

## Review

## Psychosocial aspects of epilepsy: a wider approach

Marco Mula and Josemir W. Sander

**Summary**

Epilepsy is one of the most serious neurological conditions and has an impact not only on the affected individual but also on the family and, indirectly, on the community. A global approach to the individual must take into account cognitive problems, psychiatric comorbidities and all psychosocial complications that often accompany epilepsy. We discuss psychosocial issues in epilepsy with special focus on the relationship between stigma and psychiatric comorbidities. Social barriers to optimal care and health outcomes for people with epilepsy result in huge disparities, and the public health system needs to invest in awareness programmes to increase public knowledge and reduce stigma in order to minimise such disparities.

**Declarations of interest**

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Epilepsy is among the most common serious neurological conditions with incidence rates, in high-income countries, ranging between 40 and 70 per 100 000 persons per year and generally higher in young children and in the elderly.<sup>1–3</sup> In resource-poor countries, the incidence is usually much higher, often above 120/100 000/year, and in high-income countries, poor people also seem to have a higher incidence.<sup>4,5</sup> Poor sanitation, inadequate health delivery systems and higher risk of brain infections and infestations may contribute to this.<sup>1,6</sup> Prevalence studies have reported lifetime rates between 4 and 10/1000 in developed countries,<sup>2,7</sup> but data from resource-poor countries clearly suggest higher lifetime prevalence rates in the region of 23.2–32.1/1000<sup>8</sup> up to 57/1000 in some selected cases in rural areas.<sup>9</sup>

Many people with epilepsy live a normal life, but there is no doubt that the long-term prognosis of epilepsy is poor in many cases owing to increased morbidity and mortality.<sup>10</sup> This can be because of physical causes (e.g. fractures, scalding, bruising) as well as comorbidity with other systemic diseases<sup>11</sup> and increased psychosocial problems.<sup>12</sup> People with epilepsy, particularly if chronic, have an increased risk of premature death.<sup>6,13,14</sup> Sudden unexpected death, trauma, suicide, pneumonia and status epilepticus have been identified as being more common in people with epilepsy.<sup>14,15</sup> Symptomatic epilepsy may reduce life expectancy by up to 18 years.<sup>11</sup> Little is known about mortality in resource-poor countries as only a few adequate studies have been carried out to address this issue. Circumstantial evidence, however, suggests that the mortality rate is higher, helping to explain the discrepancy between the higher incidence and relatively low prevalence of active epilepsy in these countries.<sup>1</sup>

In May 2015, the World Health Assembly approved the WHO Resolution on the Global Burden of Epilepsy which provides a powerful tool to engage national governments into implementing effective actions to improve medical and social services for people with epilepsy, promote public awareness about epilepsy and allocate resources to epilepsy research.<sup>16</sup> The resolution calls on the WHO Secretariat to continue to lead and coordinate support to member states in addressing the global burden of epilepsy so that people with epilepsy can receive timely treatment and can benefit from educational and occupational opportunities, free from stigma and discrimination.

**The global perspective**

Apart from good seizure control, numerous factors are involved in quality of life (QoL) of people with epilepsy. It is now well recognised that other factors, such as comorbid depression and adverse effects of medications, are far stronger predictors.<sup>17</sup> Even in those in whom remission is achievable, if this is at the expense of unacceptable side-effects, adherence and QoL remain poor.

