EPILEPSY

Introduction

An epileptic seizure is defined as the manifestation of an abnormal or excessive discharge of neurons in the brain. Epilepsy is defined as recurrent seizures, specifically two or more seizures separated by 24 hours but within 18 months of one another. This is based on the finding that children who experience one seizure have a 50% chance of recurrence within two years. Febrile seizures are normally excluded from these definitions [1].

The incidence of childhood epilepsy (number of new cases) has been reported to be around 80 per 100,000, which is higher than in the adult population. The prevalence of epilepsy (existing cases at any point in time), ranges from 4−7 per 1,000 depending on the study cited [1].

Epilepsy is commonly grouped into three categories: genetic, metabolic/structural and idiopathic/unknown. Genetic disorders include diseases with a known genetic defect, where seizures are the main manifestation. Metabolic/structural causes include head injuries, central nervous system infections, and tumours. Most children with epilepsy have epilepsy of unknown origin [1].

In developed countries, it has been consistently shown that people with epilepsy have a 2–3 fold increase in risk of mortality. Almost all of the excess in risk in children with epilepsy is in those with severe neurological conditions. Risk factors which increase the risk of mortality include onset of seizures in the first year of life, status epilepticus before diagnosis and poor seizure control. In contrast, mortality risk is only minimally elevated in children with epilepsy who are neurologically normal [2].

An audit of epilepsy related deaths in the UK found that 59% of deaths during childhood could have potentially or probably have been avoided had sufficient attention been given to appropriate drug management, access to specialist care, or adequate investigations [3]. Good seizure control is one of the most important aspects of prevention [2]. The appropriate management of status epilepticus is also important, as it is associated with significant mortality (3% in paediatric population data, and up to 32% in patients with refractory status epilepticus in paediatric intensive care). In light of this, a set of Australasian practice guidelines outlining the optimal management of status epilepticus in the emergency department setting have recently been released [4].

The following section reviews hospital admissions in children and young people aged 0−24 years with any mention of epilepsy or status epilepticus in any of the first 15 diagnoses.

Data Source and Methods

Definition

1. *Hospital admissions for children and young people aged 0–24 years with epilepsy or status epilepticus listed in any of the first 15 diagnoses*
2. *Mortality for children and young people aged 0–24 years with epilepsy or status epilepticus listed as the main underlying cause of death or as a contributory cause*

Data Source

1. National Minimum Dataset

Numerator: Hospital admissions for children and young people aged 0–24 years with epilepsy (ICD-10-AM G40) or status epilepticus (ICD-10-AM G41) in any of the first 15 diagnoses.

2. National Mortality Collection

Numerator: Mortality in children and young people aged 0–24 years with epilepsy (ICD-10-AM G40) or status epilepticus (ICD-10-AM G41) listed as the main underlying cause of death, or as a contributory cause.

Denominator: Statistics New Zealand Estimated Resident Population (projected from 2007)

Notes on Interpretation

Note 1: This analysis focuses on hospital admissions and mortality for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses, or as a main underlying or contributory cause of death. The rationale for looking beyond the primary diagnosis was the need to identify the full spectrum of health issues experienced by those with epilepsy and their consequent need for acute health services.

Note 2: A review of the secondary diagnoses in those admitted with a primary diagnosis of epilepsy or status epilepticus also highlighted the fact that a number had other underlying conditions (e.g. cerebral palsy, developmental delay, congenital anomalies) which may have increased their risk of developing of epilepsy.

Note 3: Children and young people with febrile or unspecified convulsions were not included in the analysis unless they also had a diagnosis of epilepsy or status epilepticus, on the basis that for many, such seizures are one off events which do not lead to a subsequent diagnosis of epilepsy.

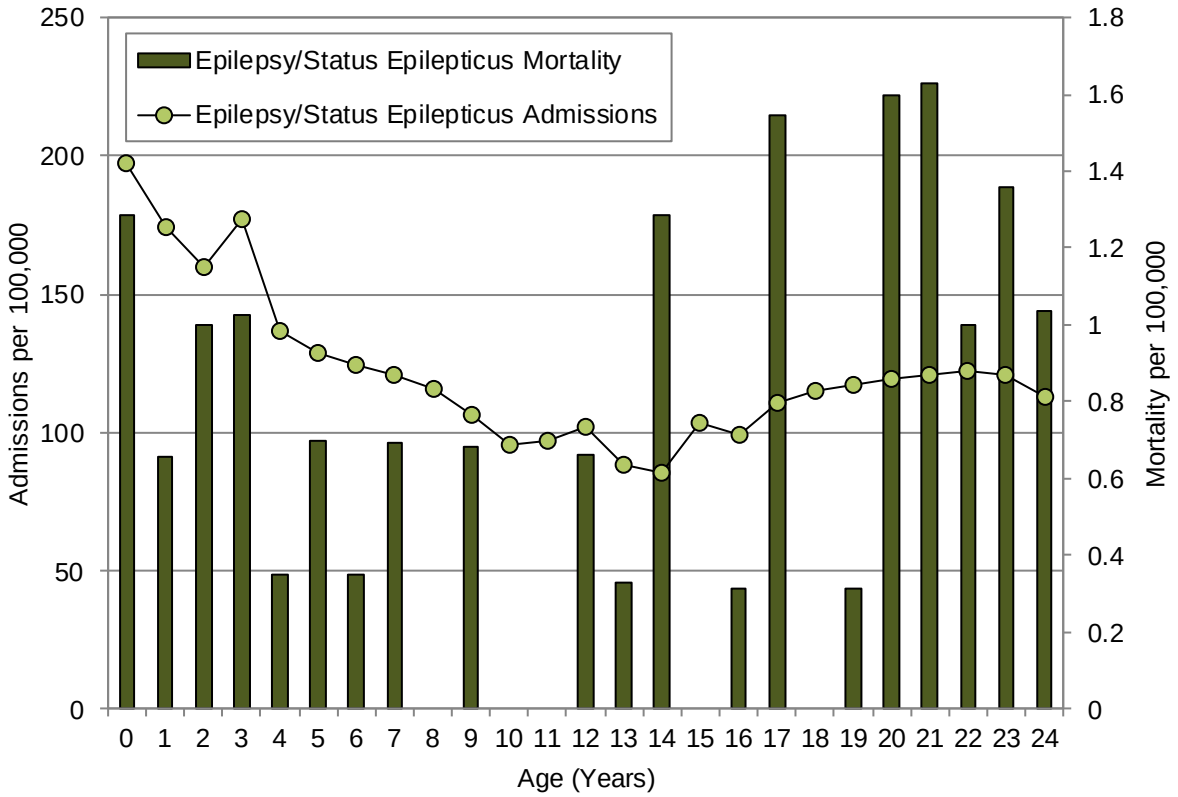
Note 4: If no mention of epilepsy or status epilepticus was made in any of the first 15 diagnoses, these cases were not included, even if the patient had been assigned an epilepsy-related code on a previous admission.

New Zealand Distribution and Trends

Distribution by Age

In New Zealand during 2008–2012, hospital admissions for those with epilepsy or status epilepticus were highest during the first four years of life, with rates declining during childhood, to reach their lowest point at 14 years. Rates then increased again slightly, to reach a plateau amongst those in their late teens and early twenties. Mortality during 2006–2010 occurred sporadically across the age range, although rates were generally higher for those in their early twenties, than for those in late childhood (**Figure 1**).

