COMMENTS RECEIVED FROM CONSTULATION, NOVEMBER 2018

SIGN Epilepsies in children and young people

All reviewers submitted declarations of interests which were viewed prior to the addressing of comments.

Invited reviewers			**Type of response and declared interests**
AQ	Dr Alan Quigley	Consultant Paediatric Radiologist, RHSC, Edinburgh	Individual response.
AJ	Dr Alice Jollands	Consultant Paediatric Neurologist, NHS Tayside, Dundee	Individual response
FB	Professor Frank Besag	Consultant Neuropsychiatrist, East London Foundation NHS Trust, CAMHS, Bedford	Individual response. Remuneration from consultancy - I have, in the past, been sponsored to epilepsy conferences by various pharmaceutical firms but none of these sponsorships have been within the last five years and none are current.
CR	Professor Catherine Riney	Paediatric Neurologist & Epidemiologist, Queensland Children's Hospital, Brisbane, Australia.	Individual response. Remuneration as holder of paid office - I would declare the following: I have received speaker honoraria, travel support, advisory board honoraria and/or research funding from: UCB Pharma, Eisai Australia, Novartis Pharmaceuticals, Zogenix International Inc, AFT Pharmaceuticals Ltd, LivaNova Australia Pty Ltd and Janssen-Cilag Pty Ltd. Remuneration from consultancy - As noted above, I have received speaker honoraria, travel support, advisory board honoraria and/or research funding from: UCB Pharma, Eisai Australia, Novartis Pharmaceuticals, Zogenix International Inc, AFT Pharmaceuticals Ltd, LivaNova Australia Pty Ltd and Janssen-Cilag Pty Ltd
CS	Ms Christine Sutton	Portfolio Lead, HIS, Edinburgh	Individual response.
PG	Dr Pradnya Gadgil	Consultant Paediatric Neurology, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai	Individual response.
HC	Professor Helen Cross	The Prince of Wales's Chair of Childhood Epilepsy and Honorary Consultant in Paediatric Neurology, UCL Great Ormond Street Institute of Child Health, London	Individual response Remuneration of self-employment: I see a limited number of private patients, who are not entitled to NHS care.

			Non-financial interests: I am clinical advisor to the national Childrens Epilepsy Surgery Service, and the update of the NICE .guideline for childhood epilepsies Non-personal support: I am an investigator in clinical trials with Zogenix, GW Pharma, Ovid and Vitaflo I have acted on advisory boards for Zogenix, GW Pharma, I have spoken at educational symposia for Nutricia, Zogenix, GW Pharma Remuneration for all has been made to my department.
IM	Dr Ian Morrison	Consultant Neurologist, NHS Tayside, Dundee	Individual response. Remuneration from employment: Received payment from advisory boards and speaking from UCB, Eisai and Pfizer. Educational awards from UCB, Eisai and Cyberonics. Remuneration from consultancy: See earlier.
JC	Dr Judith Carrier	Reader Primary Care/Public Health Nursing, School of Healthcare Sciences, Cardiff University	Individual response.
MK	Professor Martin Kirkpatrick	Consultant Paediatric Neurologist, Tayside Children's Hospital, Ninewells, Dundee.	Individual response.
KKT	Dr Krishnaraya Kamath Tallur	Consultant Paediatric Neurologist, Honorary Senior Lecturer, University of Edinburgh. Clinical Lead, Scottish Paediatric Epilepsy Network (SPEN), Department of Paediatric Neurosciences, Royal Hospital for Sick Children, Edinburgh	Individual response. Non-financial interests: Being the Clinical lead for SPEN, I originally set up the chair and initial working group (Carsten Mandt being the manager). Hence, I would like to think that I was mainly responsible for bringing about the entire project with Carsten's help.
LD	Dr Liam Dorris	Consultant Paediatric Neuropsychologist, Royal Hospital for Children, Glasgow	Individual response. Remuneration from employment: Employee of NHS Greater Glasgow & Clyde.

			Remuneration from self-employment: Director of Dorris Consulting Ltd Non-Financial interests: Non-Executive Director of Epilepsy Scotland
AF	Dr Alan Forster	Consultant Clinical Neurophysiologist, Aberdeen Royal Infirmary, Aberdeen	Individual response. Honorarium for advising Bespoke healthcare, which includes intraoperative monitoring, but has no impact on SIGN output and specifically no epilepsy involvement to date.
MO	Dr Mary O'Regan	Consultant Paediatric Neurologist, Our Lady's Children's Hospital, Dublin	Individual response. Remuneration from consultancy: Drug Advisory Boards for Biogen and Novartis
NS	Dr Natasha Schoeler	Research Dietitian, UCL Great Ormond Street Institute of Child Health, London	Individual response.
PB	Dr Phillipus Brink	Consultant Paediatric Neurologist, Tayside Children's Hospital, Dundee	Individual response.
SD	Dr Susan Duncan	Consultant Neurologist, Dept of Clinical Neurosciences, Western General Hospital, Edinburgh	Individual response.
TS	Tommy Stodberg	Senior Consultant Pediatric Neurology, Karolinska University Hospital and Karolinska Institutet, Stockholm	Individual response.
VW	Mrs Victoria Whiteley	Advanced Practitioner in Ketogenic Therapies, Royal Manchester Childrens Hospital, Manchester	Individual response. Non-financial interests: Co-Chair of Ketogenic Dietitians Research Network Trustee of The Daisy Garland charity
RC	Dr Richard Chin	Senior Clinical Lecturer, Centre for Clinical Brain Sciences, Muir Maxwell Epilepsy Centre and MRC Centre for Reproductive Health, University of Edinburgh	Individual response. No DOI received
DS	Mr Drahoslav Sokol	Consultant Paediatric Neurosurgeon, Royal Hospital for Sick Children, Edinburgh	Individual response. No DOI received

Section		Comments received	Development group response
	TS	The literature review seems ambitious and well performed. Compared to the SIGN 81 this draft is a lot more difficult to read. Sometimes difficult to follow the thread of thought. This is partly due to the presentation of references/studys within the text which makes a clear structure more needed. Presenting all references in the text, as in a Cochrane or other Review document, has pros and cons. The purpose of this guideline makes it important that its easy to read, easy to follow. This is in my impression most problematic in the chapters on investigation and pharmacological treatment. The parts going through studies need to be, one way or another, very clearly separated from introductions, summarys, conclusions. Going back and forth between these different types of texts creates unclarity and confusion. The impression of lack of structure in some parts of the document I think is reinforced by the fact that the text is still immature in terms of language and will be better after proof reading etc.	The guideline has been edited with these comments in mind. The sections highlighted have been restructured to be clearer and more readable.
	MK	I would like to make some general comments which apply to varying degrees across the whole guideline. I appreciate and remember very clearly in the previous edition of this guideline that the draft at this stage was very far from the finished product. It is clear that there has already been very significant work entailed in pulling this guideline together and it is a commendable piece of work. I hope that the comments that I make are thus not construed to be critical but are meant to be entirely constructive. **General comments** In very general terms the guideline is too long to be for a typical reader. I do not think that, for example, many of the epilepsy syndromes need to be described in any detail and I would argue that that information could be found in places outwith this guideline. Evidence i. Finding high level evidence with which to make recommendations in the field of paediatric epilepsy is challenging. There are numerous Cochrane reviews referred to throughout the guideline that seem almost invariably to have been assigned a level 1++ but within the accompanying text are comments on, for example, only very small numbers of children or that the evidence was only of moderate of poor quality. This must be a source of bias to a greater	The guideline has been edited to make it more concise and the detailed epilepsy syndromes removed. The Cochrane/Systematic reviews are graded by the quality of how the systematic review is conducted, ie how reliable it is that it has gathered, appraised and reported the evidence in a systematic, unbiased way. Where the trials identified in the review are of poor quality or small numbers this has been described in the text.

		or lesser degree and I wonder whether all these Cochrane review are appropriately graded.	
		There are points where the NICE clinical guideline on epilepsies is referenced and appears to have been allocated 1++ as an evidence level. In any event I wonder about the wisdom to reference another guideline as evidence – since it will probably not have been formally reviewed by the group.	The NICE guideline has been rated level 4 as the recommendations include expert opinion as well as underpinning evidence.
		C. Recommendations i. The key to the Recommendations section defines two levels of Recommendation. It is not clear within the guideline itself which of the two levels a recommendation is being put forward.	This is in the use of the terminology strong= should and conditional = should consider. This is linked also to the harms versus benefits, feasibility and patient preferences as well as the results of the evidence.
		A better understanding of the strength of each Recommendation would help the reader.	
		ii. I am concerned about the internal consistency within the guideline between a Recommendation that "should be used" compared to one that "should be considered" and that there needs to be a view taken on this in the round across the guideline. Addressing this in isolation within one section has the potential to mislead a reader in considering the guideline as a whole.	The strength of each recommendation is based on a number of factors, including the robustness of the evidence base, but also other factors, such as balance between benefit and harms, and acceptability to patients. Each recommendation has been considered and worded individually to take these factors into account.
		iii. Even with individual sections there appears to be a lack of consistency. For example it is not logical to make a Recommendation that a ketogenic diet "should be used as a treatment option in the paediatric population for drug resistant epilepsy" (6.1) when in later sections of the same chapter it "could be considered" as a treatment option in specific diseases (the significant majority of which will have drug resistant epilepsy).	Thank you. This has now been changed to 'should be offered' in the ketogenic diet section.
		iv. That same consistency needs to be applied when reviewing Recommendations made following "traditional" SIGN evidence levels compared to Recommendations following qualitative studies.	We have reviewed this and feel there is internal consistency on the recommendations based on the qualitative evidence, (transition and discussions about SUDEP) based on the overall good quality of evidence reported.
		I welcome the use of qualitative studies in this guideline – it is potentially a really important step forward in guideline methodology – but there needs to be clarity on the strength of Recommendations that follow what most would regard as different	There are still some methodological issues to address around how to grade qualitative/mixed methods evidence (see section 8.2). We presented the quality of the evidence based on tools/methods currently available, within the text or at the side. We sought internal and expert external feedback on how best to present quality grading for the

