

How to understand and address the cultural aspects and consequences of diagnosis of epilepsy, including stigma

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ABSTRACT – Epilepsy is one of the most prevalent serious neurological diseases. It is unique, being the only severe and disabling neurological disease that is fully treatable in the majority of cases, but on the other hand, associated with stigma, prejudice and discriminatory practices, which negatively impact people's everyday life in important areas, such as access to education, employment, marriage and social integration. For centuries, people with epilepsy (PWE) were stigmatized in all societies, with the consequences of prejudice and discrimination adding to the medical burden of the disease. Myths and misconceptions about this disease still occur, mostly in low-resources settings, however, in many industrialized countries, the knowledge regarding epilepsy is still limited in the population. The stigma is perceived as a negative attribute that is undesirable for the community to which the individual belongs. PWE are intrinsically undervalued, both by themselves ("felt stigma") and by the others. Actual discrimination by peers and institutions generates what is referred to as "enacted stigma". Misconceptions, stigma and negative attitudes towards PWE dramatically decrease quality of life, affecting the most sensitive areas, such as marriage, employment and driving. The Resolution 68.28 of the World Health Assembly (2015), the WHO-ILAE-IBE Global Report "*Epilepsy: a public health imperative*", advocates for strengthening and implementing national policies and legislation to promote and protect the rights of PWE, reducing misconceptions about epilepsy and improving access to care. Consolidated efforts are required from different organizations, public health managers, healthcare providers, PWE and their families to work together to improve socialization and quality of life of PWE. Educational programs and awareness to support activities among the general population, health service providers and PWE are the best way to reduce all types of stigma and discrimination.

Key words: epilepsy, stigma, discrimination, quality of life, marriage, employment, driving, non-adherence, educational programs



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PWE have suffered from prejudice and discrimination since ancient times. The number and absurdity of myths about this disease, many of which still exist, are no less surprising than their persistence in the minds of people. For example, the myth of the contagion of epilepsy existed from time immemorial to the middle ages, and in some countries -until the 18th century (De Boer, 1995). PWE considered as being contagious, crazy and possessed by demons, bewitched or punished by gods are typical misconceptions that are still prevalent in a number of countries, such as Zambia, Ghana, Cameroon, and Burkina Faso (ILAE, 2018).

At the beginning of the 20th century, patients with frequent seizures, status epilepticus, cognitive decline and psychosis were isolated from society on the assumption that they were incurable, unable to support a family and have healthy children. In the late 19th century, Samt (1876) called epilepsy the “death of the spirit”, claiming that epilepsy patients have the tendency to cruelty and excessive religiosity. It was believed that a patient with epilepsy should not expect to have a successful career, marriage or have children. The semiology of epileptic seizures (for example, impaired awareness and various automatisms) made the patients appear mentally ill, resulting in persistent fear from the public. However, in reality, epilepsy is rarely associated with intellectual disability. In contrast, there have been many outstanding PWE, for instance, Alexander the Great, Lewis Carroll, and Fyodor Dostoevsky.

In the 20th century, new drugs and non-drug treatments emerged, but, unfortunately, prejudice against PWE did not vanish, manifesting in legislations in various countries where patients were forbidden to marry or even called to be sterilized (WHO, 2019).

Prejudice and lack of knowledge lead to discrimination and stigmatization of PWE and even their family members. Fisher et al. (2000) reported stigma as the second worst consequence of an epilepsy diagnosis experienced by PWE (after fear and the unpredictability of seizures). Beyond the direct effects of stigma, such as loss of self-esteem and quality of life, its indirect consequences are even worse and manifest as social isolation, deterioration of health-seeking behaviour, and poor epilepsy control.

In this paper, we aim to provide the conceptual framework of stigma and social consequences of misconceptions and prejudice in epilepsy, illustrating cultural variations, in order to address *Learning Objective 2.1 of the ILAE Curriculum For Epileptology* (Blümcke, 2019).

Misconceptions of epilepsy: history

Epilepsy is believed to be a disease as old as mankind, and has attracted great public interest through the

millennia with the first descriptions in recorded history dating as far back as 2000 BC (Magiorkinis et al., 2010). The word “epilepsy” is derived from the Greek verb “epilambanein”, which means “to seize”. Over the ages, however, various names have been assigned to describe epilepsy.

For example, in the first reports found out in ancient Mesopotamian text, a PWE was thought to be attacked by the vengeance of Mene, the Moon goddess, and as such, an exorcism was the recommended treatment (Gottfried et al., 1805). Among the ancient Babylonians, seizures were thought to be caused by “the possession by demons” or “evil spirits” with several descriptions made of the various clinical presentations (Chaudhary et al., 2011). This finding is no different from what was noted in Africa, where epilepsy is still sometimes thought to be caused by ancestral spirits, “poisoning” or witchcraft. Also, in Christian biblical teaching, seizures are viewed as “the punishment from God” or a result of “possession by demons” requiring spiritual cleaning (Jilek-Aall, 1999).

In ancient Greek and Latin astrology, an evil position of the moon was linked to making a person convulse or prone to fits (Gross, 1992). The ancient Greeks also believed that epilepsy was a result of a divine punishment for sinners, with specific manifestations during the epileptic seizures attributed to the different deities, such as Poseidon if the patient screamed like a horse, or Cybele if there was gnashing of the teeth (Hippocrate, 1849).

In contrast, the author of the book “On the Sacred Disease” (a follower of Hippocrates, 400 BC), disputed the supposed divine or demonic origin of epilepsy. The author stated that epilepsy “*is no more divine than other diseases, it is hereditary, its cause lies in the brain, the releasing factors of the seizures are cold, sun, and winds which change the consistency of the brain. Therefore, epilepsy can and must be treated not by magic but by diet and medications*” (Chaudhary et al., 2011).