Figure 1. Hospital Admissions (2008–2012) and Mortality (2006–2010) for New Zealand Children and Young People with Epilepsy or Status Epilepticus by Age



Source: Numerator Admissions: National Minimum Dataset, hospital admissions for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Numerator Mortality: National Mortality Collection, Deaths with epilepsy or status epilepticus listed as the main underlying or contributory cause of death; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 1. Hospital Admissions in Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Primary Diagnosis, New Zealand 2008–2012

Primary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	Admission Rate per 100,000 Population	% of Admissions in those with Epilepsy or Status Epilepticus
Epilepsy or Status Epilepticus				
Diagnoses other than Epilepsy*	2,310	462.0	30.25	24.7
Generalized: Idiopathic	2,281	456.2	29.87	24.4
Unspecified Epilepsy	1,873	374.6	24.53	20.1
Status Epilepticus	763	152.6	9.99	8.2
Grand Mal Seizures NOS	599	119.8	7.84	6.4
Focal: Symptomatic with Complex Partial Seizures	520	104.0	6.81	5.6
Focal: Symptomatic with Simple Partial Seizures	402	80.4	5.26	4.3
Generalized: Other	370	74.0	4.85	4.0
Other Epilepsy	157	31.4	2.06	1.7
Focal: Idiopathic with Localized Onset Seizures	37	7.4	0.48	0.4
Petit Mal NOS	17	3.4	0.22	0.2
Special Epileptic Syndromes	9	1.8	0.12	0.1
Total Epilepsy-Related Diagnoses	7,028	1,405.6	92.04	75.3
Total Admissions	9,338	1,867.6	122.29	100.0
*Other Diagnoses				
Diseases of the Respiratory System	424	84.8	5.55	4.5
Injury and Poisoning	316	63.2	4.14	3.4
Pregnancy, Childbirth, Puerperium	172	34.4	2.25	1.8
Other Diseases Nervous System	157	31.4	2.06	1.7
Other Infectious and Parasitic Diseases	104	20.8	1.36	1.1
Q00-Q99 Congenital Anomalies	97	19.4	1.27	1.0
Dental and Oral Health	92	18.4	1.20	1.0
Unspecified Convulsions	37	7.4	0.48	0.4
All Other Diagnoses	911	182.2	11.93	9.8
Total Other Diagnoses	2,310	462.0	30.25	24.7

Source: Numerator: National Minimum Dataset, hospital admissions by primary diagnosis for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 2. Secondary Diagnoses in Children and Young People Aged 0–24 Years Hospitalised with Epilepsy or Status Epilepticus as a Primary Diagnosis, New Zealand 2008–2012

Secondary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	% of Admissions in those with Epilepsy or Status Epilepticus as Primary Diagnosis
Secondary Diagnosis in Admissions with Epilepsy or Status Epilepticus as a Primary Diagnosis			
Respiratory Infections and Diseases	347	69.4	4.9
History of Non-Compliance with Treatment	310	62.0	4.4
Cerebral Palsy and Other Paralytic Syndromes	297	59.4	4.2
Other Diseases of the Nervous System	221	44.2	3.1
Tobacco Use	213	42.6	3.0
Injury and Poisoning	202	40.4	2.9
Other Congenital Anomalies	167	33.4	2.4
Developmental Delay	149	29.8	2.1
Congenital Anomalies Nervous System	121	24.2	1.7
Viral Infection, Unspecified	101	20.2	1.4
Mental Retardation	98	19.6	1.4
Autism and Other Pervasive Developmental Disorders	94	18.8	1.3
Gastroenteritis	91	18.2	1.3
Sequelae of Head Injuries	74	14.8	1.1
Mental and Behavioural Disorders due to Alcohol	55	11.0	0.8
Otitis Media	53	10.6	0.8
Other Infectious and Parasitic Diseases	52	10.4	0.7
Epilepsy or Status Epilepticus	41	8.2	0.6
Other Diagnoses	1,241	248.2	17.7
No Secondary Diagnosis	3,101	620.2	44.1
Total	7,028	1,405.6	100.0

Source: Numerator: National Minimum Dataset, hospital admissions by secondary diagnosis for children and young people with epilepsy or status epilepticus listed as their primary diagnosis; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Distribution by Primary and Secondary Diagnosis

Primary Diagnosis: In New Zealand during 2008–2012, 75.3% of all hospital admissions in children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses, had an epilepsy-related diagnosis listed as the primary reason for admission. Generalised idiopathic epilepsy (24.4%) and unspecified epilepsy (20.1%) were the most frequent epilepsy-related diagnoses. A further 24.7% of admissions were for conditions unrelated to epilepsy, with respiratory conditions and injury and poisoning being the most frequent non epilepsy-related diagnoses (**Table 1**).

Secondary Diagnosis: During the same period, the secondary diagnoses assigned to children and young people admitted with epilepsy or status epilepticus as a primary diagnosis, fell into two main categories: those conditions which may have increased the risk of the child or young person developing epilepsy (e.g. cerebral palsy, congenital anomalies, and other diseases of the nervous system); and acute concurrent illnesses such as respiratory and viral infections (**Table 2**).

Distribution by Ethnicity and Gender

In New Zealand during 2008–2012, hospital admissions for those with epilepsy or status epilepticus were *significantly* higher for males. Admission rates were also *significantly* higher for Māori and Pacific children and young people, than for European/Other, and then Asian/Indian children and young people (**Table 3**).

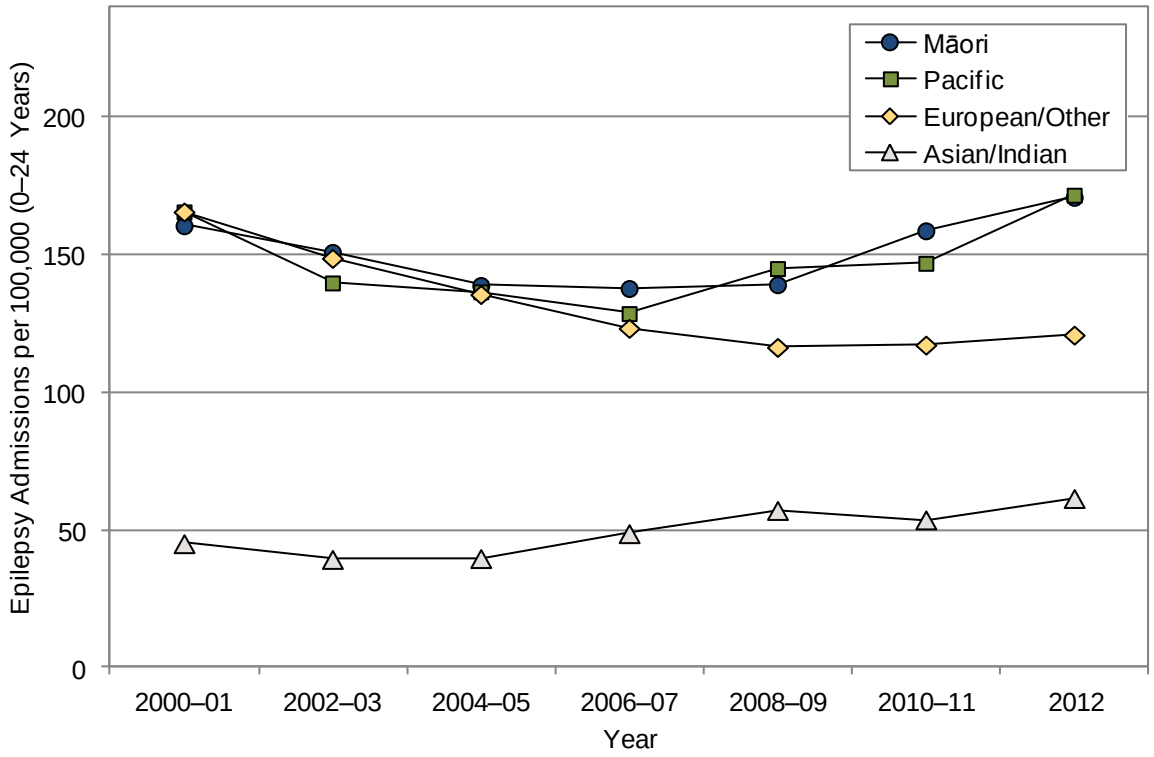
Similarly during 2000–2012, hospitalisations for Asian/Indian children and young people with epilepsy or status epilepticus were consistently lower than for Māori, Pacific and European/Other children and young people. While rates for Māori, Pacific and European/Other children and young people were similar during the early 2000s, diverging trends saw rates for Māori and Pacific children and young people become higher than for European/Other children and young people from 2008–09 onwards (**Figure 2**).

