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Cowan LD. The epidemiology of the epilepsies in children. Mental Retardation and Developmental Disabilities Res Reviews, 2002; 8: 171-181	Review article		Paediatric patients							Discusses incidence and prevalence rates of epilepsy by Age, Sex and Race/ethnicity. Describes frequencies of seizures types and epilepsy syndromes in children Discusses epilepsy and developmental disabilities, aetiology, specific types of childhood seizures and prognosis.
Tudor-Smith C et al. Phenytoin versus valproate monotherapy for partial onset seizures and generalized onset tonic clonic seizures. Cochrane database of Systematic Reviews 2001. Issue 4 Art No CD001769 DOI:10.1002/14651858.CD002769	Systematic review. Randomized controlled trials in children or adults with partial onset seizures or generalized onset tonic-clonic seizures. Trials must have included a comparison of phenytoin monotherapy with valproate monotherapy.	Data were available for 669 individuals from five trials, representing 60% of the participants recruited into the eleven trials that met the inclusion criteria	Of the five trials for which individual patient data were provided, one recruited individuals of all ages (Ramsay 1992), one recruited children only (de Silva 1996), two recruited adults only (Heller 1995; Turnbull 1985) and one trial recruited elderly people (Craig 1994). Newly diagnosed people were recruited in all five	To review the effects of phenytoin compared to valproate when used as monotherapy in people with partial onset seizures (simple/complex partial with or without secondarily generalization) or generalized onset tonic-clonic seizures (with or without other generalized seizure types).	Phenytoin compared to valproate when used as monotherapy		Analysis on an intention-to-treat basis. Results are expressed as a hazard ratio (HR) and 95% confidence interval, and by convention a HR greater than one indicates that an event is more likely on phenytoin. Time to withdrawal of allocated treatment	***Time to withdrawal of allocated treatment*** •For this outcome, a HR greater than one indicates a clinical advantage for valproate. ***Time to achieve 12 month remission*** •For this	**External sources of support** •Medical Research Council UK •NHS R&D UK **Internal sources of support** •University of Liverpool UK •Walton	

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			trials.				(retention time) was chosen as the primary outcome. Participants achieved this outcome if allocated treatment was withdrawn for poor seizure control, adverse effects, non-compliance or if additional add-on treatment was initiated (i.e. allocated treatment had failed). This is a combined outcome reflecting both efficacy and tolerability and is an outcome to which the individual contributes. It is the primary outcome measure recommended by the Commission on Antiepileptic Drugs of the International League Against Epilepsy (Commission 1998). (2) Time to achieve 12 month remission (seizure free period).	outcome, a HR greater than one indicates a clinical advantage for phenytoin. ***Time to achieve six month remission*** •For this outcome, a HR greater than one indicates a clinical advantage for phenytoin. ***Time to first seizure post randomization*** •For this outcome, a HR greater than one indicates a clinical advantage for valproate.	Centre for Neurology and Neurosurgery UK	

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							(3) Time to achieve six month remission. (4) Time to first seizure post randomization. (5) Quality of life measures if available.			
Tudor-Smith C et al Carbamazepine versus phenytoin monotherapy for epilepsy. Cochrane database of Systematic Reviews 2002, Issue 2 Art No CD001911 DOI:10.1002/14657858.CD001911	Systematic review	551 participants (adults and children) in 3 Trials, available for analysis. This is 61% of the participants in the 9 trials that met the inclusion criteria	Adults or Children with partial onset seizures or generalised onset tonic-clonic seizures.	To review the best evidence comparing carbamazepine and phenytoin when used as monotherapy in people with partial onset seizures or generalised onset tonic-clonic seizures.	Comparison of carbamazepine monotherapy with phenytoin monotherapy	12 months	a)time to withdrawal of allocated treatment b)12 remission c)6 month remission d) first seizure post randomisation. Results were expressed as hazard ratios plus confidence intervals, where a HR greater than 1 indicates an event is more likely on phenytoin	A)Time to withdrawal of allocated treatment HR=0.97 (95% CI 0.74-1.28) B)Time to 12 month remission HR=1 (95% CI 0.78-1.29) C)Time to 6 month remission 1.10 (95% CI 0.87 -1.39 D)Time to first seizure 0.91 (95% CI 0.74-1.12)		The results suggest no overall difference between carbamazepine and phenytoin for these outcomes, but confidence intervals are wide.
Taylor S et al. Phenobarbitone versus phenytoin monotherapy for partial onset seizures and generalized onset tonic-clonic seizures. Cochrane Database of Systematic Reviews 2003. issue 2 Art No CD002217 DOI:10,1002/14651858. CD002217	Systematic review	599 participants (adults and children) in 4 trials. This is 65% of the participants in the 10 studies meeting the inclusion criteria	Adults and children with partial onset seizures or generalised onset tonic-clonic seizures.	To review the effects of phenobarbitone compared to phenytoin when used as monotherapy in patients with partial onset seizures or generalised tonic-clonic seizures	Comparison of phenobarbitone monotherapy and phenytoin monotherapy	12 months	A)Time to withdrawal of allocated treatment B)12 month remission C) First seizure post-randomisation. Results were expressed as Hazard ration and 95% confidence interval, where a HR >1 indicates	A)Time to withdrawal of treatment HR=1.62 995% CI 1.22-2.14) B)Time to 12 month remission HR=0.93 (95% CI 0.7-1.23) C)Time to first seizure HR=0.84 (95% CI 0.68-		These results indicated a statistically significant clinical advantage for phenytoin in terms of treatment withdrawal (probably related to adverse effects associated with