Chinese traditional medicine is based on the belief that epilepsy results from the blockage of acupoint channels by phlegm and salivation. Therefore, acupuncture is provided as treatment to balance the Yin and Yang and terminate convulsions by exposing acupoint channels and amending life energy, blood, and “waking” the brain (Xia, 2010). In Ayurveda medicine, a traditional eastern Indian healing system, still in practice to date, epilepsy is called *apasmara*, meaning loss of consciousness of the body caused by weakened nutrition of the brain or nerve blockage. Ayurveda medicine strives to treat epilepsy by clearing out the channels of the heart and the mind that may be blocked by the excess of *doshas* (humor fluids that circulate in the body that are responsible for creating physiological balance) (Karam, 2012).

Despite the fact that even in the second century, some ancient doctors and surgeons, such as Aretaeus the Cappadocian, proposed trepanation as a treatment for epilepsy, the view that demons and evil spirits or punishment from god might cause fits prevailed throughout the Middle Ages obstructing the progress of science and, consequently, medicine (Temkin, 1971; Wolf, 2014).

Indeed, in the history of epilepsy, there were iniquitous examples of discrimination against PWE. Among them was witch hunting during the Middle Ages, when women with seizures were identified as witches, tortured and persecuted (Masia and Devinsky, 2000). Eugenic tenets and campaigns, preventing PWE from having children, with forced sterilization of PWE in Nazi Germany according to the 1933 Law for the Prevention of Hereditarily Diseased Descendants, should be also noted (Cohen, 2010).

Excellent description of different periods of epilepsy history can be found in Temkin's *"The Falling Sickness"*, as well as in papers by Wolf (2014), Shorvon (2011), and many others.

Since mid 1900, there have been significant advances in the understanding of the aetiology of epilepsy, based on achievements in electroencephalography, neuroimaging, molecular genetics, and clinical and molecular biochemical techniques (Shorvon, 2011).

Despite these achievements over the years, people from some low-resource settings in Africa and Asia still believe that PWE are possessed by demons or evil spirits. Whereas misconceptions in the high-resource settings may be different, the knowledge regarding the causes of epilepsy is still limited (De Boer, 2010). It is no wonder then that these community perceptions have led PWE to be stigmatized, isolated and treated with contempt and pity based on the ignorance, prejudice and fears of the community. Culturally appropriate strategies are required to address the stigmatizing beliefs and develop new approaches that address stigma reduction and create positive affective reactions.

Stigma and epilepsy

Perceived as a negative attribute that is undesirable for the community to which the individual belongs, stigma has been extensively applied to seizures and epilepsy across the centuries, affecting all regions of the world (figure 1).

Definitions and concepts

PWE are intrinsically undervalued, both by themselves ("felt stigma") and others. Actual discrimination by

peers and institutions generates what is referred to as "enacted stigma".

Felt stigma arises both from the experience of being discriminated against (Choi, 2011) and from self-evaluation in the context of culturally learnt expectations. It is not only the source of anxiety and depression, but initiates a vicious circle of self-isolation and loss of opportunities. PWE may feel that they do not deserve love or company, they may not be able to study or get a job, and may even feel that they do not deserve to live which might contribute to higher suicidal rates compared to the general population (Pompili *et al.*, 2005).

Enacted stigma, meaning actual discriminatory behaviour, is usually approached through investigation of attitudes of other people towards someone with epilepsy. This ranges from the exclusion from sports, social and educational activities, to using the disease as a negative attribute with regards to evaluating candidates for an academic or work position, firing someone because of a seizure, or direct discrimination including bullying and isolation (Bandstra, 2008). Institutionalized stigma is a type of enacted stigma, in which governmental institutions (insurance and educational institutions, from schools to universities, ministries of health and healthcare providers) establish laws or rules supposedly devoted to protecting people with certain conditions (epilepsy, in this case), but are, in fact, an additional source of discrimination. This can happen either because of the excessive nature of the limitations imposed by the rules, or because of an inability to provide alternatives for the full development of an individual's capacities and valuable integration into the community (WHO, 2019).

Determinants of stigma and attitudes towards PWE

One of the major challenges to unravel the magnitude and characteristics of stigma in a certain population is to develop an appropriate tool for its measurement. This difficulty arises from the complex nature of this concept and its components (felt and enacted stigma), cultural factors that must be taken into account and from the bias derived from personal interviews on sensitive topics. Multiple factors influencing stigma cause additional concerns for interpreting these results (*i.e.* socio-economic background, educational level, specific training, personality traits and other sources of stigma in a certain community, such as gender-race discrimination, *etc.*).

Many studies on stigma apply questionnaires to evaluate attitudes towards PWE, and sometimes simultaneously to assess knowledge, attitudes and practices (KAP). Although these questionnaires have topics in

