COMMENTS RECEIVED FROM EXTERNAL REFEREES, FEBRUARY 2019

SIGN Epilepsies in children and young people

All reviewers submitted declarations of interests which were viewed before comments were addressed.

Invited reviewers			**Type of response and declared interests**
AB	Dr Andreas Brunklaus	Consultant Paediatric Neurologist, Royal Hospital for Children, Glasgow	Individual response. Remuneration as holder of paid office, director of an undertaking, partner in a firm – I am a consultant Paediatric Neurologist with no commercial interests.
CH	Christine Hepburn	Principal Pharmaceutical Analyst, SMC, Healthcare Improvement Scotland	Individual response.
Open consultation			
BACD		Dr Karen Horridge commenting on behalf of the British Academy of Childhood Disability (BACD)	Group/organisation response. Nature and purpose of your organisation: BACD operates as an affiliate group of the British Association of Community Child Health, a specialty group of the Royal College of Paediatrics and Child Health, and as the UK branch of the European Academy of Childhood Disability. Membership is encouraged from all disciplines working in the field of childhood disability. The aims of the BACD are: to be a means of networking and mutual support for all those working in district and tertiary level services for children with neurodevelopmental disability to promote communication between Child Development Teams to organise regular national multidisciplinary meetings on child development and disability

			to promote the development of quality standards, guidelines for good practice and audit in the field of child development and disability to encourage debate and promote research into the many outstanding questions in childhood disability to work closely with voluntary organisations and others to advocate for children with disabilities and their families. The BACD committee has representation from the disciplines of Paediatrics, Psychiatry, Speech and language therapy, Physiotherapy, Occupational therapy, Psychology, Nursing and Education. BACD is a registered charity. How might the statements and recommendation in the draft impact on your organisation's functions: BACD welcome this guideline, especially as it has been developed with input from patients and families. BACD look forward to the patient version of the guideline.
DJ	Dr Dinakaran Jayachandran	Consultant Paediatrician, Darlington Memorial Hospital, CDDFT, Darlington	Individual response. Nothing declared.
EA	Epilepsy Action	Louise Cousins on behalf of Epilepsy Action	Group/organisation response. Nature and purpose of your organisation: Epilepsy Action is a UK-wide voluntary organisation which exists to improve the lives of everyone affected by the

			condition. As a member-led organisation, we are led by and represent people with epilepsy, their friends, families and healthcare professionals. How might the statements and recommendation in the draft impact on your organisation's functions: Our organisation - or more specifically, our members and the people we represent - would be strengthened following a recommendation in favour of this intervention as it could improve care and increase management options for patients in Scotland.
GB	Dr Gunjan Baweja	Paediatrician, Government Multispecialty Hospital, Chandigarh	Individual response. Nothing declared.
RCPCH		Dr Helen Lewis commenting on behalf of Royal College of Paediatrics and Child Health	Group/organisation response. How might the statements and recommendation in the draft impact on your organisation's functions: RCPCH may refer to guideline in formulating its own guidelines and for teaching and training.
SA	SUDEP Action	Sammy Ashby commenting on behalf of SUDEP Action	Group/organisation response. Nature and purpose of your organisation: Voluntary organisation dedicated to tackling epilepsy-related deaths and specialised in supporting those bereaved by epilepsy across the UK and internationally. How might the statements and recommendation in the draft impact on your

			organisation's functions: *[see comments below under 'General']*
UCBP	UCB Pharma	Iain McJennett commenting on behalf of UCB Pharma	Group/organisation response. Nature and purpose of your group or organisation: Pharmaceutical manufacturer How might the statements and recommendation in the draft impact on your organisation's functions: *[see comments below under 'General']*
Group members			
AM	Ailsa McLellan	Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh	
CJ	Chris Jeans	Development Officer for Scotland, SUDEP Action Scotland, Livingston	

Section		Comments received	Development group response
	RCPCH	Proof editing needed – to make English clearer and less wordy, as stated in introduction.	The guideline has been edited before publication.
	BACD	Overall the guideline is very easy to read and follow, well laid out and generally easier to understand than some other guidelines. BACD welcome the patient version and look forward to seeing this and hearing feedback from families.	Thank you.
	EA	We would like to thank SIGN for this comprehensive and detailed draft guidance and for the opportunity to comment. We believe the draft guideline has the potential to improve the diagnosis and treatment of epilepsies in children in Scotland. Epilepsy Action would welcome the opportunity to further engage with this guideline development other relevant processes.	Thank you.
	SA	As an organisation we are deeply concerned by this draft guideline and the potential impact it could have particularly regarding the discussion of SUDEP and epilepsy risks, the management of these risks, and support for families who are bereaved by epilepsy. The information and recommendations within section 9 particularly appear in many places to be a backwards step from previous guidance and information provision in Scotland, and in comparison, to other existing UK guidelines. If such a guideline was released in its current form it could prove incredibly detrimental to the work of our organisation and of clinicians across the UK, who have worked over many years to develop good practice regarding discussing and reducing epilepsy mortality. Comments regarding consistency and proofing provided in earlier sections.	Section 9 has been revised. Specific comments from the reviewer are addressed in section 9. The guideline has been edited before publication.
	UCBP	UCB welcome the opportunity to comment on the Epilepsies in children and young people: Investigative procedures and management national clinical guideline (Scottish Intercollegiate Guidelines Network.	

