                                                                                                                                                                                                                                            |
| 2017 | Fu-Li Wang et al. | Influence of Marital Status on the Quality of Life of Chinese Adult Patients with Epilepsy      | China    | Adult outpatients with epilepsy     | 805 | Linear regression analysis | QOLIE-31 | PHQ-9, GAD-7 | NA | 9 | cross-sectional | The scores of married adult patients with epilepsy on QOLIE ( $61.8 \pm 15.3$ ) and social function ( $70.9 \pm 22.7$ ) were higher than the scores of the unmarried patients aged between 20 and 44 years. The scores of married adult epileptics on the QOLIE ( $58.4 \pm 14.6$ ) and the energy/fatigue ( $62.1 \pm 20.4$ ) were higher than the scores of the unmarried patients (QOLIE = $58.4 \pm 14.6$ and the energy/fatigue = $62.1 \pm 20.4$ ) aged between 45 and 59 years. For the adult epilepsy patients, depression, anxiety, seizures within the last year, disease course, medical expense category, and marriage* age are negatively correlated with the quality of life. |

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| 2017 | Camara-Lemarro y et al. | Affective symptoms and determinants of health-related quality of life in Mexican people with epilepsy                          | Mexico               | PWE                       | 145 | Simple logistic regression       | QOLIE-10    | BDI, BAI     | NA | 9  | cross-sectional | PWE had more depressive/anxiety symptoms when compared with controls. QOLIE-10 scores were significantly inversely correlated with poor sleep quality, insomnia symptoms, depressive/anxiety symptoms, and number of anti-seizure medicines used, but not with seizure type or number of seizures per month. A poor QOL was independently associated only with anti-epileptic drug polytherapy.                                                                                                                                                      |
| 2017 | Ives-Deliperi, Butler   | Quality of life one year after epilepsy surgery                                                                                | South Africa         | Epilepsy surgery patients | 25  | T test for paired samples        | QOLIE-89    | BDI-II       | NA | 10 | longitudinal    | Overall, there was a significant improvement in QOL, reduction in depressive symptoms, and decline in naming one year after surgery. Positive clinically important improvement in QOL was achieved in 76% of patients, meaningful reduction of depressive symptoms was achieved in 20%, and clinically important naming declines were observed in 48% of the cohort. Sixteen patients were seizure-free one year after surgery, but there was no significant correlation between changes in QOL and seizure outcome, depressive symptoms, or naming. |
| 2017 | Alsaadi et al.          | Potential factors impacting health-related quality of life among patients with epilepsy: Results from the United Arab Emirates | United Arab Emirates | PWE                       | 160 | Multivariate regression analysis | WHOQOL-BREF | PHQ-9, GAD-7 | NA | 9  | cross-sectional | Depression, anxiety, seizure freedom, and the use of anti-depressants had significant positive correlation with HRQOL in univariate analysis. However, depression, followed by seizure freedom, had the strongest association with HRQOL in a multivariate regression analysis                                                                                                                                                                                                                                                                       |

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| 2018 | Chen et al.    | Associated and predictive factors of quality of life in patients with temporal lobe epilepsy                                                        | China | patients with temporal lobe epilepsy | 47  | Multivariate regression analysis          | QOLIE-31 | SAS, SDS | NA | 9  | cross-sectional | In the final multivariate regression model, anxiety, long durations of seizures, adverse effects of ASMs, and depression explained approximately 60.6% (adjusted $R^2 = 0.606$ , $R$ coefficient = 0.800) of the QOLIE-31 overall score variance.                                                                                                        |
| 2018 | Ehrlich et al. | Beyond depression: The impact of executive functioning on quality of life in patients with temporal lobe epilepsy                                   | USA   | patients with temporal lobe epilepsy | 52  | Hierarchical multiple regression analysis | QOLIE-31 | BDI-II   | NA | 9  | cross-sectional | Of the clinical variables, only number of anti-seizure medicines contributed to QOLIE scores. As expected, severity of depressive symptoms was the most significant predictor of QOLIE Total Score, explaining 43.4% of the variance in total QoL.                                                                                                       |
| 2018 | Puri et al.    | Quality of Life and Its Determinants in Adult Drug Refractory Epilepsy Patients Who Were Not Candidates for Epilepsy Surgery: A Correlational Study | India | Drug Refractory Epilepsy Patients    | 129 | Correlational analysis                    | QOLIE-31 | NA       | NA | 11 | longitudinal    | In comparison to QOL status during the pre-surgical evaluation, there was statistically significant worsening of QOL in all domains ( $p < 0.01$ ). Seizure severity significantly correlated with almost all QOL domains ( $p \leq 0.01$ ), while seizure frequency significantly correlated with only the single domain of overall QOL ( $p = 0.03$ ). |

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| 2019 | Hamed-Shahraki et al.     | Health-related quality of life and medication adherence in elderly patients with epilepsy                                         | Iran   | Elderly population (60 years or older) | 766 | Multiple linear regression analysis      | QOLIE-31    | NA    | NA | 12 | longitudinal    | Medication adherence was significantly correlated with both seizure severity ( $\beta = -0.33$ , $p < 0.0001$ ) and serum AED level ( $\beta = 0.29$ , $p < 0.0001$ ) after adjusting for demographic and clinical characteristics. Neither QoL nor its sub-classes were correlated with seizure severity. In addition, a significant correlation was not observed between serum AED level and QoL. However, medication adherence was significantly correlated with QoL ( $\beta = 0.30$ , $p < 0.0001$ ). The mediating effects of medication adherence on the association between serum AED level ( $Z = 3.39$ , $p < 0.001$ ) and seizure severity ( $Z = -3.47$ , $p < 0.001$ ) with QoL were supported by the Sobel test. |
| 2019 | Eleftheria Siarava et al. | Depression and quality of life in patients with epilepsy in Northwest Greece                                                      | Greece | PWE                                    | 140 | Hierarchical regression                  | WHOQOL-BREF | PHQ-9 | NA | 11 | cross-sectional | The PHQ-9 score was higher in patients compared to controls and slightly higher than reported in patients with epilepsy. PHQ-9 was significantly associated with the AEP score. Our patients had a poorer QoL compared to controls. The level of education, the AEP and the PHQ-9 scores were associated to QoL, the last two being the most powerful predictors of QoL.                                                                                                                                                                                                                                                                                                                                                       |
| 2019 | Kaddumukasa et al.        | Seizure severity is associated with poor quality of life in people living with epilepsy (PLWE) in Uganda: A cross-sectional study | Uganda | PWE                                    | 48  | Spearman's rank correlation coefficients | QOLIE-31    | NA    | NA | 9  | cross-sectional | Over 57.4% of the study participants were unemployed. The mean (standard deviation (SD)) of QOLIE-31 and Seizure Severity Score was 62.5 (14.5) and 62.4 (1.6), respectively. There was no gender difference in the seizure severity scores ( $p = 0.451$ ). An inverse relationship existed between seizure severity and the total QOLIE-31 score (Spearman's rank correlation coefficient, $r = -0.48$ , $p = 0.001$ ), and seizure worry ( $r = -0.31$ , $p = 0.030$ ).                                                                                                                                                                                                                                                     |

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| 2019 | Lotfinia et al. | Health-related quality of life after epilepsy surgery: A prospective, controlled follow-up on the Iranian population                                       | Iran     | Epilepsy surgery patients | 60  | T test for paired samples           | WHOQOL-BREF | NA   | NA | 11 | longitudinal    | The difference in QoL between the healthy group and the operated patients was significant in all domains of QoL, except in social and life environment domains, while the non-operated patients had lower scores in all domains of QoL compared to the operated patients.                                                                                                                                                                                                                                                                                                                                             |
| 2019 | Abadigal et al. | Health-related quality of life and associated factors among epileptic patients on treatment follow up at public hospitals of Wollega zones, Ethiopia, 2018 | Ethiopia | PWE                       | 392 | Multiple linear regression analysis | WHOQOL-BREF | HADS | NA | 9  | cross-sectional | The overall mean total score on the WHOQOL-BREF scale was 60.47 with $\pm$ 23.07 SD. Monthly income $\leq$ 500 EB ( $\beta$ = - 12.49, $P < 0.001$ ), living alone ( $\beta$ = - 7.11, $P = 0.007$ ), adverse drug reaction ( $\beta$ = - 10.86, $P < 0.001$ ), comorbidity of anxiety ( $\beta$ = - 12.99, $P < 0.001$ ), perceived social stigma ( $\beta$ = - 9.73, $P < 0.001$ ) and frequency of seizure once per week ( $\beta$ = - 8.41, $P = 0.001$ ) were negatively associated with quality of life of epileptic patients. The mean quality of life of patients living with epilepsy in this study was low. |
| 2020 | Lin et al.      | Social functioning and health-related quality of life trajectories in people with epilepsy after epilepsy surgery                                          | Taiwan   | Epilepsy surgery patients | 76  | GEE with identity links             | QOLIE-89    | NA   | NA | 9  | longitudinal    | The majority of the study participants had a good overall HRQOL. In general, a low level of HRQOL score was significantly associated with the marital status of single/widowed/divorced, low level of education, low level of monthly income, co-morbidity, uncontrolled seizure, and poly-pharmacy; irrespective of HRQOL domains.                                                                                                                                                                                                                                                                                   |

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| 2019 | Tefera et al. | Health-related quality of life and its determinants among ambulatory patients with epilepsy at Ambo General Hospital, Ethiopia: Using WHOQOL-BREF | Ethiopia | Ambulatory patients with epilepsy                   | 121 | Multivariate linear regression analyses | WHOQOL-BREF | NA     | NA  | 11 | cross-sectional | Total QOLIE-89 improved 3 months after surgery, while overall SOFSE showed no significant improvement until 6 months after surgery. The presurgical Full-Scale Intelligence Quotient (FSIQ) of the Wechsler Adult Intelligence Scale-III and years of education were significantly associated with time-dependent improvement for both total QOLIE-89 and overall SOFSE (p value < 0.001). At one year after surgery, overall SOFSE and total QOLIE-89 scores were significantly higher in the seizure-free group than in the non-seizure-free group (p value = 0.040 and 0.032, respectively). |
| 2020 | Deleo et al.  | Quality of life, psychiatric symptoms, and stigma perception in three groups of persons with epilepsy                                             | Italy    | 3 groups of persons with epilepsy (DRE, DSE, DREES) | 181 | Linear regression analysis              | QOLIE-31    | SCL-90 | ESS | 10 | cross-sectional | We found that QoL is higher and psychiatric symptoms are lower in persons with DSE compared with DRE and that patients with DREES, who were drug-resistant before surgery, are in between DSE and DRE for both measures. Perceived stigma level is different in DSE and in DRE, that report the highest levels of stigma, and is between the other two groups in DREES.                                                                                                                                                                                                                         |

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| 2020 | Maria et al. | Quality of life perception in patients with epilepsy for a period of 4 years | Brazil | PWE | 129 | Linear regression analysis | QOLIE-31 | NA | NA | 10 | longitudinal | Quality of life was compromised by increasing the number of anti-seizure medicines (AED) taken [total score (-8.53), social functioning (-14.70)] or by maintaining the use of polytherapy [social functioning (-12.89)]. Fewer seizures were associated with a better QoL [total score (7.99), social (17.88) and cognitive functioning (16.30)]. The reduction in seizures was not associated with a better QoL [total and social functioning score], and the increase in seizures did not change QoL perception (cognitive functioning). There was a reduction in the QoL perception in medication effects in temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) (8.92) and with an increase in age in one year (-0.44). |
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| 2020 | Winslow et al. | Longitudinal trajectory of quality of life and psychological outcomes following epilepsy surgery | USA | Epilepsy surgery patients | 229 (178 followed up) | Linear Modelling | QOLIE-10 | PHQ-9, GAD-7 | NA | 11 | longitudinal | After adjusting for gender, age, marital status, and type of surgery using linear modelling, the mean QOLIE-10 score decreased by 1.157 points/year, mean PHQ-9 score by 0.331 points/year, and mean GAD-7 score by 0.299 points/year. Improvement in QOL continued to be observed throughout the follow-up duration, whereas both depression and anxiety improved the most within the first postoperative year and then stabilized. Seizure freedom was strongly correlated with improved QOL ( $p = 0.001$ ), while depressive symptoms showed a non-statistically significant correlation with worse QOL ( $p = 0.07$ ). Patients who underwent frontal resection had significantly superior QOL and depression symptom improvement compared with temporal resections during full data analysis (QOLIE-10, $p = 0.024$ ; PHQ-9, $p = 0.027$ ), but only significant depression symptom improvement on secondary analysis of complete follow-up patients only (PHQ, $p = 0.040$ ; QOL, $p = 0.104$ ). |
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|------|----------------------|------------------------------------------------------------------------------------------------------------------------------|---------|----------------------|-----|-----------------------------------------|----------------|------|----|----|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2020 | Kazeem Ayinde et al. | Determinants of quality of life in adults living with epilepsy                                                               | Nigeria | Adults with epilepsy | 74  | Logistical Regression Analysis          | WHOQOL-BREF-26 | MINI | NA | 10 | cross-sectional | The presence of psychiatric disorder, long duration of epilepsy, and being single were predictive of poor QOL. Psychiatric disorder was found in 33 (44.6%) of the respondents. The presence of these psychiatric disorders was predictive of poor score on the overall QOL (odds ratio [OR] = 0.382; 95% confidence interval [CI] = 0.145-0.983; P = 0.0046), physical (OR = 0.269; 95% CI = 0.100-1.722; P = 0.009), and psychological health domain (OR = 0.269; 95% CI = 0.102-0.709; P = 0.008). Longer duration of epilepsy was predictive of a poor score on the health satisfaction item (OR = 0.202; 95% CI = 0.06-0.679; P = 0.010) while being single was predictive of poor score on the social relationship domain (OR = 0.177; 95% CI = 0.065-0.482; P = 0.001). |
| 2021 | Ogundare et al.      | Quality of life among patients with epilepsy in Nigeria: predictors and barriers to routine clinical use of QOLIE-31         | Nigeria | PWE                  | 270 | Multivariate linear regression model    | QOLIE-31       | NA   | NA | 10 | cross-sectional | Following multivariate logistic regression analysis, social support (OR = 29.51, 95% CI = 2.87 - 302.66, p = 0.004) appeared as the independent determinant of HRQOL in PWE.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 2020 | Iwuzo et al.         | Determinants of Health-related Quality of Life in Persons with Epilepsy Seen at a Tertiary Hospital in North Western Nigeria | Nigeria | PWE                  | 103 | Multivariate linear regression analyses | WHOQOL-BREF-26 | NA   | NA | 9  | cross-sectional | Factors associated with poorer QOL include seizure frequency, depression, and family history of epilepsy.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |