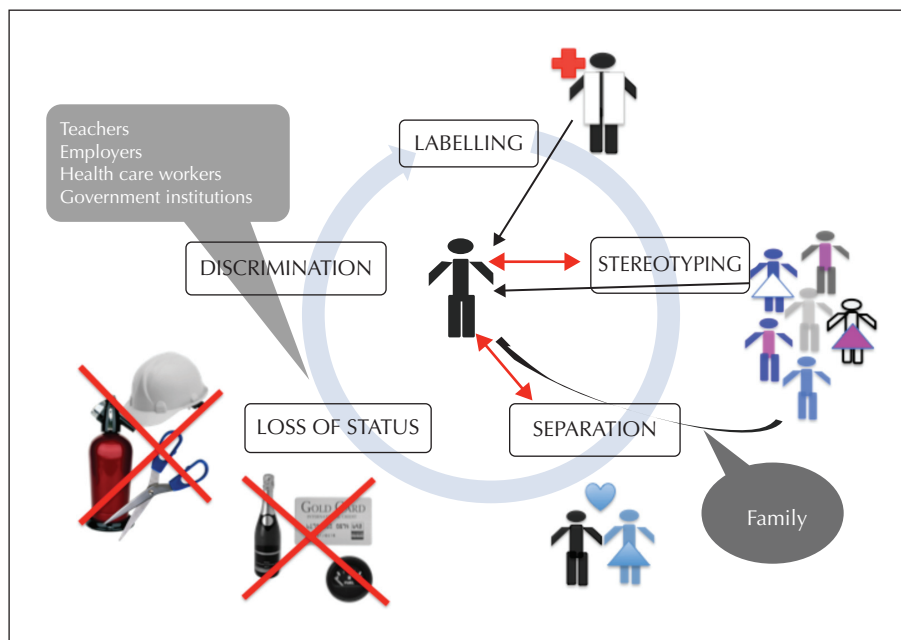


Figure 1. The origin of stigma in PWE relative to personal history and life experience (based on the stigma model proposed by Link and Phelan [2001]). Labelling occurs when the diagnosis is established, and a stereotype with negative attributes is then applied by people, increasing interpersonal distance (separation); this may affect family and intimate relationships. This social stigma adds to actual discrimination (enacted stigma, i.e. limitations on studying and working) to generate a global loss of status. Self-stigma (red arrows) enhances separation and stereotyping, leading to a vicious circle.

common, there is extensive variation among studies; ad-hoc instruments are often developed by research teams. These instruments are different for PWE, the general public, caregivers, and teachers. Some well-developed and validated tools were reported for adults (Antonak, 1990; Diiorio *et al.*, 2004) or children (Lowe-Pearce and Camfield, 2005; Martiniuk *et al.*, 2007) without epilepsy. Other instruments are used for adults (Jacoby, 1994; Dilorio *et al.*, 2006; Rao *et al.*, 2009; Taylor *et al.*, 2011) and children (Austin, Huberty, 1993; Heimlich *et al.*, 2000; Austin *et al.*, 2004) with epilepsy or with chronic illnesses including epilepsy.

Most studies on the topic have explored *felt stigma*, that was identified in 25-66% of adults, 17-41% of children and up to 71% of adolescents, in different countries. These studies confirmed the association with anxiety, depression (Kwon, Park 2013), lower self-esteem, self-concept and mastery across all age groups. Scarce knowledge about epilepsy, low levels of social support and low quality of life were also associated with increased internalized stigma (Leaffer *et al.*, 2014). In adults, other determinants for high-level felt stigma were: younger age (below 50 years old), lower educational level (Ghanean *et al.*, 2013), unemployment (Bellon *et al.*, 2013), and adverse effects of antiepileptic medication (Jacoby, 1994, Taylor *et al.*, 2011). In children and adolescents, felt stigma also correlated with younger age (below 12

years old), behavioural problems, higher seizure frequency (Heimlich *et al.*, 2000; Austin *et al.*, 2004), and shame of having seizures in public (Austin *et al.*, 2004). Patients with drug-resistant epilepsy showed higher levels of felt stigma (Viteva and Semerdjieva, 2012), and a decrease in seizure frequency or achieving remission (through medication or epilepsy surgery) was shown to be the best instrument for reducing felt stigma (Bautista *et al.*, 2015).

Felt stigma was shown to be extended to parents of children with epilepsy, and found to be associated with depression, perceived behavioural problems of the child and lack of self-confidence on how to manage epilepsy (Austin *et al.*, 2004). Those expressing a lower level of stigma were less worried about their children's seizures and shared more leisure activities with them. On the other hand, in some cultures, close relatives are a source of further enacted stigma, isolating and concealing the patient because of shame in order to protect the rest of the family from social isolation and blame.

Negative attitudes and behaviours towards PWE have been a longstanding problem in many countries, despite many attempts to enhance awareness and decrease fear and misunderstanding of epilepsy (table 1). The level of *enacted stigma* varies according to living in rural vs urban settings, religious beliefs and practices, female gender, lower social status and

Table 1. The attitude towards PWE in different countries (as a percentage of positive response) (modified from Guekht *et al.* [2017]).

	Austria (Spatt <i>et al.</i> , 2005)	Croatia (Bagić <i>et al.</i> , 2009)	Hungary (Mirnics <i>et al.</i> , 2001)	Czech Republic (Novotna and Rektor, <i>al.</i> , 2002)	Greece (Diamantopoulos <i>et al.</i> , 2006)	Turkey (Degirmenci <i>et al.</i> , 2010)	Russia (Guekht <i>et al.</i> , 2017)*	Korea (Kim <i>et al.</i> , 2003)	Hong Kong (Fong and Hung, 2002)	Thailand (Saengpattachai <i>et al.</i> , 2010)	Ethiopia (Fekadu <i>et al.</i> , 2019)
I have heard about epilepsy	89	97	89	94	94	-	77	93	58	81	-
I personally know someone with epilepsy	40	56	41	-	39	-	44	55	19	19	11
Epilepsy is curable	-	-	-	-	22	-	38	47	48	-	-
Epilepsy is a mental illness	11	3	17	29	15	7	24	34	10	32	-
I agree that PWE should be educated normally	89	93	84	87	86	-	53	50	89	83	-
I agree that a PWE may marry	85	-	59	-	34	12	43	6	68	56	6
I agree to take on a PWE for a permanent job	84	-	62	74	73	65	-	48	-	53	7

"-" — not assessed. * Standardized data.

educational level, and familiarity of epilepsy (Neni et al., 2010; Baker et al., 2018).