		Draft 1.60, 05 November 2018). UCB are committed to ensuring that treatment decisions for people with Epilepsy are a collaborative process that supports patients, and their carers, to reach an informed decision about their care. Clinicians are increasingly moving towards an approach of tailoring treatment, ensuring people get the right choice of medicines, at the right time, and are engaged in the process by their clinical team. This medicines optimisation approach, where a suite of drugs is available so that patients' treatment can be individualised, improves the outcomes for patients, prescribers and health economies. We are disappointed that the guidelines do not include lacosimide (Vimpat®) in line with its Scottish Medicines Consortium January 2018 assessment. The advice is summarised as follows: ADVICE: following an abbreviated submission lacosamide (Vimpat®) is accepted for restricted use within NHS Scotland. Indication under review: as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adolescents and children from 4 years of age with epilepsy. SMC restriction: patients with refractory epilepsy. Treatment should be initiated by physicians who have appropriate experience in the treatment of epilepsy. SMC has previously accepted lacosamide for restricted use as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older. (SMC No 1301/18 UCB Pharma Ltd https://www.scottishmedicines.org.uk/media/3108/lacosamide_vimpat_abbreviated_final_jan_2018_for_website.pdf)	We accept that this is available however the evidence available was insufficient to support a recommendation (SMC, data was extrapolated). It is, however, listed in Annex 5, as an adjunctive therapy, under the NICE recommendations. As above.

		UBC request that the final guideline includes Vimpat in line with this assessment, in line with SMC assessment. Finally, we would like to draw your attention to the imminent publication of the SMC assessment of brivaracetam (Briviact®) for the treatment of partial onset seizures with or without secondary generalisation in children from 4 years of age to 15 (SMC2113 https://www.scottishmedicines.org.uk/medicines-advice/brivaracetam-briviact-abbreviated-smc2113/). The advice is due on December 6th 2018 and we ask that this be considered for inclusion within the final guideline document.	Brivaracetam was included in the search as SMC data was extrapolated from adult studies.
	CH	paragraph 3: the text should refer to …marketing *authorisation*, not marketing *licence*	Amended
	RCPCH	I have read the draft guideline to refresh my understanding of new evidence and techniques, as I was (until recent retirement) Consultant Paediatrician, special interest in Neurodevelopmental Disorders. I do not wish to comment on the detail of the guidance but there are errors in English syntax and use of English. The documents need proof reading and correction. I might be able to help but not within tight time frame.	The guideline has been edited before publication.
	BACD	BACD agree.	No action required.
1.1.1	BACD	BACD look forward to seeing the patient version of the guideline, also to learning about feedback on it from families in due course.	No action required.
	EA	Quality of Life – Questions around participation in leisure and play activities are often raised with Epilepsy Action by the parents or care givers of children with epilepsy. This has particular significance for children who have developed epilepsy as a result of a head injury. In these instances a consultant's opinion is often needed before a child is allowed to participate. We recommend explicit inclusion of 'Leisure and Play Activities' under the 'Quality of Life' subheading.	Leisure and play included in section 10.3. We are not addressing seizures following head injury in this guideline. The information provided following head injury depends on the type of injury and this is best addressed in brain injury/head injury guidelines.
1.1.2	BACD	A wide range of views have been	Thank you.

		included which BACD welcome.	
1.2	BACD	Reads well.	Thank you.
1.2.1	BACD	Very clear objectives.	Thank you.
	UCBP	UCB welcome the opportunity to comment on the Epilepsies in children and young people: Investigative procedures and management national clinical guideline (Scottish Intercollegiate Guidelines Network. Draft 1.60, 05 November 2018). UCB are committed to ensuring that treatment decisions for people with Epilepsy are a collaborative process that supports patients, and their carer's, to reach an informed decision about their care. Clinicians are increasingly moving towards an approach of tailoring treatment, ensuring people get the right choice of medicines, at the right time, and are engaged in the process by their clinical team. This medicines optimisation approach, where a suite of drugs is available so that patients' treatment can be individualised, improves the outcomes for patients, prescribers and health economies.	Thank you for the feedback.
1.2.2	BACD	All clear and link with UK NICE guidance.	Thank you.
1.2.3	BACD	Although targeted at professionals, it will be interesting to hear the views of families, once the family version is published.	Views and information points have also been included in appropriate sections throughout the guideline.
1.2.4	BACD	BACD look forward to seeing this, but are disappointed not to have had the opportunity to also comment on this.	This has not been developed yet. Your interest is noted and details passed to Patient Information Officer.
1.3	BACD	This is clear.	No action required.
1.3.1	BACD	This is clear.	No action required.
1.3.2	BACD	This explains the situation well.	Thank you.
1.3.3	BACD	Clear.	No action required.
3.1	BACD	This clear and matches the NICE guideline.	Thank you.
3.2	BACD	BACD has a strong view on this. Whilst understanding that for those presenting for the first time with possible epilepsy, in the context of no previous long term disabling conditions, the "diagnosis of epilepsy is most appropriately delivered in the setting of a dedicated first-seizure or epilepsy clinic" as stated in the	Now section 3.4. This has been amended to a dedicated neurology or neurodisability clinic.

		guideline. However, for disabled children and young people who are already cared for by paediatricians with disability expertise, then it would be preferable for this group to receive their epilepsy diagnosis from their usual lead clinician who knows them and their family well, as long as this lead clinician has the epilepsy competences laid out in the guideline.	This has been amended to a trained paediatrician with experience in epilepsy.
	GB	Paediatrician should be included in person who can make diagnosis along with epilepsy specialist.	Now section 3.4. Thank you the wording of this has been changed to paediatrician.
3.3	BACD	Excellent section.	Thank you.
3.4	BACD	Very clear.	Thank you.
3.5	BACD	BACD welcome the inclusion of the new international League Against Epilepsy classification. This section will need to be updated as the classification evolves.	We have made reference to this in section 3.2 and stated that the 2017 classification is used in this guideline.
	AM	The classification of epileptic seizures should include most up to date ILAE which at the moment is Fisher 2017, Epilepsia.	The ILAE 2017 classification has been included in section 3.2.
General	BACD	This section is clear and helpful.	Thank you.
4.1.1	BACD	Clear and helpful.	Thank you.
	EA	We welcome reference to the use of EEG data and video information concurrently to aid interpretation and correlation of EEG findings with clinical events. Similarly, we welcome the inclusion of factors that should be considered when deciding on the types of EEG investigation to use as second line as suggested best practice. We recommend more explicit reference to the provision and use of specialist facilities with video-EEG monitoring capabilities for the diagnostic investigation of children with highly complex seizure disorders and co-morbidities.	Provision and use of specialist facilities is now covered in the implementation section
4.1.2	BACD	This is helpful.	Thank you.
4.1.3	BACD	This is helpful.	Thank you.
4.1.4	BACD	This is helpful.	Thank you.
4.1.5	BACD	This is helpful.	Thank you.
4.2	BACD	This is helpful.	Thank you.
4.3	BACD	This is clear and helpful.	Thank you.
4.3.1	BACD	This is clear.	Thank you.
4.3.2	BACD	This is clear.	Thank you.