Successful integration of people with epilepsy into society is another important goal in epilepsy care. Educational level, intellectual ability, psychological stability, family and social support, the ability to overcome stigma, transportation and mobility issues, and employment opportunities are important determinants of successful integration.<sup>18</sup> The combination of these factors influences the life of people with epilepsy and what they consider meaningful.<sup>19</sup> For this reason, sport and leisure is becoming a new topic in epilepsy care and the International League against Epilepsy has a specific task force dedicated to Epilepsy and Sport and a report is now available.<sup>20</sup>

The QoL of people with epilepsy also appears to be related to the level of social support they receive through the various societal structures, including emotional support, informational support, instrumental support, appraisal, social companionship and affectionate support.<sup>21</sup> Social support mechanisms help people to overcome many of the difficulties they encounter. Individuals with good social support usually have an increased sense of control over their lives, enabling them to have better coping mechanisms for handling adversities.<sup>21</sup> It is now clear that people with the highest level of social support have significantly lower reported stigma scores.<sup>22</sup>

Epilepsy is a condition still highly stigmatised, and stigma greatly affects the QoL of people with epilepsy, leading to increased anxiety and depression and poor adherence with medication.<sup>23</sup> Unfortunately, even today, stigma is present in both high-income and resource-poor countries.<sup>1</sup> Stigma is not only responsible for poor QoL but also seems to play a role in mood and anxiety problems in both people with epilepsy and their caregivers. Perceived stigma is also responsible for increased rates of aggressive behaviour associated with depression and anxiety.<sup>24</sup> In low- and middle-income countries, 20% of mothers of children with epilepsy feel stigmatised because of their child's neurological condition,<sup>25</sup> and the caregiver's perception of burden, together with the level

of family function, are indirectly correlated with depressive symptoms in people with epilepsy via the mediating effect of caregiver depression.<sup>26</sup> This is also present in high-income countries where social aspects of stigma are an important determinant of anxiety and depression.<sup>27</sup>

The US Centers for Disease Control and Prevention, Epilepsy Program, pointed out that one in five of those with epilepsy lives alone and less than one in four live in households with two adults and children.<sup>28</sup> Adults with epilepsy living alone may be at increased risk of injury associated with uncontrolled seizures, mental distress associated with social isolation, lower QoL and early mortality. Stigma affects attitude towards epilepsy and the more intimate life domains such as cohabitation and marriage. A number of studies have shown that people with epilepsy are less likely to be married and people suffering from the enacted stigma are significantly more likely to get divorced in comparison with others.<sup>29–31</sup>

In resource-poor countries, stigma directly affects access to healthcare<sup>32,33</sup> and probably contributes to the discrepancy between the incidence and prevalence of epilepsy in lower-income regions of the world because diagnoses and clinical information are sometimes unreliable.<sup>34</sup> As already stated, perceived stigma is a problem even in high-income countries and is probably a major determinant of poor adherence with medications.<sup>23</sup> The information–motivation–behavioural skills model is a useful framework for understanding the pathways linking perceived stigma and adherence in the population with epilepsy.<sup>35</sup> Living in a European country with better health system performance and higher health expenditure per capita does not necessarily lead to a reduction in perceived discrimination, unless the public health system invests in awareness programmes to increase public knowledge and reduce stigma.<sup>36</sup> Low socio-economic status alone does not account for felt stigma, but depressive symptoms and poor social supports have the greatest impact on reported felt stigma in people with epilepsy.<sup>37</sup> Social barriers to optimal care and health outcomes for people with epilepsy result in huge disparities.<sup>38</sup> Disparities are a complex phenomenon that requires research and action. A systematic review has identified five domains of potential disparities in epilepsy care: access to medical and surgical treatment, outcomes following medical/surgical treatment, attitudes/knowledge about epilepsy, epidemiology and disability.<sup>39</sup> Data on these domains were, however, limited. For example, a US national study has shown that White people and those privately insured were found to be more likely to have surgery compared with their respective minority and publicly insured counterparts.<sup>40</sup> Furthermore, robust data collection and surveillance to identify points of intervention are urgently needed.

