Supplementary table for Lewis-Smith D *et al.* Early-onset genetic epilepsies reaching adult clinics. Brain 2020. https://doi.org/10.1093/brain/awaa029

Estimates of the number of children with genetic epilepsy onset before 3 years of age who will require adult neurology care

Syndrome and gene	*n* in Symonds *et al.* (2019)			Evidence for prognostication	Estimate of active cases at transition
	Total	Therapy-resistant seizures	Neurodevelopment		
Self-limited infantile epilepsy *PRRT2*	15	0	Moderate delay = 1 Mild delay = 1 Normal = 12 Missing data = 1	Typical *PRRT2*-related self-limited infantile epilepsy remits in early childhood in 89-98%, about a quarter of those with self-limited epilepsy in early childhood may develop paroxysmal kinesigenic dyskinesia as juveniles or adolescents, which commonly improves during adulthood (Ebrahimi-Fakhari *et al.*, 2015).	0-3
Dravet syndrome *SCN1A*	11	11	Moderate delay = 6 Mild delay = 3 Normal = 2	The childhood mortality of *SCN1A*-postive Dravet syndrome is 16%-21% and whilst seizures may become less frequent or even enter remission, adults continue to require anti-epileptic treatment (Jansen *et al.*, 2006; Akiyama *et al.*, 2010; Catarino *et al.*, 2011; Genton *et al.*, 2011; Cooper *et al.*, 2016).	9-11
GLUT1-deficiency syndrome *SLC2A1*	7	2 Missing data = 2	Mild delay = 3 Normal = 4	A third of people with seizures due to Glut1-deficiency syndrome continue to experience seizures in adulthood and many develop a movement disorder (Leen *et al.*, 2014).	1-7
Self-limited neonatal epilepsy *KCNQ2*	6	0	Normal = 6	These are self-limited in early childhood but 18% have seizures in adolescence or adulthood (Miceli *et al.*, 2010; Grinton *et al.*, 2015).	0-1
Early infantile-onset developmental and epileptic encephalopathy *CDKL5*	4 (1 male)	4	Severe delay = 3 Moderate delay = 1	A quarter of girls presenting with *CDKL5*-related epilepsy before 3 years old may enter treatment-free remission and another third may enter remission on continuing treatment (Bahi-Buisson *et al.*, 2008), the remainder are likely to have seizures refractory to current treatments (Muller *et al.*, 2016). Boys may have a more severe phenotype than girls (Liang *et al.*, 2019).	3-4
Unclassified epilepsy *SLC6A1*	3	2	Profound delay = 1 Moderate delay = 1	A significant minority of people with epilepsy and developmental delay beginning before 3 years of age and due to *SLC6A1* variants may enter remission, but many relapse and the majority continue to require antiepileptic medication (Carvill *et al.*, 2015c; Johannesen *et al.*, 2018a).	2-3
PCDH19-related epilepsy *PCDH19*	3	3	Profound delay = 1 Moderate delay = 1 Normal = 1	*PCHD19*-related seizures become less frequent at puberty as behavioural and psychiatric features become more prominent (Trivisano *et al.*, 2018). Beyond 15 years old 80% may be seizure-free for two years but relapse after long seizure-free intervals is reported (van Harssel *et al.*, 2013) and many patients require follow up into adulthood because of seizures, continuing anti-epileptic medication and suspected seizures.	1-3
Focal epilepsy *DEPDC5*	3	1	Normal = 3	*DEPDC5*-related epilepsies are usually active and require treatment into adulthood, although half of those amenable to surgery may achieve remission through this (Baldassari *et al.*, 2019).	2-3
Self-limited familial neonatal epilepsy *KCNQ3*	2	0	Normal = 2	These are self-limited in early childhood (Miceli *et al.*, 2014).	0-0
KCNQ2-related encephalopathy *KCNQ2*	2	1	Profound delay = 1 Moderate delay = 1	Seizures of *KCNQ2*-related epilepsy usually remit in childhood even if encephalopathy continues; both adults reported had become seizure-free for several years albeit with one remaining on anti-epileptic medication (Weckhuysen *et al.*, 2013).	0-2
Self-limited infantile epilepsy *KCNQ2*	1	0	Normal	These are self-limited in early childhood but 10-18% have seizures in adolescence or adulthood (Miceli *et al.*, 2010; Grinton *et al.*, 2015).	0-0
Genetic epilepsy with febrile seizures plus *SCN1A*	1	1	Normal	This participant had treatment-resistant febrile seizures plus with focal seizures. Most people with febrile seizures plus and focal seizures have active epilepsy into adulthood (Zhang *et al.*, 2017) and whilst many people become seizure-free, roughly half remain on medication (de Lange *et al.*, 2019).	0-1
Absences with eyelid	1	1	Moderate delay	People with onset of absences with eyelid myoclonia prior to 3 years of age are likely to remain refractory to antiepileptic	1-1