4.3.3	BACD	Whilst understanding the importance of more detailed imaging, the practicalities of delivering 3 Tesla MRI in an equitable way, taking into account remote and rural populations, should be addressed.	Thank you the text below has been added to the implementation section (section 11.3.) for clarity: 3T imaging will be available in Edinburgh, Glasgow, Dundee and Aberdeen. GA facilities will be limited except in Edinburgh where GA 3T will be standard. Where there has been failure of medical therapy and further imaging is required, it is not unreasonable to expect that imaging in one of the larger centres will be required. GA 3T imaging will be available at the national epilepsy surgery site.
4.4	BACD	This is clear and helpful.	Thank you.
4.4.1	BACD	Clear and helpful.	Thank you.
4.4.2	BACD	Clear and helpful.	Thank you.
5.1	CH	Paragraph 6: should refer to SMC *advice*, rather than SMC *recommendations*	This sentence has been removed, and relevant SMC advice added to the appropriate sections.
	DJ	Although there are good details about anti-epileptic drugs, I couldn't find details about the recommendations for rescue medications like Buccal Midazolam which is in common practice for prolonged convulsive seizures lasting for more 5 minutes. Could SIGN make some recommendations for Buccal Midazolam and also suggest that Buccal is safe and better than rectal diazepam as some professionals like ambulance crew would still continue to use Rectal diazepam in preference to Buccal Midazolam. Could SIGN throw some evidence or recommendation on the use of Intranasal Midazolam instead of Buccal Midazolam for children who have copious secretion during their convulsive seizures.	Outwith scope. Covered by APLS and flow chart in NICE 2012. Outwith scope. Outwith scope.
	BACD	Clear and helpful	Thank you.
	EA	Epilepsy Action recognises the omission of the treatment of status epilepticus from this draft guideline in light of its inclusion in the Royal College of Emergency Medicine and Advance Paediatrics Life Support guidelines. Despite this, we recommend including information about administering emergency medicines in the community	This is not within the remit of this guideline.

		and the importance of individual care plans, specifically for parents and care givers, within this guideline. https://www.epilepsy.org.uk/info/firstaid/emergency-treatment-seizures-last-long-time.	
	SA	Information regarding Sodium Valproate, the Pregnancy Prevention Progamme and pre-conception counselling should be provided in a balanced way to ensure young women with epilepsy are able to make informed choices about their care in the context of being aware of epilepsy risks including risk of SUDEP/Mortality. Previous maternal death reports have demonstrated this need following women with epilepsy ceasing medication and not adequately accessing services which may have enabled informed choices to be made about their treatment and lifestyle. References: *1. Centre for Maternal and Child Enquiries (CMACE). Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006–08. The Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG 2011;118(Suppl. 1):1–203.* *2. Knight M, Nair M, Tuffnell D, ShakespeareJ, Kenyon S, Kurinczuk JJ (Eds.)onbehalfof MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–15. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2017.* *3. https://sudep.org/article/closer-look-mbrrace-maternal-deaths-report-what-does-mean-mothers-epilepsy*	The link to the MHRA website has been added to direct readers to the most current advice on use of sodium valproate, to allow for informed discussion.
5.2	BACD	Clear and helpful	Thank you.
5.2.1	BACD	Clear and helpful	Thank you.
5.2.2	BACD	Clear and helpful	Thank you.
	UCBP	Lacosamide (Vimpat®) is accepted for restricted use within NHS Scotland. Indication under review: as adjunctive therapy in the treatment of partial-onset seizures with or without secondary	Both drugs are licensed using extrapolated data. Both were included in the literature search but no direct evidence was identified.

		generalisation in adolescents and children from 4 years of age with epilepsy. SMC restriction: patients with refractory epilepsy. Treatment should be initiated by physicians who have appropriate experience in the treatment of epilepsy. SMC has previously accepted lacosamide for restricted use as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy aged 16 years and older. (SMC No 1301/18 UCB Pharma Ltd https://www.scottishmedicines.org.uk/media/3108/lacosamide_vimpat_abbreviated_final_jan_2018_for_website.pdf) We would also like to draw your attention to the imminent publication of the SMC assessment of brivaracetam (Briviact®) for the treatment of partial onset seizures with or without secondary generalisation in children from 4 years of age to 15 (SMC2113 https://www.scottishmedicines.org.uk/medicines-advice/brivaracetam-briviact-abbreviated-smc2113/ The advice is due on December 6th 2018 and we ask that this be considered for inclusion within the final guideline document.	
5.3	BACD	Clear and helpful	Thank you.
	EA	We welcome the inclusion of additional warnings around the use of sodium valproate and specific reference to the 2018 MHRA safety advice on the use of valproate medicines in women and girls of childbearing age and associated Pregnancy Prevention Programme. We would recommend a reference to ongoing work and potential updates to the guidance in light of developments in this area. Reference to potential teratogenic effects of other relevant medications should also be acknowledged.	Noted, thank you. The latest updates and links to MHRA have been added. Common adverse effects reported in studies are discussed, however, prescribers should consult up-to-date advice from the BNF and MHRA before prescribing.
5.3.1	BACD	Clear and helpful, although time will tell how acceptable families find ethosuxamide and its side effect profile, as compared to sodium valproate.	No action required. The section has been edited to allow for further discussion of the NICE recommendations.