### Cognitive problems

About 40% of people with epilepsy aged between 4 and 15 years have one or more additional neurological problems, the most common being intellectual disabilities, speech and language difficulties or other specific cognitive disabilities.<sup>1</sup> In addition, intellectually disabled individuals are at an increased risk of behavioural problems.<sup>41</sup> Those severely affected have higher healthcare needs than others because of the concomitant presence of other neurological disabilities (i.e. feeding and swallowing difficulties, inability to walk).<sup>42</sup>

Epilepsy can have an impact on cognition in several ways. A degree of impairment in cognitive functions is frequently reported by people with epilepsy, ranging between 44% for difficulties in learning and psychomotor retardation to 59% for sleepiness or tiredness.<sup>43,44</sup>

In clinical practice, the majority of cognitive problems have multifactorial origins with many different variables often interlinked.<sup>44</sup> Cognitive dysfunction in epilepsy is generally regarded as either trait dependent or state dependent.<sup>45</sup> Trait-dependent dysfunction is a stable condition owing to the underlying brain disorder, while state-dependent dysfunction is a potentially reversible condition owing to modifiable factors such as anti-epileptic drugs (AEDs), seizure frequency and pattern, and psychiatric comorbidities.

Whether poorly controlled epilepsy is associated with progressive cognitive deterioration is still controversial, and this has been demonstrated only for some specific syndromes: mesial temporal lobe epilepsy and epileptic encephalopathies.<sup>46</sup> Different epileptic encephalopathies seem to have specific patterns of cognitive deficits such as short-term visuospatial memory problems, executive dysfunction and frontal lobe dysfunction in Unverricht–Lundborg syndrome,<sup>47,48</sup> language dysfunction in Landau–Kleffner syndrome<sup>49</sup> and poor language acquisition and visuospatial defects in Dravet<sup>50</sup> and Rett syndrome.<sup>51</sup> Finally, epileptic encephalopathies associated with frequent and uncontrolled seizures during sleep are characterised by memory and language problems.<sup>52</sup>

Cognitive problems are important in the long-term management of people with epilepsy, having an impact on QoL and everyday functioning.<sup>53,54</sup> A US study showed that a self-management intervention targeting cognitive dysfunction can significantly improve not only cognitive performance but also QoL.<sup>55</sup> Access to investigations, appropriate testing and review are important parts of the management.

Epilepsy has also a clear impact on relatives and carers of people with epilepsy, especially when seizures start during childhood. A Swedish study showed that mothers and fathers of children with drug-resistant epilepsy have poorer QoL compared with population norms, and symptoms of anxiety seem to be common especially among mothers.<sup>56</sup>

### Psychiatric problems

Psychiatric disorders are relatively frequent comorbidities in epilepsy, with a lifetime history identified in one in three people with epilepsy.<sup>57</sup> Mood and anxiety disorders are the most frequently reported<sup>58</sup> for both biological and psychosocial reasons. The burden of stigma, social limitations and discrimination in epilepsy lead to demoralisation and poor self-esteem, but the pathophysiology of epilepsy *per se* is interlinked with mood problems as demonstrated by neuroanatomical and neurochemical principles. The involvement of the temporal lobes<sup>59</sup> and the psychotropic effects of AEDs<sup>60</sup> seem to be relevant contributors to the increased rates of psychiatric problems in epilepsy but much remains unknown regarding the role of shared versus syndrome-specific variables and the role of cortico-subcortical networks. In addition, a number of epidemiological studies have suggested that the relationship between epilepsy and psychiatric problems is not necessarily unilateral but rather bidirectional and some people may present with a psychiatric disorder before the emergence of seizures.<sup>61–63</sup>

Depression is an important predictor of poor QoL,<sup>64</sup> seizure severity,<sup>65</sup> drug-resistance<sup>66</sup> and a poor outcome after epilepsy surgery.<sup>67</sup> Nonetheless, mood disorders are still under-recognised, under-treated and sometimes fully ignored, unless they are severe enough to reach medical attention. A number of reasons can explain the diagnostic delay and inaccuracy, including individuals' reluctance spontaneously to volunteer information about existing psychiatric problems, a paucity (or total lack) of training for the treating neurologist to recognise psychiatric symptoms and a lack of time in very busy clinics to screen for them. The result is

that epilepsy is often complicated and burdened by psychiatric disturbances or behavioural problems that are not adequately addressed or managed.