Multiple factors influence *attitudes towards PWE*. The media contribute to the misrepresentation of information about epilepsy. According to Krauss et al. (2000), a search through English-language printed media between 1991 and 1996 revealed 210 publications on epilepsy: by physicians (43%), public sources, such as police and legal spokespersons (22%), patients and their families (18%), epilepsy associations (11%), and corporate sources, predominantly pharmaceutical manufacturers (5%). Thirty one percent of the publications contained incorrect information, including scientific inaccuracies (14%), severe exaggeration of treatment benefits (9%), and an exaggeration of the risk of seizures, etc. (5%). Most celebrities with recurring seizures denied having epilepsy. Seizures were described with demonic imagery in 6% of the reports. The term “epileptics” was used in 45% reports despite the recommendation by the United States Epilepsy Association to avoid it as this has been related to increased negative attitudes (Fernandes et al., 2009).

Negative attitudes towards PWE have been associated with lower educational level worldwide (Antonak, 1990; Dilorio 2006; Chung et al., 2010; Neni et al., 2010; Guekht et al., 2017). For instance, people with a university degree were less frequently reported to be against their child marrying a PWE (Guekht et al., 2017). Healthcare professionals in certain areas of expertise have also been shown to have different attitudes: doctors and nurses specialized in neurology showed more positive attitudes towards epilepsy than those without expertise in neurology based on a recent study in southern China (Yang et al., 2019). Moreover, younger non-neurologist physicians with fewer years of clinical practice tended to be more negative towards PWE, and nurses were more negative towards epilepsy compared to doctors.

A relatively low level of understanding of essential aspects of epilepsy in the general population was demonstrated by a study in Russia. Four out of ten respondents ranked epilepsy as the “least preferred” among the following other five chronic conditions: disability, depression, a disfigured face (burns or scars), cardiac problems, and diabetes. The association of educational level with the understanding of epilepsy was also shown (Guekht et al., 2017).

A number of studies have addressed the long-term development of public attitude towards PWE. According to a long-term follow-up study in the Czech Republic, the quality of information about epilepsy increased significantly between 1981 and 1998, 1981 and 2009, and 1998 and 2009. Gradual improvement in knowledge about epilepsy was demonstrated (Novotná et al., 2017).

Clinical vignette

A 37-year-old male patient presented to the outpatient epilepsy clinic. He was born in a small village and lives in a rural area close to that village. He did not complete secondary school. There was no relevant past medical history, apart from epilepsy. He was told by the family members that he had an aunt with epilepsy, but he could not provide any additional data.

His seizures started during the first year of life. His parents had passed away, and no other informants were present. He did not remember much about the characteristics of his seizures during childhood and adolescence, but he cannot remember a single year of his life without seizures. At present, seizures normally start with either epigastric discomfort or an unpleasant, unexplained smell. In most cases, they are followed by impairment of consciousness and when he is told he behaves in a certain way, he cannot remember. These seizures frequently evolve to convulsions (his best estimation is six per month), usually followed by prolonged confusional states. He recognized a lack of antiepileptic medication (non-compliance), sleep deprivation, stress and fever as precipitating factors to his seizures. No history of status epilepticus was identified. However, he described a history of seizure-related injuries (he has scars due to burns in his left hand and right leg).

He complained of frequent seizures that have not improved under trials of different antiepileptic medications (carbamazepine, lamotrigine, levetiracetam, and clonazepam) at adequate doses and in different combinations, without relevant adverse events. There was no history of cognitive decline or psychiatric comorbidities. The neurological examination was normal.

He does not work at present due to frequent seizures, moreover, he lives in isolation because his only sister is afraid of his seizures and he is forbidden from visiting his nephews. He came with a friend to get advice on the possibility of epilepsy surgery.

Comments- *Negative social consequences and stigma associated with epilepsy can be clearly identified in this clinical case:*

- 1. *Unemployment due to persistent seizures.*
- 2. *Social isolation and inability to have a romantic partner throughout his life.*
- 3. *Insufficient knowledge and institutional support act as perpetrators of non-compliance and poor seizure control.*
- 4. *Enacted stigma underlies the isolation from his own family (sister, nephews).*

A study in the USA (Cui *et al.*, 2015) showed that a significantly higher percentage of adults in 2013 than in 2005 strongly or moderately agreed that PWE “can do anything as well as anyone else and can cope with everyday life”.

Strategies to decrease stigma

Global awareness campaigns aimed at combating stigma associated with epilepsy have been launched and sustained for decades, but effective changes in public attitudes are still to be achieved.

Whatever intervention is planned, it has to be targeted to specific groups, with in-depth analyses used to inform and guide the specific foci for the intervention. Interventions need to take into account local conditions and be multifaceted in approach.

Interventions tested so far to decrease stigma are focused on education. Most educational interventions were developed on specific groups and have shown a favourable change in knowledge and attitudes related to epilepsy, when evaluated immediately after the intervention. Delayed evaluations were rarely performed. More sustained effects were found with more prolonged exposure to the topic or by using interactive strategies (Atadzhanov *et al.*, 2016).

On the other hand, a peer self-support group intervention achieved a significant decrease in felt stigma (Elafros *et al.*, 2013).

General recommendations for physicians and health-care providers to address stigma in PWE are:

- To discuss felt and enacted stigma at first visit and periodically with all patients.
- If a formal evaluation tool is used, consider the target population for which it was designed and available information on its validation in the particular country/culture.
- To contribute to self-empowerment of PWE through education, both providing accurate information and guidance to trustworthy resources.
- To be able to deliver professional counselling and support as necessary in the context of the community or educational or work settings.

Social aspects: marriage, employment, driving

Misconceptions, stigma and negative attitudes towards PWE dramatically decrease quality of life (QOL), affecting the most sensitive areas, such as marriage, employment and driving (*table 1*).

Marriage

According to Kaplan and Kronick (2006), marriage is associated with longer survival; having never been married is the strongest predictor of premature mortality. It seems that marriage might help chronically ill persons to cope more effectively with the disease, retaining better psychological and physical health (Kiecolt-Glaser, 2001).