Table 3. Hospital Admissions for Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Ethnicity and Gender, New Zealand 2008–2012

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
Epilepsy or Status Epilepticus							
Asian/Indian	56.6	0.48	0.44–0.53	Female	119.4	1.00	
European/Other	117.6	1.00		Male	125.0	1.05	1.01–1.09
Māori	153.5	1.31	1.25–1.37				
Pacific	151.3	1.29	1.20–1.37				

Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: Ethnicity is Level 1 Prioritised; Rate is per 100,000 population

Figure 2. Hospital Admissions for Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Ethnicity, New Zealand 2000–2012



Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: Ethnicity is Level 1 Prioritised

South Island DHBs Distribution and Trends

South Island Distribution

In the South Island during 2008–2012, 96 Nelson Marlborough, 46 South Canterbury, 404 Canterbury, 27 West Coast, 157 Otago and 134 Southland children and young people were hospitalised with a diagnosis of epilepsy or status epilepticus. Admission rates per 100,000 in Southland were *significantly* higher than the New Zealand rate, while in South Canterbury, Canterbury, the West Coast and Otago rates were *significantly* lower. While also lower, rates in Nelson Marlborough were not *significantly* different from the New Zealand rate (**Table 4**).

South Island Trends

In the South Island DHBs during 2000–2012, large year to year variations (likely as a result of small numbers) made individual DHB's trends in admission rates difficult to interpret. However admissions in South Canterbury were lower than the New Zealand rate throughout 2000–2012, while rates in Nelson Marlborough, Canterbury and Otago were lower for the majority of this period (**Figure 3**).

Table 4. Hospital Admissions for Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus, South Island DHBs vs. New Zealand 2008–2012

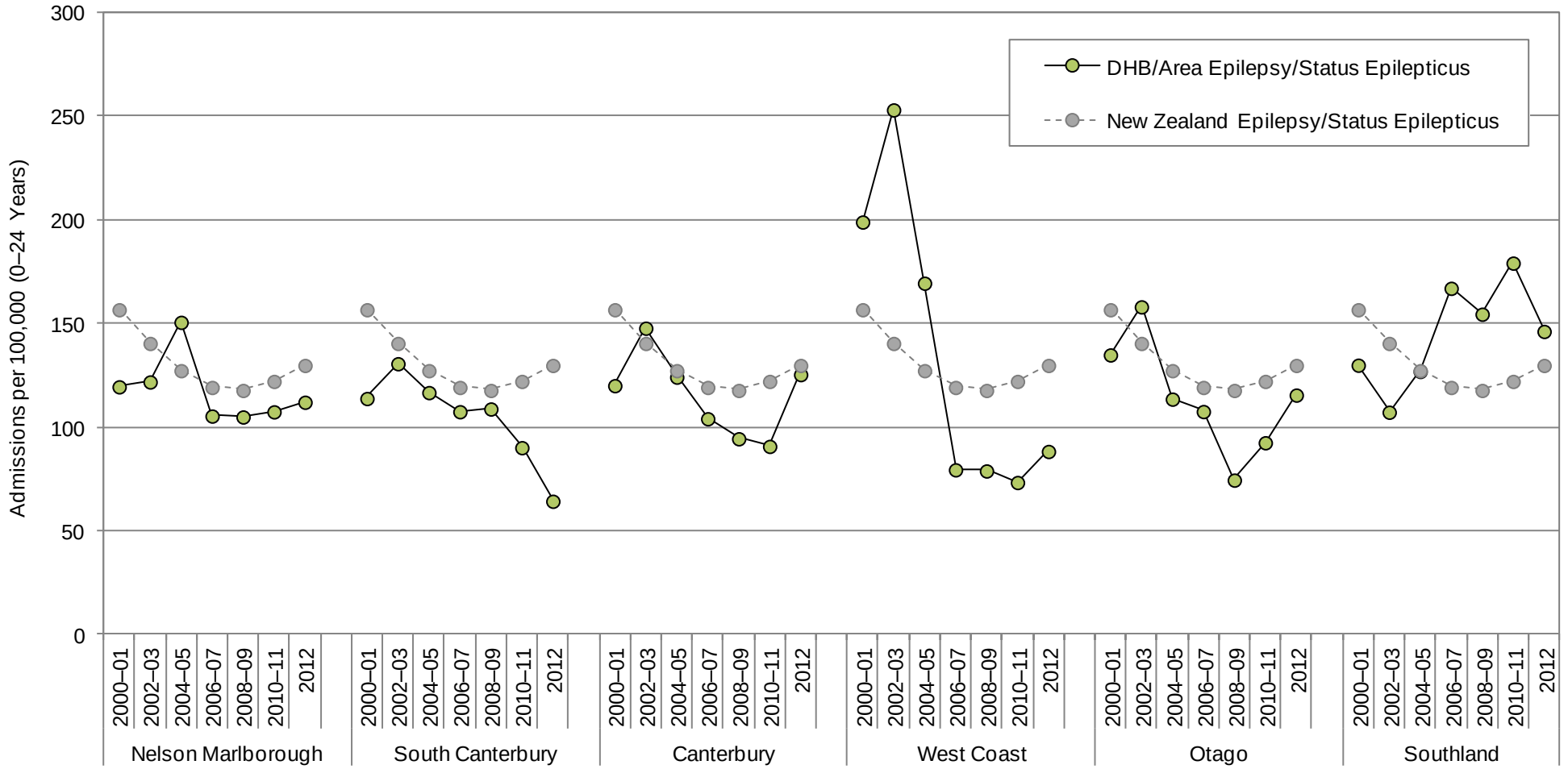
DHB/Area	Total Number of Individuals 2008−2012		Total Number of Admissions 2008−2012	Average Number of Admissions per Individual per Year	Admission Rate per 100,000 Population	Rate Ratio	95% CI
	A*	B*					
Epilepsy or Status Epilepticus							
Nelson Marlborough	95	96	229	0.48	107.73	0.88	0.77–1.00
South Canterbury	42	46	79	0.34	92.76	0.76	0.61–0.95
Canterbury	401	404	827	0.41	99.44	0.81	0.76–0.87
West Coast	25	27	40	0.30	78.91	0.65	0.47–0.88
Otago	150	157	303	0.39	90.31	0.74	0.66–0.83
Southland	130	134	299	0.45	163.11	1.33	1.19–1.50
New Zealand	4,163		9,338	0.45	122.29	1.00	

Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: A*: Each individual only counted once in DHB in which they first reside (DHB total = NZ total); B*: Each individual counted once in each DHB in which they reside (sum of DHB totals exceeds NZ total); Rate Ratios are compared to NZ rate and have not been adjusted for population demographics

Distribution by Primary Diagnosis

In the South Island DHBs during 2008–2012, around three quarters (range 67.1%–80.0%) of all hospital admissions in children and young people with epilepsy or status epilepticus listed in the first 15 diagnoses had an epilepsy-related diagnosis listed as the primary reason for admission. In all South Island DHBs, generalised idiopathic epilepsy and unspecified epilepsy were the most frequent primary diagnoses in those admitted with epilepsy or status epilepticus (**Table 5**–**Table 7**).