Suicide is a severe complication of untreated and undiagnosed depression. In the context of epilepsy, suicide is gaining increasing attention, and it has been recently reinvigorated by the Food and Drug Administration alert on a supposedly increased risk of suicidal ideation and behaviour in people taking AEDs.<sup>68</sup> In the general population, suicide is the 11th cause of death and the second in the age group between 25 and 34 years.<sup>69</sup> It is now evident that the overall risk of death by suicide is about three times higher in people with epilepsy than in the general population.<sup>70–72</sup> Several studies have attempted to identify reasons for this increased risk. In the general population, about 90% of people who die by suicide have at least one psychiatric disorder at the time.<sup>73</sup> Epilepsy is burdened by psychiatric comorbidities, but it is unlikely that such a problem is the only responsible element. A Danish study reported that the rate ratio of suicide in people with epilepsy is still doubled even after excluding people with psychiatric comorbidity and adjusting for various factors.<sup>72</sup> Some have suggested a link with temporal lobe epilepsy,<sup>70</sup> but a recent study, using retrospective and prospective methods, found no epilepsy-related factors.<sup>74</sup> The issue of epilepsy and suicide is still far from being elucidated, but it is likely to be multifactorial with biological, constitutional and psychosocial variables being implicated. It seems evident that suicide prevention is another relevant issue in epilepsy care deserving further clinical attention.

People with epilepsy historically have been considered to have an increased risk of developing psychotic disorders. Epidemiological evidence suggests that the incidence of non-organic, non-affective psychoses, including schizophrenia and schizophrenia spectrum disorders, is generally over-represented among people with epilepsy compared with the general population or other chronic medical conditions.<sup>75</sup> A family history of psychoses and a family history of epilepsy were significant risk factors for psychosis suggesting strong neurobiological underpinnings.<sup>76</sup> In general terms, psychoses represent a rare but serious complication of epilepsy. Close attention to the relationship between psychotic symptoms and seizure pattern is crucial to identify seizure-based phenomena such as postictal psychoses or the forced normalisation phenomenon.<sup>77</sup> Chronic interictal schizophrenia-like psychoses can be occasionally seen and deserve careful consideration.

The increasing attention to the psychiatric comorbidities of epilepsy brings to light the issue of double stigma. No studies investigated the relative contribution of the two conditions, epilepsy and mental health issues, but the problem of double stigma is well-known in other medical conditions such as obesity and mental health<sup>78</sup> or the comorbidity between HIV and tuberculosis<sup>79</sup> in low-income countries. Double stigma means double challenge and for this reason it becomes even more important to invest energies and resources.

Epilepsy is one of the most common neurological conditions, and it has an impact not only on the individual with epilepsy but also on the family and, indirectly, on the community. A global approach to the individual must take into account the cognitive problems and psychiatric comorbidities that often accompany epilepsy. The burden of epilepsy concerns not only the physical hazards of epilepsy but also the psychosocial consequences involved, such as the negative attitudes of people towards the patients, manifested as social stigma, social isolation and lack of support. Social barriers to optimal care and health outcomes for people with epilepsy result in huge disparities, and the public health

system should invest in awareness programmes to increase public knowledge and reduce stigma in order to minimise such disparities.

**Marco Mula**, MD, PhD, Atkinson Morley Regional Neuroscience Centre, St George's University Hospitals NHS Foundation Trust, London, UK; South West London and St George's Mental Health Trust, London, UK; Institute of Medical and Biomedical Sciences, St George's University of London, London, UK; **Josemir W. Sander**, MD, PhD, FRCP, Department of Clinical and Experimental Epilepsy, NIHR UCL Hospitals Biomedical Research Centre, UCL Institute of Neurology, London, UK; Epilepsy Society, Chalfont St Peter, UK; Stichting Epilepsie Instellingen Nederland – SEIN, Heemstede, The Netherlands