|      |                   |                                                                                          |       |                      |     |                                     |          |              |          |    |                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------|-------------------|------------------------------------------------------------------------------------------|-------|----------------------|-----|-------------------------------------|----------|--------------|----------|----|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2021 | Tombini et al.    | Epilepsy and quality of life: what does really matter?                                   | Italy | PWE                  | 122 | Stepwise multiple regression        | QOLIE-31 | BDI-II, DERS | SSE, JSS | 9  | cross-sectional | Quality of life is inversely correlated mostly with psychosocial features, as DS, emotion dysregulation, and stigma perception, as well as with epilepsy-related factors, as the seizure frequency and number of ASMs. The combination of DS, perceived stigma, and number of ASMs best explained the QoL. Worse features of QoL were detected in females and in patients with age of epilepsy onset in adulthood. |
| 2021 | Salas-Puig et al. | Quality of life in adult patients with idiopathic generalised epilepsy. The EPILAK study | Spain | Adults with epilepsy | 546 | Multiple linear regression analysis | QOLIE-10 | NA           | NA       | 11 | cross-sectional | Mean score on the QOLIE-10: 71.4 ± 19.1. Being female (p = 0.006), greater frequency of seizures (p < 0.001), polytherapy (p < 0.001), psychiatric comorbidity (p < 0.001) and unemployment (p < 0.001) were significantly associated with a worse QoL.                                                                                                                                                            |

*Note.* AED= Anti-Epileptic Drug; AKA= Awareness, Knowledge and Attitudes; ANCOVA= Analysis of Covariance; ANOVA= Analysis of Variance; ASM= Antiseizure Medications; BAI= Beck Anxiety Inventory; BDI= Beck Depression Inventory; CES-D= Center for Epidemiologic Studies Depression Scale; CIDI= Composite International Diagnostic Interview; DERS= Difficulties of Emotion Regulation Scale; DRE= Drug Resistant Epilepsy DSE= Drug Sensitive Epilepsy; DREES= Drug Resistant Epilepsy- Epilepsy Surgery; DS= Depressive Symptoms; Epi-QoL= Epilepsy Quality of Life; ESS= Epilepsy Stigma Scale; FSQ= Functional status questionnaire; GAD= Generalized Anxiety Disorder; GEE= Generalized Estimating Equations; GHQ= General Health Questionnaire; HADS= Hospital Anxiety and Depression Scale; HAMD= Hamilton Depression Rating Scale; HARS= Hamilton Anxiety Rating Scale; HRQOL= Health-related Quality of Life; HRSD= Hamilton Rating Scale for Depression; ICD= International Classification of Diseases; JSS= Jacoby's Stigma Scale; LSSS= Liverpool Seizure Severity Scale; MADRS= Montgomery-Asberg Depression Rating Scale; MANCOVA= Multivariate Analysis of Covariance; MINI= Mi.ni International Neuropsychiatric Interview; MMPI= Minnesota Multiphasic Personality Inventory; NA= non-applicable; NDDI-E= Neurological Disorders Depression Inventory for Epilepsy; PHQ= Patient Health Questionnaire; PLWE= People Living with Epilepsy; POMS= Profile of Mood States; PWE= People with Epilepsy; QOLIE= Quality of Life in Epilepsy Inventory; SAS = Self-rating Anxiety Scale; SCID= Structured Clinical Interview for DSM; SCL= Symptom Checklist; SDS= Self-rating Depression Scale; SF-36= Short-Form Health Survey; SHE= Subjective Handicap of Epilepsy Scale; SKATE= Scale of Knowledge and Attitudes Toward Epilepsy; SSE= Stigma Scale of Epilepsy; STAI= State-Trait Anxiety Inventory; TLE= Temporal Lobe Epilepsy; UK= United Kingdom; USA= United States of America; WHOQOL-BREF= World Health Organization Quality of Life Brief Version.

## Chapter 4:

### Results

As Figure 1 (the PRISMA flow diagram) illustrates, we screened the titles and abstracts of 468 unique records and subsequently reviewed full-text copies of 257 papers for potential inclusion. Of that 257, 100 met all study criteria and hence were included in the final review sample. The papers excluded from the review sample were those that (a) included no standard QoL measure, (b) were not focused on PWE, (c) included paediatric samples, (d) included PWE participants with confounding health conditions, (e) were not written in English, (f) were reviews or letters discussing previously published papers, and (g) were of low methodological quality.

#### Characteristics of Included Studies

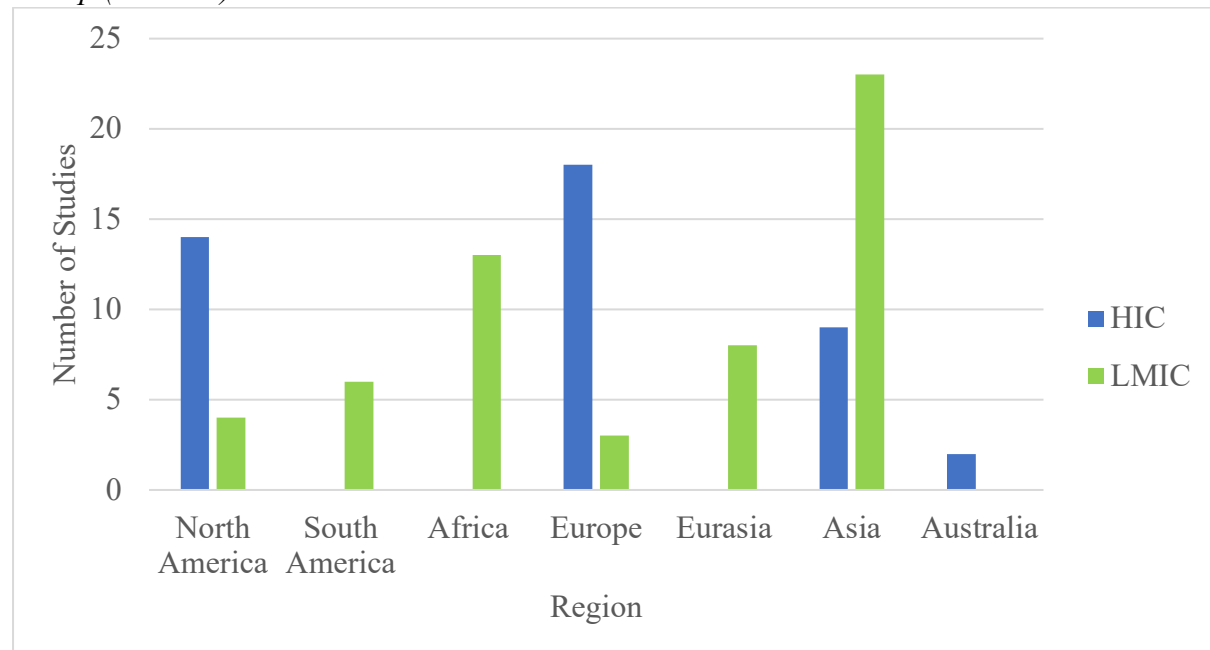
Table 1 presents a comprehensive summary of the major characteristics of the study sample ( $N = 100$ ). These studies were all published in English (by design, given the inclusion criteria), and all were published between 1997 and 2021. More than half (about 52%) were published within past decade (i.e., since 2012), indicating a slight uptick in rate of publication over time.

Of the 100 included studies, 87 were of cross-sectional design and 13 of longitudinal design (Cankurtaran et al., 2005; Chou et al., 2015; Cunha & Oliveira, 2010; Hamed-Shahraki et al., 2019; Ives-Deliperi & Butler, 2017; Lin et al., 2020; Lotfinia et al., 2019; Markand et al., 2000; Puri et al., 2018; Sillanpää et al., 2004; Tanriverdi et al., 2008; Tedrus et al., 2020; Winslow et al., 2020).

Figure 2 presents a summary of the geographical regions in which the studies were conducted. The largest proportion of studies (32 of 100) emerged from Asia. Relatively equal numbers emerged from Europe and North America (21 and 18, respectively). Thirteen were from Africa, 8 from Eurasia, 6 from South America, and 2 from Australia. Somewhat surprisingly, more studies (57 of the 100) had been conducted in LMICs (spread across North America, South America, Africa, Europe, Eurasia, and Asia) than in HICs ( $n = 43$ ; spread across North America, Europe, Asia, and Australia). Most LMIC studies ( $n = 23$ ) were conducted in Asia.

**Figure 2.**

*Review Samples: Studies Classified by Geographical Region and Nation-Based Income Group (N = 100)*



*Note.* In this figure, North America includes countries in Central America (Mexico) and the Caribbean (Jamaica). Eurasia refers to transcontinental countries (Turkey, Georgia, Russia).

Table 3 and Table 4 provide further detail in this regard, specifying, respectively, the country in which each LMIC and each HIC study was conducted. Unsurprisingly, the single country that provided the largest number of studies for the review was the United States (12 of the 100 studies). China was the most prolifically publishing of the LMICs ( $n = 8$ ).

Table 3.

*Review Sample: Studies Conducted in Low- and Middle-Income Countries (N = 57)*

| Geographic Region             | Country               | Number of Studies |
|-------------------------------|-----------------------|-------------------|
| Africa ( <i>n</i> = 13)       | Ethiopia              | 2                 |
|                               | Kenya                 | 1                 |
|                               | Nigeria               | 6                 |
|                               | South Africa          | 1                 |
|                               | Togo and Benin (West) | 1                 |
|                               | Uganda                | 1                 |
|                               | Zimbabwe              | 1                 |
|                               |                       |                   |
| Asia ( <i>n</i> = 23)         | Bhutan                | 1                 |
|                               | China                 | 8                 |
|                               | India                 | 5                 |
|                               | Iran                  | 3                 |
|                               | Lebanon               | 1                 |
|                               | Malaysia              | 3                 |
|                               | Thailand              | 2                 |
|                               |                       |                   |
| Eurasia ( <i>n</i> = 8)       | Georgia               | 1                 |
|                               | Russia                | 1                 |
|                               | Turkey                | 6                 |
| Europe ( <i>n</i> = 3)        | Bulgaria              | 2                 |
|                               | Serbia                | 1                 |
| North America ( <i>n</i> = 4) | Jamaica               | 1                 |
|                               | Mexico                | 3                 |
| South America ( <i>n</i> = 6) | Brazil                | 4                 |
|                               | Colombia              | 2                 |

*Note.* In this table, North America includes countries in Central America (Mexico) and the Caribbean (Jamaica). Eurasia refers to transcontinental countries.

Table 4.