		(and may or may not be weaker) levels of evidence. It is currently unclear to a reader how a Recommendation or Good Practice Point is made when this follows qualitative evidence. I accept there needs to be an assessment of the balance of benefits and harms but this should not outweigh the other factors on weight, consistency and applicability of published evidence. v. Key Recommendations – (Section 2): there are not a huge number of recommendations contained within this guideline, some 25 or so, and the rationale for highlighting only 6 is not clear. At the least I suggest it does not flow well to a reader and perhaps there are not so many that precludes them all being listed in one section of the guideline. I like this idea but am not sure that it works well and is accurate. In my experience, most young people, above all, want their seizures to go away! I think it is difficult for the guideline group to be sure those quotes are reasonably representative of the young people's epilepsy community. For example, in 4.1 young people are quoted as finding the wires "painful". I not believe that is representative at all – and have confirmed this with a number of my EEG technologist colleagues. ii. Importantly, while I welcome having the views of young people, this needs to include the views of parents too. iii. I do not know how extensive the consultation with young people and parents has been beyond the two third sector organisations mentioned. Overall I do wonder whether there is a sufficiently broad scope of young people's and parents opinion to provide the appropriate spread of views. In considering a "Patient Perspective" (section 1.1.1) then it would be helpful to review the published (reasonably extensive qualitative) literature. Williams (Seizure, 2018) published over 3000 PREM responses on the views of parents and young people analysing their perspective on factors influencing their satisfaction with an epilepsy service.	qualitative evidence within the guideline. Thank you we have clarified this in this in preceding text. This quote has been removed. This has been added.

	PB	Quoting of statistical parameters have been commented on and not in SIGN 81/143. Their styles make for easier reading. Summaries of studies in fewer lines like SIGN 143 does would make for easier readability. The words 'should' and 'consider' are not always in line with the levels of evidence in recommendations, sometimes used together and needs to be kept separate. I need to add other points: it would have been nice to keep Annex 3 ,p. 38 from SIGN 81 from a practical point of view. To SIGN: Give Reviewers please more time to do reviews, e.g. 2-3 months , so as to be able to do this thoroughly and not under pressure.	It is SIGN practice to include statistical results to support statements made and allow readers to see the effect size. The guideline has been edited to be more succinct. The wording of the recommendations is dependent on the reliability of the evidence and the balance between the potential benefit and harm. Annex 3 has been replaced by SPEN care standards, which include ECG after first convulsive seizure (https://www.spen.scot.nhs.uk/wp-content/uploads/2017/12/2017-11-Pathway-1-First-Seizure-1.pdf) SIGN appreciate that peer reviewers carry out this work as an addition to their routine work. However, it takes around 18 months to develop a guideline. SIGN request a response to peer review within four weeks to ensure the guideline can be published timeously after the literature review has been conducted.
	AJ	I find the draft very detailed but feel the material is not organised in a way that a clinician can quickly access and use in clinical practice. Guidelines are usually only helpful and used if succinct and to the point	The guideline has been edited to be more succinct.
	AF	Main style issue for me the classification of seizures - I would suggest giving definition of current classification, then the previous versions - which could be put in an appendix to keep the main document a little 'lighter'.....	Amended.
	PG	No addition- just wanted to say this is superbly written.	Thank you.
	MO	Some sections in my opinion are excellent such as the one on mortality in epilepsy and SUDEP so is the section on transition and co-morbidities. However it is not really clear who this guideline is for ; specialist in epilepsy or professionals in primary/secondary care. Why would an A&E practitioner need so much detail on the management of the use of the ketogenic diet in Glut 1 deficiency or sections on epilepsy surgery containing mostly adult data. It seems like there were many vested interests producing this guideline and all had their say when it was relevant to the target audience or not. Great emphasis was made that young people were asked their views and these were put	Thank you. Different aspects of a child's epilepsy are managed by different professionals. This guideline has information for anyone involved in the the management of epilepsy. We acknowledge that some sections are more relevant to some professions than others. These issues will be addressed in the patient and young people's versions. Epilepsy nurses - The second paragraph in

		into the document but I don't feel their needs were address. The young people wanted access to epilepsy nurses, information about investigations, they expressed concern regarding adverse effects of drugs. I read nothing in the guideline about the overall incidence of adverse effects from drugs. The young people wanted multidisciplinary clinics never addressed in the document there was nothing on models of care. It was stated that the guideline was going to use the term focal seizure and then throughout the guideline used partial seizure	section 10.2 references how patients prefer talking to an epilepsy nurse. Transition recommendation also refers to 1:1 with a HCP/nurse. Information about investigations – we have said in the guideline that professionals should offer information and the patient version will go into detail about each investigation. Information point for HCP in section 5.1 includes talking to patients about adverse effects. Information points for HCP are included to address what young people told us. This has also been clarified in section 1. Adverse effects are noted after each drug in section 5, overall incidence has now been added. This term has been amended throughout.
	KKT	Excellent piece of work. Thank you all.	Thank you.
	RC	Will there be a way to readily distinguish between strong and conditional?	This is in the wording of the recommendation – 'should' for strong, an 'could be considered' or 'may be considered' for conditional.
	FB	As mentioned elsewhere, this guideline is full of valuable information. It requires considerable editing, most of the necessary corrections/alterations are obvious. The information is somewhat dense in a number of areas. In some cases, notably the section on classification of seizures, only the up-to-date information should appear in the main guideline. Information on previous classifications could be put into an appendix, for information.	Amended.
1.1	TS	Clear and adequate.	Thank you.
	PB	Agree that guidance is helpful and harmonises practice.	Thank you.
	MK	It is not true that many of the anti-epileptic drugs have no marketing licence. It is rather that they either are used outside the indication for which they are licensed or outside the age range for which they are licensed, i.e. they are used "off-label".	Amended.
	CR	Paragraph 2, line 2: It is important to identify the specific epilepsy syndrome wherever possible to refine the choice of medication to maximise benefit and minimise adverse effects. Would the authors consider that it is the epilepsy aetiology that is of central importance and of broader importance than specific syndromes (which in themselves have importance because of direction	Amended.

		towards specific aetiologies). For example Dravet syndrome is genetic in aetiology with the genetics predisposing towards efficacy of specific drugs, and adverse effects from others. Consider: It is important to identify the specific epilepsy aetiology wherever possible to refine the choice of treatment to maximise benefit and minimise adverse effects.	
	JC	This is clearly articulated with appropriate literature drawn upon an depidemiological data provided.	Thank you.
	NS	'The epilepsies are a heterogeneous group of childhood conditions' - perhaps better to omit the word 'childhood' here?	'Childhood' removed.
	IM	No issues with content	No action required.
	AF	Makes sense	No action required.
	CS	Clearly evidenced in introduction - target audience also clear NB may also be useful for advocates for patients and their families to know what they can expect of services	Services are different and variable across Scotland and access to tertiary care is not addressed in this guideline. The SPEN pathway in Annex 3 highlights this.
	VW	2nd paragraph, 3rd line, replace medication with treatment (guideline covers both AEDs and other treatment options and service users very keen to ensure info about 'other' options) 4th paragraph, first sentence doesn't read well. Final line - has there been a survey to determine the issues raised	'Medication' replaced with 'treatment'. Sentence edited for clarity. Issues clarified in additional section 1.1.2 'Patient perspective'.
	AJ	'There is a need for a guideline to provide a standardised service across all settings for the different aspects of epilepsy management.' I wonder if this sentence should be substituted with a comment that the guideline does not address all aspects of epilepsy management but has focused on 'key areas' of care. 'Children and their parents deserve information appropriate to their particular type of epilepsy' Not sure this is helpful in this paragraph and not sure that the guideline ultimately addresses this need Are we going to 'add' additionally to SIGN guideline 143 - if so should we state this? e.g transition. I also wondered if the guideline should state that this guideline does not replace SIGN guideline 81 as it addresses different or selected issues and refer the reader to NICE of other current guidelines in general as SIGN 81 is now regarded as obsolete (this is	Sentence amended. The guideline group discussed this comment and feel this is appropriate as it gives the user perspective. SIGN 143 will not be added to. A sentence has been added for clarity. Different issues were raised for this guideline based on stakeholder consultation. SPEN were consulted around the key questions and topics for inclusion. SIGN 81 is archived. The SPEN pathways have taken this into account.

		a pity as it remains an excellent guideline in key areas of the diagnosis and management of epilepsy in children and young people)	New evidence on diagnosis was felt to be limited/poor.
	MO	The case for the guideline is well set out. Epilepsy is common and many new anti-epileptic drugs have emerged in recent years. There is also a need to address issues such as SUDEP and mortality in epilepsy and address the co-morbidities in epilepsy	No action required.
	KKT	Accepted	No action required.
	LD	No specific concerns.	No action required.
	RC	Need a bridging statement to link concept that epilepsy is not one single thing but a group of conditions and thus epilepsies. eg. “There is increasing awareness that epilepsy is a heterogeneous group of childhood...outcomes leading to the condition to be increasingly referred to as the epilepsies.”	Thank you. This has been highlighted and reference is made to ILAE 2017. We did not review evidence specifically for different epilepsy classifications.
	RC	And there are few head to head clinical trials of AEDs. How does the patient version differ?	Reviewed all AED trials in children after 2012. This guideline will be for patients and parents to read based on the evidence review. This will be simplified as some of the children diagnosed to have epilepsy may find this medical writing hard to follow.
	FB	At the end of the first sentence of the second paragraph, to the words "widely differing outcomes" I recommend adding in terms , not only of seizure control but also in terms of implications for learning and behaviour.	Added.
1.1.1	TS	The sentence "By listening to the people that are directly affected empowers young people to raise issues that are important to them and that they want to see reflected in the in guidelines for practitioners and support networks” needs correction. "The views and preferences from patients, carers and service users are presented throughout the guideline where this symbol is shown." Why italics? Confuses it with the citations in italics. Symbol still to be included. The list of issues is long but relevant and well structured.	Now section 1.1.2. Punctuation in this quotation has been amended for clarity. The italics are to make it look different from the standard guideline text. No action required.
	JC	Comprehensive include user views plus a focused literature search	No action required.
	MK	See my comments above on sourcing published qualitative literature. Gaining a literature based patient perspective would add significantly to the guideline.	The section includes results from the literature search, which included qualitative and quantitative evidence.
	AF	makes sense: p3 -'where this symbol is shown' - ? what symbol?? to be added in final version?	The symbol will be added pre-publication at graphic design.
	CR	No comments. Regarding the sentence: The views and preferences from patients,	