myoclonia *CHD2*				medications and to develop intellectual disability (Caraballo *et al.*, 2009). Only a quarter of the few reported individuals with *CHD2*-related epilepsy and treatment outcomes have obtained seizure-freedom and these required continuing medication (Carvill *et al.*, 2015a).	
Early infantile-onset developmental and epileptic encephalopathy *SCN8A*	1	1	Profound delay	*SCN8A*-related seizures with developmental delay usually require continuing antiepileptic therapy and mortality is estimated at 5%, mostly in early childhood (Johannesen *et al.*, 2018b). Seizures may come less frequent in adolescence with sodium channel multiple medications (Gardella *et al.*, 2018) and seizure-freedom is possible from the third decade (Larsen *et al.*, 2015).	1-1
Early infantile-onset developmental and epileptic encephalopathy *STXBP1*	1	0	Severe delay	A third of people with *STXBP1*-related epilepsy become seizure-free but late relapse has been observed and neurological follow up may be required for movement disorders (Stamberger *et al.*, 2016).	0-1
Epilepsy of infancy with migrating focal seizures *GABRA1*	1	1	Profound delay	Epilepsy of infancy with migrating focal seizures has a poor prognosis with continuing seizures, intellectual disability and risk of premature death in childhood (McTague *et al.*, 2013; McTague *et al.*, 2016), and *GABRA1*-associated epileptic encephalopathies have been reported reaching adulthood with refractory seizures (Johannesen *et al.*, 2016). However, the association between *GARBRA1* and this syndrome is yet to be described in sufficient people to inform prognostication in greater detail.	1-1
Epilepsy with myoclonic-atonic seizures *SLC6A1*	1	0	Moderate delay	A significant minority of people with epilepsy with *SLC6A1*-related myoclonic-atonic seizures and developmental delay beginning before 3 years of age may enter remission but many experience relapse and the majority continue to require antiepileptic drugs in adolescence (Carvill *et al.*, 2015c; Johannesen *et al.*, 2018a).	1-1
Epilepsy with myoclonic-atonic seizures *STX1B*	1	1	Normal	Familial *STX1B*-associated epilepsies including febrile seizures appear to have good prognoses with seizures remitting or responding to treatment in most people with normal intellectual development (Wolking *et al.*, 2019).	0-1
Ohtahara syndrome *KCNT1*	1	1	Profound delay	Early-onset *KCNT1*-related epileptic encephalopathies are associated with treatment-resistant epilepsy and limited neurodevelopment (Ohba *et al.*, 2015; McTague *et al.*, 2018). Their long-term outcomes and mortality have not been reported (Gertler *et al.*, 2018) but the epilepsy may progress to other epileptic encephalopathies such as Lennox-Gastaut syndrome which require follow up.	1-1
Progressive myoclonus epilepsy *POLG* (compound heterozygous)	1	1	Profound delay	Survival into adulthood following infant-onset bi-allelic *POLG*-related myoclonic epilepsy with status epilepticus and profound developmental delay is very rare at present (Wolf *et al.*, 2009; Lamperti and Zeviani, 2016).	0-1
Rett syndrome *MECP2*	1	0	Severe delay	In epilepsy associated with *MECP2*-positive Rett syndrome seizures become less frequent in adulthood but often remains active or requires antiepileptic medication (Steffenburg *et al.*, 2001) and neurological follow up is often needed to differentiate stereotypies from seizures (Glaze *et al.*, 2010).	0-1
Unclassified epilepsy *COL4A1*	1	1	Profound delay	*COL4A1* variants are associated with developmental structural abnormalities of the brain with most patients requiring continuing antiepileptic medication and treatment resistance is common (Zagaglia *et al.*, 2018).	0-1
Unclassified epilepsy *PCDH19*	1	1	Normal	*PCHD19*-related seizures become less frequent at puberty as behavioural and psychiatric features become more prominent (Trivisano *et al.*, 2018). Beyond 15 years old 80% may be seizure-free for two years but relapse after long seizure-free intervals is reported (van Harssel *et al.*, 2013) and many patients require follow up into adulthood because of seizures, continuing anti-epileptic medication and suspected seizures.	0-1
Unclassified epilepsy *PRRT2*	1	0	Normal	This individual presented with a febrile focal seizure aged 6 months and presumably had an afebrile seizure to result in a diagnosis of unclassified epilepsy without developmental delay and not requiring antiepileptic medication within the trial (before 4 years of age). Febrile seizures have been reported in patients with *PRRT2* variants but their detection may be due to coincidence rather than true association (Ebrahimi-Fakhari *et al.*, 2015) thus it is possible that this individual has had both self-limited infantile epilepsy and a coincidental febrile seizure, and therefore has a good prognosis.	0-1