**Correspondence:** Josemir W. Sander, National Hospital for Neurology and Neurosurgery, Box 29, Queen Square, London WC1N 3BG, UK. Email: l.sander@ucl.ac.uk

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## References

- de Boer HM, Mula M, Sander JW. The global burden and stigma of epilepsy. *Epilepsy Behav* 2008; **12**: 540–6.
- Duncan JS, Sander JW, Sisodiya SM, Walker MC. Adult epilepsy. *Lancet* 2006; **367**: 1087–100.
- MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain* 2000; **123**: 665–76.
- Heaney DC, MacDonald BK, Everitt A, Stevenson S, Leonardi GS, Wilkinson P, et al. Socioeconomic variation in incidence of epilepsy: prospective community based study in south east England. *BMJ* 2002; **325**: 1013–6.
- Ngugi AK, Kariuki SM, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Incidence of epilepsy: a systematic review and meta-analysis. *Neurology* 2011; **77**: 1005–12.
- Sander JW, Bell GS. Reducing mortality: an important aim of epilepsy management. *J Neurol Neurosurg Psychiatry* 2004; **75**: 349–51.
- Forsgren L, Beghi E, Öun A, Sillanpää M. The epidemiology of epilepsy in Europe – A systematic review. *Eur J Neurol* 2005; **12**: 245–53.
- Bell GS, Neligan A, Sander JW. An unknown quantity – the worldwide prevalence of epilepsy. *Epilepsia* 2014; **55**: 958–62.
- Sander JW, Shorvon SD. Epidemiology of the epilepsies. *J Neurol Neurosurg Psychiatry* 1996; **61**: 433–43.
- Cockerell OC, Johnson AL, Sander JW, Shorvon SD. Prognosis of epilepsy: a review and further analysis of the first nine years of the British National General Practice Study of Epilepsy, a prospective population-based study. *Epilepsia* 1997; **38**: 31–46.
- Gaitatzis A, Sisodiya SM, Sander JW. The somatic comorbidity of epilepsy: a weighty but often unrecognized burden. *Epilepsia* 2012; **53**: 1282–93.
- Gaitatzis A, Trimble MR, Sander JW. The psychiatric comorbidity of epilepsy. *Acta Neurol Scand* 2004; **110**: 207–20.
- Lhatoo SD, Johnson AL, Goodridge DM, MacDonald BK, Sander JW, Shorvon SD. Mortality in epilepsy in the first 11 to 14 years after diagnosis: multivariate analysis of a long-term, prospective, population-based cohort. *Ann Neurol* 2001; **49**: 336–44.
- Neligan A, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. *Brain* 2011; **134**: 388–95.
- Gaitatzis A, Sander JW. The mortality of epilepsy revisited. *Epileptic Disord* 2004; **6**: 3–13.
- Covanis A, Guekht A, Li S, Secco M, Shakir R, Perucca E. From global campaign to global commitment: The World Health Assembly's Resolution on epilepsy. *Epilepsia* 2015; **56**: 1651–7.
- Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. *Epilepsia* 2002; **43**: 535–8.
- Hermann B, Jacoby A. The psychosocial impact of epilepsy in adults. *Epilepsy Behav* 2009; **15**(suppl 1): S26–30.