*Review Sample: Studies Conducted in High-Income Countries (N = 43)*

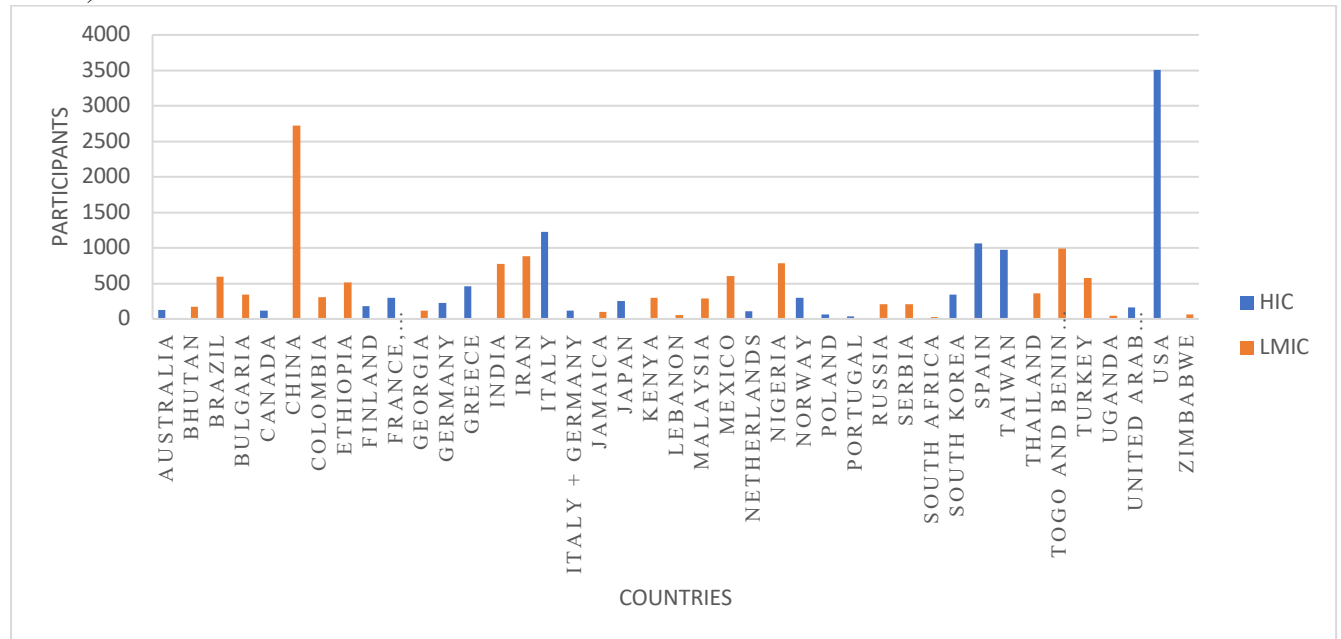
| Continent                  | Country                         | Number of Studies |
|----------------------------|---------------------------------|-------------------|
| Asia ( $n = 9$ )           | Japan                           | 2                 |
|                            | South Korea                     | 2                 |
|                            | Taiwan                          | 4                 |
|                            | United Arab Emirates            | 1                 |
| Australasia ( $n = 2$ )    | Australia                       | 2                 |
| Europe ( $n = 18$ )        | Finland                         | 1                 |
|                            | France, Germany, United Kingdom | 1                 |
|                            | Germany                         | 1                 |
|                            | Greece                          | 3                 |
|                            | Italy                           | 4                 |
|                            | Italy + Germany                 | 1                 |
|                            | Netherlands                     | 1                 |
|                            | Norway                          | 2                 |
|                            | Poland                          | 1                 |
|                            | Portugal                        | 1                 |
|                            | Spain                           | 2                 |
| North America ( $n = 14$ ) | Canada                          | 2                 |
|                            | United States                   | 12                |

## Participants

Across the review sample, all studies included (by design) PWE older than the age of 18 years. The total sample size was 20601. Individual-study sample sizes ranged from 25 to 1931 ( $M = 206$ ,  $SD = 258$ ) with majority of the participants from the United States ( $n = 1931$ ) and the least number of participants from South Africa ( $n = 25$ ; see Figure 3).

**Figure 3.**

*Review Sample: Number of Participants per Country from Which the Studies Emerged (N = 20601)*



*Note.* HIC = high-income countries; LMIC = low- and middle-income countries.

Some studies compared PWE with matched healthy controls, others compared patients with medically intractable epilepsy to those who were seizure-free, and still others followed up on patients who had undergone surgery to relieve their seizures. More specifically, 13 studies focused on patients with medically refractory epilepsy (Akdemir et al., 2016; Alonso-Vanegas et al., 2013; Chou et al., 2015; Deleo et al., 2020; Espinosa Jovel et al., 2016b; Garcia et al., 2015; Markand et al., 2000; Meldolesi et al., 2006; Pauli et al., 2012; Puri et al., 2018b; Szaflarski et al., 2006; E. Viteva, 2013b; E. I. Viteva & Zahariev, 2009). Twelve studies included patients that had undergone epilepsy surgery (Aydemir et al., 2004; Cunha & Oliveira, 2010; Elliott et al., 2012; Elsharkawy et al., 2009; Ives-Deliperi & Butler, 2017; Kanchanatawan & Kasalak, 2012; Lin et al., 2020; Lotfinia et al., 2019; Stavem et al., 2008; Tanriverdi et al., 2008; Vergara Palma et al., 2015; Winslow et al., 2020). One study included three groups of PWE: those with drug-resistant epilepsy, those with drug-sensitive epilepsy, and those with drug-resistant epilepsy who had undergone epilepsy surgery (Deleo et al., 2020).

Eleven studies focused specifically on patients with temporal lobe epilepsy (Alonso-Vanegas et al., 2013; Aydemir et al., 2004; Cankurtaran et al., 2005; Y. yu Chen et al., 2018b; Chou et al., 2015; Cunha & Oliveira, 2010; Ehrlich et al., 2019; Elsharkawy, May,

Thorbecke, Koch-Stoecker, et al., 2009; Markand et al., 2000; Meldolesi et al., 2006; Pauli et al., 2012).

Two studies focused on samples of PWE drawn from low-income populations (Jovel et al., 2016; Palma et al., 2015), another two focused on older adults (Hamedi-Shahraki et al., 2019; Laccheo et al., 2008). One study focused solely on women from the baseline phase of a clinical treatment trial (Harden et al., 2007). For one study, patients were recruited during childhood but their QoL was measured at adulthood (Sillanpää et al., 2004).

### **Measures of Quality of Life**

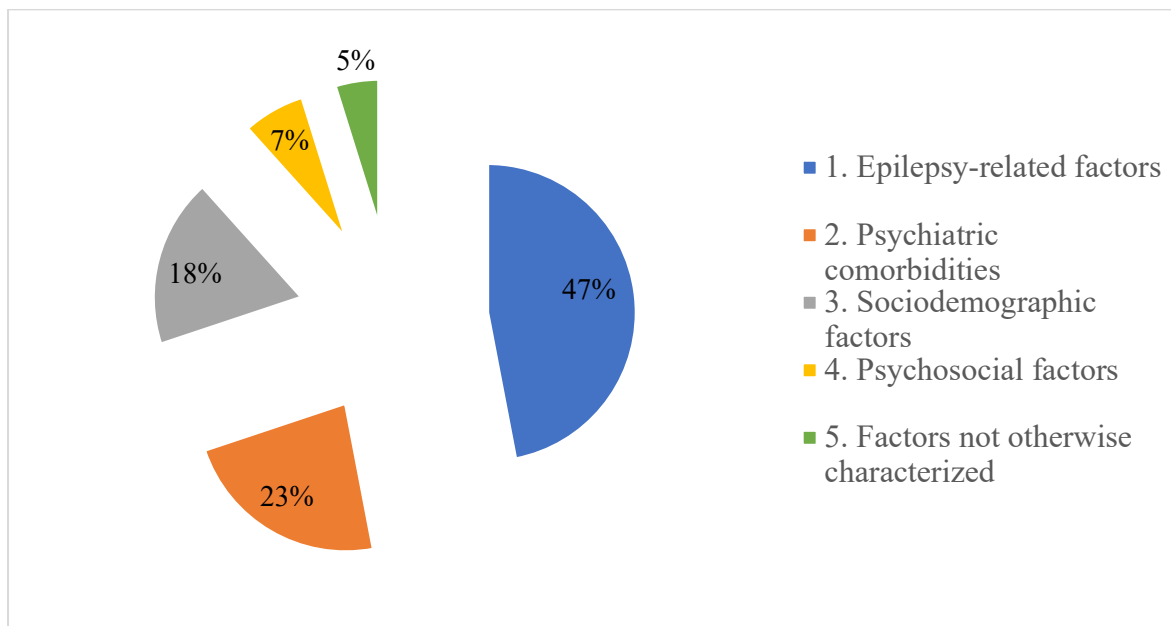
By design, all studies included in this review used an objective quantitative measure to characterize QoL in adults PWE. Forty-nine studies used the Quality of Life in Epilepsy (QOLIE-31), two of them using it in conjunction with either the World Health Organization Quality of Life (WHOQOL-100) or the Short Form Health Survey (SF-36). Fifteen studies used the QOLIE-89, two of them using it in conjunction with either the WHOQOL-100 or the Sheehan Disability Scale. Thirteen studies used the World Health Organization Quality of Life Brief Version (WHOQOL-BREF) only, 11 used the QOLIE-10 only, and 6 used the SF-36 only. Each of the following instruments was used in only one study: the Epilepsy Quality of Life (Epi-QoL), the Epilepsy Surgery Inventory (ESI-55), the FSQ, the Malay QOLIE-30, and the WHOQOL-100. Table 2 includes information about which study used which instrument.

### **Determinants of Quality of Life: A Global Perspective**

These determinants were categorized into five domains: epilepsy-related factors, psychiatric comorbidities, sociodemographic factors, psychosocial factors, and factors not otherwise categorized. Each of Tables 5–9 presents, for one of the domains, the individual factors within that domain, the number of studies that reported a significant relationship between a factor and QoL, and the total number of studies that examined each factor. As Figure 4 shows, almost half of the studies in the review sample investigated the relationship between QoL and at least one epilepsy-related factor (e.g., seizure type, seizure frequency, disease duration). Almost a quarter of the studies investigated the relationship between QoL and psychiatric comorbidities (depression and/or anxiety), and a slightly smaller proportion investigated relations between QoL and sociodemographic factors (e.g., age, gender, education). Less than 10% of studies investigated relations between (a) psychosocial factors, such as stigma and social support, and (b) factors not otherwise categorized, such as sleep disruption and cognitive impairment.

**Figure 4.**

*Proportion of the Reviewed Studies that Investigated at Least One Determinant of Quality of Life, Grouped by the Five Major Categories of Variable (N = 100)*



**Epilepsy-related Factors.** As Table 5 shows, *seizure frequency* was the most frequently studied of these factors. Of the 46 studies in which it was assessed, 39 found that it bore a statistically significant relationship to QoL. The most consistent finding in this regard was that higher seizure frequency was associated with lower QoL. The two longitudinal studies in this group reported that seizure frequency was significantly inversely correlated with overall QoL in patients (a) with medically intractable epilepsy who were not candidates for surgery and (b) who had undergone anterior temporal lobectomy.

*Disease duration* was the second most frequently studied of these factors. Of the 17 studies in which it was assessed, 10 found that it bore a statistically significant relationship to QoL. The most consistent finding in this regard was that longer duration of epilepsy was associated with lower overall QoL (or at least with a poor score on one of the subdomains of QoL, such as health satisfaction). Only one study reported that shorter disease duration was associated with lower QoL.

Several medication-related factors (*AED polytherapy*, *adverse effects of ASMs*, and *lack of or non-adherence to ASMs*) were also significantly and consistently associated with QoL. Fifteen of the 16 studies that assessed effects of polytherapy reported that using multiple different ASMs was associated with lower QoL – the greater the number of ASMs a patient used, the more likely they were to experience poorer QoL. All 10 studies that assessed

adverse effects of ASMs reported that this factor was associated with poorer QoL in PWE. One study reported that lack of or unavailability of AED treatment was significantly associated with poorer QoL in West African PWE. In terms of treatment adherence, one study reported that non-adherence to ASMs was associated with poorer overall QoL.

All 15 of the studies that investigated *seizure freedom* found that it was associated with better QoL: patients tended to show significantly improved QoL after successful surgery. Similarly, 11 of the 12 studies that investigated *seizure severity* found that it was inversely associated with QoL.

Smaller numbers of studies reported that *seizure worry*, *seizure type*, and *epilepsy aetiology* were predictors of QoL. That is to say, patients with more seizure worry had poorer QoL. Moreover, patients experiencing generalized seizures, as compared to those experiencing other seizure types, had better QoL, and patients with idiopathic epilepsy had relatively good QoL especially when viewed in light of the relatively poor QoL of those with structural/metabolic aetiology of epilepsy.

Finally, all four studies that investigated the effects of *age at onset* found that patients diagnosed later in life tended to experience poorer QoL.

**Psychiatric Comorbidities.** *Depression* was the most frequently investigated of these factors (see Table 6). Of the 45 studies in which its relationship to QoL was assessed, 38 found a statistically significant association. Of the 24 studies in which relations between anxiety and QoL was assessed, 19 found a statistically significant association. Unsurprisingly, when significant associations were detected they indicated that PWE who experienced depression and/or anxiety symptoms had poorer QoL outcomes.