Figure 3. Hospital Admissions for Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus, South Island DHBs vs. New Zealand 2000–2012



Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 5. Hospital Admissions in Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Primary Diagnosis, Nelson Marlborough and South Canterbury 2008–2012

Primary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	Rate per 100,000 Population	% of Admissions in those with Epilepsy or Status Epilepticus
Nelson Marlborough				
Diagnoses other than Epilepsy	62	12.4	29.17	27.1
Generalized: Idiopathic	48	9.6	22.58	21.0
Unspecified Epilepsy	34	6.8	16.00	14.8
Other Epilepsy	23	4.6	10.82	10.0
Status Epilepticus	21	4.2	9.88	9.2
Focal: Symptomatic with Complex Partial Seizures	14	2.8	6.59	6.1
Generalized: Other	10	2.0	4.70	4.4
Focal: Symptomatic with Simple Partial Seizures	8	1.6	3.76	3.5
Grand Mal Seizures NOS	5	1.0	2.35	2.2
Unspecified Convulsions	4	0.8	1.88	1.7
Nelson Marlborough Total	229	45.8	107.73	100.0
South Canterbury				
Diagnoses other than Epilepsy	26	5.2	30.53	32.9
Unspecified Epilepsy	29	5.8	34.05	36.7
Generalized: Idiopathic	9	1.8	10.57	11.4
Status Epilepticus	5	1.0	5.87	6.3
Generalized: Other	3	0.6	3.52	3.8
Grand Mal Seizures NOS	3	0.6	3.52	3.8
Other Epilepsy	4	0.8	4.70	5.1
South Canterbury Total	79	15.8	92.76	100.0

Source: Numerator: National Minimum Dataset, hospital admissions by primary diagnosis for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 6. Hospital Admissions in Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Primary Diagnosis, Canterbury and the West Coast 2008–2012

Primary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	Rate per 100,000 Population	% of Admissions in those with Epilepsy or Status Epilepticus
Canterbury				
Diagnoses other than Epilepsy	226	45.2	27.18	27.3
Generalized: Idiopathic	214	42.8	25.73	25.9
Unspecified Epilepsy	163	32.6	19.60	19.7
Status Epilepticus	60	12.0	7.21	7.3
Focal: Symptomatic with Complex Partial Seizures	55	11.0	6.61	6.7
Focal: Symptomatic with Simple Partial Seizures	39	7.8	4.69	4.7
Grand Mal Seizures NOS	30	6.0	3.61	3.6
Generalized: Other	19	3.8	2.28	2.3
Other Epilepsy	10	2.0	1.20	1.2
Unspecified Convulsions	7	1.4	0.84	0.8
Focal: Idiopathic with Localized Onset Seizures	4	0.8	0.48	0.5
Canterbury Total	827	165.4	99.44	100.0
West Coast				
Diagnoses other than Epilepsy	8	1.6	15.78	20.0
Unspecified Epilepsy	11	2.2	21.70	27.5
Generalized: Idiopathic	7	1.4	13.81	17.5
Status Epilepticus	6	1.2	11.84	15.0
Focal: Symptomatic with Simple Partial Seizures	3	0.6	5.92	7.5
Other Epilepsy	5	1.0	9.86	12.5
West Coast Total	40	8.0	78.91	100.0

Source: Numerator: National Minimum Dataset, hospital admissions by primary diagnosis for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 7. Hospital Admissions in Children and Young People Aged 0–24 Years with Epilepsy or Status Epilepticus by Primary Diagnosis, Southern DHB 2008–2012

Primary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	Rate per 100,000 Population	% of Admissions in those with Epilepsy or Status Epilepticus
Otago				
Diagnoses other than Epilepsy	72	14.4	21.46	23.8
Generalized: Idiopathic	73	14.6	21.76	24.1
Unspecified Epilepsy	61	12.2	18.18	20.1
Focal: Symptomatic with Complex Partial Seizures	33	6.6	9.84	10.9
Focal: Symptomatic with Simple Partial Seizures	27	5.4	8.05	8.9
Grand Mal Seizures NOS	13	2.6	3.87	4.3
Status Epilepticus	10	2.0	2.98	3.3
Generalized: Other	8	1.6	2.38	2.6
Other Epilepsy	6	1.2	1.79	2.0
Otago Total	303	60.6	90.31	100.0
Southland				
Diagnoses other than Epilepsy	64	12.8	34.91	21.4
Generalized: Idiopathic	85	17.0	46.37	28.4
Unspecified Epilepsy	63	12.6	34.37	21.1
Status Epilepticus	24	4.8	13.09	8.0
Focal: Symptomatic with Complex Partial Seizures	16	3.2	8.73	5.4
Generalized: Other	16	3.2	8.73	5.4
Grand Mal Seizures NOS	15	3.0	8.18	5.0
Focal: Symptomatic with Simple Partial Seizures	13	2.6	7.09	4.3
Other Epilepsy	3	0.6	1.64	1.0
Southland Total	299	59.8	163.11	100.0

Source: Numerator: National Minimum Dataset, hospital admissions by primary diagnosis for children and young people with epilepsy or status epilepticus listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Policy Documents and Evidence-Based Reviews Relevant to the Diagnosis or Management of Epilepsy or Status Epilepticus

International guidelines, along with a range of evidence-based reviews are briefly summarised in **Table 8.** (Note: It was beyond the scope of this review to consider publications which explored the efficacy of individual drugs in the management of epilepsy, with the focus of the table below being on broader management principles).

Table 8. Policy Documents and Evidence-Based Reviews Relevant to the Diagnosis or Management of Epilepsy or Status Epilepticus