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							an event is more likely to occur earlier on phenobarbitone then phenytoin	1.05)		phenobarbitone), and a non-significant advantage in terms of 12 month remission. Results for time to first seizure suggest a non-significant clinical advantage for phenobarbitone
Muller M et al Oxcarbazepine versus phenytoin monotherapy for epilepsy. Cochrane Database of Systematic reviews 2006 Issue 2. Art No CD003615 DOI 10.1002/14651858. CD003615. pub2	Systematic Review of randomised controlled trials	Data were available for 480 patients from 2 trials, representing 100% of the patients recruited into the 2 trials that met the inclusion criteria.	Adults and children with epilepsy	To review the best evidence comparing oxcarbazepine and phenytoin when used as monotherapy in patients with epilepsy	Comparison of oxcarbazepine monotherapy with phenytoin monotherapy in children and adults with epilepsy.		A)Time on allocated treatment B)Time to achieve 6, 12 and 24 month remission C)Time to first seizure post-randomisation D) Quality of life measures if available. Results are expressed as Hazard ratios (HR) and 95% confidence intervals, where HR>1 indicates an event is more likely on phenytoin	A)Time to withdrawal of treatment HR=1.64 (1.09-2.47) B)Time to 6 month remission HR=0.89 (0.66-1.22) Time to 12 month remission HR=0.92 (0.62-1.37) C)Time to first seizure HR=1.07 (0.83-1.39)		No significant advantage for either drug for patients with generalised onset seizures could be identified. A potentially important advantage in time to withdrawal for oxcarbazepine for patients with partial onset seizures was identified. However, current data do not allow a statement as to whether

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										oxcarbazepine is equivalent, superior or inferior to phenytoin in terms of seizure control.
Forsythe I et al. Cognitive improvement in new cases of epilepsy randomly assigned to carbamazepine, phenytoin and sodium valproate. Developmental Medicine and Child Neurology 1991:33;524-34	Randomised, prospective blind study of children allocated to monotherapy with phenytoin, carbamazepine or sodium valproate compared to with controls	64	Children aged 5-14 years of age who had had a) three tonic clonic seizures, 2) three complex partial seizures or 3)three partial seizures with secondary generalisation 31 children referred because of nocturnal enuresis and 9 with migraine acted as controls.	Effect of carbamazepine, phenytoin and sodium valproate on cognitive function in newly diagnosed epilepsy.	Active treatment group versus control group	12 months	Cognitive assessments: 1.Visual recall 2.Auditory recall 3.Visual scanning 4.Strrop test (concentration) 5.Speed of information processing 6. Standard scales of intellectual functioning and reading	Memory tests: no significant difference between medications (although impaired recent recall was noted on carbamazepine at 6 months and 1 year. Vigilance: No significant differences between medications Speed of Information processing: No significant difference between the drug groups, although it was impaired y both carbamazepine and phenytoin. Concentration: no significant differences between the drug groups	1.NHS 2. Ciba Geigy PLC Sanofi PLC	

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								Standard tests of intelligence and reading. Difference between carbamazepine and phenytoin at 1 year.		
Thilothammel et al. Comparison of phenobarbitone, phenytoin with sodium valproate randomized double blind study. Indian Paediatrics 1996 33;549-55	Randomised, double-blind clinical trial	151	Paediatric outpatients (4-12 years of age) with generalised tonic-clonic convulsions in a tertiary care hospital (India)	Comparison of efficacy and side effects of phenytoin, phenobarbitone or sodium valproate in controlling generalised tonic-clonic seizures.	Administration of active drug (phenobarbitone or phenytoin or sodium valproate) versus placebo	2 years	Recurrence of convulsion and side effects. Clinical, haematological and biochemical parameters were assessed monthly. Serum drug levels were assesses periodically	The proportion of children with recurrence did not differ amongst the 3 groups. More than 1 side effect was observed in 32% of children on Phenobarbitone; 40% of children on phenytoin and 19% of children on sodium valproate. This difference was statistically significant	International clinical epidemiology network. Boots Pharmaceuticals, Reckitt and Coleman India Ltd. & Rhone Poulenc India Ltd.	Most side effects with phenytoin disappeared on adjustment of dosage. Least expensive, phenobarbitone may be preferred as the drug of first choice, but only in pre-school children. Sodium valproate is preferred for schoolchildren.
de Silva M et al. Randomised comparative monotherapy trial of phenobarbitone, phenytoin, carbamazepine or sodium valproate for newly diagnosed childhood epilepsy. The Lancet 1996; 347:709-13 (Alder Hey Library)	Randomised, comparative trial of monotherapy (with phenobarbitone, phenytoin, carbamazepine, sodium valproate) in newly diagnosed epilepsy	167	Children aged 3-16 years of age who had had at least 2 previously untreated tonic-clonic or partial seizures with or without secondary generalisation	Random allocation to treatment with one of the 4 anti-epileptic drugs	Comparative efficacy of the drugs	Median duration 44 months (3-88 months)	Time to first seizure recurrence after the start of therapy. Time to achieve a 1-year remission from all seizures (or the last date of follow up summarised by a Kaplan Meier of	Overall outcome for all 4 drugs was good. 20% of children remained seizure free and 73% had achieved a 1-year remission by 3 years of follow up. Phenytoin was	Medical Research Council. Health promotion trust, Ciba-Geigy, Parke-Davis, Sanofi.	