- 19 Bautista RED, Shapovalov D, Saada F, Pizzi MA. The societal integration of individuals with epilepsy: perspectives for the 21st century. *Epilepsy Behav* 2014; **35C**: 42–9.
- 20 Capovilla G, Kaufman KR, Perucca E, Moshé SL, Arida RM. Epilepsy, seizures, physical exercise, and sports: a report from the ILAE Task Force on Sports and Epilepsy. *Epilepsia* 2016; **57**: 6–12.
- 21 Amir M, Roziner I, Knoll A, Neufeld MY. Self-efficacy and social support as mediators in the relation between disease severity and quality of life in patients with epilepsy. *Epilepsia* 1999; **40**: 216–24.
- 22 Dilorio C, Osborne Shafer P, Letz R, Henry T, Schomer DL, Yeager K, et al. The association of stigma with self-management and perceptions of health care among adults with epilepsy. *Epilepsy Behav* 2003; **4**: 259–67.
- 23 Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimens. *Seizure* 1997; **6**: 87–93.
- 24 Seo J-G, Kim J-M, Park S-P. Perceived stigma is a critical factor for interictal aggression in people with epilepsy. *Seizure* 2015; **26**: 26–31.
- 25 Elafros MA, Bowles RP, Atadzhanov M, Mbewe E, Haworth A, Chomba E, et al. Reexamining epilepsy-associated stigma: validation of the Stigma Scale of Epilepsy in Zambia. *Qual Life Res* 2015; **24**: 1483–9.
- 26 Han SH, Kim B, Lee SA, Korean QoL in Epilepsy Study Group. Contribution of the family environment to depression in Korean adults with epilepsy. *Seizure* 2015; **25**: 26–31.
- 27 Peterson CL, Walker C, Shears G. The social context of anxiety and depression: exploring the role of anxiety and depression in the lives of Australian adults with epilepsy. *Epilepsy Behav* 2014; **34**: 29–33.
- 28 Program UCFDCAPE. Nearly one in five adults with active epilepsy lives alone based on findings from the 2010 and 2013 US National Health Interview Surveys. US Centers for Disease Control and Prevention, Epilepsy Program. *Epilepsy Behav* 2015; **51**: 259–60.
- 29 Friedrich L, Taslak M, Tomasovic S, Bielen I. How does the label ‘epileptic’ influence attitudes toward epilepsy? *Seizure* 2015; **33**: 54–9.
- 30 Riasi H, Rajabpour Sanati A, Ghaemi K. The stigma of epilepsy and its effects on marital status. *Springerplus* 2014; **3**: 762.
- 31 Tedrus GMAS, Fonseca LC, Pereira RB. Marital status of patients with epilepsy: factors and quality of life. *Seizure* 2015; **27**: 66–70.
- 32 Nehra A, Singla S, Bajpai S, Malviya S, Padma V, Tripathi M. Inverse relationship between stigma and quality of life in India: is epilepsy a disabling neurological condition? *Epilepsy Behav* 2014; **39C**: 116–25.
- 33 Ali DB, Tomek M, Lisk DR. The effects of epilepsy on child education in Sierra Leone. *Epilepsy Behav* 2014; **37C**: 236–40.
- 34 Mathern GW, Beninsig L, Nehlig A. Reasons for discrepancy between incidence and prevalence of epilepsy in lower income countries: Epilepsia’s survey results. *Epilepsia* 2015; **56**: 163–5.
- 35 Chesaniuk M, Choi H, Wicks P, Stadler G. Perceived stigma and adherence in epilepsy: evidence for a link and mediating processes. *Epilepsy Behav* 2014; **41**: 227–31.
- 36 Brigo F, Igwe SC, Ausserer H, Tezzon F, Nardone R, Otte WM. Epilepsy-related stigma in European people with epilepsy: correlations with health system performance and overall quality of life. *Epilepsy Behav* 2015; **42C**: 18–21.
- 37 Leaffer EB, Hesdorffer DC, Begley C. Psychosocial and sociodemographic associates of felt stigma in epilepsy. *Epilepsy Behav* 2014; **37C**: 104–9.