International Guidelines and Useful Websites
National Institute for Health and Clinical Excellence. 2012. **The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (Clinical guideline no. 137).** London: National Institute for Health and Clinical Excellence. http://www.nice.org.uk/nicemedia/live/13635/57779/57779.pdf These clinical guidelines, which are an abbreviated version of the full guideline below, provide guidance on best practice for the care of children, young people and adults with epilepsy. They do not contain details of the evidence on which the recommendations are based.
National Clinical Guideline Centre. 2012. **The epilepsies: The diagnosis and management of the epilepsies in adults and children in primary and secondary care.** London: National Clinical Guideline Centre. http://www.nice.org.uk/nicemedia/live/13635/57779/57779.pdf These very comprehensive 600-page guidelines cover, in detail, specific topics relating to the treatment and management of people with epilepsy. They are a partial update of the original guideline published in 2004. Each section of the guideline, apart from the introductory chapters, is laid out in the same way. There is an introduction followed by a series of clinical questions. For each question there is a brief answer followed evidence statements with grades to indicate the strength of the evidence and details of the relevant systematic reviews and primary papers which make up the evidence. There are summary tables to present key information regarding comparisons between treatments (where this is available). The appendices to the guideline can be found here: http://guidance.nice.org.uk/CG137/Guidance/Appendices
Go CY, Mackay MT, Weiss SK, et al. 2012. **Evidence-based guideline update: medical treatment of infantile spasms. Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society**. Neurology 78(24) 1974-80. http://www.neurology.org/content/78/24/1974.long This review addressed the following clinical questions: 1. Are other forms of corticosteroids as effective as ACTH for short-term treatment of infantile spasms? 2. Are low-dose ACTH regimens effective for short-term treatment of infantile spasms? 3. Is ACTH more effective than VGB for short-term treatment of infantile spasms? 4. Is there a role for the ketogenic diet or for AEDs other than VGB in managing infantile spasms? 5. Does the successful short-term treatment of infantile spasms lead to long-term improvement of neurodevelopmental outcomes or a decreased epilepsy incidence? Twenty-six articles were included in the analysis. For each question, evidence was analysed sequentially and then summarized to determine the overall strength of the evidence and to formulate recommendations. The conclusions of the review process were as follows: There is insufficient evidence to determine whether other forms of corticosteroids are as effective as adrenocorticotropic hormone (ACTH) for short-term treatment of infantile spasms (IS) but low-dose ACTH is probably as effective as high-dose ACTH. ACTH is more effective than vigabatrin (VGB) for short-term treatment of children with IS (apart from those with tuberous sclerosis complex). There is insufficient evidence to show that other agents or combination therapy are effective for short-term treatment of IS. Short lag time to treatment leads to better long-term developmental outcome. Successful short-term treatment of cryptogenic IS with ACTH or prednisolone leads to better long-term developmental outcome than treatment with VGB. The review authors recommended that**:** Low-dose ACTH should be considered for treatment of IS. ACTH or VGB may be useful for short-term treatment of IS and ACTH is to be preferred over VGB. Hormonal therapy (ACTH or prednisolone) may be considered for use in preference to VGB in infants with cryptogenic IS, to possibly improve developmental outcome. A shorter lag time to treatment of IS with either hormonal therapy or VGB possibly improves long-term developmental outcomes.
Cincinnati Children's Hospital Medical Center. 2009. **What effect do inpatient support groups can have on families/parents of children with intractable epilepsy?** Cincinnati, OH: Cincinnati Children's Hospital Medical Center. http://www.cincinnatichildrens.org/WorkArea/linkit.aspx?LinkIdentifier=id&ItemID=88037&libID=87725 This brief publication (a 'Best evidence statement') discusses the evidence regarding the effect of inpatient support groups on families and parents of children hospitalised with intractable epilepsy. There were eleven relevant studies identified by the review authors and at least one was a RCT. The authors state that the evidence indicates that parent support groups can improve parental attitudes and knowledge and decrease parental anxiety. They recommended that mutual support groups for parents and families of vulnerable paediatric patients (i.e. children with intractable epilepsy) in the inpatient care setting should be developed.

The International League Against Epilepsy http://www.ilae.org/

This site has a number of useful evidence-based guidelines and reports which can be found here: http://www.ilae.org/Visitors/Centre/Guidelines.cfm. Among them are:

Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. (2013)

Antiepileptic drugs – Best practice guidelines for therapeutic drug monitoring: A position paper by the subcommission on therapeutic drug monitoring, ILAE Commission on Therapeutic Strategies, (2008)

Guidelines for imaging infants and children with recent-onset epilepsy (2009)

Guidelines on Neonatal Seizures (WHO, ILAE) (2011)

Genetic testing in the epilepsies: Report of the ILAE Genetics Commission (2010)

Epilepsia: Guidelines and special reports Virtual Issue
http://onlinelibrary.wiley.com/journal/10.1111/%28ISSN%291528-1167/homepage/virtual_issue__guidelines_and__special_reports.htm

This web page, published by the journal Epilepsia, provides links to a variety of recent special reports and guidelines related to epilepsy. It states that "These reports offer guidelines, expert opinion, and state-of-the art position papers – from the International League Against Epilepsy and from other groups with special (and usually authoritative) expertise. The Editors hope that by gathering such reports from the past few years into a Virtual Issue, we make these reports more accessible to the Epilepsia readership".

Gaillard WD, Chiron C, et al. **Guidelines for imaging infants and children with recent-onset epilepsy.** Epilepsia 2009; 50(9):2147-53. http://www.ilae.org/Visitors/Documents/pedsneuroimageguideilaecom2009epilepsia.pdf

These guidelines are the result of a review by the Subcommittee for Pediatric Neuroimaging of the International League Against Epilepsy (ILAE) which examined published series reporting the use of computed tomography (CT) and magnetic resonance imaging (MRI) for the evaluation of children with new-onset seizure(s). The reviewers reported that nearly 50% of imaging studies in these children were abnormal and they provide details on the findings on imaging (or lack of them) and their diagnostic, prognostic and management implications for particular types of epilepsy. They recommend imaging, preferably with MRI if this is available, (because of the lack of radiation and its superior resolution and versatility), when localization-related epilepsy is known or suspected, when there is doubt about the epilepsy classification, or when there is suspicion of an epilepsy syndrome with remote symptomatic cause

Scottish Intercollegiate Guidelines Network (SIGN). **Diagnosis and management of epilepsies in children and young people**. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN), 2005. http://www.sign.ac.uk/guidelines/fulltext/81/index.html

These Scottish guidelines are aimed at health care professionals involved in the diagnosis and management of childhood epilepsies. They do not cover issues relating to babies less than one month of age, non-epileptic seizures, surgical treatments or reproductive issues. (These last are addressed in the adult guidelines). There is an evidence grading system for the research evidence on which the guidelines are based and each recommendation in the guidelines is accompanied by a grade reflecting the strength of the evidence on which it is based. SIGN recommends that these guidelines should be used with caution given their age.

Recent Systematic and other Reviews

Cochrane reviews of drug treatments

There are now a large number of Cochrane reviews dealing with single drugs for the treatment of epilepsy, or comparisons between drugs. There is not space to provide details of all of them here. The following drugs have been the subjects of Cochrane reviews published in the years indicated: sulthiame (2013), phenytoin vs. valproate (2013), calcium antagonists (2013), gabapentin (2013), oxcarbazepine vs. phenytoin (2013), vigabatrin (2013), phenobarbitone vs. phenytoin (2013), pregabalin monontherapy (2012), levetiracetam (2012), propofol vs. thiopental sodium (2012), tiagabine (2012), melatonin (2012), losigamone (2012), cannabinoids (2012), vigabatrin vs. carbamazepine (2012), pregabalin add-on (2012), remacemide (2012), immediate-release vs. controlled-release carbamazepine (2011), clobazam add-on (2011), felbamate add-on (2011), lamotrigine add-on for refractory generalized tonic-clonic seizures (2010), lamotrigine add-on for drug-resistant partial epilepsy (2010), carbamazepine vs. phenytoin (2010, oxcarbazepine vs. carbamazepine (2009), carbamazepine vs. valproate (2009), zonisamide add-on (2009), corticosteroids including ACTH (2009) and lamotrigine vs. carbamazepine (2009).

Cochrane reviews relating to the prevention of epilepsy in particular circumstances

A number of Cochrane review have addressed the prevention of epilepsy in particular circumstances related to brain damage (topics are followed by date of publication): after sub-arachnoid haemorrhage (2013), post craniotomy (2013), in viral encephalitis (2012), following acute traumatic brain injury (2012), in adults with brain tumours (2011), after intracranial venous thrombosis (2011), after stroke (2010), and in people with brain tumours (2009).

Krishnaiah B, Ramaratnam S, Ranganathan NL. 2013. **Subpial transection surgery for epilepsy**. Cochrane Database of Systematic Reviews(8).

Around 30% of patients with epilepsy still have seizures despite multiple trials of anti-epileptic drugs. It is believed that early surgical intervention may prevent seizures at a younger age and improve the intellectual and social status of children. This review aimed to determine to determine the benefits and adverse effects of subpial transection, one of many types of surgery for refractory epilepsy, for partial-onset seizures and generalised tonic-clonic seizures in children and adults. The review authors did not find any relevant RCTs or quasi-randomised parallel group studies and so they concluded that there is no evidence to support or refute this surgery.

Hancock EC, Osborne JP, Edwards SW. 2013. **Treatment of infantile spasms.** Cochrane Database of Systematic Reviews(6).