**Table 5.** *Studies Reporting on Epilepsy-Related Determinants of Quality of Life in People with Epilepsy*

| Factor                       | Studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Cross-Sectional                            | Longitudinal | Total |                                 |
| Seizure frequency            | Abadiga et al., 2019; Alanis-Guevara et al., 2005; Alonso-Vanegas et al., 2013; Alsaadi et al., 2017; Au et al., 2002; Aydemir et al., 2004; Azuma & Akechi, 2014; Bautista & Tannahill Glen, 2009; Canuet et al., 2009; H. F. Chen et al., 2016; Y. yu Chen et al., 2018; Choi-Kwon et al., 2003; Chou et al., 2015; Djibuti & Shakarishvili, 2003; Edefonti et al., 2011; Kinyanjui et al., 2013; Kwan et al., 2009; Leidy et al., 1999; Liou et al., 2005; McLaughlin et al., 2008; McLaughlin et al., 2010; Melikyan et al., 2012; Mohamed et al., 2014; Mosaku et al., 2006; Norsa'adah et al., 2013; Nubukpo et al., 2004; Ogundare et al., 2021; Pauli et al., 2012; Piperidou et al., 2008; Puri et al., 2018; Rakesh et al., 2012; Ranjana et al., 2014; Salas-Puig et al., 2021; Şenol et al., 2007; G. M. de A. S. Tedrus et al., 2013; Tefera et al., 2020; van Hout et al., 1997; Wang et al., 2017; Yue et al., 2011 | 37                                         | 2            | 39    | 46                              |
| Disease duration             | Au et al., 2002; Ayanda & Sulyman, 2020; Djibuti & Shakarishvili, 2003; Gordon-Perue et al., 2011; Pauli et al., 2012; Piperidou et al., 2008; Szaflarski et al., 2006; Tanriverdi et al., 2008; Wang et al., 2017; Zhao et al., 2011                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 9                                          | 1            | 10    | 17                              |
| Number of ASMs (polytherapy) | Aydemir et al., 2004; Camara-Lemarroy et al., 2017; Choi-Kwon et al., 2003; Ehrlich et al., 2019; Giray et al., 2009; Gordon-Perue et al., 2011; Kwan et al., 2009; Mosaku et al., 2006; Pimpalkhute et al., 2015; Piperidou et al., 2008; Salas-Puig et al., 2021; Tedrus et al., 2020; Tefera et al., 2020; Tombini et al., 2021; Yue et al., 2011                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 14                                         | 1            | 15    | 16                              |
| Surgery (seizure-free)       | Cankurtaran et al., 2005; Chou et al., 2015; Cunha & Oliveira, 2010; Elliott et al., 2012; Elsharkawy et al.,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 6                                          | 9            | 15    | 15                              |

|                                       |                                                                                                                                                                                                                                                       |    |   |    |    |
|---------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|---|----|----|
|                                       | 2009; Ives-Deliperi & Butler, 2017; Kanchanatawan & Kasalak, 2012; Lin et al., 2020; Lotfinia et al., 2019; Markand et al., 2000; Mikati et al., 2006; Stavem et al., 2008; Tanriverdi et al., 2008; Vergara Palma et al., 2015; Winslow et al., 2020 |    |   |    |    |
| Seizure severity                      | Adebayo et al., 2014; Bautista & Glen, 2009; Cramer et al., 2003; Fawale et al., 2014; Harden et al., 2007; Jehi et al., 2011; Kaddumukasa et al., 2019; Milovanović et al., 2014; Puri et al., 2018; Zhao et al., 2011; Zou et al., 2014             | 10 | 1 | 11 | 12 |
| Side effects of ASMs                  | Abadiga et al., 2019; Azuma & Akechi, 2014; Chen et al., 2016; Chen et al., 2018; Jovel et al., 2016; May et al., 2009; Milovanović et al., 2014; Ranjana et al., 2014; Siarava et al., 2019; Yue et al., 2011                                        | 10 | 0 | 10 | 10 |
| Seizure worry                         | Barahmand & Haji, 2014; Cramer et al., 2003; Kaddumukasa et al., 2019; Markand et al., 2000; Myers et al., 2015; Norsa'adah et al., 2013                                                                                                              | 5  | 1 | 6  | 9  |
| Seizure type                          | Alonso-Vanegas et al., 2013; Giray et al., 2009; Ranjana et al., 2014                                                                                                                                                                                 | 3  | 0 | 3  | 7  |
| Seizure aetiology                     | Jovel et al., 2016; Milovanović et al., 2014                                                                                                                                                                                                          | 2  | 0 | 2  | 5  |
| Age at onset                          | Alonso-Vanegas et al., 2013; Gülpek et al., 2011; Pauli et al., 2012; Szaflarski et al., 2006                                                                                                                                                         | 4  | 0 | 4  | 4  |
| Lack of AED treatment / non-adherence | Hamed-Shahraki et al., 2019; Nubukpo et al., 2004                                                                                                                                                                                                     | 1  | 1 | 2  | 2  |

*Note.* AED = anti-epilepsy drugs.

**Table 6.** *Studies Reporting on Psychiatric Comorbidities as Determinants of Quality of Life in People with Epilepsy*

| Factor     | Studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Cross-Sectional                            | Longitudinal | Total |                                 |
| Depression | Akdemir et al., 2016; Alsaadi et al., 2017; Ayanda & Sulyman, 2020; Azuma & Akechi, 2014; Camara-Lemarroy et al., 2017; Canuet et al., 2009; Chen et al., 2016; Chen et al., 2018; Choi et al., 2011; Choi-Kwon et al., 2003; Cramer et al., 2003; Deleo et al., 2020; Ehrlich et al., 2019; Espinosa Jovel et al., 2016; Garcia et al., 2015; Gülpek et al., 2011; Hessen et al., 2009; Jehi et al., 2011; Kwan et al., 2009; McLaughlin et al., 2010; Meldolesi et al., 2006; Melikyan et al., 2012; Milovanović et al., 2014; Mohamed et al., 2014; Mosaku et al., 2006; Myers et al., 2015; Ogundare et al., 2021; Saadi et al., 2016; Salas-Puig et al., 2021; Şenol et al., 2007; Siarava et al., 2019; Szaflarski et al., 2006; Tedrus et al., 2015; Tedrus et al., 2013; Tombini et al., 2021; Viteva & Zahariev, 2009; Wang et al., 2017; Whatley et al., 2010 | 38                                         | 0            | 38    | 45                              |
| Anxiety    | Abadiga et al., 2019; Au et al., 2002; Ayanda & Sulyman, 2020; Camara-Lemarroy et al., 2017; Chen et al., 2016; Chen et al., 2018; Choi-Kwon et al., 2003; Deleo et al., 2020; Gülpek et al., 2011; Kwan et al., 2009; Meldolesi et al., 2006; Milovanović et al., 2014; Mosaku et al., 2006; Rakesh et al., 2012; Salas-Puig et al., 2021; Tedrus et al., 2015; Tedrus et al., 2013; Wang et al., 2017; Yue et al., 2011                                                                                                                                                                                                                                                                                                                                                                                                                                               | 19                                         | 0            | 19    | 24                              |

**Sociodemographic Factors.** As Table 7 shows, *age* was the most frequently studied of these factors. Of the 15 studies in which its relationship to QoL was assessed, 7 observed a statistically significant inverse correlation (i.e., older age was associated with diminished QoL).

*Education* was the second most frequently studied of these factors. Of the 13 studies in which its relationship to QoL was assessed, 10 observed a statistically significant positive relationship (i.e., lower levels of education were associated with poorer QoL outcomes).

For each of the sociodemographic factors of *employment status*, *household income*, and *marital status*, more than 70% of the studies that assessed the factor found that it was significantly associated with QoL in PWE. Specifically, being unemployed, lower household income, and being single/divorced or widowed rather than married were all associated with worse QoL. Both studies that assessed associations between *driving ability* and QoL reported that an inability to drive when one could independently drive before was a significant predictor of poorer QoL.

Interestingly, findings with regard to *gender* were more mixed. Of the 8 studies that assessed the relationship between this factor and QoL, 3 found that being female was significantly associated with poorer QoL, 1 found that being male was significantly associated with poorer QoL, and 4 found no significant associations.

Table 7.

*Studies Reporting on Sociodemographic Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor                   | Studies                                                                                                                                                                                                                        | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                          |                                                                                                                                                                                                                                | Cross-Sectional                            | Longitudinal | Total |                                 |
| Age                      | Chen et al., 2016; Choi-Kwon et al., 2003; Djibuti & Shakarishvili, 2003; Melikyan et al., 2012b; Rakesh et al., 2012; Saadi et al., 2016; Zhao et al., 2011; Zou et al., 2014                                                 | 7                                          | 0            | 7     | 15                              |
| Education                | Akdemir et al., 2016; Choi-Kwon et al., 2003; Djibuti & Shakarishvili, 2003; Kinyanjui et al., 2013; Rakesh et al., 2012; Saadi et al., 2016; Siarava et al., 2019; Tefera et al., 2020; Zhao et al., 2011; Zou et al., 2014). | 10                                         | 0            | 10    | 13                              |
| Employment status        | Akdemir et al., 2016; Azuma & Akechi, 2014; Choi-Kwon et al., 2003; Elsharkawy et al., 2009; Gu et al., 2016; Hessen et al., 2009; Kinyanjui et al., 2013; Salas-Puig et al., 2021                                             | 8                                          | 0            | 8     | 11                              |
| Household income         | Abadiga et al., 2019; Alanis-Guevara et al., 2005; Argyriou et al., 2004; Chen et al., 2016; Choi-Kwon et al., 2003; Kinyanjui et al., 2013; Rakesh et al., 2012; Tefera et al., 2020; Zhao et al., 2011                       | 9                                          | 0            | 9     | 10                              |
| Gender                   | Alanis-Guevara et al., 2005b; Chen et al., 2016b; Mosaku et al., 2006; Salas-Puig et al., 2021                                                                                                                                 | 4                                          | 0            | 4     | 8                               |
| Marital status           | Ayanda & Sulyman, 2020; Giray et al., 2009; Rakesh et al., 2012; Tefera et al., 2020; Wang et al., 2017; Zou et al., 2014                                                                                                      | 6                                          | 0            | 6     | 6                               |
| Inability to drive a car | Elsharkawy et al., 2009; Tiamkao et al., 2009                                                                                                                                                                                  | 2                                          | 0            | 2     | 2                               |

**Psychosocial Factors.** *Stigma* was the most frequently investigated of these factors (see Table 8). Of the 10 studies in which its relationship to QoL was investigated, 9 found that the greater the experience of stigma the poorer the QoL. Similarly, all 8 of the studies that investigated associations between *social support* and QoL observed that individuals with greater levels of such support reported better overall QoL outcomes as compared to those with either poor or a complete lack of support from family and/or friends.

**Factors Not Otherwise Categorized.** *Activities of daily living (ADLs)* and *sleep disturbances* were the joint most-frequently investigated of these factors (see Table 9). All 4 of the studies assessing the relationship of ADLs to QoL found that an inability to perform such activities was associated with lower QoL. Similarly, all 4 of the studies assessing the relationship of sleep disturbances to QoL observed that difficulties with obtaining quality sleep, in particular, were associated with lower QoL.

Two studies reported that diminished performance in specific cognitive domains was associated with poor QoL. One study reported that impairments in *attention*, *learning*, and *processing speed* were related to lower QoL, while another study reported that impairments in *executive functioning* were similarly related to lower QoL.

Table 8.

*Studies Reporting on Psychosocial Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor         | Studies                                                                                                                                                                                                         | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                |                                                                                                                                                                                                                 | Cross-Sectional                            | Longitudinal | Total |                                 |
| Stigma         | Abadiga et al., 2019;<br>Fawale et al., 2014;<br>Kumari et al., 2009;<br>Lua & Neni, 2011;<br>McLaughlin et al.,<br>2008; Saadi et al.,<br>2016; Tombini et al.,<br>2021; Viteva, 2013;<br>Whatley et al., 2010 | 9                                          | 0            | 9     | 10                              |
| Social support | Au et al., 2002; Chen<br>et al., 2016; Choi-<br>Kwon et al., 2003;<br>Gülpek et al., 2011;<br>Iwuozo et al., 2020;<br>Saburi et al., 2006;<br>Whatley et al., 2010;<br>Zou et al., 2014                         | 8                                          | 0            | 8     | 8                               |

Table 9.