At the same time, PWE of both genders with seizure onset within matrimony demonstrated higher levels of anxiety and perceived stigma versus those diagnosed with epilepsy prior to marriage (Deli *et al.*, 2019).

The likelihood of marriage is low for PWE and divorce is high, due, in part, to legislation restricting marriage among PWE throughout the world which is still the case in several countries, especially for arranged marriages (Singh *et al.*, 2018). Until 1999, India was the only country in the world where marriage could be solemnized on the condition that neither party suffered from insanity or epilepsy (according to the Hindu Marriage Act, 1955 and the Special Marriage Act, 1958). Moreover, according to an amendment of this act (passed in 1976), a person subjected to recurrent attacks of insanity or epilepsy could not have a legally valid marriage, and such a marriage would have been annulled.

This discriminatory law was withdrawn in 1999, and today, PWE can have a legally valid marriage, and epilepsy can no longer be claimed as grounds for divorce. However, for marriage and epilepsy in India, the reality is in stark contrast to legal jurisdiction. It is not uncommon to hear about cases of absolved marriages, and estrangement/ abandonment after a single episode of seizure. Not surprisingly, it is the women who are at the receiving end of mistreatment, but very rarely men also struggle with failed marriages due to epilepsy. The primary reason for failure of marriage in cases of epilepsy is due to a PWE or the family choosing not to disclose this medical condition before marriage. Consequently, such a revelation after marriage is taken to be a breach of trust and it is not uncommon to hear about women being sent home by the in-laws. In some unfortunate cases, domestic violence and harassment have also been encountered. Even educated women from well-to-do families have been victims of the same practice.

As recourse, doctors often suggest that not hiding their epilepsy status from potential marriage partners is a good strategy. However, this can be a double-edged sword given the highly prevalent social stigma, myths and misconceptions surrounding epilepsy. Patients, especially women, often complain that nobody wants to marry them because they have epilepsy and this holds true even when the seizures have ceased to occur completely. Patients also worry whether epilepsy could trickle down to their

children and whether pregnancy would be safe with antiepileptic medications. Thus, PWE of marriageable age often require extensive counselling and emotional support.

However, in India and other countries, there are many women and men with epilepsy who have gone on to have successful relationships and raised healthy children. In all these “success stories”, a positive attitude from both the patients as well as their families plays a huge role.

Employment

According to many studies, driving, independence and employment are the most significant predictors of QOL in epilepsy (Gilliam *et al.*, 1997; Melikyan *et al.*, 2012). PWE can be legally employed in most professions barring those involving driving motorized vehicles including flying airplanes, working at unprotected heights or with open and/or moving machinery and live electric cables, operating trains and other related duties, as well as certain jobs in the defence services. However, PWE are frequently unemployed (globally, the mean adjusted employment rate is 58% [Wo *et al.*, 2015]) and under-employed (12-50% PWE in the USA are unemployed [Krumholz *et al.*, 2016]). Employers are often unwilling to bear any financial costs that may come from employing a PWE, *i.e.* insurance costs, paid sick leave, *etc.* As a result, PWE often do not inform their co-workers and employers about their disease, especially in cases of less frequent seizures. The main reason for this is the fear of losing their job and being stigmatized and treated unfairly (Majkowska-Zwolinska *et al.*, 2012).

Depression, anxiety, and enacted and felt stigma are significant factors associated with unemployment status. Mobility and marital status (especially in Asian countries) seem to increase the chance of employment. In contrast, PWE with uncontrolled seizures or seizure onset during childhood are more likely to be unemployed (Gilliam *et al.*, 2003; Fiest *et al.*, 2014; Wo *et al.*, 2015).

The guidelines developed by the International Bureau for Epilepsy’s Employment Commission (1989) state that in cases with restriction regarding particular types of employment, decisions must be based on fair and individual assessments of both the demands associated with the work and those of PWE concerned, otherwise such restrictions are discriminatory.

Physicians, neurologists and epileptologists should be aware of the legislation on employment of PWE in their country, and be ready to advise PWE and employers based on working conditions and the specific manifestations of a patient’s seizures.

Driving

The ability to drive enables a high degree of social and personal comfort, increasing the chance of employment, and is associated with better QOL (Joshi *et al.*, 2019). A ban on driving causes serious stress, especially for those patients who have been driving for a long time, and this correlates with depression (Tracy *et al.*, 2007).

Rules regarding driving for PWE vary among countries and, in the USA, vary among states (Krauss *et al.*, 2001; Krumholz *et al.*, 2016). In most European countries, PWE may be considered fit to drive after 6- to 12-month seizure-free intervals, but this period varies from three months (in some states in the US) to two years (in Australia, New Zealand, and Japan) (Krumholz *et al.*, 2016; ILAE, 2010; WHO, 2019).

However, a lifelong driving ban for PWE still exists in some countries (Ali *et al.*, 2011). For example, in India, according to the Motor Vehicle Act of 1939, the transport authorities are not permitted to give a driving license to anyone who has had a single seizure at any point in his/her life. Following a series of modifications, current regulations require all applicants to fill in an “application for declaration of physical fitness” form. Thus, according to current Indian law, a PWE cannot drive. This law was drafted with the safety of the passenger, as well as other vehicles and traffic and road conditions in India in mind.

The reality, again, contrasts the legal jurisdiction. It is not uncommon to hear that PWE, especially those with controlled seizures, are driving four/two-wheeled vehicles. Such behaviour is especially common among youngsters who are eager to explore without much concern about the risk this poses. Very rarely, there have been cases of patients with accidents or injury due to a seizure while driving.