5.4	BACD	Clear and helpful.	Thank you.
	EA	Cannabidiol – While recognising that there are currently no licensed cannabidiol-based drugs for the treatment of epilepsies we would see merit in referencing the NICE appraisal of 'Cannabidiol for adjuvant treatment of seizures associated with Lennox-Gastaut Syndrome', ID1211. As a minimum, we would recommend a reference to ongoing monitoring and potential updates to the guidance in light of developments in this area.	The draft has been updated with more recent evidence.
5.5	BACD	Clear and helpful.	Thank you.
5.6	BACD	Clear and helpful.	Thank you.
5.7	BACD	Clear and helpful.	Thank you.
	EA	Cannabidiol – While recognising that there are currently no licensed cannabidiol-based drugs for the treatment of epilepsies we would see merit in referencing the NICE appraisal of 'Cannabdiol for adjuvant treatment of seizures associated with Dravet Syndrome', ID1308. As a minimum, we would recommend a reference to ongoing monitoring and potential updates to the guidance in light of developments in this area.	The draft has been updated with recent evidence and SMC advice included.
5.8.1	BACD	Clear and helpful.	Thank you.
6.1	BACD	Clear and helpful	Thank you.
6.1.1	BACD	Clear and helpful	Thank you.
6.1.2	BACD	Clear and helpful	Thank you.
	AB	As child neurologist I run the ketogenic diet clinic at the RHC in Glasgow. The ketogenic diet is the only curative treatment available for Glut 1 deficiency syndrome and is the only treatment that will be able to prevent these individuals from developing a learning disability. The ketogenic diet should therefore be the RECOMMENDED treatment for Glut 1D. Given that this is the only curative treatment for this disorder it would be unethical to perform any RCT in this regard.	Agree – this has been changed to 'recommended'.
6.1.3	BACD	Clear and helpful	Thank you.
	AB	Similar to the above PDH deficiency can only be treated in a meaningful way by the ketogenic diet to optimise future outcome. It has been shown that this	This goes into metabolic disorders and is therefore out of the scope of this guideline.

		improves later cognitive outcomes and can be explained biochemically. Therefore the ketogenic diet should be the RECOMMENDED treatment for PDH deficiency.	
6.1.4	BACD	Clear and helpful	Thank you.
6.1.5	BACD	Clear and helpful	Thank you.
6.1.6	BACD	Clear and helpful	Thank you.
6.2	BACD	Clear and helpful	Thank you.
6.2.1	BACD	Clear and helpful	Thank you.
6.2.2	BACD	BACD especially welcomes the attention to these issues, which can have more impact than the epilepsy itself.	No action required.
6.2.3	BACD	BACD warmly welcomes attention to this important area.	No action required.
6.2.4	BACD	Clear and helpful.	Thank you.
6.3	BACD	Clear and helpful.	Thank you.
	AM	In the R for VNS take out refer to SPESS but include if not suitable candidate for epilepsy surgery evaluation (then maybe reference epilepsy surgery section).	This has been updated.
6.4.1	BACD	BACD warmly welcomes attention to this important area.	No action required.
7.1.1	BACD	BACD welcomes attention to the recognised association between the epilepsies, autism spectrum, attention deficit and mental health conditions.	No action required.
	EA	Epilepsy Action welcomes the inclusion of a detailed and comprehensive section on psychology in the draft guideline. This is an important area of focus given the noted higher prevalence of neurodevelopmental disorders in children with epilepsy. Given that this is an area that has previously been somewhat overlooked, this is particularly welcome.	Thank you.
7.1.2	BACD	BACD welcomes the signposting to expert assessment pathways for those with red flags for autism spectrum conditions. This section would be strengthened by emphasis on the importance of timely assessment and diagnosis, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists, some of three years or more.	The authors acknowledge that timely assessment and diagnosis is crucial for all neurodevelopmental disorders and this is emphasised in the introductory paragraph (see section 7.1.1 – second paragraph: *"Early and appropriate identification of comorbidities can help tailor appropriate interventions and modifications to lessen their impact on the child or young person's development and wider functioning.*" For the sake of brevity, this point is

			made once in reference to all conditions.
7.1.3	BACD	BACD agree that screening is not evidence-based, but agree that identification of red flags for autism conditions and referral on to appropriate multidisciplinary assessment pathways is important. BACD welcomes the signposting to expert assessment pathways for those with red flags for autism spectrum conditions. This section would be strengthened by emphasis on the importance of timely assessment and diagnosis, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists, some of three years or more.	See response to comment in 7.1.2.
7.1.4	BACD	BACD welcomes the signposting to expert assessment pathways for those with red flags for attention deficit conditions. BACD welcomes the signposting to expert assessment pathways for those with red flags for autism spectrum conditions. This section would be strengthened by emphasis on the importance of timely assessment and diagnosis, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists.	See response to comment in 7.1.2.
7.1.5	BACD	BACD agree that whilst population screening is not evidence-based, identification of red flags for attention deficit conditions and referral on to appropriate multidisciplinary assessment pathways is important. BACD welcomes the signposting to expert assessment pathways for those with red flags for autism spectrum conditions. This section would be strengthened by emphasis on the importance of timely assessment and diagnosis, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists.	See response to comment in 7.1.2.
7.1.6	BACD	BACD welcome inclusion of this important section, but are concerned as to equity of availability and access to neuropsychological services for all with epilepsies who may need them, taking into account populations in remote and	Now section 7.2. The good practice points have been reworded to highlight the lack of specialist neuropsychology services in some areas and include reference to appropriate local services/alternatives.