*Studies Reporting on Factors Not Otherwise Categorized as Determinants of Quality of Life in People with Epilepsy*

| Factor                | Studies                                                                                                          | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|-----------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                       |                                                                                                                  | Cross-Sectional                            | Longitudinal | Total |                                 |
| ADLs                  | Au et al., 2002;<br>Choi-Kwon et al.,<br>2003; Gordon-<br>Perue et al., 2011;<br>Sillanpää et al.,<br>2004       | 3                                          | 1            | 4     | 4                               |
| Sleep disturbance     | Alanis-Guevara et<br>al., 2005; Camara-<br>Lemarroy et al.,<br>2017; Jovel et al.,<br>2016; Kwan et al.,<br>2009 | 4                                          | 0            | 4     | 4                               |
| Learning              | Engelberts et al.<br>(2002)                                                                                      | 1                                          | 0            | 1     | 2                               |
| Attention             | Engelberts et al.<br>(2002)                                                                                      | 1                                          | 0            | 1     | 1                               |
| Processing speed      | Engelberts et al.<br>(2002)                                                                                      | 1                                          | 0            | 1     | 1                               |
| Executive functioning | Ehrlich et al.<br>(2019)                                                                                         | 1                                          | 0            | 1     | 1                               |

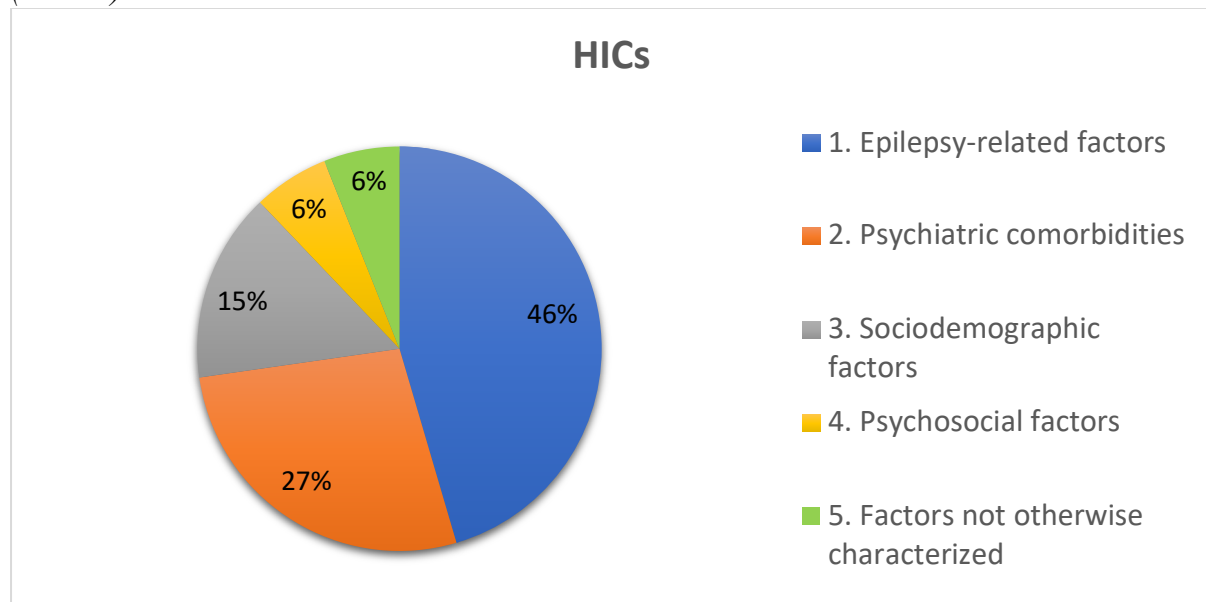
*Note.* ADLs = activities of daily living.

### Determinants of Quality of Life: PWE in High-Income Countries

In this section, I focus on summarizing, reviewing, and analysing the results from the 43 studies conducted in HICs. As in the major section above, determinants of QoL in PWE were categorized into the following five domains: epilepsy-related factors, psychiatric comorbidities, sociodemographic factors, psychosocial factors, and factors not otherwise categorized. Each of Tables 10–14 presents, for one of the domains, the individual factors within that domain, the number of studies that reported a significant relationship between a factor and QoL, and the total number of studies that examined each factor. As Figure 5 shows, almost half of the studies in the review sample investigated the relationship between QoL and at least one epilepsy-related factor (e.g., seizure severity, seizure frequency, disease duration). Slightly more than a quarter of the studies investigated the relationship between QoL and psychiatric comorbidities (depression and/or anxiety), and a slightly smaller proportion investigated relations between QoL and sociodemographic factors (e.g., age, gender, education). Less than 10% of studies investigated relations between (a) psychosocial factors, such as stigma and social support, and (b) factors not otherwise categorized, such as sleep disruption and cognitive impairment.

**Figure 5.**

*Proportion of the Reviewed Studies Conducted in High Income Countries that Investigated at Least One Determinant of Quality of Life, Grouped by the Five Major Categories of Variable (N = 43)*



**Epilepsy-related Factors.** Again, *seizure frequency* was the most frequently studied of these factors (see Table 10). Of the 17 studies in which it was assessed, 15 found that it bore a statistically significant relationship to QoL. The most consistent finding in this regard was that higher seizure frequency was associated with lower QoL. The longitudinal study in this group reported that seizure frequency was significantly inversely correlated with overall QoL in patients from Taiwan who had undergone anterior temporal lobectomy (Chou et al., 2015).

In contrast to what was observed for the overall sample, the second most frequently studied epilepsy-related factor in the HIC subsample of studies was *seizure freedom* – patients who had undergone surgery tended to report improved QoL post-operatively. Of note here is that of the 15 studies in the overall sample that found a significant association between seizure freedom and QoL, 9 were conducted in HICs.

*Disease duration* was also one of the most frequently studied of these factors. However, of the 9 studies in which it was assessed, only 3 found that it bore a statistically significant relationship to QoL. The most consistent finding in this regard was that longer duration of epilepsy was associated with lower overall QoL. In contrast, one study reported that shorter disease duration was associated with lower QoL (Szaflarski et al., 2006).

A smaller number of studies reported that lower QoL was associated with a) *adverse effects of ASMs* (b) *AED polytherapy* (c) *greater seizure severity*, and (d) *more seizure worry*. In most of these cases, all or all but one of the published studies reported significant findings in the same direction. For seizure worry, the other half of the studies that investigated this factor found no significant associations regarding QoL. Finally, a single study reported that *older age at onset* was associated with lower QoL.

**Psychiatric Comorbidities.** Similar to the pattern for the overall sample of reviewed studies, in HIC-based studies psychiatric comorbidities were the second-most studied determinants of QoL (see Figure 5).

*Depression* was not only the most frequently investigated psychiatric comorbidity but was also the overall most frequently assessed factor related to QoL in HICs (see Table 11). Of the 24 studies in which its relationship to QoL was assessed, 21 found a statistically significant association. A smaller number of studies found a significant association between *anxiety* and QoL. Of the 8 studies in which relations between anxiety and QoL was assessed, 5 found a statistically significant association. Unsurprisingly, when significant associations were detected they indicated that PWE who experienced depression and/or anxiety symptoms had poorer QoL outcomes.

Table 10.

*Studies Conducted in High Income Countries Reporting on Epilepsy-Related Determinants of Quality of Life in People with Epilepsy*

| Factor                       | Studies                                                                                                                                                                                                                                                                                                                                           | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                              |                                                                                                                                                                                                                                                                                                                                                   | Cross-Sectional                            | Longitudinal | Total |                                 |
| Seizure frequency            | Alsaadi et al., 2017; Azuma & Akechi, 2014; Bautista & Tannahill, 2009; Canuet et al., 2009; Chen et al., 2016; Choi-Kwon et al., 2003; Chou et al., 2015; Edefonti et al., 2011; Leidy et al., 1999; Liou et al., 2005; McLaughlin et al., 2008; McLaughlin et al., 2010; Piperidou et al., 2008; Salas-Puig et al., 2021; van Hout et al., 1997 | 14                                         | 1            | 15    | 17                              |
| Surgery (seizure-free)       | Chou et al., 2015; Cunha & Oliveira, 2010; Elliott et al., 2012; Elsharkawy et al., 2009; Lin et al., 2020; Markand et al., 2000; Stavem et al., 2008; Tanriverdi et al., 2008; Winslow et al., 2020                                                                                                                                              | 3                                          | 6            | 9     | 9                               |
| Disease duration             | Piperidou et al., 2008; Szaflarski et al., 2006; Tanriverdi et al., 2008                                                                                                                                                                                                                                                                          | 3                                          | 0            | 3     | 9                               |
| Number of ASMs (polytherapy) | Choi-Kwon et al., 2003; Ehrlich et al., 2019; Piperidou et al., 2008; Salas-Puig et al., 2021; Tombini et al., 2021                                                                                                                                                                                                                               | 5                                          | 0            | 5     | 5                               |
| Seizure severity             | Bautista & Tannahill, 2009; Cramer et al., 2003; Harden et al., 2007; Jehi et al., 2011                                                                                                                                                                                                                                                           | 4                                          | 0            | 4     | 5                               |
| Side effects of ASMs         | Azuma & Akechi, 2014; Chen et al., 2016; Elsharkawy et al., 2009; Siarava et al., 2019                                                                                                                                                                                                                                                            | 4                                          | 0            | 4     | 4                               |
| Seizure worry                | Cramer et al., 2003; Markand et al., 2000; Myers et al., 2015                                                                                                                                                                                                                                                                                     | 2                                          | 1            | 3     | 6                               |
| Age at onset                 | Szaflarski et al., 2006                                                                                                                                                                                                                                                                                                                           | 1                                          | 0            | 1     | 1                               |

*Note.* AED = anti-epilepsy drugs.

Table 11.

*Studies Conducted in High Income Countries Reporting on Psychiatric Comorbidities as Determinants of Quality of Life in People with Epilepsy*

| Factor     | Studies                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Cross-Sectional                            | Longitudinal | Total |                                 |
| Depression | Alsaadi et al., 2017; Azuma & Akechi, 2014; Bala et al., 2016; Canuet et al., 2009; Chen et al., 2016; Choi et al., 2011; Choi-Kwon et al., 2003; Cramer et al., 2003; Deleo et al., 2020; Ehrlich et al., 2019; Garcia et al., 2015; Hessen et al., 2009; Jehi et al., 2011; McLaughlin et al., 2010; Meldolesi et al., 2006; Myers et al., 2015; Salas-Puig et al., 2021; Siarava et al., 2019; Szaflarski et al., 2006; Tombini et al., 2021; Whatley et al., 2010 | 21                                         | 0            | 21    | 24                              |
| Anxiety    | (H. F. Chen et al., 2016c; Choi-Kwon et al., 2003; Deleo et al., 2020; Meldolesi et al., 2006; Salas-Puig et al., 2021)                                                                                                                                                                                                                                                                                                                                               | 5                                          | 0            | 5     | 8                               |

**Sociodemographic Factors.** Consistent with the overall sample of reviewed studies, in HIC-based studies a smaller proportion of studies investigated the impact of sociodemographic factors on QoL (see Figure 5).

As Table 12 shows, *employment status* was the most frequently studied of these factors in the HIC subsample. Of the 7 studies in which its relationship to QoL was assessed, 5 observed a statistically significant positive correlation (i.e., being unemployed was associated with poorer QoL outcomes).

For each of the sociodemographic factors of *household income* and *education*, most of the studies that assessed the factor found that it was significantly associated with QoL in PWE. Specifically, having a lower household income or a lower level of education, was associated with worse QoL. However, for *age* only 1 of the 6 studies that investigated this factor found a significant association between age and QoL (i.e., being older was associated with poorer QoL).

The single study that assessed associations between *driving ability* and QoL reported that an inability to drive when one could independently drive before was a significant predictor of poorer QoL.

Again, the findings with regard to *gender* were more mixed. Of the 4 studies that assessed the relationship between this factor and QoL, 1 found that being female was significantly associated with poorer QoL (Salas-Puig et al., 2021) whilst 1 found a similar relationship but with regards to males (Chen et al., 2016) and the rest of the studies reported no significant gender-based findings.

Table 12.

*Studies Conducted in High Income Countries Reporting on Sociodemographic Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor                   | Studies                                                                                                             | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|--------------------------|---------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                          |                                                                                                                     | Cross-Sectional                            | Longitudinal | Total |                                 |
| Employment status        | Azuma & Akechi, 2014; Choi-Kwon et al., 2003; Elsharkawy et al., 2009; Hessen et al., 2009; Salas-Puig et al., 2021 | 5                                          | 0            | 5     | 7                               |
| Education                | Choi-Kwon et al., 2003; Siarava et al., 2019                                                                        | 2                                          | 0            | 2     | 4                               |
| Household income         | Argyriou et al., 2004; Chen et al., 2016; Choi-Kwon et al., 2003                                                    | 3                                          | 0            | 3     | 3                               |
| Age                      | Choi-Kwon et al., 2003                                                                                              | 1                                          | 0            | 1     | 6                               |
| Gender                   | Chen et al., 2016; Salas-Puig et al., 2021                                                                          | 2                                          | 0            | 2     | 4                               |
| Inability to drive a car | Elsharkawy et al., 2009                                                                                             | 1                                          | 0            | 1     | 1                               |

**Psychosocial Factors.** *Stigma* and *social support* were the most frequently investigated of these factors (see Table 13). All the studies in which these relationships were assessed with regards to QoL found a significant association between QoL and stigma or social support. Poorer QoL was associated with greater levels of stigma experienced. The few studies that investigated associations between social support and QoL observed that individuals with greater levels of such support reported better overall QoL outcomes as compared to those with either poor or a complete lack of support from family and/or friends.

**Factors Not Otherwise Categorized.** *Activities of daily living (ADLs)* and diminished performance in specific cognitive domains were the joint most frequently investigated of these factors (see Table 14). Both of the studies assessing the relationship of ADLs to QoL found that an inability to perform such activities was associated with lower QoL.

Two studies reported that diminished performance in specific cognitive domains was associated with poor QoL. One study reported that impairments in *attention*, *learning*, and *processing speed* were related to lower QoL, while another study reported that impairments in *executive functioning* were similarly related to lower QoL.