		carers and service users are presented throughout the guideline where this symbol is shown. I could not work out what symbol was intended to be shown in this location.	The symbol will be added at the graphic design stage.
	IM	No issues with content	No action required.
	FB	Good to include this	No action required.
	CS	Reference to work with the youth group was particularly helpful - this section evidences how specific themes identified impacted on the development of the guideline	No action required.
	VW	Typo in the quoted section from the youth worked 'in the in guidelines' where is this symbol shown? There is no symbol, just bold itallic text Last 2 paragraphs explaining who was invited and process should be before the listed outcomes of the sessions	Now section 1.1.2. Amended. The symbol will be added at the graphic design stage. This has been retained and clarified.
	HC	There is a good patient and family perspective throughout, with a variety of methods utilised to gain opinion. This is reported throughout	No action required.
	AJ	'This is a new and focused SIGN guideline reflecting the most recent evidence around key issues and replaces SIGN 81'. I strongly feel that this guideline may address key issues identified but does NOT replace many of the key areas addressed by SIGN guideline 81	Some of the commentaries and guidelines for clinicians have been taken up by SPEN and Paediatric Epilepsy Training (PET) courses. The guideline therefore focused on key questions/topics directed by SPEN.
	KKT	Accepted	No action required.
	LD	No specific concerns.	No action required.
	RC	“third sector organisations are invited”. Change ‘are’ to ‘were’ What symbol?	Corrected to ‘were’ (now section 1.1.2). This formatting issue will be addressed at layout.
1.1.2	TS	Ok	No action required.
	JC	Evident from the document	No action required.
	MK	Does this guideline replace SIGN 81 or in fact is a new guideline sitting in its own right? SPEN is an acronym that needs to be defined.	This is a new guideline. SIGN 81 has been withdrawn. Amended (now section 1.1.1).
	IM	Not especially detailed. Stakeholders involved in gathering views not identified in detail.	The majority of stakeholders are mentioned in the preceding sections and for conciseness are not detailed in full.
	AF	things have changed since 2005 - update appropriate	No action required.
	CS	More clarity in this section about how this impacted on the actual development of the guideline may be helpful	The guideline group feel this is adequate for overall conciseness.
	VW	Give full name/title of SPEN before using acronym.	This has been added (now section 1.1.1).
	MO	The group have sought the view of a wide community having a SPEN members day to discuss guidelines	No action required.

	LD	No specific concerns.	No action required.
	KKT	Accepted	No action required.
	FB	Worthwhile exercise. No additional comment.	No action required.
1.2	PB	-1.2.2 advise- advice? -'convulsion11' needs superscripting	Both amended.
	JC	Clearly stated inclusion and exclusion criteria	No action required.
	FB	It is a broad remit.	No action required.
	IM	I'm not sure why it doesn't include seizures in children less than one month, diagnosis of epilepsy and management of non-epileptic seizures. It would be helpful to expand on the reasons why not.	The majority of babies < 1 month have symptomatic seizures and are managed not by the paediatric epilepsy service but by neonatologists.
	AJ	I wonder if the guideline should expressly state which areas it has NOT covered in SIGN guideline 81 and refer the reader to NICE or similar more recently published guidelines again which cover the key issues omitted.	The topics covered in this SIGN guideline were agreed after consultation with SPEN. We reference NICE throughout the guideline where relevant and used work from NICE where necessary.
	MO	Appropriate to exclude neonatal seizures. I think the guideline has attempted to deal with too many topics such as epilepsy surgery, neurostimulation and epileptic encephalopathies	This was due to inclusion of the patient perspective. Topics were selected after wide consultation with SPEN and subsequent issues that the evidence led us to.
	LD	No specific concerns.	No action required.
	KKT	Accepted	No action required.
	RC	“A convulsion or convulsive seizure”. Check.	Now section 1.2.2. Formatting of reference citation amended in this paragraph.
1.2.1	TS	Suggestion: state that status ep is not covered, why it is not and refer to appropriate/alternative guideline. "A convulsion 11 or..." needs to be corrected.	A UK resus guideline is updated frequently. A sentence on emergency management of seizures and the resus council has been added. Corrected.
	FB	As stated above, it is a broad remit, with wide ranging objectives.	No action required.
	CR	Second last line: convulsion11 (this is a typo?)	Removed.
	AF	Typos -para 2 MHRA advise -? should be advice - convulsion11 in last paragraph:	Both amended.
	PB	It would have been helpful for focused comments on metabolic investigations in epilepsy- indications and what investigations in what circumstances	Some aspects of metabolic treatment have been addressed, e.g. Glut 1. Investigations of individual metabolic syndromes are outwith the scope of this guideline. There is a SPEN pathway for managing complex epilepsies.
	JC	Clearly stated, definitions provided	No action required.
	NS	Would benefit from some minor grammatical changes for ease of reading, e.g. 'and [COMMA] although surgery is addressed [COMMA] this guideline does not cover specific surgery treatment...' typo: 'convulsion11'	Sentence amended. Superscript addressed.

	IM	See response to 1.2	Response covered in 1.2.
	VW	delete 'the specific topics' in first line - not needed 5th line, delete the 'a' before paediatric settings 2nd paragraph, 6th line - epilepsy is associated.. should be new paragraph as different topic 3rd paragraph, 3rd line - convulsion11 - is this a typo for a reference?	All amended. Specific aspects needed – see comments from other reviewers.
	HC	Appear appropriate	No action required.
	AJ	The overall objective should state that it covers SPECIFIC aspects The flow of writing may be better if the objectives are first discussed before stating what is excluded. Could this whole section be condensed as detail is provided in subsequent sections?	Specific aspects are now stated.
	MO	Whilst I fully appreciate the amount of work involved in producing this guideline I am not sure who this guideline is for. It seems to have been written primarily for those with clinicians with a special interest in epilepsy rather than those in primary or secondary care. The details of whether the ketogenic diet is effective pyruvate dehydrogenase deficiency is not really of relevance to a school or practice nurse. The needs of young people with epilesy was gathered and their words incorporated into every section but apart from the part of SUDEP seems to have been ignored. I do apologise if that seems harsh I think this document has been trying to serve too many masters.	This guideline has information for everyone involved in the management of epilepsy. We acknowledge that some sections are more relevant to some professionals than others. We anticipate that users will refer to sections that are relevant to their practice. This is a pilot of using patient quotes and we have incorporated them where there was a quote which was relevant and acceptable to reviewers. Thank you for your feedback.
	LD	No specific concerns.	No action required.
	KKT	Accepted	No action required.
1.2.2	TS	I don´t really understand how this fits into or serves a purpose in 1.2.	Section removed as per all comments for this section – covered in section 7.
	PB	public-health - spell rather public health?	Now section 1.2.1. Amended to 'public health'.
	JC	Defined and appropriate	No action required.
	MK	It is clear that other comorbidities including cognition and development have been reviewed within this guideline. These need to be listed in this section.	Removed section. However See section 1.1.1 and also added psychiatric comorbidities and neurodevelopment, to reflect the new title of section 7 in section 1.2.1 3rd para.
	CR	No comment other than this seems a redundant section with only one bullet point.	Section removed.
	IM	No issues with content	No action required.
	VW	feels out of place	Now within section 1.2.1. Introduction restructured.
	HC	Would it be appropriate to indicate, neurodevelopment, learning and behaviour would all be included under the term 'psychological'	Section has been removed.

	AJ	Common comorbidities and coexisting health issues which have been considered when reviewing the evidence for this guideline are: • psychological comorbidities (see section 7). The above does not make sense. Section 7 seems to address: 1) the identification of cognitive, developmental and psychiatric co-morbidities but also 2) addresses the management of co-morbid anxiety and depression and ADHD ? rewrite so this makes sense in the context of section 7.	This has been revised and incorporated into section 1.2.1.
	MO	These have been well set out and are comprehensively listed	No action required.
	KKT	Accepted	No action required.
	RC	"Psychological comorbidities". Change 'psychological' to 'psychiatric'?	Now section 1.1, para 5. Amended to 'psychiatric comorbidities'.
	FB	Some reference should be made to learning, since about 30% of children and some epidemiological studies have intellectual disability.	Section removed see additions to section 1.1.1 – added and above comment.
1.2.3	TS	Last sentence already stated in the first sentence...	Sentence removed.
	JC	Clearly stated	Thank you.
	AF	? comma after clinical inappropriate - presumably clinical psychologists?? Last sentence not English! This guideline will be of interest to healthcare professionals that working in epilepsy. ?lose 'that' – or 'are after it...?	Amended.
	CR	Some typos noted, otherwise no comments. 1. clinical, neuropsychologists 2. to healthcare professionals that working in epilepsy	Amended.
	FB	No additional comment. It should be noted that there is a typing error and the last sentence: should "that working" be replaced with "that are working"?	Removed.
	MK	The primary target users should include general paediatricians and community paediatricians.	Added, and list has been amended to alphabetical order.
	NS	'This guideline will be of interest to healthcare professionals that [ARE] working in epilepsy.'	Sentence removed.
	IM	No issues with content	No action required.
	CS	This is clear - good to see range of professional groups referenced	Thank you.
	VW	Include Allied Health Professionals in the list Delete the final sentence 'This guideline will be of interest to healthcare professionals that working in epilepsy.' - has been said in previous sentences	Allied health professionals added. Sentence removed.
	AJ	'This guideline will be of interest to healthcare professionals that working in epilepsy.'	Sentence removed.