		rural areas.	Other feedback has included concerns about whether a neuropsychological assessment should be first step and so recommendations/ good practice points have been worded to reflect this and emphasise more stepped intervention based on available resources.
7.1.7	BACD	BACD welcome inclusion of this important section, but are concerned as to equity of availability and access to neuropsychological services for all with epilepsies who may need them, taking into account populations in remote and rural areas.	Now section 7.2.1. See above; good practice point has been reworded to highlight lack of access to these services in some areas.
7.1.8	BACD	BACD warmly welcomes this important section. This section would be strengthened by emphasis on the importance of timely assessment, diagnosis and treatment, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists.	See response to section 7.1.2.
7.1.9	BACD	BACD welcomes this important section.	No action required.
7.2.1	BACD	BACD warmly welcomes this important section. This section would be strengthened by emphasis on the importance of timely assessment, diagnosis and treatment, which could act as a lever for those services struggling to improve their resources that currently have long waiting lists.	See response to comment in section 7.1.2.
7.2.2	CH	Referring to the recommendation that sertraline or venlafaxine could be considered in children/adolescents with epilepsy and comorbid depression, note that the SPC for venlafaxine states that it is not recommended for use in children and adolescents. Therefore this recommendation is outwith the terms of the product licence for this medicine (note there is no relevant SMC advice for these medicines since they predate the establishment of SMC).	The recommendation specifically for venlafaxine has been removed.
8.1	BACD	Clear and helpful	Thank you.
8.2	BACD	Clear and helpful	Thank you.
8.3	BACD	Clear and helpful, although mostly geared to those with epilepsies without complexing disabling conditions. The importance of processes of transition addressing each and every need of the latter group would be very helpful, as although hand over for	We have looked again at the studies and there was insufficient evidence to provide more specific advice on young people with complex needs.

		epilepsy care may go well, there also needs to be transition planning around the whole array of complex needs that young people with complex disabling conditions and their families experience.	
	EA	We welcome the reference to self-management within the recommendations and the additional mention of individualised approaches to both transition and self-management. Epilepsy Action would encourage the inclusion of additional guidance around structured self-management plans.	This will be addressed in the patient/young person's/parent and carer's guidance.
General	BACD	Important section.	No action required.
	EA	We welcome the inclusion of information about causes of death in epilepsy beyond SUDEP. We recommend explicit inclusion of information and preventive measures related to other causes of death in epilepsy, beyond SUDEP, in the associated recommendation.	There is now text in the draft on information and preventive measures related to other causes of death in epilepsy, beyond SUDEP, in the associated recommendation.
	SA	Proof reading required throughout – some whole sections have been repeated or contain errors (eg: section 9.2, paragraphs 6 & 7; 9.3 para 3;) Opening line – 'although death is rare in childhood' is inaccurate, can help to downplay individual's risk levels in both clinicians and patients minds and bereaved families in particular find this very difficult to read. There has been research published recently which shows the rates are similar to those for adults: available and I believe more is soon to be published also showing this (Keller et al, 2018: doi:10.1212/WNL.0000000000005762). The other causes of 50% of epilepsy-related deaths and epilepsy risks which can lead to death in general are not covered here in much depth at all other than a couple of sentences here. Caution should be taken on focusing too heavily on just SUDEP as other causes of epilepsy mortality are also known to be potentially avoidable.	The guideline has been edited before publication. We have now amended this to include epidemiology data from the evidence, including citing the Keller paper. As above comment – text on other causes now included.
	CJ	'Although death is rare' - it is NOT rare – and I do not think 'rare' is the correct terminology to use.	This sentence has been removed. See comment above – amended to

		This could affect Health Professionals [non epilepsy specialists] in not giving out the correct information and patients in not fully understanding about ALL risks. **Maybe that is why I did not learn about this until my son died -**which is obviously not the way to find out. Fatal Accident Enquiry could have been mentioned – discussing risk. SUDEP conversation should be repeated over time – NOT just given once, people could become complacent in risk management. Research was heavy, which I found quite daunting initially and felt that although some used was not paeds specific, others more recent could have been included.	epidemiology data from Keller article There is now a GPP on the importance of repeating risks of mortality, including SUDEP over time. Qualitative and quantitative studies identified in the literature search have been included.
9.1	BACD	Well explained.	Thank you.
	SA	There has been research published recently (since the AAN guidelines which are referenced) which shows the rates of SUDEP in children are similar to those for adults: available and I believe more is soon to be published also showing this (Keller et al, 2018: doi:10.1212/WNL.0000000000005762).	The Keller paper is now referenced.
9.2	BACD	Clear guidance.	Thank you.
	SA	The Scottish Fatal Accident Inquiries appear to not have been included as evidence for this section, though they provide significant insight and learnings to why discussing SUDEP & Epilepsy risks is vital to help prevent deaths. Is there a rationale behind their exclusion given the evidence that has been included still references the legal implications of this topic? Concern about the high SUDEP mortality rates in the UK were first expressed more than 20 years ago now. Pressure from relatives of the deceased and epilepsy charities eventually resulted in the UK funding the National Sentinel Audit of Epilepsy Deaths and in the holding of two major SUDEP inquiries in Scotland, the first in 2002 and another in 2010/11. These two inquiries into SUDEP were highly critical of the reasons given by neurologists for not communicating with patients about SUDEP in relation to the	FAI are based on the opinions of the sherriff in relation to the differing evidence presented. Evidence presented is not based on medical perspective but other evidence. FAI often look at whether there was something wrong with processes and can often relate to the legal context around previous cases. As such they are not considered as robust clinical evidence.