In fact, the risk of a serious motor vehicle accident among PWE is reported to be 1.13 to 2.16-fold higher than in the general population (Tiller, 2007; Sundelin *et al.*, 2018). The risk due to driving for PWE depends on the frequency of seizures and other clinical parameters of epilepsy, and is clearly lower compared to that related to alcohol. According to Sheth *et al.* (2004), in the USA, only 0.2% of motor vehicle-related deaths during 1995-97 were associated with seizures compared to 30% which were alcohol related. PWE were reported to have a nearly two-fold increased risk of accidents, however, the general cause of most vehicle accidents was shown to be due to driver error (Taylor *et al.*, 1996; Krumholz *et al.*, 2016).

Taking into account the increased risk of accidents for PWE, in most countries various types of driving legislation restrictions have been developed, and the degree

of restriction usually depends on whether it is a question of driving for personal or professional reasons. For culturally-appropriate counselling on driving, both the regulations in a country and a balanced, individually tailored risk profile, taking into account the context regarding the relevance of this practice relative to culture and region and its impact on quality of life as well as available alternatives for transportation, should be considered.

Non-adherence and treatment gap

The epilepsy treatment gap is defined as the proportion of PWE who require treatment but do not receive it or are on inadequate treatment, expressed as a percentage of the total number with active epilepsy (Meinardi *et al.*, 2001). Adherence to antiepileptic drugs (AEDs) is defined as the extent to which patients take drugs as prescribed by their health-care providers (Osterberg *et al.*, 2005). The evaluation of the epilepsy treatment gap is vital for healthcare planning, both on a public health level as well as an individual level. According to Malek *et al.* (2017), the prevalence of significant medication non-adherence in epilepsy varied between 26% and 79%. There are several AEDs available which may reduce or eliminate seizures by 70-80%, but non-adherence to medication is a major problem in PWE. Hence, seizure control in non-adhering patients can be challenging. Uncontrolled seizures lead to major morbidity and mortality, including not only physical injury, such as head trauma, fractures and burns, but also psychosocial problems, such as depression, anxiety disorders, decreased quality of life, and sudden unexpected death.

A meta-analysis of 27 studies, 12 from Africa, nine from Asia, and six from Latin America, revealed that the overall estimate of the treatment gap was 56/100 (95% CI: 31.1-100.0) (Mbuba *et al.*, 2008).

In India, there is a link between the treatment gap and non-adherence to treatment. The magnitude of the epilepsy treatment gap ranges from 22% (for those in urban regions with average income) to 90% (for those in villages) (Meyer *et al.*, 2010). This can be partly explained by the fact that in India, Kenya and some other countries, especially in rural areas, people are often initially seen by traditional healers (who may use chants, incantations, confession and other rituals, or herbs, *etc.*), and only afterwards by primary care providers (WHO, 2019). Task-sharing models to train traditional medicine healers can be used to improve referral for appropriate health care (WHO, 2015a).

Most PWE do not receive appropriate treatment due to a lack of diagnosis and poor access to treatment as

they reside in resource-limited areas; this gap can be attributed to poor education, poverty, cultural beliefs, stigma, and poor healthcare infrastructure (Dixit *et al.*, 2017).

Many essential AEDs are not readily available in several regions, particularly in the public sector, and the price of these medicines in low-income countries (LIC) is several times higher compared with high-income countries (HIC) (Covanis *et al.*, 2015). Most governments have not set up national epilepsy programs or allocated funds to implement policies and plans for epilepsy despite recognizing its global burden (Meyer *et al.*, 2010). A large project aimed at addressing the community-based treatment gap in five provinces of rural China led to a reduction of stigma by 13% and significantly decreased costs to the health system (Wang *et al.*, 2008).

Unintentional non-adherence might be due to forgetfulness or an inability to follow treatment instructions due to poor understanding or impairment (e.g., poor eyesight), whereas intentional non-adherence arises when the patient rejects either the doctor's diagnosis or recommended treatment. Between 25% and 75% of PWE do not follow prescribed drug regimens, leading to uncontrolled seizures and reduced quality of life (Buck *et al.*, 1997).

A study found that a significant number of PWE in India discontinued epilepsy treatment within a year of therapy initiation because of poor knowledge regarding outcome following discontinuation (Das *et al.*, 2007). Based on the study published by Dash *et al.*, a significant difference in selfcare of PWE with and without comorbid illness was reported. PWE with comorbid illness had a lower self-care score compared to the other groups. This confirms the efficacy of structured educational programs in improving drug adherence in a cohort of PWE with low educational background (Dash *et al.*, 2015). Health education is a powerful tool which can have a positive impact on both drug adherence and self-management skills in order to address the treatment gap for PWE.

In Egypt, two studies found that the treatment gap in Al Kharga and Al-Quseir ranged from 61.5% to 83.8%. This is consistent with the report by the International League Against Epilepsy/International Bureau for the Epilepsy/World Health Organization in their introduction to the Global Campaign against Epilepsy, "Epilepsy out of the Shadows", stating that, globally, 85% of PWE are either inappropriately treated or not treated at all (El-Tallawy *et al.*, 2013; El Tallawy *et al.*, 2016).

In order to reduce the treatment gap in the context of limited resources, it would be necessary to specify the main causes of the treatment gap in a particular community, e.g. availability of phenobarbitone versus unwillingness to seek treatment, as well as specify the

most cost-effective resource for a particular situation, e.g. focusing on increasing specialized training versus improving training for primary healthcare workers (Bharucha, 2012).

Quality of life

Definitions and concepts

QOL is a theoretical construction that evaluates perceptions of the degree of wellbeing, both in different areas (social, mental, physical) and at different levels (personal, community). Although we all have an implicit understanding of what “quality of life” means, there is significant variation among individuals, including patients, healthcare providers and researchers.