		Is this sentence necessary - this has already been stated in this paragraph?	
	MO	The guideline is trying to cover the needs of a practice nurse in primary care to a specialist a very wide remit and I am not sure that it is possible to do both Much in the guideline is the remit of the epileptologist not related to professionals in primary or secondary care	As per comments in section 1.2.
	LD	There is an extra word 'clinical' between obstetricians and neuropsychologists.	Superfluous comma removed.
	KKT	Accepted	No action required.
	RC	Delete 'This guideline will be of interest to healthcare professionals that working in epilepsy'.	This superfluous sentence has been deleted during editing.
1.2.4	TS	"...publication if this guideline." needs correction	Section amended.
	JC	Not yet available	No action required.
	CR	Typo noted: 1. if this guideline	Amended.
	FB	This is not part of the current guideline and consequently no comment will be made. It would be of interest to me to comment on it separately at a later stage.	Thanks for expressing an interest in this our PPI Advisor will contact you in due course.
	NS	after the publication if [OF] this guideline.	Section amended.
	VW	of not if, 3rd to last word	Section amended.
	MO	not available at that of review	Section amended.
1.3	TS	Ok	No action required.
	JC	Clear and transparent	Thank you.
	IM	No issues with content	No action required.
	AF	1.3 -1st sentence: ? phrasing...? ? true meaning??? –how about- 'This guideline is not intended to be, or be construed or to serve as, a standard of care.' This guideline is not intended to be construed as, or to serve as, a standard of care.	The wording is correct as it stands.
	CS	Clearly set out	Thank you.
	FB	The statement of intent should start off with a comment on what the guideline is, rather than what it is not.	Section 1.2 covers what the guideline is (recommendations based on evidence).
	KKT	Accepted	No action required.
	RC	Add 'and the rationale for doing so' before 'should be documented in the patient's medical records'.	This is standard SIGN text.
1.3.1	TS	I don´t really understand how this fits into or serves a purpose here. Better in chapter 13?	This is standard SIGN text, to make readers aware of interests before reading the guideline. It applies to the full guideline, not just Chapter 13.
	PB	Important paragraph	No action required.
	CR	One typo noted: working` with	Amended.
	JC	Transparent	No action required.

	FB	A necessary section. No additional comment.	No action required.
	IM	No issues with content	No action required.
	VW	should state if the guideline has been influenced by charities	Views were sought from a wide range of patient groups and healthcare professionals – not unduly influenced by any specific charity. This section explains how influence or bias is mitigated throughout the development of the guideline.
	MO	Important to state	No action required.
	KKT	Accepted	No action required.
1.3.2	TS	Better placed in chapter 5?	It is standard to have this as part of the introduction. This also applies to Chapter 7 on psychology. Chapter 5 refers back to it.
	JC	Comprehensive	No action required.
	MK	This paragraph could be rationalised and shortened and the recommendations in annex 2 are better highlighted.	This is a statement that has been agreed by the Royal Pharmaceutical Society and the Scottish Medicines Consortium, to explain the use of unlicensed pharmacological therapies. We would not want to shorten it and miss out key points.
	AF	sounds right - but outside my expertise -(I'm a Clinical Neurophysiologist)	No action required.
	CR	No comments other than references at the bottom of this page require updating as they are partially completed.	Amended.
	FB	Would it be worth stating that some medicines do not have marketing authorisation simply because the pharmaceutical companies have not considered to be financially in their interest to obtain it. The implication of stating this would be that the medication might, nevertheless, be worthwhile and helpful to the individual.	It would not be appropriate to state this as it is not the case that every medication in such circumstances is worthwhile.
	IM	No issues with content	No action required.
	AJ	Could this section state that where evidence is available we sometimes prescribe 'off label' or in exceptional circumstance may prescribe an 'unlicensed' product and then refer the reader to the GMC, MHRA and Scottish equivalent with links to their guidance rather than state all this in the guideline?	This is standard SIGN text. The last sentence of this section addresses unlicensed medicines and refers to Annex 2.
	MO	Very well explained why this occurs in paediatric practice and the problems associated with their use. At present this is unavoidable in paediatric practice	Thank you.
	KKT	Accepted	No action required.
	RC	"An unlicensed medicine is a medicine which does not have MA for medicinal use in humans". Consider move to section just above use of unlicenced medicines. Decide on whether using abbreviation or full text and remain consistent throughout. If using abbreviations then a glossary needed.	This is standard template text. The guideline has been edited to ensure that all abbreviations are defined on first use. A list of abbreviations is included towards the end of the guideline.

1.3.3	TS	Better placed in chapter 5 or 11?	As this is relevant to more than one chapter, it is standard practice to include this in the introduction of each SIGN guideline.
	PB	'NHSScotland' numerous times in document-should have space between? 'newly-licensed'- rather newly licensed?	Correct without the space. Amended to 'newly licensed'.
	JC	Clear and transparent	No action required.
	IM	No issues with content	No action required.
	MK	I am not sure that this section adds helpfully to the guideline but perhaps it is standard for all SIGN guidance?	This is standard for all SIGN guidance.
	AJ	Is this relevant to this guideline and can this be summarised more succinctly?	This is standard SIGN text. Note there are two NICE technology assessments on cannabidiol.
	FB	This section provides technical information on the roles of the various governmental bodies relating to medication. I wonder whether it could be placed in an appendix.	This is standard text for all SIGN guidelines.
	AF	P7- bottom line – 1st bit was red and am sure for finalising – last bit was in black....was that a note to yourself?!?- made bold! -this bit -(COPIED TO YOUR FORM CAN'T MAKE BOLD! CAPITALISED...also 'ENDNOTE'=?! 1 The British National Formulary. Guidance on prescribing. add to endnote library 2 General Medical Council (GMC). Good practice in prescribing and managing medicines and devices. London: General Medical Council; 2013. [cited 06 Sept 2017]. Available from url: http://www.gmc-uk.org/Prescribing_guidance.pdf_59055247. pdf 3 electronic Medicines Compendium (eMC). [CITED XXX]. Available from url: www.medicines.org.uk 4 Medicines and Healthcare products Regulatory Agency. Off label use or unlicensed medicines: prescribers' responsibilities. Drug Safety Update 2009;2(9):6. add to endnote library.	Formatting amended.
	KKT	Accepted	No action required.
General	MK	See my comments above	Response as above.
2.1	TS	I think there should be two more key recommendations/investigation emphasised. How to express them could be discussed: 1.Neuroradiology/MRI in confirmed epilepsy with indication for neuroradiology (where structural etiology cannot be excluded) as deemed by a pediatric neurologist or pediatrician with expertise in epilepsy. 2.Routine EEG in suspected epilepsy (as deemed by ...a doctor(pediatrician?) with experience and knowledge of epilepsy in children or after consultation with pediatric	The key recommendations are highlighted as areas that require a change in practice and/or may have the greatest benefit for patients. In Scotland EEG is not used routinely as a diagnostic tool (see PET and SPEN pathway) unless a diagnosis of epilepsy is strongly suspected.

		neurologist or pediatrician with expertise in epilepsy). Even though EEG has a relatively low sensitivity and specificity its a piece in the diagnostic puzzle when used in an appropriate way, in a selected population and by the right healthcare professional. Can help estimate risk of seizure recurrence and support epilepsy diagnosis.	
	PB	Fine	No action required.
	JC	Transparent and provide clear advice for clinicians	Thank you.
	AF	Yes	No action required.
	FB	This recommendation appears to be a little too dogmatic. An EEG is not always "required" for further classification of epilepsy. With the word "recommended" be more appropriate?	Amended to recommended.
	IM	No issues with content	No action required.
	CR	No comments The recommendation presented in the guideline is appropriate.	No action required.
	AJ	'If a clinical diagnosis of epilepsy has been made, EEG is required for further classification of epilepsy. If routine EEG is normal, as second line EEG investigation, consider an ambulatory or sleep deprived recording.' I wonder if the second sentence should not read If routine EEG is normal, consider an ambulatory or sleep recording.' (Sleep recording could be further clarified i.e. melatonin sleep induced, sleep deprived or combination as all of these are discussed in the evidence. Also wondered if sleep study should be specified first as although a prolonged ambulatory study may yield more, this is much more labour intensive and requires more resource). Evidence and recommendations subsequently include imaging and genetics so not sure why key recommendations in this regards are not made.	The wording of this recommendation has been revised. The group discussed the relative advantages and disadvantages of each method in detail in the text and could find no strong evidence in favour of any particular method of obtaining sleep. The evidence was not strong enough and the number of key recommendations is limited.
	MO	These are appropriate	No action required.
	RC	What about MR imaging?	A recommendation on MRI is included in section 4.2.3 and will be reproduced in section 2.
2.2	TS	Ok	No action required.
	PB	statement rather be 'The ketogenic diet should be available as a treatment option...'?	Changed to ‘offered’.
	JC	Clearly laid out	Thank you.
	AF	Yes P9 – 2.2 -comma in last sentence redundant	Amended.