		deaths that were investigated. An ombudsman report into the complaint that formed part of the 2011 inquiry also drew attention to the harm experienced by bereaved families, where there had been no communication about risk and where the patient and family were excluded from considerations about risk. It is widely believed that these inquiries, and the resulting reports, raised awareness and resulted in a reduction in SUDEP fatalities in the UK. However, it is no secret that the neurology profession in the UK was very unhappy with these inquiries, although perhaps supportive of some of the findings v. For example, this dissatisfaction in relation to the second inquiry is reflected in the comments of one neurologist quoted in a 2017 publication, "...I don't think that was an amazingly useful event that ruling". Medico-Legal context: The 2004 Beran article used in the guideline reflects one school of thought that at that time considered that none of the known risks of SUDEP were amenable to modification. At the time it went against the school of thought informed by the National Audit of Epilepsy Deaths that found 42% of epilepsy deaths in UK were potentially avoidable. Population audits and research since 2002 have strengthened the evidence base on reduction of risks and avoidability of deaths. There is now an overwhelming body of evidence however which suggests that much can be done to reduce risks. The 2004 article is also out of date in terms of the development of medical negligence law on discussion of risk in the UK jurisdiction and also excludes the wider medico-legal context in the aftermath of a sudden death which may be avoidable. This wider context includes individual complaints, the Ombudsman and state triggered Fatal Accident Inquiries. It also excludes consideration of the benefits of guidance that would support learnings and support for families and	The medico-legal section has been removed/ The guideline group decided that the medico legal aspect should not be commented on as the group is not qualified to make legal recommendations.

		clinicians in the aftermath of deaths. The article which is suggestive of information on SUDEP causing harm also lacks any evidence base or legal basis. Information giving temporary anxiety is expected in other medical disciplines as part of the natural adaptation (Martineau). Legal case law does not support temporary distress as a `harm'. General Medical Council guidance in 2008 provided: "You should not withhold information necessary for making decisions for any (other) reason unless you believe that giving it would cause the patient serious harm. In this context "serious harm' means more than that the patient might become upset or decide to refuse treatment" and "If you withhold information from the patient you must record your reason for doing so in the patient's medical records and you must be prepared to explain and justify your decision". The Ombudsman 2009 also supported this, with reasons for not telling (the risk of upset) not being "in step with the direction of travel of NHS Scotland towards a mutual NHS". The case of Montgomery v Lanarkshire Health Board (Scotland) (2015), the UK Supreme Court has now decided how clinicians should communicate risk. Before Montgomery, this was assessed by whether or not a clinician had acted in line with the views of a responsible body of medical opinion. Montgomery confirms the duty to advise of material risk, then goes on to examine what a material risk is. It concludes that the clinician has to understand the effect on the particular patient - on his or her life and decision-making - and so must consider non-medical as well as medical factors. Materiality of risk is fact-sensitive and sensitive to the characteristics of the patient. The way to do this, Montgomery says, is by having meaningful dialogue about risk with the patient. A clinician can't wait to be asked, as a patient may not know there is anything to ask about, nor can a clinician assume that the patient does not need to know or would not attach significance to a risk.	This case was not in relation to SUDEP, the evidence was regarding what a doctor would do and what a patient would expect.

		The Montgomery judgment now confirms in law principles that were already evolving in the guidance to clinicians from their professional bodies (for example, the General Medical Council, the Nursing & Midwifery Council). This Scottish legal system also includes complaints and public inquiries which have different remit and include purpose of making recommendations on whether preventative measures 'might' have saved a life. Scotland rulings: The first Fatal Accident Inquiry into epilepsy investigated the sudden death of a young woman, aged 17 years (Taylor, 2002). It found a catalogue of failures for the appropriate care of the deceased including: 1) failure on the part of specialists to alert the general practitioner as to what circumstances required re-referral; 2) failure on the part of the general practitioner to prescribe appropriate doses of medication; 3) failure to re refer the deceased when the seizures did not stop after 2 years; 4) failure to re-refer the deceased when the intensity, form, and duration of her seizures changed as the deceased matured; and 5) failure by the medical team to discuss with the deceased's family, the diagnosis, the attendant risks, and how these risks might be properly managed. The sheriff stated that given the association between seizures and SUDEP and the potential for control, that it was a 'short step' to the view that if the deceased had been referred for review she might not have died. He determined that the family ought to have been informed that the deceased was suffering from epilepsy, the risks of SUDEP explained, and a discussion held on how her condition might be managed. The most important recommendation was considered to be the need for a personal care plan. The Sheriff suggested that all the key issues would have been addressed if a care plan, '. . . shared or otherwise' had been	

		produced, and '. . . it might have saved her life' (Taylor, 2002). In Scotland in 2003 SIGN produced guidelines aimed at health professionals in respect of the diagnosis and treatment of epilepsy. The SIGN guidelines recommended the use of a checklist "to help healthcare professionals to give patients and carers the information they need in an appropriate format". An "example checklist" was provided and listed information about SUDEP as essential. These guidelines were challenged in the Erin Casey Fatal Accident Inquiry in 2011 when it was argued that it was up to clinicians to reach their own judgement and that the legal test was whether reasonable precautions such as giving advice would have prevented death. This argument was rejected as it did not meet the proper legal test for public inquiries and coronial courts: "Certainty that the accident or death would have been avoided by the reasonable precaution is not what is required. What is envisaged is not a "probability" but a real or lively possibility that the death might have been avoided by the reasonable precaution" Carmichael, Sudden Deaths and Fatal Accident Inquiries 3rd Edition page 174 para 5-75.	A mixed-methods review is now included and the wording of the recommendation changed to 'should' instead of 'should consider', based on this review.
		The research base included in this section of the draft guideline is mostly from outside of the UK, yet much work has been done on SUDEP/Epilepsy mortality within the UK that has not been included which can add much strength to this guideline.	See response above.
		Other research was included in this draft despite not being specifically about paediatric populations (Section 9.2, paragraph 4 acknowledges this), so it is concerning that much relevant, recent research on the topic has been excluded.	See response above.
		Due to the research inclusion/exclusion criteria, the recommendations in section 9.2 now cannot be 'considered strong' – should this not be revisited so that the range of information that is available to support clinicians with discussing SUDEP/Epilepsy risks is included to	There is now a GPP on repeating this over time in section 9.