Unclassified focal epilepsy *KCNA2*	1	0	Normal	*KCNA2* is associated with great neurological phenotypic heterogeneity and whilst seizures may respond well to treatment carriers often develop movement disorders that may require neurological follow up (Corbett *et al.*, 2016).	0-1
Unclassified focal epilepsy *KCNQ2*	1	1	Mild delay	Whilst the seizures of *KCNQ2*-related epilepsy usually remit in childhood even if encephalopathy continues, many continue antiepileptic medication (Weckhuysen *et al.*, 2013).	0-1
Unclassified focal epilepsy *PRRT2*	1	0	Severe delay	Focal epilepsy beginning at 19 months with severe developmental delay is not part of the typical *PRRT2* phenotypic spectrum but the heterozygous c.649dup, p.Arg217Profs*8 variant has been reported in an individual with intellectual disability and focal seizures until sudden unexpected death in epilepsy in adolescence (Labate *et al.*, 2013). However, the relatively high frequency of this most common disease-causing *PRRT2* variant suggests that its detection in other seizure disorders may be coincidental to other genetic or environmental factors influencing seizure phenotype (Ebrahimi-Fakhari *et al.*, 2015).	0-1
Unclassified generalised epilepsy *CACNA1A*	1	0	Moderate delay	*CACNA1A* variants have been associated with a range of neurological phenotypes including early-onset epileptic encephalopathies and genetic generalised epilepsies (Epi4K Consortium *et al.*, 2013; Epi4K Consortium, 2016) and whilst little is known of the long-term prognosis for epilepsy with generalised myoclonic seizures, people with disease-causing variants remain at risk of migraine, ataxia and seizures into adulthood (Damaj *et al.*, 2015).	0-1
West syndrome *DEPDC5*	1	1	Severe delay	*DEPDC5*-related epilepsies are usually active and require treatment into adulthood, although roughly half of those amenable to surgery may achieve remission (Baldassari *et al.*, 2019). In particular, West syndrome with seizures resistant to multiple antiepileptic drugs and ketogenic diet and multiple grey matter heterotopia associated with *DEPDC5* is likely to remain active (Carvill *et al.*, 2015b).	1-1
West syndrome *SCN2A*	1	1	Profound delay	This child's afebrile focal seizures in the first week of life remained resistant to sodium valproate and evolved into West syndrome with profound developmental delay. Sixty per cent of people with *SCN2A*-related epileptic encephalopathies presenting before 3 months old obtain seizure-freedom, particularly if continuing sodium channel blocking medications; however, they may develop complex neurological disorders (Wolff *et al.*, 2017).	1-1
Total	76	36	Profound delay = 9 Severe delay = 7 Moderate delay = 14 Mild delay = 8 Normal = 36 Missing data = 2		25-56 (33-74%)

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