	CR	No comments The recommendation presented in the guideline is appropriate.	No action required.
	FB	Agree	No action required.
	NS	'A ketogenic diet should be used, as a treatment option in the paediatric population for drug resistant epilepsy.' Perhaps better worded 'should be considered as a treatment option' and add 'early on in the course of treatment for specific clinical conditions' (or similar)	See section 6 and above comment.
	IM	No issues with content	No action required.
	AJ	Why have no key recommendations regarding pharmacological treatments (positive and negative) been made? The issue of cannibinoids in particular are pressing for all even if epidiolex remains unlicensed. Key recommendations are made about the use of the ketogenic diet. Don't understand why the key recommendations in regards to surgery, VNS and DBS are excluded here.	Key recommendations are limited and decided using consensus methodology. The recommendations listed are the ones which scored highest in the consensus voting.
	MO	The recommendations for the Ketogenic diet are appropriate for the evidence VNS recommendations are again appropriate Whilst I don't disagree when the recommendations for epilepsy surgery the evidence base does not support the strength of the recommendation.	Overall, there is a large body of evidence. We agree that studies are level 3 (lower quality) but a large number reach the same conclusions to support surgery.
	KKT	Accepted	No action required.
2.3	TS	One more Key recommendation: Children with psychosocial, neuropsychiatric or cognitive problems should have access to a multiprofessional team-based assessment of their difficulties. And team-based help to deal with difficulties uncovered (in house or through referral (maybe this is a second separate recommendation).	This particular evidence was prioritised due to the lack of psychological therapeutic input for children with epilepsy to drive service change, as this is a real gap.
	KKT	Accepted	No action required.
	CR	No comments The recommendation presented in the guideline is appropriate.	No action required.
	FB	Of course of depression and anxiety are important but the most frequent major diagnoses in children with epilepsy are ADHD and autism spectrum disorder. Correct management of these conditions can have a profound effect on the child and family.	See section 7 as to why this was prioritised.
	IM	No issues with content	No action required.
	HC	I note that only one recommendation ie that about depression and anxiety has been selected as prioritised for implementation. In children I would have thought that the recommendation about health professionals being made aware that all children are at increased risk of cognitive and academic impairments was equally important	Agree all are equally important, but children are more likely at present to get cognitive input, with clinicians routinely asking about education and less routinely asking about depression. The key recommendations are to highlight areas where a change in practice can improve care.

	AJ	Not sure why we should not also recommend that professionals should routinely consider and treat/ manage all cognitive, developmental and psychiatric co-morbidities as explored in section 7. Why is the key recommendation only focussed on depression and anxiety ?	As above.
	MO	Recommendations are appropriate	No action required.
2.4	TS	Ok.	No action required.
	PB	Fine	No action required.
	JC	Well written	Thank you.
	PG	Well written	No action required.
	IM	No issues with content	No action required.
	AF	1:1 - is this an abbreviation for one to one meeting/involvement? brevity fine, but clarity please!!	Amended to 'one-to-one'.
	CR	It was a little difficult to follow the sentence: direction to web based resources following a 1:1, with transition and specific disease advice I presume this means following a 1:1 education session Otherwise no comment The recommendation presented in the guideline is appropriate.	Amended for clarity. Retained as 'one-to-one conversation' rather than 'education session' to convey equal participation between patients/parents/carers and healthcare providers.
	FB	Transition is of major importance. It is not always well organised.	This is the reason for highlighting transition as a key recommendation.
	CS	This will be an area of concern for families and may also be a time when transitions are happening across other services e.g. education, social work. Particularly in complex cases, the need for multi-disciplinary approach and good communication at this time is heightened	Agree. Communication between teams is an implementation issue rather than something that will be evidence based.
	SD	Healthcare professional/Nurse led what does this mean - is a nurse different from a health care professional? does this imply that the transition clinic could be run by a physiotherapist who is a health care professional I would suggest physician/nurse led	The evidence stated a nurse and other healthcare professional.
	AJ	is it necessary to include the following in this section as this is expanded under section 8: 'This could include: • education regarding lifestyle management and self-management of health e.g. how to make an appointment, order a prescription, know the names of the doctors involved in their care, as well as advice regarding sexual health, drugs and driving • 1:1 healthcare professional/nurse led • direction to web based resources following a 1:1, with transition and specific disease advice	This is the full recommendation and therefore is included in full in this section.

		• an explanation of the differences between adult and paediatric care • educating parents and young people on epilepsy • gender appropriate advice e.g. contraception whilst on AEDs. And ideally would: • be individualised to the young person's needs/preferences • be co-ordinated between paediatric and adult services'	
	MO	Unfortunately little good evidence to support recommendations So recommendations are really good practice points but important nonetheless	Agree, the evidence base is limited. However, the recommendations also take into account other factors, such as balancing benefits and harms.
	KKT	Accepted	No action required.
2.5	TS	Maybe include SUDEP as a main theme under a wider Risk information.	Agree; heading changed.
	JC	Provides much needed guidance, well written	Thank you.
	PG	Reservations - as discussed later- about how easy is it to implement talking about SUDEP at or near diagnosis of epilepsy. A high risk checklist may help clinicians choose which patients/families need to be made aware early/ proactively	SUDEP is discussed in section 9.
	IM	No issues with content	No action required.
	AF	Makes sense: why is the word Annex used? Is this an americanism creeping into scotland? I thought that was a part of a building - whereas an appendix is an attached reference document...???	"Annex" as a term for an addition to a document or report is commonly used in British English.
	FB	This remains a very controversial area. Some families may be overwhelmed in the initial appointment and may not be ready to assimilate well-balanced information on SUDEP. I agree, however, that the starting point should be that this subject is covered in the first appointment, unless there are very good reasons for not doing so.	SUDEP is discussed in section 9.
	CS	Helpful to have set out in full in document	No action required.
	CR	The recommendation presented in the guideline is appropriate. No comments otherwise. Noted last bullet point could have use of brackets and full stops checked.	 Amended.
	SD	The title of the chapter is Mortality therefore I think in recommendations the heading should be mortality. And the recommendations should lead with information that some causes of and complications of epilepsy can lead to premature death. Hence the need for good seizure control and adherence to medication. Before going straight for SUDEP . Status causes premature death and one cause is poor adherence.	Agree; heading changed.
	MO	Very appropriate and have an evidence to support the recommendations and these recommendations are important to the third sector stake holders	No action required.

	KKT	Accepted	No action required.
3.1	TS	Ok	No action required.
	JC	Based on clinical opinion but guidance is clear	No action required.
	CR	I find it hard to understand the meaning of the sentence: The text that follows is based on clinical expertise on current standard practice to give context to this guideline. This section completely omits any section on diagnosis of the aetiology of the epilepsy, this is critical to our thinking these days and is front and foremost for patients to access the most precise therapy for their epilepsy. The authors might want to add in a specific section on this here	Sentence removed. Diagnosis of aetiology is the focus of investigations. In section 4, the third sentence has been amended to: 'The primary use of the electroencephalogram (EEG) is to help further characterise seizure types and epilepsy syndrome, and can help inform aetiology once a clinical diagnosis of epilepsy has been made.'
	IM	No issues with content	No action required.
	MO	This is the lynch pin of the management of the epilepsies It should be highlighted that the diagnosis can be difficult to make and referral to a specialist would be recommended if there is uncertainty concerning the diagnosis.	Section 3.1 now removed. This is discussed in section 3.2.
	FB	I agree that the high proportion of incorrect diagnosis should be emphasised, along with the importance of a specialist confirming the diagnosis, if there is any doubt. This is covered in the next section. Should it be in 3.1?	The introduction to this section has been removed, so it is appropriate to retain the statement in the section on who should make the diagnosis.
3.2	TS	The last paragraph is a repetition of the second last above the good practice point.	Now section 3.4. This paragraph has been removed.
	JC	Clear and transparent, user opinion identified	No action required.
	AF	P11 -3.2 – paediatrician misspelt!!! (para over tick)	Amended (now section 3.4).
	CR	This paragraph is largely repeated twice, with only minor variation, and should be considered for rationalisation: An epilepsy specialist has been defined as a trained doctor with expertise in epilepsy as demonstrated by training and continuing education in epilepsy, peer review of practice and regular audit of diagnosis. Epilepsy must be a significant part of their clinical workload (equivalent to at least one session a week).	The repetition of the paragraph 'An epilepsy specialist…' has been deleted (now section 3.4).
	FB	The guideline requires extensive editing. In this section, should the words "absence of a witnessed account" be replaced with "absence of an account of witnessed episode". The current terminology is "intellectual disability" not "learning disability". The third paragraph is repetition.	The guideline has been edited. It is felt that the term 'absence of a witnessed account' is clear and more concise than the suggested amendment. The group decided to use the term 'Learning disability' as it is widely used in Scotland. This is now section 3.4.

	VW	The first sections from what matters to young people seems out of place here, perhaps further down in this section? It does not start to answer the questions titling this section. Poorly written sentence which feels quite jumbled and repetitive. Needs to be clearer. Perhaps put the recommendation at the bottom? start with paragraph 2, then explain that an epilepsy specialist is, then the paragraph on implications of the diagnosis and then have the itallicised quote.	Now section 3.4. The positioning of the young people's quote has been adjusted, and the order of the section amended.
	AJ	An epilepsy specialist has been defined twice in this section -perhaps only once is required.	Now section 3.4. Second definition has been removed.
	MO	With the evidence used it is appropriate that a good practice point recommends that a specialist in epilepsy should make the diagnosis. However there is evidence that specialist are more effective at making the correct diagnosis but that evidence was not used and it could have strengthened the recommendation	Now section 3.4. The evidence was not reviewed here, as noted in section 3.1, so we can make only a good practice point. Section has been added to give context.
	KKT	Accepted	No action required.
3.3	TS	Ok	No action required.
	PB	Triggers? Could be lifted out in question 1. SIGN 81 p5: retain factors for epileptic vs. non epileptic staring please	These aspects are covered in BPNA's PET1 training course. In the interest of keeping the guideline succinct, these have not been included. SIGN 81 remains available.
	CR	The meaning of the word 'their' in the second line is unclear - the patient, the witness?	This sentence has been removed.
	JC	Clear and easy to follow	No action required.
	IM	I'm not sure if I agree that "a false negative diagnosis of epilepsy is probably less harmful than a false positive..." should be included. It's a very subjective statement.	This statement has been removed.
	AF	3.3 - - Awareness OR TALKING during the event -? could be useful addition?	Added.
	FB	This is broadly satisfactory.	Thank you – some revisions have been made in response to feedback from other reviewers.
	VW	suppose maybe switched to assumed?	'Suppose' has been changed to 'assume'.
	AJ	'Obtaining an accurate description of an event may be difficult. It is reasonable to suppose that their history of the seizure may be poor. It is often helpful to obtain multiple witness accounts.' I wonder if this could include a statement about a video of an event which is perhaps the most helpful 'witnessed account' 'Staring or blank spells, particularly in children with learning difficulties, often cause diagnostic difficulty. Key historical features will help select those seizures likely to be non-epileptic.' Unhelpful to make this statement and then not list or tabulate differentiating features.	Agree; statement has been added.