		strengthen the guideline and better support clinicians in having these conversations? There is significant research available from UK studies which support the standardised discussion of epilepsy risks/SUDEP/Mortality.	
		Much of this section focuses on explaining the criteria around research selection, yet does not provide much guidance into how these risks/SUDEP should be discussed with patients. As an organisation specialised in this area, this is a question we are asked often, particularly by non-specialists, so providing more information/evidence here relating to this aspect would likely prove beneficial to readers. Section 10.2 provides some additional guidance on this, though the discussion of SUDEP/risks has been well documented in multiple research studies which could be drawn upon here.	There is now a GPP on repeating this over time. There is now a GPP on repeating this over time.
		Recommendations – it is not clear when discussions about SUDEP should happen other than on or near time of diagnosis – it implies it should only happen once which could be misleading to non-specialist clinicians. There is lots of research out there to show it should happen regularly and reviews including this information should happen repeatedly.	There is now a GPP on repeating this over time
		Yet Section 10 says this info should be repeated. Differences in approach and consistency of information throughout the document currently. We would caution against the use of the phrase 'should consider' as this could imply it is optional for clinicians to share this vital information with patients. Should provide would 'Around' is an ambiguous timescale – research has shown that epilepsy risk factors can become fatal in as little as 3-6months, so if clinicians wait until the next appointment to share this vital information it could prove too late for some children, young people and their families. What happens if there are delays in diagnosis? The recommendation states information on SUDEP should be given, but no	This is a novel approach for SIGN in terms of methodology used so it is important to explain this to readers. Our audiences vary from academics, specialist and non-specialist clinicians. The quick reference guide and patient and carer versions will provide a briefer summary of the guideline.

		guidance on monitoring/reviewing or the ongoing management of the risks associated with SUDEP/Epilepsy mortality is suggested; though there is much evidence showing that this helps reduce mortality among epilepsy populations. This section overall reads incredibly 'research methodology' heavy (focusing on how evidence was selected in particular) – how helpful will this document be for non-specialist clinicians looking for support and guidance? References: *1. Hanna NJ, Black M, Sander JW, et al. The National Sentinel Clinical Audit of Epilepsy-Related Death: Epilepsy – death in the shadows. Epilepsy Bereaved; 2002.* *2. Taylor JT. Inquiry held under Fatal Accident and Sudden Deaths Inquiry (Scotland) Act 1976 into the Death of Colette Marie Findlay. Glasgow: Sheriffdom of Glasgow and Strathkelvin, 2002.* *3. Duff AJM. Determination by Sheriff Alistair JM Duff in Respect of Fatal Accident Inquiry into the deaths of Erin Casey and Christina Fiorre Ilia. Dundee: Sheriffdom of Tayside Central and Fife, 2011.* *4. Scottish Public Services Ombudsman. Case 200700075. 2009. http://www.spso.org.uk/webfm_send/2134* *5. Nisbet T, Turbull S, Mulhern S, Razvi S. 'Breaking Good News': Neurologists' experiences of discussing SUDEP with patients in Scotland. Epilepsy and Behavior 2017; 70(Pt A): 72-9.* *6. Ross D. Are we discussing SUDEP?--A retrospective case note analysis. Seizure 2013; 22(1): 74-6* *7. General Medical Council. Protocol for the Instruction of Experts to give evidence in Medical Practitioner Tribunal Service Fitness to Practise proceedings Manchester: General*	

		Medical Council; 2014. p. 11. *8. Tingle JH. Do guidelines have legal implications? Archives Disease Children 2002; 86: 387-8* *9. Shorvon S, Tomson T. Sudden unexpected death in epilepsy. The Lancet 2011; 378(9808): 2028-38.* *10. Joint Epilepsy Council. Memorandum by the Joint Epilepsy Council (JEC) (COM 104). London: UK Parliament, 2009* *11. https://sudep.org/sites/default/files/safety_tools_published_research_epsmon_and_the_checklist.pdf* *12. Keller et al 2018: doi:10.1212/WNL.0000000000005762* *13. Ridsdale L, Charlton J, Ashworth M, Richardson MP, Gulliford MC.* *13. Epilepsy mortality and risk factors for death in epilepsy: a population-based study. Br J Gen Pract. 2011;61(586):e271-8.* *14. Sidebotham et al Deaths in children with epilepsies: A UK-wide study. Seizure - European Journal of Epilepsy , Volume 30 , 113 - 119* *15. Shankar, R., Donner, E., Mclean, B., Nashef, L., Tomson, T. Sudden unexpected death in epilepsy — what every neurologist should know. Epileptic Disord. 2017;19:1–9.* *16. Shankar, R., Henley, W.H., Boland, C., Laugharne, R., Mclean, B., Newman, C. et al, Decreasing the risk of SUDEP: structured communication of risk factors for premature mortality in people with epilepsy. Eur J Neurol. 2018;*	
9.3	BACD	Helpful section.	No action required.
	SA	Compared to section 9.2, the information and evidence included in section 9.3 is very different in style and how evidence is discussed and	Section 9.2 includes the qualitative review so the reporting style is slightly different. References and evidence levels have