**Table 13.**

*Studies Conduction in High Income Countries Reporting on Psychosocial Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor         | Studies                                                                     | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|----------------|-----------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                |                                                                             | Cross-Sectional                            | Longitudinal | Total |                                 |
| Stigma         | (McLaughlin et al., 2008;<br>Tombini et al., 2021;<br>Whatley et al., 2010) | 3                                          | 0            | 3     | 3                               |
| Social support | (Chen et al., 2016; Choi-<br>Kwon et al., 2003;<br>Whatley et al., 2010)    | 3                                          | 0            | 3     | 3                               |

**Table 14.**

*Studies Conducted in High Income Countries Reporting on Factors Not Otherwise Categorized as Determinants of Quality of Life in People with Epilepsy*

| Factor                | Studies                                        | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|-----------------------|------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                       |                                                | Cross-Sectional                            | Longitudinal | Total |                                 |
| ADLs                  | Choi-Kwon et al., 2003; Sillanpää et al., 2004 | 1                                          | 1            | 2     | 2                               |
| Learning              | Engelberts et al. (2002)                       | 1                                          | 0            | 1     | 2                               |
| Attention             | Engelberts et al. (2002)                       | 1                                          | 0            | 1     | 1                               |
| Processing speed      | Engelberts et al. (2002)                       | 1                                          | 0            | 1     | 1                               |
| Executive functioning | Ehrlich et al. (2019)                          | 1                                          | 0            | 1     | 1                               |

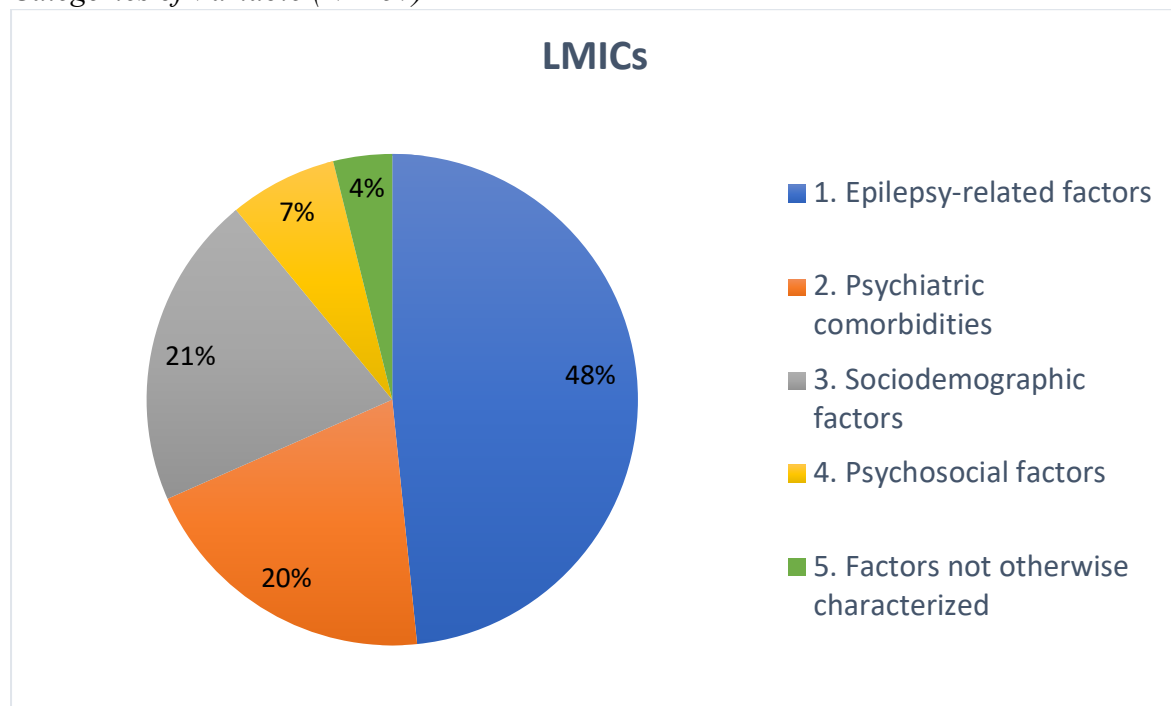
*Note.* ADLs = activities of daily living

### Determinants of Quality of Life: PWE in Low- and Middle-Income Countries

In this section, I focus on summarizing, reviewing, and analysing the results from the 57 studies conducted in LMICs. As in the two major sections above, determinants of QoL in PWE were categorized into the following five domains: epilepsy-related factors, psychiatric comorbidities, sociodemographic factors, psychosocial factors, and factors not otherwise categorized. Each of Tables 15–19 presents, for one of the domains, the individual factors within that domain, the number of studies that reported a significant relationship between a factor and QoL, and the total number of studies that examined each factor. As Figure 6 shows, almost half of the studies in the review sample investigated the relationship between QoL and at least one epilepsy-related factor (e.g., seizure type, seizure frequency, disease duration). This statistic is consistent with that presented in Table 4, for the sample as a whole (i.e., HICs and LMICs combined). Unlike the data presented in Table 4, however, almost equal proportions of studies investigated relations between QoL and psychiatric comorbidities and between QoL and sociodemographic factors. As for the sample overall, less than 10% of studies investigated relations between (a) QoL and psychosocial factors, and (b) QoL and factors not otherwise categorized, with the former group of studies being the most source of data for this sub-sample.

**Figure 6.**

*Proportion of the Reviewed Studies Conducted in Low- and Middle-Income Countries that Investigated at Least One Determinant of Quality of Life, Grouped by the Five Major Categories of Variable (N = 57)*



**Epilepsy-related Factors.** Again, *seizure frequency* was the most frequently studied of these factors (see Table 15). Of the 29 studies in which it was assessed, 24 found that it bore a statistically significant relationship to QoL – this ratio is similar to what was found for the overall review sample and for the subsample of studies conducted in HICs. Again, the most consistent finding in this regard was that higher seizure frequency was associated with lower QoL. The longitudinal study in this group reported that seizure frequency was significantly inversely correlated with overall QoL in patients from India with medically intractable epilepsy who were not candidates for surgery (Puri et al., 2018b).

In contrast to what was observed for the overall sample and for the HIC subsample, the second most frequently studied epilepsy-related factor in the LMIC subsample of studies was *AED polytherapy*. Of the 11 studies in which its relationship to QoL was assessed, 10 reported a significant correlation – the greater the number of ASMs a patient used, the more likely they were to experience poorer QoL. Of note here is that of the 15 studies in the overall sample that found a significant association between polytherapy and QoL, 10 were conducted in LMICs.

Regarding other medication-related factors, *adverse effects of ASMs* and *lack of adherence / non-adherence to ASMs* were also significantly associated with QoL. All 6 studies that assessed relations between adverse effects of ASMs and QoL found a significant inverse relation (i.e., the greater the experience of negative side effects, the lower the QoL). Of note here is that of the 10 studies in the overall sample that found a significant association between adverse effects of ASMs and QoL, 6 were conducted in LMICs.

Also of note is that the only two studies in the review sample that investigated relations between QoL and unavailability of ASMs, lack of adherence, or non-adherence were conducted in LMICs. These were all associated with poorer QoL in PWE.

In other findings unique to LMICs (because these factors were not the subject of investigation for any of HIC subsample of studies), both *seizure type* and *seizure aetiology* were reported to be significantly associated with QoL (see Table 14). That is to say, patients experiencing generalized seizures, as compared to those experiencing other seizure types, had better QoL, and patients with idiopathic epilepsy had relatively good QoL especially when viewed in light of the relatively poor QoL of those with structural/metabolic aetiology of epilepsy.

The LMIC subsample of studies was also consistent with the HIC subsample in suggesting that better QoL was associated with *seizure freedom* – patients who had

undergone surgery tended to report improved QoL post-operatively, whereas lower QoL was associated with (a) longer *disease duration*, (b) greater *seizure severity*, and (c) more *seizure worry*. In each of these cases, all or all but one of the published studies reported significant findings in the same direction.

Finally, 3 of the 4 studies reporting that *older age at onset* was associated with lower QoL were conducted in LMICs.

**Sociodemographic Factors.** In contrast to the pattern for the overall sample of reviewed studies and for the subsample of HIC studies, in LMIC-based studies sociodemographic factors were the second-most studied determinants of QoL (see Figure 6 and how it contrasts to Figure 4 and Figure 5).

As Table 16 shows, *education* was the most frequently studied of these factors in the LMIC subsample. Of the 9 studies in which its relationship to QoL was assessed, 8 observed a statistically significant positive correlation (i.e., lower levels of education were associated with poorer QoL outcomes).

For each of the sociodemographic factors of *household income*, *age*, *marital status*, and *employment status*, all or all but one of the studies that assessed the factor found that it was significantly associated with QoL in PWE. Specifically, having a lower household income, being older, being single/divorced or widowed rather than married, or being unemployed were all associated with worse QoL.

Consistent with HIC subsample, the single study that assessed associations between *driving ability* and QoL reported that an inability to drive when one could independently drive before was a significant predictor of poorer QoL.

Again, the findings with regard to *gender* were more mixed. Of the 4 studies that assessed the relationship between this factor and QoL, 2 found that being female was significantly associated with poorer QoL whereas the others reported no significant gender-based findings.

**Table 15.**

*Studies Conducted in Low- and Middle-Income Countries Reporting on Epilepsy-Related Determinants of Quality of Life in People with Epilepsy*

| Factor                       | Studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Significant Relationship with QoL Detected |                    |       | No. of Times Factor was Studied |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------------|-------|---------------------------------|
|                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cross-Sectional                            | Longitudinal Study | Total |                                 |
| Seizure frequency            | Abadiga et al., 2019; Alanis-Guevara et al., 2005; Alonso-Vanegas et al., 2013; Au et al., 2002; Aydemir et al., 2004; Chen et al., 2018; Djibuti & Shakarishvili, 2003; Kinyanjui et al., 2013; Kwan et al., 2009; Melikyan et al., 2012; Mohamed et al., 2014; Mosaku et al., 2006; Norsa'adah et al., 2013; Nubukpo et al., 2004; Ogundare et al., 2021; Pauli et al., 2012; Puri et al., 2018; Rakesh et al., 2012; Ranjana et al., 2014; Şenol et al., 2007; Tedrus et al., 2013; Tefera et al., 2020; Wang et al., 2017; Yue et al., 2011 | 23                                         | 1                  | 24    | 29                              |
| Number of ASMs (polytherapy) | Aydemir et al., 2004; Camara-Lemarroy et al., 2017; Giray et al., 2009; Gordon-Perue et al., 2011; Kwan et al., 2009; Mosaku et al., 2006; Pimpalkhute et al., 2015; Tedrus et al., 2020; Tefera et al., 2020; Yue et al., 2011                                                                                                                                                                                                                                                                                                                 | 9                                          | 1                  | 10    | 11                              |
| Disease duration             | Au et al., 2002; Ayanda & Sulyman, 2020; Djibuti & Shakarishvili, 2003; Gordon-Perue et al., 2011; Pauli et al., 2012; Wang et al., 2017; Zhao et al., 2011                                                                                                                                                                                                                                                                                                                                                                                     | 7                                          | 0                  | 7     | 8                               |
| Seizure severity             | Adebayo et al., 2014; Fawale et al., 2014; Kaddumukasa et al., 2019;                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 6                                          | 1                  | 7     | 7                               |

|                                              |                                                                                                                                                       |   |   |   |   |
|----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|---|---|---|---|
|                                              | Milovanović et al., 2014; Puri et al., 2018; Zhao et al., 2011; Zou et al., 2014                                                                      |   |   |   |   |
| Surgery<br>(seizure-free)                    | Cankurtaran et al., 2005; Ives-Deliperi & Butler, 2017; Kanchanatawan & Kasalak, 2012; Lotfinia et al., 2019; Mikati et al., 2006; Palma et al., 2015 | 3 | 3 | 6 | 6 |
| Side effects of<br>ASMs                      | Abadiga et al., 2019; Chen et al., 2018; Jovel et al., 2016; Milovanović et al., 2014; Ranjana et al., 2014; Yue et al., 2011                         | 6 | 0 | 6 | 6 |
| Seizure type                                 | Alonso-Vanegas et al., 2013; Giray et al., 2009; Ranjana et al., 2014                                                                                 | 3 | 0 | 3 | 4 |
| Seizure worry                                | Barahmand & Haji, 2014; Kaddumukasa et al., 2019; Norsa'adah et al., 2013                                                                             | 3 | 0 | 3 | 3 |
| Age at onset                                 | Alonso-Vanegas et al., 2013; Gülpek et al., 2011; Pauli et al., 2012                                                                                  | 3 | 0 | 3 | 3 |
| Seizure<br>aetiology                         | Jovel et al., 2016; Milovanović et al., 2014                                                                                                          | 2 | 0 | 2 | 2 |
| Lack of AED<br>treatment / non-<br>adherence | Hamed-Shahraki et al., 2019; Nubukpo et al., 2004                                                                                                     | 1 | 1 | 2 | 2 |

*Note.* AED = anti-epilepsy drugs.