		"An accurate history of the event should be taken from first-hand witnesses and the child". I wonder if one could not supplement this good practice point with a comment about the value of a recorded witnessed account i.e. video evidence.	This is outwith the remit of this guideline, so has not been expanded upon. Agree; added, as above.
	MO	Well written narrative	Thank you.
	KKT	Accepted	No action required.
	RC	Age of onset, frequency of episodes, longest episode, diurnal variation, lateralisation features	The checklist is a description of a particular episode. The age of the child would be known. Frequency and length of episode is included, and there is already a question around sequence timing and components of the event.
3.4	TS	"one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (at least 60% over the next 10 years), or" should be one sentence.	Now section 3.1. This sentence has been amended.
	PB	Fine	No action required.
	MO	no issues with this section	No action required.
	MK	While I do not necessarily disagree with the last paragraph, I am not sure it has a place in a clinical guideline that reflects current thinking. I suggest that this is speculation and opinion on the part of the writer.	Agree. Paragraph removed.
	CR	The bullet points here are incorrectly laid out and interfere with readability. Correct is: Epilepsy is a disease of the brain defined by any of the following conditions: 1. At least two unprovoked (or reflex) seizures occurring more than 24 hours apart 2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years 3. Diagnosis of an epilepsy syndrome I think this is worth discussing and explaining properly. This definition is important as it allows us to diagnose epilepsy after one seizure in an infant with TSC or focal cortical dysplasia, or with a single epileptic spasm cluster and hypsarrhythmia on EEG, as the risk of recurrence of seizure over the next 10 years for these infant is clearly 60% or greater. Waiting until a second seizure has been clinically seen is not the best approach and the mantra of waiting for two unprovoked seizures is often problematic for younger patients with specific aetiologies. For example a 5 month old with a focal seizure	The 2017 ILAE classification has been retained in section 3.1. In light of other peer review comments it has been agreed to keep this section (now section 3.1) concise. Rather than providing further description, readers are directed to the ILAE classification for further information. This section serves to provide background/context for the evidence we have reviewed.

		who clearly has TSC would be sent home with no diagnosis and would come back months later with spasms. The data on waiting until the occurrence of two unprovoked seizures is probably more relevant specifically to adolescent GGE's. When adolescents with potential for GGE have their first seizure, ~ 30-40% have further seizures, most of these (~90%) have seizure recurrences occur in the first year after the initial seizure. Once a second seizure occurs, around 75% of this subgroup will have further seizures, therefore epilepsy is diagnosed at that time (by definition, epilepsy means that a person has been determined to have a >60% chance of having recurring seizures). Therefore waiting for a second seizure (with discussion re specific risk of recurrence based on presumed etiology eg GGE if known) is reasonable, if acceptable risk of recurrence to the family. But waiting for a 5 month old infant with known TSC would be a serious safety risk and potentially have long term developmental consequences.	
	AF	ref 11 -correct P12 –definition – second bullet point - ? English can be improved?? ' one unprovoked (or reflex) seizure and a probability of further seizures similar to the GENERAL recurrence' - suspect a quote, but general recurrence =???? There is no 'general' after 1 seizure!!!! Don't make sense! Not generalised tonic clonic: and can't be a general pattern of 1 event....	This is a direct quote of the ILAE definition so cannot be changed (now section 3.1).
3.5	TS	I feel a bit hesitant whether it is useful and serves a purpose to relate the 1981 seizure classification in detail. I would prefer to just mention 1981 briefly /as 1989 is mentioned) and instead present the 2010 seizure classification and then 2017.	Now section 3.2. The classification has been changed to present the most recent version only (2017).
	JC	This is well laid out and useful for those accessing the guideline. Draws on established criteria	Thank you.
	MK	I wonder about the need to describe the history of the classification of epileptic seizures and syndromes? However, there is merit in describing the new 2017 ILAE classification.	History has been removed, and the most recent classification retained (now section 3.2).
	AF	P12 3.5 – Can see you've gone through classification historically - ? would it not be better (this guide should be around for a few years!!!) to say these have evolved: START with the current one, then -perhaps in appendix –give to previous definitions??? Or any reader gets the out of date stuff first.....	The historical classifications have been removed.
	FB	The guideline should not be using this out-of-date classification. It should use the up-to-date classification which is not only currently recommended but is also much better than the previous version. It should be noted that at least one Scottish consultant has been	The older classfications have been removed.

		instrumental in publicising the up-to-date classification. This classification appears later in the guideline, on page 14. It should be right at the beginning of the classification section. On page 13, the term "dyscognitive" was never widely accepted and has not been replaced. Reference to this out-of-date classification, which was even worse than the 1981 classification, should be relegated to an appendix, if it appears at all.	
	CR	I was not sure of the relevance of including older ILAE classifications. Reference to the ILAE's website www.epilepsydiagnosis.org could be considered as it is a current resource based on current ILAE seizure and epilepsy classifications. A typo was noted: myoc lonic Figure 2 uses varied capitalisation of the first letter of the seizure type Typos noted in Figure 2 legend: aware-ness, intone. Definitions and the last two sentences in the legend do not make sense unless the legend is in the actual ILAE paper.	Now section 3.2. These have been removed. Reference to ILAE website added. Figure removed.
	PB	Listing 1981 and 1989 classification - look unnecessary and can be commented on historically in one sentence under ILAE 2017: 'Generalized-onset'- leave hyphen? There is no short paragraph to describes syndromes and the new terms developmental and/or epileptic encephalopathies (Scheffer IE, Berkovic S, Capovilla G, Connolly MB, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Apr;58(4):512-521). 'myoc lonic-tonic-clonic'- myoclonic-tonic-clonic	Now section 3.2. The classification has been changed to present the most recent version only (2017). This is outwith the scope of this guideline.
	IM	It seems quite dated - is it necessary for a full historical overview of classifications?	Now section 3.2. The classification has been changed to present the most recent version only (2017).
	VW	formatting of the seizure types isnt that clear in the first section	Now section 3.2. This has been amended.
	HC	The guidelines comment that the new seizure classification of 2017 is yet to be universally accepted. Both this, and the new framework of the epilepsies (Scheffer et al Epilepsia 2017;58: 512-521) are definitive, not proposals as previously put forward, and therefore should be put forward to be utilised. I am not clear why all previous classification proposals have been discussed in detail	Now section 3.2. This has been amended.
	AJ	A brief paragraph about previous ILAE classifications of epilepsy seizure types and syndromes would be more helpful rather than	Now section 3.2. The classification has been changed to

		all the confusing history given around the different iterations. Simply stating the current 2017 operational classification of seizure types, syndromes, and aetiological classification is used is more helpful. Should the following appear as supplemental info in the appendix or perhaps be more succinctly addressed? 'The expanded ILAE 2017 operational classification of seizure types. The following clarifications should guide the choice of seizure .....Due to inadequate information or inability to place in other categories'. Throughout the guideline the most recent terminology should be used - terms like partial are repeatedly used instead of the newer terminology	present the most recent version only (2017). The ILAE classification system is continually updated. The most recent (2017) classification has been used for this guideline. Terminology has been amended throughout the guideline.
	MO	This is very confused why go into all the previous classifications and why not just use the most recent which is more approrpiate. In addition then throughout the text the authors constant interchange focal with partial seizures !! in addition use old terms like secondarily generalised this would suggest a lack of understanding of the new classification	Now section 3.2. The classification has been changed to present the most recent version only (2017). Terminology has been amended throughout the guideline.
	KKT	Accepted	No action required.
	RC	Delete 'although this is evolving and undergoing refinements'.	This has been removed during editing (now section 3.2).
General	TS	This I find is the most unfinished chapter, especially the EEG and Genetic parts. Could be better structured, less repetition ("compared to awake EEG, an EEG that captures sleep has increased sensitivity for detecting epileptiform discharges" or a similar statement is repeated at least 4 times). Clearer separation between commentating references and doing summaries and conclusions. Could be shortened without loss of content. Going through references in the text has pros and cons. SIGN81 was very accessible and easy to read. I feel ambiguous about presenting references in the text in a document like this. It is not a Cochrane report or literature review...It is important that it is readable also by people who do not have a research or explicit academic interest. Would it be possible to present all the references in an annex or a "background" document?	The guideline group have undertaken major edits to the EEG section to make it more concise and clear. No references will be written in text in the final version.
	PB	Brief comment on metabolic investigations and possible conditions to consider,e.g. such as annex 5,p. 42 ,SIGN 81 would have been helpful.	Considered outwith the scope of this guideline (as per previous comment on section 1.2.1).
	JC	These are clearly laid out and supported by evidence	No action required.
	VW	delete the quotation marks mid sentence	This has been amended.
	AJ	The general order of sections 4.1.1- 4.1.5	Significant edits to this section have been

		could be presented more logically to reflect clinical practice i.e. 1. Video including home video 2. standard (video) EEG 3. Sleep EEG including melatonin and sleep deprived 4. Ambulatory 5. Long term video EEG monitoring	undertaken with a logical presentation as suggested.
	KKT	Accepted	No action required.
	CR	Suggest sentence ends with: with epilepsy and its aetiologies	Sentence has been removed.
4.1	RC	Please consider using Rebecca Black's animation which is on YouTube https://www.youtube.com/watch?v=MO7xXL2ZXP8	Thank you. A link to this will be considered for the patient version.
	MK	I note in this section that young people have found these wires "painful". I was very surprised to read this and do not feel that this is representative of what happens during an EEG. It is certainly the case that some children and young people do not like the wires and find them a little uncomfortable but to describe this as "painful" is perhaps too strong. I have discussed this issue with my EEG technologist colleagues and they are in agreement.	The quote has been removed.
4.1.1	TS	4.1.1 to 4.1.5 all deal with EEG. So 4.1 should have the title ELECTROENCEPHALOGRAM . 4.1.1 maybe could be "General considerations"...? Routine EEG in the case of "Suspected" epilepsy should be mentioned. Even though not diagnostic and with a low sensitivity and specificity in an unselected population it has value in estimating seizure recurrence risk, support epilepsy diagnosis and as mentioned can help classify epilepsy. The text can be worked with language wise and in structure and shortened. In the end of 4.1 routine EEG in suspected epilepsy (as deemed by a health professional with adequate knowledge...) should be added to the recommendations or good practice Points. Strange if this is completely left out since it is a very common scenario and there are references to support this.	Now section 4.1. Scottish Paediatric Epilepsy Network standards of care strongly emphasise the importance of clinical diagnosis, and the avoidance of using EEG to make or refute a diagnosis of epilepsy. Utility of EEG as a "diagnostic test" clearly depends on pre-test (Bayesian) probability but no studies have performed appropriate Bayesian analysis of this question. We do not want to encourage indiscriminate use of routine EEG. The key questions were determined at the consultation phase, and use of the EEG for "suspected" epilepsy was not defined as a key question. This is standard practice in Scotland and is included within SPEN care standards.
	PB	-'Information point -Provide patients/carers with an explanation of investigative procedures'- good practice point rather	Now section 4.1. The information points are prompts for providing information, so is a form of good practice.