Infantile spasms, also known as West's syndrome, is a relatively rare condition (0.16–0.42 per 1000 live births) that includes a peculiar type of seizure, a high risk of psychomotor retardation, and usually a characteristic electroencephalographic (EEG) pattern known as *hypsarrhythmia*. Seizures usually begin in the first year of life and in most cases they resolve by the age of three. This review aimed to compare the effects of single pharmaceutical therapies used to treat infantile spasms in terms of control of the spasms, resolution of the EEG abnormality, relapse rates, psychomotor development, subsequent epilepsy, side effects, and mortality. The review authors found 16 small RCTs (< 100 participants) and two larger RCTs (> 100 participants). These 18 studies had 916 participants in total, treated with a total of 12 different drugs. Overall the studies were of poor methodological quality, partly because it is considered unethical to give placebo injections to children. Two studies showed that active treatment was better than placebo. The strongest evidence suggested that hormonal treatment (prednisolone or tetracosactide depot) leads to resolution of spasms faster (results from 2 studies) and in more infants (results from 3 studies) than does vigabatrin. Combining the results of three studies showed that 45 out of 81 patients randomly assigned to vigabatrin had resolution of their spasms compared to 57 out of 77 randomly assigned to ACTH, tetracosactide, or high-dose prednisolone (Peto Odds Ratio 0.42, 95% CI 0.21–0.80). The review authors cautioned that it is not yet clear whether these short-term benefits will lead to better long-term outcomes. The review authors also stated that if prednisone or vigabatrin is used, a high dosage is recommended and that vigabatrin may be the treatment of choice in tuberous sclerosis.

Hancock EC, Cross HJ. 2013. **Treatment of Lennox-Gastaut syndrome**. Cochrane Database of Systematic Reviews(2).

The Lennox-Gastaut syndrome (LGS) is an age-specific disorder, characterised by epileptic seizures, a characteristic electroencephalogram (EEG), psychomotor delay and behavioural disorder such as hyperactivity, aggressiveness and autistic tendencies. Between one and ten per cent of children with epilepsy have LGS. It occurs more frequently in males and onset is usually before the age of eight years, with a peak incidence at between three and five years of age. This review aimed to compare the effects of pharmaceutical therapies used to treat LGS in terms of control of seizures and adverse effects. The review authors identified nine relevant RCTs but were not able to perform any meta-analysis because the trials differed in populations studied, drugs used and outcomes measured. They concluded that the best treatment for LGS remains uncertain and that no study so far has shown any one drug to be highly efficacious but rufinamide, lamotrigine, topiramate and felbamate may be helpful as add-on therapy, and clobazam may be helpful for drop seizures. They stated that clinicians should continue to treat each patient individually, weighing up the risks and benefits of each therapy.

Oliveira MM, Conti C, Prado GF. 2013. **Pharmacological treatment for Kleine-Levin syndrome**. Cochrane Database of Systematic Reviews(8).

Kleine-Levin syndrome (KLS) is a very rare disorder affecting around one person per million mainly adolescent men. It is characterised by recurrent episodes of hypersomnia (excessive sleepiness), hyperphagia (overeating) and abnormal behaviour. The authors of this review aimed to identify and evaluate RCTs studying the effectiveness of drug treatment for Kleine-Levin syndrome but they did not find any. They stated that more research is needed.

Offringa M, Newton R. 2012. **Prophylactic drug management for febrile seizures in children.** Cochrane Database of Systematic Reviews(4).

Around 2–4% of children aged one month or more experience a seizure during a febrile illness and 30% of them go on to have another. Rapid-acting antiepileptics and antipyretics given during subsequent fever episodes have been used to prevent further seizures and avoid the adverse effects of continuous antiepileptic drugs. This review aimed to assess the effectiveness and safety of this practice. It included 36 articles describing 26 RCTs with 2740 randomised participants assessing 13 interventions of continuous or intermittent prophylaxis compared to placebo or control treatment. Most studies were of moderate to poor methodological quality. No significant benefit was found for valproate, pyridoxine, intermittent phenobarbitone or ibuprofen vs. placebo or no treatment; nor for diclofenac vs. placebo followed by ibuprofen, acetominophen or placebo; nor for intermittent rectal diazepam vs. intermittent valproate, nor phenobarbitone vs. intermittent rectal diazepam. Adverse effects were reported in up to 30% of children. The review authors concluded "given the benign nature of recurrent febrile seizures, and the high prevalence of adverse effects of these drugs, parents and families should be supported with adequate contact details of medical services and information on recurrence, first aid management and, most importantly, the benign nature of the phenomenon."

Sirven J, Sperling MR, Wingerchuk DM. 2012. **Early versus late antiepileptic drug withdrawal for people with epilepsy in remission**. Cochrane Database of Systematic Reviews(4).

Anti-epileptic drugs have long term adverse effects so when a person's epilepsy is in remission it may be in their best interest to discontinue medication. This review aimed to determine the optimal time for discontinuing anti-seizure medication in adults and children. It included seven RCTs of early (after less than two seizure-free years) vs. late (after more than two seizure-free years) withdrawal of anti-epileptic drugs (AEDs) involving 924 randomised children. There were no eligible trials in adults. The pooled relative risk for seizure relapse in early vs. late AED withdrawal was 1.32 (95% CI 1.02 to 1.70). On the basis of this estimate, the number needed to harm is ten (indicating that ten people would need to stop their medication early for one person to have a relapse seizure). Early discontinuation was associated with greater relapse rates in people with partial seizures (pooled RR is 1.52 (95% CI 0.95 to 2.41)) or an abnormal EEG (pooled RR 1.67 (95% CI 0.93 to 3.00)). The review authors concluded that the evidence supports waiting at least two seizure-free years before withdrawing AEDs in children, particularly if they have an abnormal EEG and partial seizures but that there is not sufficient evidence to establish when to withdraw AEDs in children who have had generalized seizures and no evidence to guide the timing of withdrawal of AEDs in seizure free adults.

Levy RG, Cooper PN, Giri P, et al. 2012. **Ketogenic diet and other dietary treatments for epilepsy**. Cochrane Database of Systematic Reviews(7).

The ketogenic diet is low in carbohydrates and high in fat and it is believed to decrease seizure frequency in people with epilepsy. It has mostly been used in children who have seizures despite treatment with anti-epileptic drugs. This review includes four RCTs with a total of 289 child or adolescent participants. Only one of these studies compared a ketogenic diet to a normal diet. The others compared different ketogenic diets and/or different rates of introduction of the diet. The review authors stated that the results of these studies suggest that, in children, a ketogenic diet results in short to medium term benefits in seizure control, and has an effect which is comparable to modern antiepileptic drugs. They noted that one long term study reported a high drop-out rate in the diet group which suggests that many children find the diet difficult to tolerate. They concluded that, for those with medically intractable epilepsy or those for whom surgery is unsuitable, a ketogenic diet could improve seizure control but it is difficult to tolerate.

Ramaratnam S, Sridharan K. 2012. **Yoga for epilepsy**. Cochrane Database of Systematic Reviews(1).

Yoga may reduce stress, induce relaxation and influence the electroencephalogram and the autonomic nervous system, thereby preventing or controlling seizures. If it were proved effective it would be an attractive therapeutic option with few adverse effects. This review considered two unblinded trials with a total of 50 subjects (18 who were treated with yoga and 32 who received either alternative treatment or no treatment). Due to the small size of the studies and the resulting very large confidence intervals associated with the outcome measures it was not possible to draw any reliable conclusions about the efficacy of yoga as a treatment for epilepsy.