**Table 16.**

*Studies Conducted in Low- and Middle-Income Countries Reporting on Sociodemographic Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor                   | Studies                                                                                                                                                                        | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|                          |                                                                                                                                                                                | Cross-Sectional                            | Longitudinal | Total |                                 |
| Education                | Akdemir et al., 2016; Djibuti & Shakarishvili, 2003; Kinyanjui et al., 2013; Rakesh et al., 2012; Saadi et al., 2016; Tefera et al., 2020; Zhao et al., 2011; Zou et al., 2014 | 8                                          | 0            | 8     | 9                               |
| Household income         | Abadiga et al., 2019; Alanis-Guevara et al., 2005; Kinyanjui et al., 2013; Rakesh et al., 2012; Tefera et al., 2020; Zhao et al., 2011                                         | 6                                          | 0            | 6     | 7                               |
| Age                      | Djibuti & Shakarishvili, 2003; Melikyan et al., 2012; Rakesh et al., 2012; Saadi et al., 2016; Zhao et al., 2011; Zou et al., 2014                                             | 6                                          | 0            | 6     | 6                               |
| Marital status           | Ayanda & Sulyman, 2020; Giray et al., 2009; Rakesh et al., 2012; Tefera et al., 2020; Wang et al., 2017; Zou et al., 2014                                                      | 6                                          | 0            | 6     | 6                               |
| Gender                   | Alanis-Guevara et al., 2005; Mosaku et al., 2006                                                                                                                               | 2                                          | 0            | 2     | 4                               |
| Employment status        | Akdemir et al., 2016; Gu et al., 2016; Kinyanjui et al., 2013                                                                                                                  | 3                                          | 0            | 3     | 4                               |
| Inability to drive a car | Tiamkao et al., 2009                                                                                                                                                           | 1                                          | 0            | 1     | 1                               |

**Psychiatric Comorbidities.** As was the case in the overall review sample and in the HIC subsample, *depression* was the most frequently investigated of these factors (see Table 17). Of the 21 studies in which its relationship to QoL was assessed, 17 found a statistically significant association. Similarly, of the 16 studies in which relations between anxiety and QoL were assessed, 14 found statistically significant associations.

Unsurprisingly, when significant relations were detected they indicated that PWE who experienced depression and/or anxiety symptoms had poorer QoL outcomes.

**Table 17.**

*Studies Conducted in Low- and Middle-Income Countries Reporting on Psychiatric Comorbidities as Determinants of Quality of Life in People with Epilepsy*

| Factor     | Studies                                                                                                                                                                                                                                                                                                                                                                                | Significant Relationship with QoL Detected |              |       | No. of Times Factor was Studied |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|-------|---------------------------------|
|            |                                                                                                                                                                                                                                                                                                                                                                                        | Cross-Sectional                            | Longitudinal | Total |                                 |
| Depression | Akdemir et al., 2016; Ayanda & Sulyman, 2020; Camara-Lemarroy et al., 2017; Chen et al., 2018; Jovel et al., 2016; Gülpek et al., 2011; Kwan et al., 2009; Melikyan et al., 2012; Milovanović et al., 2014; Mohamed et al., 2014; Mosaku et al., 2006; Ogundare et al., 2021; Şenol et al., 2007; Tedrus et al., 2015; Tedrus et al., 2013; Viteva & Zahariev, 2009; Wang et al., 2017 | 17                                         | 0            | 17    | 21                              |
| Anxiety    | Abadiga et al., 2019; Au et al., 2002; Ayanda & Sulyman, 2020; Camara-Lemarroy et al., 2017; Chen et al., 2018; Gülpek et al., 2011; Kwan et al., 2009; Milovanović et al., 2014; Mosaku et al., 2006; Rakesh et al., 2012; Tedrus et al., 2015; Tedrus et al., 2013; Wang et al., 2017; Yue et al., 2011                                                                              | 14                                         | 0            | 14    | 16                              |

**Psychosocial Factors.** As was the case in the overall review sample, *stigma* was the most frequently investigated of these factors (see Table 18). Of the 7 studies in which its relationship to QoL was assessed, 6 found that the greater the experience of stigma the lower the QoL. Similarly, 5 of the 6 studies that investigated associations between *social support* and QoL observed that individuals with greater levels of such support reported better overall QoL outcomes as compared to those with either poor or a complete lack of support from family and/or friends.

**Factors Not Otherwise Categorized.** All of the studies in the review sample that investigated relations between sleep disturbance and QoL in PWE were conducted in LMICs (see Table 19). As noted earlier, all 4 of those studies observed that difficulties with obtaining quality sleep, in particular, were associated with lower QoL. Similarly, both LMIC-based studies assessing the relationship of ADLs to QoL found that an inability to perform such activities was associated with lower QoL.

**Table 18.**

*Studies Conducted in Low- and Middle-Income Countries Reporting on Psychosocial Factors as Determinants of Quality of Life in People with Epilepsy*

| Factor         | Studies                                                                                                                           | Significant Relationship with QoL Detected |                    |       | No. of Times Factor was Studied |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------------|-------|---------------------------------|
|                |                                                                                                                                   | Cross-Sectional Study                      | Longitudinal Study | Total |                                 |
| Stigma         | Abadiga et al., 2019;<br>Fawale et al., 2014;<br>Kumari et al., 2009;<br>Lua & Neni, 2011;<br>Saadi et al., 2016;<br>Viteva, 2013 | 6                                          | 0                  | 6     | 7                               |
| Social support | Au et al., 2002;<br>Gülpek et al., 2011;<br>Iwuozo et al., 2020;<br>Saburi et al., 2006;<br>Zou et al., 2014                      | 5                                          | 0                  | 5     | 5                               |

**Table 19.**

*Studies Conducted in Low- and Middle-Income Countries Reporting on Factors Not Otherwise Categorized as Determinants of Quality of Life in People with Epilepsy*

| Factor            | Studies                                                                                          | Significant Relationship with QoL Detected |                    |       | No. of Times Factor was Studied |
|-------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------|--------------------|-------|---------------------------------|
|                   |                                                                                                  | Cross-Sectional Study                      | Longitudinal Study | Total |                                 |
| Sleep disturbance | Alanis-Guevara et al., 2005; Camara-Lemarroy et al., 2017; Jovel et al., 2016; Kwan et al., 2009 | 4                                          | 0                  | 4     | 4                               |
| ADLs              | Au et al., 2002; Gordon-Perue et al., 2011                                                       | 2                                          | 0                  | 2     | 2                               |

*Note.* ADLs = activities of daily living.

## **Chapter 5:**

### **Discussion**

This systematic review aimed to provide an updated integration and evaluation of knowledge on the predictors of quality of life (QoL) in adults with epilepsy. A previous systematic review, conducted over a decade ago, mainly included studies from high-income countries (HICs) and did not compare findings from studies conducted in low-income countries (LMICS; Taylor et al., 2011). A more representative review was necessary in light of increasing acknowledgement of the context-specificity of epilepsy experiences as well as the relatively higher prevalence of epilepsy in LMICs. Therefore, this review aimed to also describe how the influence of QoL predictors might differ between LMICs and HICs.

The large number of articles identified by my initial screening of the literature indicates that extensive research activity on predictors of QoL in people with epilepsy (PWE) has been published, particularly in the last decade. The more recent literature identified several broad domains into which these predictors might be grouped: epilepsy-related factors, psychiatric comorbidities, sociodemographic factors, psychosocial factors, and other factors (e.g., sleep, cognition, and activities of daily living).

#### **Associations between Epilepsy-Related Factors and QoL in PWE**

Globally (i.e., when considering studies emerging from HICs and LMICs; in other words, when considering the entire review sample of 100 studies), epilepsy-related factors were the most commonly studied domain. The review findings suggested that these factors were commonly found to be significantly associated with QoL in people with epilepsy (see, e.g., Alsaadi et al., 2017; Maschio et al., 2017; Melikyan et al., 2012; Tefera et al., 2020). For instance, high seizure frequency was a strong predictor of poor overall QoL, and this was true for studies conducted in LMICs and those conducted in HICs (see, e.g., Gebre & Haylay, 2018; Ogundare et al., 2021; Tsigebrhan et al., 2021). One way to account for this association is to note that higher seizure frequency can be debilitating in that it can limit the scope of daily activities and increase apprehension of experiencing a seizure (Pham et al., 2017). Furthermore, experiencing a greater number of seizures likely comes with more frequent pre- and post-ictal complications (e.g., confusion) that are disruptive to everyday life (Baranowski, 2018a). These restrictions on ADLs can have the knock-on effect of dampening economic prospect, which would further affect QoL.

In terms of relations between other epilepsy-related factors and QoL in PWE, there were some differences between LMICs and HICs both in terms of the extent to which individual factors were studied, and, sometimes, the effects of those individual factors on QoL. Notably more studies conducted in HICs than in LMICs investigated the relationship between epilepsy surgery and QoL. Most of these studies were longitudinal, tracking QoL in adults with medically intractable epilepsy from pre- to post-surgery. The relatively small number of LMIC-based studies might be explained by the fact that access to and use of surgery to treat medically intractable epilepsy is relatively less common in those countries (Mansouri et al., 2019). Nonetheless, studies conducted in both HICs and LMICs showed that undergoing epilepsy surgery was strongly associated with better QoL. This outcome is likely due to the fact that seizure freedom is often the result of such surgery, and that this represents a significantly improved QoL for patients whose epilepsy was otherwise intractable.

Other epilepsy-related factors that were investigated included seizure worry, seizure severity, and seizure type and aetiology. In both LMIC- and HIC-based studies, increased seizure worry was associated with lower QoL. This association is unsurprising, given that the knowledge that a seizure can occur at any time or place and sometimes without warning can be debilitating and a major point of anxiety (Landazuri et al., 2020). Similarly, both LMIC- and HIC-based studies indicated that increasing seizure worry and seizure severity impacted negatively on QoL in PWE.

These associations are understandable considering that severe seizures are likely to cause the most disturbance of patients' physical, emotional, and social wellbeing (Akosile et al., 2021; Nasir et al., 2020; Tedrus et al., 2022). However, it is important to note that some patients experience fluctuations in seizure severity (Beniczky et al., 2020; Gaston et al., 2019; Martin et al., 2019; Roehl et al., 2019), but that none of the studies included in this review accounted for these fluctuations in their evaluation of how QoL may be affected by seizure severity. Thus, there remains a knowledge gap in terms of quantifying the seizure severity a patient experiences over time, how it fluctuates, and how these fluctuations impact on their overall QoL.

Regarding seizure type and aetiology, significantly fewer studies investigated how these factors affect QoL. Interestingly, the only studies that did examine this association were conducted in LMICs. HIC studies tended to note the numbers of patients in their samples who were experiencing generalized, focal, or unclassified seizures, but they went no further. LMIC studies, however, found that both seizure type and seizure aetiology were strongly associated with QoL (Alonso-Vanegas et al., 2013; Espinosa Jovel et al., 2016b; Giray et al.,

2009; Milovanović et al., 2014b; Ranjana et al., 2014). With regards to seizure type, most studies indicated that patients experiencing generalized seizures had better QoL than those experiencing other types of seizures. However, one study reported no significant differences in QoL between those with focal and generalised seizures (Ashjazadeh et al., 2014). Of note here is that no study in the review sample investigated patients who were experiencing a combination of types of seizures. Given this fact, and the fact that only a small number of studies examined the influence of seizure type in any case, more in-depth investigations are required in this regard.

The few studies that investigated relations the influence of seizure aetiology (which, recall, were all conducted in LMICs reported that patients with idiopathic epilepsy fared better in terms of QoL compared to those with epilepsy that had structural or metabolic aetiologies. Again, however, more in-depth investigations are required in this regard because of the relatively small number of studies in this pool.

Regarding medication-related factors, AED polytherapy was consistently, across LMIC and HIC studies, associated with poorer QoL. Patients treated with monotherapy tended to report better QoL than those who were being treated with multiple different ASMs. Of note here is more LMIC than HIC studies investigated this relationship and found a strong relationship between polytherapy and QoL. This pattern of data is perhaps expected because the use of polytherapy to treat epilepsy is more common in LMICs (Kwon et al., 2022; Wagner et al., 2020).

Moreover, multiple factors may account for AED polytherapy impacting poorly on overall QoL. Firstly, patients in LMICs are more likely to receive older ASMs as this dispensation is more cost-effective (Perucca et al., 2020), and older ASMs tend to produce more intense side effects than newer ASMs (Patsalos, 2016; Zaccara & Perucca, 2014), and the greater the experience of negative side effects, the lower the QoL (Blond et al., 2016; George et al., 2015; Welton et al., 2020). Secondly, the interaction of these drugs with one another may be distressing to patients receiving them (Johannessen & Johannessen-Landmark, 2010; Lee et al., 2019; Patsalos, 2016; Verrotti et al., 2020; Zaccara & Perucca, 2014). This distress may lead to non-adherence and, consequently poor seizure control (which, as noted earlier, is directly associated with lower QoL).

Relatedly, previous studies have identified polytherapy and poor adherence to medication as the strongest risk factors for poor sleep quality in PWE (Adem et al., 2020; N. C. Chen et al., 2011; Giorelli et al., 2013; Roshan et al., 2017; Turaga et al., 2016). Disrupted sleep patterns are to have significant physical and mental consequences (Carpi et al., 2022;

Charest & Grandner, 2020; McCallum et al., 2019; Seow et al., 2020) and, therefore, to result in poorer QoL.