	MK	I suggest that this section should be re-ordered such that it should be emphasised firstly that an EEG is not a diagnostic test but secondly that can aid a syndromic diagnosis. This section contains references but no evidence levels are attached to them. If the evidence has not been reviewed then this should be explicit.	The section states that diagnosis is clinical and EEG used to characterise seizure types. There are no evidence levels against the references as they are providing background information rather than informing a recommendation.
	JC	As previously stated	No action required.
	AJ	Too much detail - can this be reduced to key points?	Now section 4.1. This section has been made more concise.
	MO	Should be stated in bold that an EEG does not diagnose epilepsy but used to inform classification	Now section 4.1. This paragraph has been edited for clarity.
	CR	"When I went to the doctor I had to get on all the wires". This made me feel nervous.". Check the extra " and . in the above sentence. I would argue that the primary use of the electroencephalogram (EEG) is to help further characterise seizure types and/or epilepsy aetiology. A focal EEG is a clue to a focal aetiology, such as a lesion. To state that it is a clue to aetiology is broader than syndromes as many syndromes are also primary aetiologies (genetic eg Dravet, complex genetic eg GGEs).	This quote has been removed as other comments indicated that it was unrepresentative. Now section 4.1. This has been reworded to: The primary use of the electroencephalogram (EEG) is to help further characterise seizure types and epilepsy syndrome, and can help inform aetiology once a clinical diagnosis of epilepsy has been made.
	KKT	Accepted	No action required.
4.1.2	TS	Ok	No action required.
	PB	-'2++'- 2+ as is one study -agree with practice point	Now section 4.1.1. This is one study rated as 2++ (high quality) – see SIGN evidence and grading key.
	JC	As previous	No action required.
	MK	The way that these sections are set out are perhaps confusing to a reader and are too long. I do not believe that describing the raw data from papers adds to the sections significantly. Setting this out as subsections of along the lines of "increasing the syndromic diagnostic yield of EEG recordings" and "ictal recordings" might be helpful. As far as I am aware the significant majority of Scotland and UK paediatric services use melatonin sleep induction and have moved away from sleep-deprived recordings. As such the evidence setting out the relative utility of these two techniques would be helpful. The Recommendations should be revised. If a clinical diagnosis has been made and a standard EEG is normal then a second-line EEG should be used. And then a statement about the relative utility of sleep deprived,	Addressed and restructured (now section 4.1.1.). Currently there is varying practice in units across Scotland, different units have differing practices. Significant numbers user melatonin others use sleep deprivation. The recommendations have been combined and amended to 'If a clinical diagnosis of epilepsy has been made, EEG is recommended for further classification of epilepsy. If standard EEG is normal, a second-line EEG should be carried out. This

		melatonin and ambulatory recordings. This may or may not be able to encompassed into a formal Recommendation depending on the view of the evidence. As they stand, the two Recommendations themselves do not easily sit side by side. In general terms the words “standard” and “routine” EEG appear to be used interchangeably.	could be an ambulatory recording, a sleep-deprived recording or melatonin-induced sleep’. Changed to ‘standard’ throughout.
	AF	4.1.2 – –COMPARE AMB /VTEM: refs in adults and kid DO exist – a quick google: best of those found quickly from Ros Kandler (she’s good!) in Sheffield did one on kids – haven’t seen whole paper, but Abstract: Seizure. 2017 Apr;47:66-70. doi: 10.1016/j.seizure.2017.02.010. Epub 2017 Feb 28. Video ambulatory EEG: A good alternative to inpatient video telemetry? Kandler R1, Ponnusamy A2, Wragg C2. Author information Abstract PURPOSE: Video ambulatory EEG (V-AEEG) is a new technique which could add increased capacity for long term EEG monitoring to overstretched inpatient video telemetry (IPVT) services. We compare V-AEEG and IPVT for diagnostic efficacy, recording quality, patient acceptability and technologist time required. METHODS: Forty-one V-AEEG and 64 IPVT adult patients were included. Patients were investigated to diagnose attacks or to obtain polysomnography (PSG) prior to multiple sleep latency test (MSLT). Number of attacks recorded, whether the diagnostic question was answered, quality of video and EEG recording and patients' preference for investigation at home or in hospital were noted. For V-AEEG patients, ease of procedure and extra technologist time required were recorded. RESULTS: Of patients investigated for diagnosis of attacks, 74% V-AEEG patients and 62% IPVT had typical attacks during the investigation. All PSGs were useful in interpreting the MSLTs. Diagnostic questions were answered by 73% V-AEEGs and 73% IPVTs. Quality of EEG and video recording was similar using V-AEEG and IPVT. Four patients had difficulty using V-AEEG equipment but diagnostic information was lost in only one. 5% of V-AEEG patients would have preferred hospital investigation	Thank you for the suggestions. The first paper is out of scope as it is in an adult population. The second paper does not answer the KQ so is outwith the scope of the guideline.

		but 45% of IPVT patients would have preferred home investigation. Extra technologist time for home visits (mean 2h) was required only for the first 7 patients. CONCLUSION: Video EEG recording quality and diagnostic efficacy from V-AEEG are similar to IPVT. V-AEEG is acceptable to most patients and does not require additional technical time. Hence, V-AEEG offers a convenient, economical alternative to IPVT. Copyright © 2017 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved -top 3 from google search! - Video ambulatory EEG: A good alternative to inpatient video telemetry? https://www.ncbi.nlm.nih.gov/pubmed/28315606 by R Kandler - 2017 - Cited by 9 - Related articles 28 Feb 2017 - PURPOSE: Video ambulatory EEG (V-AEEG) is a new technique which ... long term EEG monitoring to overstretched inpatient video telemetry (IPVT) services. We compare V-AEEG and IPVT for diagnostic efficacy, recording quality ... and EEG recording and patients' preference for investigation at home or Home video telemetry in children: A comparison to inpatient video ... https://www.ncbi.nlm.nih.gov/pubmed/30218807 by S Carlson - 2018 - Cited by 1 - Related articles 8 Sep 2018 - PURPOSE: Home Video Telemetry (HVT) combines ambulatory EEG with simultaneous video recording. No previous reports have compared G333(P) Compare the value of ambulatory EEG and video telemetry in https://adc.bmj.com/content/99/Suppl_1/A137.1 by M Iqbal - 2014 Method The EEG department database was interrogated retrospectively for children having both ambulatory EEG and video telemetry recording during the ... The value of home video with ambulatory EEG: A prospective service https://www.sciencedirect.com/science/article/pii/S1059131114000594	Outwith scope. Outwith scope.

		by E Goodwin - 2014 - Cited by 18 - Related articles In our study, home video facilities aided interpretation of ambulatory EEG recordings in ... There are two types of long term monitoring – ambulatory EEG and video telemetry (VT). ... This compared to 3 patients from a total of 11 in adults (27%).	Outwith scope.
	VW	2nd paragraph, 4th line - should all be receive - delete be	Now section 4.1.1. Amended.
	AJ	'Although this good practice point is based on only one study' Should read 'Although this good practice point is based on only one ADULT study'	Now section 4.1.1. Amended.
	MO	Excellent paper good that it is included excellent practice point	No action required.
	KKT	Accepted	No action required.
	RC	n=43 modest sample. Really class 2++ level evidence? "No studies comparing the diagnostic utility of home versus hospital video telemetry versus VT were identified." Something is wrong with this statement.	Now section 4.1.1. Agree. Downgraded to 2+. This paragraph has been deleted during editing.
	CR	Typo: should all be receive regularly VT was not defined anywhere as an abbreviation It might be best to ensure 'if safe to do so' is included in the recommendation to acquire home video, as taking video should not over-take provision of seizure first aid (a second person is best required if clinicians ask for video of events) This is a useful section as video in itself is a very important diagnostic tool.	Addressed This has been added to the GPP (now section 4.1.1).
4.1.3	TS	Ok	No action required.
	PB	'A prospective multi-centre observational study of children aged 1 month to 16 years (n=522)...'- one study, thus 2+	Now section 4.1.2. This is one study rated as 2+ (well conducted) – see SIGN evidence and grading key.
	AF	Sounds fair - might want to add in DeRoos-blinded study 2009 in kids - again sleep deprivation helped - whether or not there was sleep: Pediatrics. 2009 Feb;123(2):703-8. doi: 10.1542/peds.2008-0357. Effects of sleep deprivation on the pediatric electroencephalogram. DeRoos ST1, Chillag KL, Keeler M, Gilbert DL. Author information Abstract BACKGROUND: The routine electroencephalogram aids in epilepsy syndrome diagnosis. Unfortunately,	Thank you, this paper has been added.