Adab N, Tudur Smith C, Vinten J, et al. 2012. **Common antiepileptic drugs in pregnancy in women with epilepsy**. Cochrane Database of Systematic Reviews(6).

It is well known that taking anti-epileptic drugs (AEDs) in pregnancy may have adverse effects on the fetus but the relative risks of specific antiepileptic drug exposures remain poorly understood. This review aimed to assess the adverse effects of commonly used antiepileptic drugs on maternal and fetal outcomes in pregnancy in women with epilepsy. It focussed on neurodevelopmental outcomes in children exposed to anti-epileptic drugs in utero. The review authors identified 31 eligible studies based on 18 independent cohorts. Most studies were prospective cohort studies. Fifteen included children born to mothers without epilepsy as controls and four compared children with different AED exposures to each other. Most studies were small although only two studies had recruited fewer than 25 children with AED exposure in utero. Only seven independent cohorts had more than 50 children exposed to AEDs. Due to the wide variety of outcomes measured and methodological approaches the review authors chose to present a descriptive analysis of the studies' results. They reported that most studies were of limited quality and that there was little evidence about which specific drugs carry more risk than others to the development of children exposed in utero; that the results between studies are conflicting and that while most failed to find a significant detrimental outcome with in utero exposure to monotherapy with carbamazepine, phenytoin or phenobarbitone, this should be interpreted cautiously; that there were few studies of sodium valproate; that exposure to polytherapy in utero was more commonly associated with poorer outcomes as was exposure to any AEDs when analysis did not take into account type of AED (possibly because there was a high proportion of children in these studies who were in fact exposed to polytherapy). The review authors concluded that based on the best evidence currently available, it seems advisable for women to continue medication during pregnancy using monotherapy at the lowest dose required to achieve seizure control and that it seems best to avoid polytherapy if possible. They stated that adequately powered population studies are needed.

Cheuk KLD, Wong V. 2011**. Acupuncture for epilepsy**. Cochrane Database of Systematic Reviews(8).

Based on the results of 16 RCTs with 1468 participants, 15 conducted in China and one in Norway, authors of this review concluded that the current evidence does not support acupuncture as a treatment for epilepsy. The results of five trials indicated that compared with control treatment, needle acupuncture was not effective decreasing seizure frequency. Two trials compared acupuncture with phenytoin and found that needle acupuncture may be better for achieving at least 75% or at least 25% reduction in seizure frequency. Two trials compared acupuncture with valproate and these indicated that needle acupuncture may be better for achieving at least 50% or at least 75% reduction in seizure frequency, and be associated with better quality of life, lower frequency of impaired concentration, and higher likelihood of at least 70% improvement in epilepsy score.

Alaqeel S, Alsabhan J. 2011. **Strategies for improving adherence to antiepileptic drug treatment in patients with epilepsy**. Cochrane Database of Systematic Reviews(1).

Poor adherence to anti-epileptic medication is associated with increased morbidity and mortality. This review aimed to determine the effectiveness of interventions intended to improve adherence to medication in adults and children with epilepsy. It included six RCTs of adherence-enhancing interventions. Five studies targeted adults (222 patients in total) and one, children (51 in total). Follow-up times ranged from one to six months. The main types of intervention were educational and behavioural modification and all studies compared an intervention to 'usual care'. Because the studies differed in intervention type and how adherence was measured the review authors did not pool the studies' results. They reported that education and counselling interventions had mixed success but behavioural interventions such as the use of intensive reminders and 'implementation intention' interventions were more effective. An example of an intensive intervention is keeping a diary of medication use and seizures, using a Dosett medication container (pill organiser) and receiving prescription refill and appointment-keeping reminders. An 'implementation intervention' could be getting the patient to complete a simple worksheet linking taking medication with a particular time, place and other routine activity, such as brushing their teeth. The review authors concluded that Intensive reminders and 'implementation intention' interventions seem promising for enhancing adherence to antiepileptic mediations but further research involving well-designed RCTs is needed before a firm conclusion can be reached.

Geng J, Dong J, Li Y, et al. 2011. **Intravenous immunoglobulins for epilepsy.** Cochrane Database of Systematic Reviews(1).

People with epilepsy sometimes have various types of immunological abnormalities such as low serum IgA level, lack of IgG subclass and the presence of antibodies which are pathogenic or secondary to the primary disease. For this reason intravenous immunoglobulin (IVIg) treatment may be beneficial for some people with epilepsy. This review aimed to examine the effects of IVIg, either as alone or as an add-on treatment, on the frequency and duration of seizures, quality of life in people with epilepsy and also the adverse effects of IVIg. The review authors included only one study in the review, with 61 participants aged from two to 51 years. This study was a randomized, double-blind, placebo-controlled, multi-centre trial which compared the treatment efficacy of IVIg as an add-on with placebo add-on in patients with refractory epilepsy over a period of six weeks. This study reported no significant difference between IVIg and placebo in 50% or greater reduction in seizure frequency but it did report a statistically significant effect for global assessment in favour of IVIg. No adverse effects were noted. The review authors stated that no reliable conclusions could be drawn about the efficacy of IVIg as a treatment for epilepsy.

Ramaratnam S, Baker GA, Goldstein LH. 2011. **Psychological treatments for epilepsy**. Cochrane Database of Systematic Reviews(3).

Psychological interventions such as relaxation therapy, cognitive behaviour therapy, bio-feedback and educational interventions have been used alone or in combination in the treatment of epilepsy, with the aim of reducing seizure frequency and improving quality of life. This review aimed to evaluate such interventions. The review authors found only three small trials (with a total of 50 participants) and considered these to have poor methodological quality therefore they did not perform meta-analysis. No study found a significant effect of relaxation therapy on seizure frequency. The review authors concluded that there was no reliable evidence to support the use of psychological treatments.

Beavis J, Kerr M, Marson AG, et al. 2011. **Pharmacological interventions for epilepsy in people with intellectual disabilities**. Cochrane Database of Systematic Reviews(3).

It is common for people with intellectual disabilities to develop epilepsy. Seizures in intellectually disabled people are often complex and unresponsive to treatment. Antiepileptic drugs (AEDs) may have a profound effect upon behaviour in this patient group. This review aimed to consider RCTs of antiepileptic drug interventions in people with epilepsy and intellectual disabilities. The review authors identified 12 RCTs, with 761 randomised participants in total, comparing eight different pharmacological agents. Due to the heterogeneity between studies the review authors presented a descriptive analysis. They stated that, in general, the AEDs that have been proven effective in the general population are also effective for refractory epilepsy in people with intellectual disability and that it was not possible to comment on the relative efficacy of different medications. Side effects seemed to be similar to those observed in the non intellectually disabled population. Most studies either did not assess behavioural exacerbation or used unreliable measures of it but those that did measure it found little obvious behaviour disorder. The review authors concluded that the evidence broadly supports the use of AEDs to reduce seizure frequency in people with refractory epilepsy and intellectual disability and that side effect are similar to those in the general population, behavioural side effects leading to discontinuation are rare and other effects are under-researched.

Beavis J, Kerr M, Marson AG, et al. 2011. **Non-pharmacological interventions for epilepsy in people with intellectual disabilities.** Cochrane Database of Systematic Reviews(3).

People with intellectual disability and epilepsy are more likely than people with epilepsy but no intellectual disability to continue to experience seizures whilst taking one or more antiepileptic drugs. The authors of this review were unable to identify any RCTs of non-pharmacological interventions for people with epilepsy and intellectual disabilities except for one study still in progress. They concluded that there is a need for well-designed RCTs to assess the effect of non-pharmacological interventions on seizure and behavioural outcomes in an intellectually disabled epilepsy population.

Lindsay B, Bradley PM. 2010. **Care delivery and self-management strategies for children with epilepsy.** Cochrane Database of Systematic Reviews(12).