		presented. This section contains more speculative information and advice that is not always referenced with evidence (there are significantly less references for this section suggesting much existing on the topic has been excluded) compared to in the previous section which is narrow in focus due to the restricted evidence base selected. References: *1. Shankar, R., Newman, C., Hanna, J., Ashton, J., Jory, C., McLean, B. et al, Keeping patients with epilepsy safe: a surmountable challenge?. BMJ Qual Improv Rep. 2015;4* *2. Shankar, R., Newman, C., McLean, B., Anderson, T., Hanna, J. Can technology help reduce risk of harm in patients with epilepsy? Br J Gen Pract. 2015;65:448–449*	been added to section 9.3. These references have been checked, however, they are general reviews/opinion pieces rather than clinical evidence.
General	BACD	Helpful section.	No action required.
	CJ	Paragraph 3 Specific information could have been mentioned here e.g. SUDEP Action tools.	These tools can be accessed via the SUDEP website, which is referenced in section 10.4.
10.1	BACD	Useful links.	No action required.
10.2	BACD	Useful and practical section.	Thank you.
	SA	This section is markedly different in methodology compared to section 9. It reads much less formally and seems less restrictive on what evidence and information has been included – making the guideline read inconsistently. (This section is much easier to read though and likely to be more beneficial to non-specialists). Specific reference made to a voluntary organisation initiative in section 10.2, yet others are not included or named so specifically? A consistent approach to this would be welcomed. For example, 'epilepsy checklists available from support organisations' is mentioned, but generically and no signposting is provided so clinicians can easily access such a tool. A general epilepsy information leaflet is mentioned. Are clinical teams expected to create their own, or use a specific one? This is not made clear and could lead to huge variation in the quality of	This section is intended to be more patient-, as opposed to clinician-focused. Multiple voluntary/other organisations are named in section 10.4. Other organisations have been added based on feedback from open consultation. All clinicians in Scotland will be signposted to SPEN with regard to all aspects of epilepsy, therefore this is standardised.

		resource being distributed if not regulated and standardised somewhere.	
10.3	BACD	Useful and practical section.	Thank you.
	SA	The starred items are no longer listed as 'essential' rather they have been reduced to 'important' – this may impact on clinical decision making regarding sharing this information, which is of particular importance regarding epilepsy risks, risk management, SUDEP & Epilepsy mortality.	All stars have been removed, as we agree that many aspects are important.
10.4	BACD	Useful and practical section.	Thank you.
	EA	It's great to see Epilepsy Action's contact information included and we welcome SIGN making this information available to healthcare professionals and other readers of SIGN guidelines.	No action required.
	SA	Only some organisations are listed here, yet others are mentioned in the table in 10.3 or have been involved in the guideline creation process but are not listed ie: Young Epilepsy and Matthew's Friends – consistency of approach needed. The Joint Epilepsy Council has also formally disbanded so should be removed.	Young Epilepsy and Matthew's Friends have been included in this list. Joint Epilepsy Council has been removed.
General	BACD	Clear section.	The section has been revised to provide further detail.
11.1	BACD	Clear section.	No action required.
	SA	Is there evidence that the previous Children guidelines were implemented? How are clinicians/trusts, particularly those who are non-specialists, going to be supported to implement these guidelines (especially if they have not previously been)? Is there additional funding for them to implement the aspects surrounding discussion of SUDEP and the management of risks for example?	This is outwith the remit of the current SIGN guideline. Guideline implementation is done locally. Section 11 details implementation considerations. SIGN has no funding for implementation. The section has been revised to section 11.3, and highlights resource requirements.
11.2	BACD	Well explained.	Thank you.
11.3	BACD	Very helpful. How will this be monitored?	The implementation of the guideline is being addressed by SPEN.
	SA	The SUDEP and Seizure Safety Checklist can be used as an audit tool to understand epilepsy risks among patient caseloads. It has been used in primary and secondary care to do this and has resulted in early interventions being applied to patients at risk who	The purpose of the audit tools suggested are to check the recommendations in the guideline are being implemented. Appraisal of additional tools is outwith the remit of the guideline, and cannot

		were previously not known to their clinicians. Will audit tools such as this have the opportunity to be included or signposted to? (While it is currently based on adult research, it is approved for use with transition patients, and a paediatric version is also in development). References: *1. Shankar, R., Henley, W.H., Boland, C., Laugharne, R., Mclean, B., Newman, C. et al, Decreasing the risk of SUDEP: structured communication of risk factors for premature mortality in people with epilepsy. Eur J Neurol. 2018;* *2. Gales A, Shankar R. SUDEP Checklists in primary care; RACGP; 2016. Available from:* *http://www.rcgp.org.uk/clinical-and-research/bright-ideas/sudep-checklists-in-primarycare.aspx*.	be recommended. If the paediatric version is developed it could be considered for future updates of the guideline.
11.3.1	BACD	Helpful section.	Thank you.
11.3.2	BACD	Helpful section.	Thank you.
11.3.3	BACD	Clear and helpful.	Thank you.
11.4	CH	Additional advice to NHSScotland and from Healthcare Improvement Scotland and the Scottish Medicines Consortium: This section is not comprehensive in that it doesn't include all the relevant SMC advice on medicines for children with epilepsy. For example, there is recent SMC advice for eslicarbazepine (SMC 2087) and brivaracetam (SMC2113) in children and also a number of other relevant pieces of advice that are not included. All previous SMC advice is published on our web-site and can be searched by BNF category- please let me know if you'd like help in identifying previous relevant advice.	Further SMC advice is now included for recommended drugs.
	BACD	Helpful section	Thank you.
12.1	BACD	Helpful for those who want all the details.	No action required.
12.1.1	BACD	Very helpful section, welcomed by BACD.	Thank you.
12.1.2	BACD	Helpful for those who want all the details.	No action required.
12.2	BACD	Helpful section.	No action required.

	EA	We recommend including a call for additional data to determine the long term efficacy and safety of Cannibidiol for the treatment of Lennox-Gastaut Syndrome. A similar recommendation for Dravet Syndrome is currently included twice. In light of political developments and compelling anecdotal evidence we would also recommend research into cannabis-derived medicinal products (CDMPs) containing >0.2% THC for the treatment of severe childhood epilepsies. This would include RCTs and additional data to determine the long term efficacy and safety of these products.	The list of recommendations has been edited, but reflects the general nature of the guideline. More recent evidence on cannabidiols has been added.
12.3	BACD	Helpful section.	No action required.
	BACD	Helpful to understand the process.	No action required.
	BACD	Clear and helpful information.	Thank you.
	BACD	These are very practical and clear.	Thank you.
	BACD	These are very practical and clear.	Thank you.