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							recurrence free follow-up. Frequency of unacceptable side- effects necessitating withdrawal	more likely to be withdrawn 9%) than carbamazepine (4%) or sodium valproate (4%)		
Guerreiro M et al. A double-blind controlled clinical trial of oxcarbazepine versus phenytoin in children and adolescents with epilepsy. Epilepsy Research 1997; 27(2):205-13	Multi-centre, randomised, parallel group trial with 3 phases: a retrospective baseline assessment, double-blind treatment and a long term open extension	193 patients enrolled. 153 included in the results	Children aged 5-18 years with newly diagnosed epilepsy with partial seizures or generalised tonic-clonic seizures. Recruitment centres were located in Brazil and Argentina	Monotherapy with oxcarbazepine or phenytoin	Comparison of efficacy, tolerability and treatment retention in patients receiving monotherapy with oxcarbazepine or phenytoin for the management of partial seizures or generalised tonic- clonic seizures.	56 weeks	A)efficacy B)Tolerability C)Treatment retention	A) Overall 61% and 60% of patients were seizure free during the maintenance period in the oxcarbazepine and phenytoin groups respectively. No statistically significant difference noted. B) Tolerability: 2 oxcarbazepine recipients and 14 phenytoin recipients were withdrawn due to adverse experiences. This was a statistically significant difference in favour of oxcarbazepine. The proportion of patients experiencing at least 1 adverse effect was 82.3% and 89.4% for	Novartis Pharma	

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								oxcarbazepine and phenytoin respectively. Patients and physicians assessment of tolerability on a 4 point scale favoured oxcarbazepine treatment C)Treatment retention: 24 patients on oxcarbazepine and 34 patients on phenytoin discontinued the trial prematurely		
Temkin NR. Antiepileptogenesis and seizure prevention trials with antiepileptic drugs: meta-analysis of controlled trials. Epilepsia 2001;42(4):515-524	Meta-analysis of controlled trials (47 in total) identified from Medline, Embase and the Cochrane Clinical Trials Register. Seventeen trials included phenytoin as a single or comparative agent.	Between 49 and 404 patients were included in the different studies	Adults and children	1.Alcohol related conditions (phenytoin versus placebo or no treatment) 2.Brain tumour (phenytoin versus placebo or phenobarbital) 3.Craniotomy (phenytoin versus placebo; or phenytoin versus carbamazepine 4. Traumatic brain injury phenytoin versus placebo, no treatment or carbamazepine)	To review the effects of phenytoin versus placebo, no treatment, phenobarbital or carbamazepine in preventing seizures associated with alcohol or associated with craniotomy/traumatic brain injury		Relative risk (ratio of seizure rate in the drug group to seizure rate in the control group) and 95% confidence interval for each drug. A probability (p) value for the test of no treatment effect (i.e. RR =1) was obtained. All p values are 2 sided	Phenytoin for provoked seizures after craniotomy or traumatic brain injury (RR 0.42;CI 0.25-0.71	Drug identified as effective for a condition if the overall test indicates that fewer people assigned to the active treatment had a seizure at the 2-sided 0.05 level.	
Tandon M et al. serum albumin-adjusted phenytoin levels: an approach for predicting drug efficacy in patients	Observational study over 6 months	50 patients	Male and female Indian patients, aged 15 years – 60 years, with newly diagnosed epilepsy	To investigate whether serum albumin adjusted phenytoin levels predicted clinical outcome better	Comparison of serum albumin adjusted phenytoin levels with total levels.	Six month duration 3 visits at 2 monthly intervals. Phenytoin	1. Serum albumin level 2.Serum phenytoin concentration	Post-graduate institute of Medical education and Research Chandigarh,		

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with epilepsy, suitable for developing countries. International Journal of Clinical Pharmacology and Therapeutics. October 2004;42(10):550-5				than total phenytoin levels.	Corrected phenytoin levels were calculated using the Sheiner- Tozer equation	was given for at least 1 month to allow steady state to be achieved.	3. Corrected phenytoin level obtained at visit 1	India		