Various models of service delivery for children with epilepsy have been developed in response to perceived inadequacies in quality of care but it is unclear what the best kind of service for children with epilepsy is. This review aimed to assess the effectiveness of specialist or dedicated teams or individuals for the care of children with epilepsy compared to usual care services. Studies were eligible for inclusion in this review if they were RCTs, controlled or matched trials, cohort studies or other prospective studies with a control group, or time series studies. Four studies and five reports were included. They reported on four different education and counselling programmes for children, children and parents, or teenagers and parents. All of the programmes showed some benefits for the wellbeing of children with epilepsy but all of the trials had methodological flaws and no single programme was evaluated by more than one study. The review authors noted that the impacts of the programmes were extremely variable and no programme showed benefits across the full range of outcomes. They stated that there were no detrimental effects demonstrated for any programme in the studies and they concluded that the evidence in favour of any single programme is insufficient to make it possible to recommend one programme over another.

Privitera MD, Welty TT, Ficker DD, et al. 2010. **Vagus nerve stimulation for partial seizures**. Cochrane Database of Systematic Reviews(7).

Vagus nerve stimulation (VNS) is used as an adjunct treatment for some types of epilepsy. The procedure involves implanting a pacemaker-type device under the skin of the chest and connecting a stimulator wire to the left vagus nerve in the neck. The frequency, intensity and duration of nerve stimulation can be varied by programming the device. This review aimed to determine the effects of high-level VNS compared to low-level (presumed sub-therapeutic dose) VNS in adults and children with drug-resistant partial seizures by reviewing relevant RCTs. The review authors identified two RCTs sponsored by Cyberonics as part of their pre-approval programme for VNS and involving 312 randomised participants. All participants had a stimulator implanted, but the control group received less frequent and lower intensity stimulation. In addition, those in the control group did not receive any electrical current when the device was activated by the hand-held magnet. The outcomes assessed in the studies were: (1) 50% or greater reduction in total seizure frequency; (2) treatment withdrawal (any reason); (3) adverse effects. Summary odds ratios (ORs) were estimated for each outcome. The overall odds ratio for 50% responders across all studies was 1.93 (95% CI 1.1 to 3.3), implying that those in the intervention group were almost twice as likely to experience a 50% or greater reduction in seizure frequency. The overall odds ratio for withdrawal for any reason was 1.08 (95% CI 0.07 to 17.51) indicating that those in the intervention group were no more likely to withdraw than those in the control group. The statistically significant adverse effects associated with implantation (compared to baseline) were hoarseness, cough, pain, and paresthesia. Statistically significant adverse effects associated with stimulation (high vs. low) were hoarseness and dyspnea, suggesting the implantation is associated with hoarseness, but the stimulation produces additional hoarseness. From these results the review authors concluded that VNS for partial seizures appears to be effective and well tolerated (since dropouts were rare). They noted that VNS does not produce the side effects typically associated with anti-epilepsy drugs such as ataxia, dizziness, fatigue, nausea, and somnolence.

Appleton R, Macleod S, Martland T. 2010. **Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children.** Cochrane Database of Systematic Reviews(10).

Convulsive status epilepticus (currently defined as a grand mal convulsion lasting at least 30 minutes) and tonic-clonic (grand mal) convulsions are medical emergencies and demand urgent and appropriate anticonvulsant treatment. First choice drugs in these situations include benzodiazepines, (diazepam, lorazepam, midazolam), phenobarbitone, phenytoin and paraldehyde. This review aimed to review the evidence comparing the efficacy and safety of these drugs for treating children with tonic-clonic convulsions and convulsive status epilepticus in hospital. It included four trials involving 383 participants (all RCTs or quasi-RCTs comparing one drug with another). The main results were as follows: (1) Intravenous lorazepam is as effective as intravenous diazepam in the treatment of acute tonic clonic convulsions, 19/27 (70%) versus 22/34 (65%), RR 1.09 (95% CI 0.77 to 1.54), has fewer adverse events and rectal lorazepam may be more effective than rectal diazepam, 6/6 versus 6/19 (31%), RR 3.17 (95% CI 1.63 to 6.14), (2) Buccal midazolam controlled seizures in 61/109 (56%) compared with 30/110 (27%) of rectal diazepam treated episodes with acute tonic-clonic convulsions, RR 2.05 (95% CI 1.45 to 2.91), (3) Intranasal midazolam is as effective as intravenous diazepam in the treatment of prolonged febrile convulsions, 23/26 (88%) versus 24/26 (92%), RR 0.96 (95% CI 0.8 to 1.14), (4) There is moderate evidence that intranasal lorazepam is more effective than intramuscular paraldehyde for acute tonic-clonic convulsions and patients treated with intranasal lorazepam are significantly less likely to require further anticonvulsants to control continuing seizures, 8/80 (10%) versus 21/80 (26%), RR 0.58 (95% CI 0.42 to 0.79). The review authors concluded that, since the previous Cochrane review on this topic (which included only one study), the situation has changed and there is now evidence that intravenous lorazepam is at least as effective as intravenous diazepam for the treatment of acute tonic-clonic convulsions and is associated with fewer adverse events. They stated that where intravenous access is unavailable there is evidence from one trial that buccal midazolam is the treatment of choice.

Tomson T, Dahl M, Kimland E. 2010. **Therapeutic monitoring of antiepileptic drugs for epilepsy**. Cochrane Database of Systematic Reviews(5).

This review aimed to assess the evidence regarding the effects of therapeutic drug monitoring upon outcomes in epilepsy. The review authors identified only one relevant RCT, with180 participants aged six to 65 years who were taking one of a variety of anti-epileptic drugs as monotherapy. Sixty per cent of the patients randomised to therapeutic drug monitoring (intervention group) achieved 12-month remission from seizures as did 61% in the control group. A total of 56% in the intervention group and 58% in the control group were seizure free during the last 12 months of follow up. Adverse effects were reported by 48% in the intervention group and 47% in the control group. Of those randomised to therapeutic drug monitoring, 62% completed the two-year follow up compared with 67% of the control group. The review authors concluded that there was no clear evidence to support routine measurement of serum concentration of antiepileptic drugs with the aim of reaching predefined target ranges in order to optimise treatment of patients with newly-diagnosed epilepsy who are receiving antiepileptic drug monotherapy. They stated that this does not exclude the possibility that therapeutic drug monitoring of specific antiepileptic drugs may be useful during polytherapy, in special situations, or in selected patients, although evidence is lacking.

Other Relevant Publications

Babl FE, Sheriff N, et al. **Emergency management of paediatric status epilepticus in Australia and New Zealand: Practice patterns in the context of clinical practice guidelines**. Journal of Paediatrics & Child Health 2009; 45(9): 541–6.

This paper reports on a study that reviewed clinical practice guidelines and reported physician practice concerning the management of paediatric status epilepticus in the largest Australian (n=9) and New Zealand (n=2) paediatric emergency departments within the Paediatric Research in Emergency Departments International Collaborative (PREDICT) network. There were seven different guidelines in use in ten of the sites and one site didn't have a guideline. Initial management of seizure was similar at all sites with benzodiazepines being the first line strategy, consistent with Advanced Paediatric Life Support (APLS) guidelines. There was more variation in the second and third line strategies used for persistent seizures. The authors noted that there is a lack of evidence comparing the efficacy of different second and third line agents and regarding the use or non-use of rapid sequence intubation and that this is reflected in the variations in practice. They considered that further research in this area would be beneficial.

Note: The publications listed were identified using the search methodology outlined in Appendix 1 (Search Methods for Policy Documents and Evidence-Based Reviews)

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