Regarding other medication-related factors, only two studies in the review sample (both, again, conducted in LMICs) investigated relations between QoL and unavailability of ASMs or lack of adherence to medication. Hence, there is a definitely lack of knowledge about how these factors might impact QoL. Filling that knowledge gap is particularly important for patients and clinicians in LMICs considering the high treatment gaps in those countries and the fact that unavailability of treatment and / or lack of adherence will almost certainly have a negative impact on QoL.

### **Associations between Psychiatric Comorbidities and QoL in PWE**

Overall, this review's findings indicated that the presence of psychiatric comorbidities impacted negatively on QoL in adults with epilepsy. In both the LMIC and HIC study subsamples, depression was the most frequently investigated of these comorbidities. Moreover in HICs, depression was the most frequently investigated factor throughout the other classes of predictors (more commonly assessed than seizure frequency). Anxiety was also commonly investigated, either in conjunction with depression or independently. Unsurprisingly, when significant relations were detected they indicated that PWE who experienced depression and/or anxiety symptoms had poorer QoL outcomes.

In the current literature, the high prevalence of depression and anxiety in PWE is associated with suboptimal patient outcomes, including lower QoL (Ertem et al., 2017b; Hermann et al., 2000; Lu et al., 2021; Tao et al., 2021). Moreover, a recent systematic review by Lu et al. (2021) found that in adults with epilepsy, major depressive disorder was the most common mood disorder with a prevalence of 24.2%. Post-traumatic stress disorder (PTSD) had the highest reported prevalence among anxiety disorders, at 14.2%, followed by generalized anxiety disorder at 11.1%. Other commonly observed psychiatric comorbidities included substance abuse (7.9%), bipolar disorder (6.2%), psychotic disorders other than schizophrenia (5.7%), obsessive-compulsive disorder (3.8%), and schizophrenia (1.7%). These epidemiological statistics confirm that the focus of QoL-epilepsy research on depression and anxiety is warranted. It is equally clear, however, that more studies should focus on other psychiatric comorbidities (primarily, perhaps, substance abuse and bipolar disorder).

Of note here is that the association between the presence of a particular psychiatric comorbidity and QoL may vary based on seizure type and treatment responsiveness

(Hermann et al., 2000; Kováts et al., 2017b; Pulsipher et al., 2006b; Tao et al., 2021). For instance, in the Lu et al (2021) review, partial seizures were associated with a higher prevalence of depression than generalized seizures. Furthermore, the review noted that it was quite difficult to establish the directionality of the relationship between epilepsy and psychiatric disorders; it is almost certain, in fact, that there are bidirectional relations.

### **Associations between Sociodemographic Factors and QoL in PWE**

In the overall sample of reviewed studies and in the subsample of HIC studies, psychiatric comorbidities were the second-most studied determinant factors of QoL in PWE. In LMIC-based studies, however, sociodemographic factors were the second-most studied such determinants. These sociodemographic factors included age, gender, education, household income, employment status, marital status, and the ability to drive oneself.

Overall, the findings from the review sample indicated that being older, having a relatively low household income, having attained a lower level of education, being unemployed, being single/widowed/divorced instead of being married and being unable to drive oneself were all predictive of poorer QoL. Findings were inconclusive with regards to gender. The findings from both LMICs and HICs were mixed (three studies found that being female was associated with worse QoL, whereas one study found this association in males and the four other studies investigating this factor reported no significant gender-based differences in QoL).

In the previous systematic review by Taylor et al. (2011), some of the factors mentioned above were found to be either of no significance to QoL (age, gender, marital status) or to have an unclear predictive influence (education and employment status). The findings from the current updated systematic review indicate that, particularly in LMICs, sociodemographic factors can have a significant impact on QoL in PWE. Thus, interventions to improve QoL in adults with epilepsy in these countries must focus on ensuring that these factors are taken into consideration. For example, job security is precarious in PWE – many are insecurely employed (e.g., working on 3-month contracts), and overall they are disproportionately unemployed as compared to the rest of the population (Chrastina & Vysloužilová, 2018; Dorota et al., 2014; Marinas et al., 2011; Pirker et al., 2021; Pivoriene & Sediene, 2019; Zhao et al., 2021). So, in order to improve QoL more work must be done to address the systemic factors (e.g., education, employment) that can be targets for intervention, rather than simply noting that there are personal factors (e.g. age) that are beyond the control of the clinician/researcher.

### **Associations between Psychosocial Factors and QoL in PWE**

Within this domain, stigma and social support were the most widely studied factors. In HICs both these factors were jointly the most frequently investigated. However, in LMICs stigma was the most frequently investigated of the two, and findings were consistent in suggesting that experiencing higher levels of stigma is associated with lower QoL. These findings are unsurprising: Stigma restricts the personal, educational, economic, and social opportunities of PWE, and therefore has a profound impact on QoL. Interestingly, most studies did not specify what type of stigma they were investigating. Because epilepsy stigma has three different levels (internalized, interpersonal, and institutional; Jacoby & Austin, 2007), this may be an important distinction to make. Internalized stigma pertains to stigmatizing oneself, interpersonal stigma involves being stigmatized by others, and institutional stigma is systematic (e.g., as manifested in employer hiring practices). More studies need to be conducted to evaluate how each type of stigma affects QoL, and to outline potential differences in these effects. The findings from these studies are potentially important in terms of intervention design. For instance, if internalized stigma has larger negative effects than other forms of stigma, intervention programs can focus on interpersonal therapies that attempt to change the patient's perspective on themselves and their relation to epilepsy.

In terms of the social support factor, findings were also consistent across LMICs and HICs. Social support was directionally proportional to QoL: the greater the social support (e.g., from friends and family) the patient reported experiencing, the better the overall QoL. Because epilepsy can be a disabling condition, it is strongly beneficial for one to have a strong support system in order to manage the illness and its consequences. Strong social support systems in PWE are associated with better mental wellbeing, the adoption of better coping mechanisms, and reductions of depression, anxiety, and stress (Keikelame et al., 2017b). All of these have a direct influence on overall QoL.

### **Associations between Factors Not Otherwise Categorized and QoL in PWE**

Prior to conducting the systematic search and literature screening, only factors that could be classified within one of the four domains addressed so far in this chapter (i.e., epilepsy-related factors, psychiatric comorbidities, sociodemographic factors, and psychosocial factors) were considered to have an effect on QoL in PWE. This consideration was consistent across LMIC- and HIC-based studies. However, after initial screening and review of potentially eligible studies, it became apparent that a few other factors not easily

categorized as being part of the established domains had been found to be related to QoL in PWE.

Four studies (two conducted in LMICs and two in HICs, with findings consistent across sites) found that the inability to perform one's ADLs was associated with poorer QoL. Although few studies have investigated this association, it is perhaps important to shore up this literature given that inability to perform ADLs not only affects mental wellbeing but affects personal independence.

Another four studies conducted in LMICs investigated associations between sleep disturbances and QoL in PWE. Findings suggested that difficulties obtaining quality sleep were associated with lower QoL. Poor sleep quality in PWE may be commonplace, accounted for by the presence of nocturnal seizures or other epilepsy-related sleep disruptions. Hence, the fact that so few studies examine the effects of this factor on QoL is surprising. Furthermore, sleep and QoL might have a bidirectional relationship where one is equally capable of influencing the other; this is established in other clinical conditions, and should be examined in PWE. Again, it is important to shore up this aspect of the literature.

Lastly, two studies (both conducted in HICs) studied and reported a significant relationship between performance in specific cognitive domains and QoL. In one study, impairments in attention, learning, and processing speed were associated with lower QoL (Engelberts et al., 2002). The other study reported that impairments in executive functioning (e.g., performance on tests of set-shifting and response inhibition) were related to lower QoL (Ehrlich et al., 2019). These findings are unsurprising as the cognitive domains they investigated are commonly affected in PWE, especially those with uncontrollable seizures. Impairments in cognition can lead to poorer QoL as this can limit the ability of PWE to perform ADLs successfully, to achieve economic independence, and to maintain a job. Hence, it is somewhat surprising that LMIC-based studies have not attempted to replicate these results, particularly as findings may have direct implications for therapeutic interventions.

### **Limitations and Directions for Future Research**

Four primary limitations constrain the power of inferences one might make on the basis of the current findings. First, there was great variance in terms of the sample sizes of the reviewed studies ( $N$  range = 22 to 1931). Studies with smaller samples might have skewed the review's findings, given that they were likely statistically underpowered with increased likelihood of Type I error (Rusticus & Lovato, 2014). Thus, future research should ensure

that power is improved, and Type I error probability reduced by recruiting larger samples with equal numbers of people in each comparison group.

Second, it was common for investigators to study a heterogeneous sample composed of adults who varied in a number of ways, including age, type(s) of epilepsy, and phase of treatment or follow-up. These factors all have an impact on QoL, either individually or in interaction, and many studies did not attempt to (or did not have the statistical power to) tease out the main from the interaction effects. Future studies should either recruit larger samples that will allow them to analyse such interactions, or they should recruit more homogeneous samples and generalize findings only to specific portions of the population of PWE.

Third, the review sample included only studies conducted in English. Consequently, some valuable and insightful studies may have been excluded based on this language restriction, and the current review might be biased toward research conducted by English-speaking researchers. It remains unknown, therefore, whether other factors affecting QoL are being studied by researchers publishing in other languages. Given that this research is likely to be based in LMICs, future studies should endeavour to remove the language restriction and give a truly global perspective.

Finally, the current study compared LMIC-based studies to HIC-based studies but did not go further to investigate what are known differences in factors affecting QoL in urban versus rural contexts. This finer-grained perspective would have provided further knowledge on the context-specificity of how epilepsy is experienced. Future studies should adopt this perspective.

## Summary and Conclusion

Several individual factors (including the patient's sociodemographic profile, epilepsy-related clinical characteristics, psychiatric comorbidities, and psychosocial influences) affect how people with epilepsy perceive their general wellbeing and thus affects their quality of life. Understanding these factors and the ways in which they affect QoL is crucial in managing the condition and in developing interventions to enhance overall health and wellbeing in PWE.

The systematic review presented here provided a narrative synthesis that summarized, integrated, and evaluated current knowledge on the predictors (sociodemographic, clinical, psychiatric, psychosocial, and other) of QoL in PWE. To a certain extent, then, the current work represents an update on the review published more than a decade ago by Taylor et al. (2011).

The current review found that, globally, seizure frequency was the most commonly studied predictor of QoL. This finding is largely consistent with that of Taylor et al. (2011). In contrast to that systematic review, however, this study found that sociodemographic and psychosocial factors were strongly associated with QoL in PWE. Moreover, a few studies found that sleep, activities of daily living, and cognition were also associated with QoL outcomes. This difference in findings can be accounted by the inclusion of a larger sample of studies in the review, with a slightly disproportionate number of studies from LMICs and HICs. Hence, a critical aspect of the novelty of this study is that it compared the influence of these predictors in LMICs against that in HICs, and then made an attempt to identify the best predictors of QoL in PWE who live in LMICs.

For LMICs, the influence of sociodemographic factors on QoL was profound and showed that this factor is just as crucial in determining QoL in these populations as compared to the widely studied epilepsy-related clinical factor. Given that the burden of epilepsy is more profound in LMICs than in HICs, it is crucial that clinicians and researchers are aware of how the influence of these predictors might differ from one geographic region to another – such awareness will allow the design or adjustment of interventions to optimize them for use in different countries. Future research must ensure that more studies are conducted that depict the differences in QoL between rural, urban, and suburban areas within these countries. Such research will enable the design of interventions to be as clinically sound as possible.

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## Appendices

### Appendix A

#### List of Criteria Assessing the Methodological Quality of Reviewed Studies

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##### QOL Assessment:

- A A standardised or valid quality of life questionnaire is used.
- B A reason is given for choosing a certain questionnaire.

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##### Study Population:

- C A description is given of the sample's socio-demographic data (at least age, gender and educational status).
- D Description of epilepsy variables (at least type, age of onset, duration and treatment) is given.
- E Information is given about the ratio of non-responders versus to responders.
- F Participation and response rates for patient groups have to be described and be more than 75%.
- G Inclusion and/or exclusion criteria are considered (at least age and relevant co-morbidity).
- H The setting of requirement is given (i.e. general practice, hospital, occupational setting, nursing home, etc).
- I The process of data collection is described (e.g. interview or self-assessment, etc).

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##### Study Design:

- J The study size consists of at least 50 persons.
  - K The data are prospectively gathered.
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L

The follow-up period is at least six months.

M

Drop-out/loss to follow up <20%.

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QOL Results:

N

The results are reported for overall and for specific QoL domains (at least mean and standard deviation).

O

The results compared are between two groups or more (e.g. health population, groups with different severity of epilepsy or age).

P

The results are compared with at least two time points (e.g. longitudinally or pre-versus post treatment).

Q

Predictors are described using regression analyses or structural modelling.

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