- 38 Szaflarski M. Social determinants of health in epilepsy. *Epilepsy Behav* 2014; **41**: 283–9.
- 39 Burneo JG, Jette N, Theodore W, Begley C, Parko K, Thurman DJ, et al. Disparities in epilepsy: report of a systematic review by the North American Commission of the international league against epilepsy. *Epilepsia* 2009; **50**: 2285–95.
- 40 Englot DJ, Ouyang D, Garcia PA, Barbaro NM, Chang EF. Epilepsy surgery trends in the United States, 1990–2008. *Neurology* 2012; **78**: 1200–6.
- 41 Caplan R, Austin JK. Behavioral aspects of epilepsy in children with mental retardation. *Ment Retard Dev Disabil Res Rev* 2000; **6**: 293–9.
- 42 Kerr M, Linehan C, Thompson R, Mula M, Gil-Nagal A, Zuberi SM, et al. A White Paper on the medical and social needs of people with epilepsy and intellectual disability: the Task Force on Intellectual Disabilities and Epilepsy of the International League against Epilepsy. *Epilepsia* 2014; **55**: 1902–6.
- 43 Meador KJ. Cognitive and memory effects of the new antiepileptic drugs. *Epilepsy Res* 2006; **68**: 63–7.
- 44 Mula M, Trimble MR. Antiepileptic drug-induced cognitive adverse effects: potential mechanisms and contributing factors. *CNS Drugs* 2009; **23**: 121–37.
- 45 Mula M. Cognitive dysfunction in patients with epilepsy: focus on clinical variables. *Future Neurol* 2015; **10**: 41–8.
- 46 Avanzini G, Depaulis A, Tassinari A, De Curtis M. Do seizures and epileptic activity worsen epilepsy and deteriorate cognitive function? *Epilepsia* 2013; **54**(suppl 8): 14–21.
- 47 Giovagnoli AR, Canafoglia L, Reati F, Raviglione F, Franceschetti S. The neuropsychological pattern of Unverricht-Lundborg disease. *Epilepsy Res* 2009; **84**: 217–23.
- 48 Ferlazzo E, Gagliano A, Calarese T, Magaudo A, Striano P, Cortese L, et al. Neuropsychological findings in patients with Unverricht-Lundborg disease. *Epilepsy Behav* 2009; **14**: 545–9.
- 49 Billard C, Fluss J, Pinton F. Specific language impairment versus Landau-Kleffner syndrome. *Epilepsia* 2009; **50**: 21–4.
- 50 Wolff M, Cassé-Perrot C, Dravet C. Severe myoclonic epilepsy of infants (Dravet syndrome): natural history and neuropsychological findings. *Epilepsia* 2006; **47**: 45–8.
- 51 Siegel MS, Smith WE. Psychiatric features in children with genetic syndromes: toward functional phenotypes. *Pediatr Clin North Am* 2011; **58**: 833–64.
- 52 Tassinari CA, Cantalupo G, Rios-Pohl L, Giustina ED, Rubboli G. Encephalopathy with status epilepticus during slow sleep: ‘the Penelope syndrome’. *Epilepsia* 2009; **50**(suppl 7): 4–8.
- 53 Reilly C, Atkinson P, Das KB, Chin RFM, Aylett SE, Burch V, et al. Factors associated with quality of life in active childhood epilepsy: a population-based study. *Eur J Paediatr Neurol* 2015; **19**: 308–13.
- 54 Mula M, Cock HR. More than seizures: improving the lives of people with refractory epilepsy. *Eur J Neurol* 2015; **22**: 24–30.
- 55 Caller TA, Ferguson RJ, Roth RM, Secore KL, Alexandre FP, Zhao W, et al. A cognitive behavioral intervention (HOBSCOTCH) improves quality of life and attention in epilepsy. *Epilepsy Behav* 2016; **57**: 111–7.
- 56 Reilly C, Taft C, Nelander M, Malmgren K, Olsson I. Health-related quality of life and emotional well-being in parents of children with epilepsy referred for presurgical evaluation in Sweden. *Epilepsy Behav* 2015; **53**: 10–4.