Calman (1984) postulated that health-related quality of life (HR-QOL) could be used to evaluate the gap between expectations and actual experiences of an individual, within a particular time period. Later, the WHO (1995) defined HR-QOL as “*an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment*”.

Tools to evaluate QOL

The development of HR-QOL can be summarized in three stages (Levine, 2002): an early stage to ensure that QOL instruments are valid and reproducible; a second stage of integration of QOL as an outcome measure in clinical research (initially in cancer trials); and a final stage of evaluation of the potential impact of these QOL measurements on health-related decision-making, either at an individual or community level (health policies). Evaluation of QOL in epilepsy patients should include investigation of physical and somatic complaints, cognitive functioning, the psychological state, social performance, economical aspects, as well as adaptability to cope with seizures and treatment.

The development of QOL assessment tools for PWE began in the 1990s. The SF-36 Role-Physical scale, used to measure social and role functioning and mental health, led to a clearer distinction of patients suffering with a greater seizure-related impact (Ware, 1992). The Quality-Of-Life In Epilepsy-89 (QOLIE-89) includes 17 subscales addressing different domains, such as fear of occurrence of seizures, effectiveness of antiepileptic drugs, cognitive functions (attention, memory, etc.),

social aspects, among others (Devinsky et al., 1995). This tool was later validated in many countries and provided the basis for shorter questionnaires such as QOLIE-31 (Cramer et al., 1998) and QOLIE-10 (Cramer et al., 1996).

Internationally used questionnaires, such as SF 36 (Wagner et al., 1995) or QOLIE 31 (Cramer et al., 1998), have shown similar results worldwide. The SF-36 Role Physical scale, measuring social and role functioning and mental health, allows patients suffering from a greater seizure-related impact to be more easily identified. Some tools, developed in certain regions, have been designed to capture and identify additional factors and regional specificities (Wang et al., 2013). Specific scales for children have also been developed (Lai et al., 2015).

A lack of a “gold standard” diagnostic test, inter-individual and transcultural differences, as well as the multiplicity of factors determining QOL remain unsolved challenges.

Determinants of QOL in epilepsy

Quality of life in PWE has multiple determinants; the most important are discussed below.

Epilepsy-related variables: presence, frequency and/or severity of seizures, duration of the disease as well as adverse effects of antiepileptic drugs were found to be, as expected, determinants of QOL in epilepsy patients (Guekht et al., 2007; Taylor et al., 2011). On the other hand, the impact of specific epilepsy types is unclear.

Psychiatric and somatic comorbidities should be systematically explored in epilepsy patients. Anxiety and depression clearly influence self-perception of wellbeing, and have a relevant impact on QOL in this population, although the specificity of this finding is debatable. Psychiatric disturbances and psychological profiles may specifically impact on the results of any self-reported test for QOL. Therefore, the common interpretation of depression as the most relevant factor affecting QOL in PWE should be considered with caution (Melikyan et al., 2012; Keezer et al., 2016).

Many neurological diseases or conditions underlying the patients’ seizures may create cognitive and physical impairments (CNS neoplasm, head injury, stroke, encephalopathy) (Keezer et al., 2016), with additional impact on QOL.

Educational and employment status, number of antiepileptic drugs (AEDs) and AED side effects have been shown to have a heterogeneous effect on QOL across studies, while age, gender and marital status seemed not to be associated with HR-QOL (Taylor et al., 2011). No differences were found in QOL measures or determinants in younger versus older adults (Baranowski, 2018).

In the subgroup of drug-resistant epilepsy patients, AED side effects and depression were the most relevant determinants of QOL, rather than seizures themselves. Consequently, Luoni *et al.* (2011) proposed that actively treating depressive symptoms and optimizing pharmacotherapy to reduce adverse effects may be the most effective interventions to improve QOL in this subgroup of patients, particularly when they are not good candidates for other non-pharmacological interventions.

An improvement in QOL has been observed in the follow-up of patients referred for epilepsy surgery. Fewer concerns, improved mood, working status and ability to drive were the most frequent factors associated with this improvement (Gilliam *et al.*, 1999). Shifting of priorities after surgery would explain additional changes in QOL measures (Sajobi *et al.*, 2014). In children, seizure freedom was the main predictive factor for improved QOL after epilepsy surgery (Maragkos *et al.*, 2019).

Results of QOL studies in children with epilepsy and their parents are fairly heterogeneous. While some studies revealed relatively good QOL measures in both children and parents (Ferro *et al.*, 2017), a systematic review revealed that parents of children with epilepsy had a reduced quality of life, similar to parents of children with other chronic conditions; mothers were more affected than fathers (Puka *et al.*, 2018). QOL was inversely associated with socioeconomic status, anxiety and depression, but seemed not to be correlated with the child's seizure frequency (Ferro *et al.*, 2017; Puka *et al.*, 2018), although a recent study found that

children with higher seizure frequency and younger age at onset presented with lower QOL scores (Liu *et al.*, 2015).

The main reported determinants of both felt stigma and QOL are summarized in *table 2*. Available evidence shows a major effect of epilepsy-related factors on QOL, while demographic features seem to have more impact on stigma. Depression and anxiety significantly modulate the scores of both stigma and QOL scales.

Strategies to improve QOL

There are few published studies on interventions specifically designed to improve quality of life in PWE. Psychosocial interventions aiming to help cope with the diagnosis, addressing concerns and fears, as well as leading to a gradual empowerment of PWE should have a favourable impact on both patients and families (Wu *et al.*, 2014). Telemedicine has been shown to be a useful tool in a Malaysian study in which an SMS-based epilepsy education programme was associated with better QOL (Lua *et al.*, 2013).