- 57 Lin JJ, Mula M, Hermann BP. Uncovering the neurobehavioural comorbidities of epilepsy over the lifespan. *Lancet* 2012; **380**: 1180–92.
- 58 Tellez-Zenteno JF, Patten SB, Jette N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. *Epilepsia* 2007; **48**: 2336–44.
- 59 Quiske A, Helmstaedt C, Lux S, Elger CE. Depression in patients with temporal lobe epilepsy is related to mesial temporal sclerosis. *Epilepsy Res* 2000; **39**: 121–5.
- 60 Perucca P, Mula M. Antiepileptic drug effects on mood and behavior: molecular targets. *Epilepsy Behav* 2013; **26**: 440–9.
- 61 Hesdorffer DC, Hauser WA, Annegers JF, Cascino G. Major depression is a risk factor for seizures in older adults. *Ann Neurol* 2000; **47**: 246–9.
- 62 Hesdorffer DC, Hauser WA, Olafsson E, Ludvigsson P, Kjartansson O. Depression and suicide attempt as risk factors for incident unprovoked seizures. *Ann Neurol* 2006; **59**: 35–41.
- 63 Hesdorffer DC, Ishihara L, Mynepalli L, Webb DJ, Weil J, Hauser WA. Epilepsy, suicidality, and psychiatric disorders: a bidirectional association. *Ann Neurol* 2012; **72**: 184–91.
- 64 Boylan LS, Flint LA, Labovitz DL, Jackson SC, Starner K, Devinsky O. Depression but not seizure frequency predicts quality of life in treatment-resistant epilepsy. *Neurology* 2004; **62**: 258–61.
- 65 Cramer JA, Blum D, Reed M, Fanning K. The influence of comorbid depression on seizure severity. *Epilepsia* 2003; **44**: 1578–84.
- 66 Hitiris N, Mohanraj R, Norrie J, Sills GJ, Brodie MJ. Predictors of pharmacoresistant epilepsy. *Epilepsy Res* 2007; **75**: 192–6.
- 67 Kanner AM. Depression in epilepsy: a complex relation with unexpected consequences. *Curr Opin Neurol* 2008; **21**: 190–4.
- 68 Mula M, Sander JW. Suicide and epilepsy: do antiepileptic drugs increase the risk? *Expert Opin Drug Saf* 2015; **14**: 553–8.
- 69 Gelder MG. *New Oxford Textbook of Psychiatry*. 2nd edn. Oxford University Press, 2009.
- 70 Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *Br J Psychiatry* 1997; **170**: 205–28.
- 71 Bell GS, Gaitatzis A, Bell CL, Johnson AL, Sander JW. Suicide in people with epilepsy: how great is the risk? *Epilepsia* 2009; **50**: 1933–42.
- 72 Christensen J, Vestergaard M, Mortensen PB, Sidenius P, Agerbo E. Epilepsy and risk of suicide: a population-based case-control study. *Lancet Neurol* 2007; **6**: 693–8.
- 73 Cavanagh JT, Carson AJ, Sharpe M, Lawrie SM. Psychological autopsy studies of suicide: a systematic review. *Psychol Med* 2003; **33**: 395–405.

- 74 Hara E, Akanuma N, Adachi N, Hara K, Koutroumanidis M. Suicide attempts in adult patients with idiopathic generalized epilepsy. *Psychiatry Clin Neurosci* 2009; **63**: 225–9.
- 75 Bredkjaer SR, Mortensen PB, Parnas J. Epilepsy and non-organic non-affective psychosis: national epidemiologic study. *Br J Psychiatry* 1998; **172**: 235–8.
- 76 Qin P, Xu H, Laursen TM, Vestergaard M, Mortensen PB. Risk for schizophrenia and schizophrenia-like psychosis among patients with epilepsy: population based cohort study. *BMJ* 2005; **331**: 23.
- 77 Mula M. The Landolt's phenomenon: an update. *Epileptologia* 2010; **18**: 39–44.
- 78 Mizock L. The double stigma of obesity and serious mental illnesses: promoting health and recovery. *Stigma Heal* 2015; **1**: 86–91.
- 79 Daftary A. HIV and tuberculosis: the construction and management of double stigma. *Soc Sci Med* 2012; **74**: 1512–9.