If QOL is additionally considered as one of the targets for treatment in patients with chronic diseases and particularly in epilepsy patients, strategies and actions should be planned and executed for its particular improvement, both at the individual (medical assistance) and social (institutional policies) levels. Preventing seizures remains an important goal in the epilepsy clinic, as is the more recent treatment of depression. Support, academic and professional

Table 2. Most relevant determinants of, and their impact on felt stigma and quality of life in PWE, according to the literature.

		Felt stigma	Quality of life
Epilepsy-related factors	Seizures	Heterogeneous	Decreased
	Seizures frequency/ severity	Heterogeneous	Decreased
	AEDs adverse effects	Increased	Decreased
	Longer epilepsy duration	No data	Decreased
	Drug resistance	Increased	Decreased
Demographic factors	Age	Increased	No effect
	Low educational level	Increased	Heterogeneous
	Unemployment	Increased	Heterogeneous
Comorbidities	Anxiety / Depression	Increased	Decreased
	Behavioral problems	Increased	No data

orientation and anti-stigma measures may be additional components of our treatment algorithms (WHO, 2019).

The following are some general recommendations to address QOL in PWE:

- explore QOL determinants in all patients;
- if a formal QOL instrument is used, it should be carefully selected according to predefined goals and considering cross-cultural differences;
- the patient's perspective should be taken into account, and the existence of dynamic temporal shifts in personal priorities should be considered by healthcare professionals.

Conclusion

Epilepsy is the most common serious chronic neurological disease. Because of increasing life expectancy and the increasing proportion of people surviving epilepsy-provoking insults, such as birth injury, head trauma, cerebral infection and stroke, the number of PWE is bound to increase further around the world. Epilepsy carries a high burden of comorbidities, including depression, psychosis, anxiety, autistic spectrum disorder, cognitive impairment and migraine. Unlike the overwhelming majority of other diseases, epilepsy can be associated with stigma, prejudice and discriminatory practices, which negatively impact people's everyday life in important areas, such as access to education, employment, marriage and social integration. Importantly, epilepsy is fully treatable in the majority of cases.

In fact, as shown in the Pan American Health Organization (PAHO) Report (2013), only 36% of Latin America and the Caribbean countries had a program/plan of action to care for PWE and only 20% of the surveyed countries had national legislation related to epilepsy. However, legislation was updated since 2002 in Chile, Colombia, and Venezuela (PAHO/WHO, 2014; WHO, 2019).

In 2015, the World Health Assembly (WHA) approved unanimously Resolution 68.20 on the "Global Burden of Epilepsy and the Need for Coordinated Action at the Country Level to Address its Health, Social and Public Knowledge Implications". The Resolution highlights the need for governments to formulate, strengthen and implement national policies as well as legislation to promote and protect the rights of PWE. The importance of involving non-specialist healthcare providers to reduce the epilepsy treatment gap was declared. The need for reducing misconceptions about epilepsy and improving access and affordability of AED medicines was emphasized (WHO, 2015b).

The WHO-ILAE-IBE Global Report (2019) "Epilepsy: a public health imperative" presented a compre-

hensive picture of the impact that the condition has on PWE, their families, communities and societies. Across the world, PWE and their families suffer from stigma and discrimination. Many children with epilepsy do not go to school and adults are denied work and the right to drive or marriage. The violation of human rights faced by PWE around the world is unacceptable.

Consolidated efforts are required from different organizations, public health managers, healthcare providers, and PWE and their families to work together to improve socialization and quality of life of PWE. Educational programs and awareness to promote activities for the general population, health service providers and PWE are the best way to reduce all types of stigma and discrimination. □

Supplementary data.

Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.

None of the authors have any conflict of interest to declare.

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TEST YOURSELF



(1) Who is the author of the book “On the Sacred Disease”?

- A. A follower of Hippocrates
- B. A follower of Galen
- C. Homer
- D. Paracelsus

(2) What are the type(s) of stigma?

- A. Felt
- B. Partial
- C. Enacted
- D. Institutionalized

(3) Felt stigma is:

- A. Associated with anxiety and depression
- B. Not demonstrated among children
- C. Similar to internalized stigma
- D. Associated with a low quality of life

(4) Which of the following is true?

- A. Negative attitude towards PWE in the population is associated with lower educational level
- B. More than 80% of people worldwide accept that their child may marry a PWE
- C. More than 80% of people worldwide think that epilepsy is a mental illness
- D. In European countries, only 10% of employers agree to take a person with epilepsy on for a permanent job

(5) Which of the following determinant(s) is(are) reported to decrease QOL in PWE:

- A. Seizures frequency
- B. Smoking
- C. Generalised tonic-clonic seizures
- D. Anxiety/depression

(6) Resolution 68.28 of the World Health Assembly (2015) advocates for:

- A. Strengthening and implementing national policies and legislation to promote and protect the rights of PWE
- B. Reducing misconceptions about epilepsy
- C. Improving access to care
- D. Offering disability status to all PWE

(7) The Global Report "Epilepsy: a public health imperative" was created by the:

- A. European Academy of Neurology
- B. International Brain Research Organization
- C. WHO in collaboration with the ILAE and IBE
- D. International Committee of the Red Cross

(8) Which of the following is true?

- A. PWE may be considered fit to drive after 6- to 12-month seizure-free intervals in many European countries
- B. PWE may be considered fit to drive after at least 10 years of remission in many European countries
- C. The risk of a serious motor vehicle accident among PWE is not higher than that in the general population
- D. The risk of death due to PWE-related and alcohol-related motor vehicle accidents is equal.

(9) The employment status in PWE is:

- A. Equal to that in the population
- B. Higher when PWE are in remission
- C. Associated with the level of stigma
- D. Associated (in some countries) with marital status

(10) Tools to evaluate QOL in PWE include:

- A. QOLIE-89
- B. QOLIE-31
- C. Mini-Mental State Examination (MMSE)
- D. Montreal Cognitive Assessment (MOCA test)

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".