		routine outpatient electroencephalogram results are normal in roughly half of children with epilepsy. To increase the yield, practice guidelines recommend electroencephalograms with sleep and sleep deprivation. The purpose of this study was to rigorously evaluate this recommendation in children. METHODS: We conducted a randomized, blinded comparison of routine electroencephalograms versus sleep-deprived electroencephalograms in 206 children aged 0 to 18 years. Electroencephalograms were ordered for standard indications after a neurologist's clinical assessment indicated > or =1 seizure (83%) or unclear spell (17%). The primary outcome was the proportion of normal routine electroencephalogram results versus sleep-deprived electroencephalogram results. Logistic regression modeling was used to assess the influence of sleep, as well as other clinical factors. RESULTS: Although children with sleep-deprived electroencephalograms had less sleep the night before (4.9 vs 7.9 hours) and more sleep during electroencephalograms (73% vs 55%), the increase in electroencephalogram yield was borderline significant (56% normal sleep-deprived electroencephalogram versus 68% normal routine electroencephalogram). Moreover, sleep during the electroencephalogram did not increase its diagnostic yield. Sleep-deprived electroencephalogram yield tended to be higher in children with preelectroencephalogram clinical diagnosis of seizure(s) and at older ages (>3 years). CONCLUSIONS: Sleep deprivation, but not sleep during the electroencephalogram, modestly increases the yield of the electroencephalogram in children diagnosed with seizures by neurologists. Compared with a routine electroencephalogram, the number needed to test with sleep-deprived electroencephalogram to identify 1 additional child with epileptiform discharges is approximately 11.	
	JC	As previous	No action required.
	CR	Typo: who had a normal, routine (remove comma) No other comments.	This sentence has been removed (now section 4.1.2).
	VW	No conclusion or recommendation	Recommendations are at the end of the section.
	AJ	Paragraph 1 is all about adults - is it necessary to put this in?	Now section 4.1.2.

		Ref 33 could simply be added after the last statement in paragraph 2 which reference adult studies are consistent with the single paeds study discussed. why is there no recommendation on the basis of the evidence reviewed?	The order of paragraphs has been switched to feature studies including children first. The adult study is still included, as this adds strength to the recommendation. Recommendation is at the end of section 4.1.
	MO	My only issue with this is the difficulty of achieving sleep deprivation in children under 5. Also no mention has been made of acquiring a sleep and awake recording together naturally	Now section 4.1.2. This is now included in paragraph 3 of sleep-deprived EEG section. An additional sentence has now been included for clarification.
	FB	A necessary section.	No action required.
	KKT	Accepted	No action required.
4.1.4	TS	Ok	No action required.
	FB	A worthwhile section.	No action required.
	AF	must be a lot of old literature on this: a fairly good 2016 ref- 1803 pts- is: Neurology. 2016 Apr 19;86(16):1524-30. doi: 10.1212/WNL.0000000000002592. Epub 2016 Mar 16. Routine vs extended outpatient EEG for the detection of interictal epileptiform discharges. Burkholder DB1, Britton JW2, Rajasekaran V2, Fabris RR2, Cherian PJ2, Kelly-Williams KM2, So EL2, Nickels KC2, Wong-Kisiel LC2, Lagerlund TD2, Cascino GD2, Worrell GA2, Wirrell EC2. Author information Abstract OBJECTIVE: To compare the yield of epileptiform abnormalities on 30-minute recordings with those greater than 45 minutes. METHODS: We performed a prospective observational cross-sectional study of all outpatient routine EEGs comparing the rate of interictal epileptiform discharges (IEDs) and clinical events during the initial 30 minutes (routine) with those occurring in the remaining 30-60 minutes (extended). A relative increase of 10% was considered clinically significant. RESULTS: EEGs from 1,803 patients were included; overall EEG duration was 59.4 minutes (SD ±6.5). Of 426 patients with IEDs at any time during the EEG, 81 (19.1%, 95% confidence interval 15.6-23) occurred only after the initial 30 minutes. The rate of late IEDs was not associated with age, indication, IED type, or sleep deprivation. Longer recording times also increased event capture rate by approximately 30%.	Outwith scope.

		CONCLUSIONS: The yield of IED and event detection is increased in extended outpatient EEGs compared to 30-minute studies	
	CR	Typo: by a two neurophysiologists who (remove a) Typo: during routine part (change part to EEG, add the before routine) Typo: Sensitivity of ambulatory was 58% (insert EEG).	The section has been edited, so these no longer apply.
	PB	-'The 30 minute portion and the 23.5 hour portion were analysed separately by a two neurophysiologists who were blinded to the patient details and clinical question. The reference standard was diagnosis of epilepsy as judged by one neurologist.' - necessary? -one study-2+ SIGN 143 ,81, do not state statistical values-RR, confidence interval, p values unless within sentence and not in brackets(e.g sometimes RR)	Now section 4.1.2. This section has been edited and this paragraph removed. It is standard SIGN style to include supporting statistics. They have now been changed to the standard SIGN format.
	JC	As previous	No action required.
	VW	No conclusion or recommendation	Recommendation is at the end of section 4.1.
	AJ	'AMBULATORY EEG VERSUS STANDARD EEG' Are we trying to define the use of ambulatory vs standard EEG in children for who a diagnosis of epilepsy has been made or use this to determine the nature of clinical events or both? Heading should be clear as in 4.1.3 Think that this can be simplified to say that and adult study demonstrated value but that there are no studies in children. Recommendation - there is no data to support the use of prolonged ambulatory EEG to classify seizure types or make a syndromic diagnosis (note - ambulatory EEG without video is also unhelpful when trying to establish if an event is epileptic or not)	Now section 4.1.2. This section focuses on the diagnostic utility of various types of EEG for detecting epileptiform discharges when a clinical diagnosis of epilepsy has been made. We have made this clearer by adjusting the structure of this section.
	MO	All the studies were in adults not children of course an ambulatory study captures sleep thereby increasing the yield	Now section 4.1.2. This has been addressed in the rewritten section.
	KKT	Accepted	No action required.
	RC	Since not data in children, really class 2++ evidence?	Now section 4.1.2. The evidence level is linked to the way the study has been conducted. The strength of the recommendation is affected by the evidence being extrapolated from an adult population.
4.1.5	TS	Needs more structure and better flow to be easier to follow. The melatonin part is better placed after the	Now section 4.1.2. The guideline group have undertaken major edits to the EEG section to make it more

		paragrafh "SD EEG and ambulatory EEG are both more sensitive than standard EEG at capturing epileptiform activity."	concise and clear.
	MK	The way that these sections are set out are perhaps confusing to a reader and are too long. I do not believe that describing the raw data from papers adds to the sections significantly. Setting this out as subsections of along the lines of "increasing the syndromic diagnostic yield of EEG recordings" and "ictal recordings" might be helpful. As far as I am aware the significant majority of Scotland and UK paediatric services use melatonin sleep induction and have moved away from sleep-deprived recordings. As such the evidence setting out the relative utility of these two techniques would be helpful. The Recommendations should be revised. If a clinical diagnosis has been made and a standard EEG is normal then a second-line EEG should be used. And then a statement about the relative utility of sleep deprived, melatonin and ambulatory recordings. This may or may not be able to encompassed into a formal Recommendation depending on the view of the evidence. As they stand, the two Recommendations themselves do not easily sit side by side. In general terms the words "standard" and "routine" EEG appear to be used interchangeably.	These sections have been edited, and restructured with a subsection for melatonin (now section 4.1.2). The recommendations have been combined and amended to clarify the second-line EEG method. Changed to 'standard' throughout.
	PB	-paragraph one -SIGN 143 ,81, do not state statistical values- RR, confidence interval, p values -Could the summary paragraph not just be fleshed out a little more and brief sentences on sleep deprived EEG and melatonin in regards their usefulness with evidence alongside that (above recommendations) and leave out the detail paragraphs?	Now section 4.1.2. SIGN style is to state CI where cited and *P*-values if not. The guideline group have undertaken major edits to the EEG section to make it more concise and clear.
	JC	As previous	No action required.
	AF	You could include another retrospective study - also not brilliant as possible bias& retrospective - but compared sleep deprived EEG as first test - - found best in focal: from pubmed: , -Clin Neurophysiol. 2013 Nov;124(11):2101-7. doi: 10.1016/j.clinph.2013.04.342. Epub 2013 Jun 18. Usefulness of a simple sleep-deprived EEG protocol for epilepsy diagnosis in de novo subjects.	This was an adult retrospective study so not included.

		Giorgi FS1, Perini D, Maestri M, Guida M, Pizzanelli C, Caserta A, Iudice A, Bonanni E. Author information Abstract OBJECTIVE: In case series concerning the role of EEG after sleep deprivation (SD-EEG) in epilepsy, patients' features and protocols vary dramatically from one report to another. In this study, we assessed the usefulness of a simple SD-EEG method in well characterized patients. METHODS: Among the 963 adult subjects submitted to SD-EEG at our Center, in the period 2003-2010, we retrospectively selected for analysis only those: (1) evaluated for suspected epileptic seizures; (2) with a normal/non-specific baseline EEG; (3) still drug-free at the time of SD-EEG; (4) with an MRI analysis; (5) with at least 1 year follow-up. SD-EEG consisted in SD from 2:00 AM and laboratory EEG from 8:00 AM to 10:30 AM. We analyzed epileptic interictal abnormalities (IIAs) and their correlations with patients' features. RESULTS: Epilepsy was confirmed in 131 patients. SD-EEG showed IIAs in 41.2% of all patients with epilepsy, and a 91.1% specificity for epilepsy diagnosis; IIAs types observed during SD-EEG are different in generalized versus focal epilepsies; for focal epilepsies, the IIAs yield in SD-EEG is higher than in second routine EEG. CONCLUSIONS: This simple SD-EEG protocol is very useful in de novo patients with suspected seizures. SIGNIFICANCE: This study sheds new light on the role of SD-EEG in specific epilepsy populations.	
	CR	Typo: a clinical diagnosis of epilepsy sensitive Typo: Sensitivity of SD EEG of 45% (?? was 45%, check this whole sentence) Typo: .None of the economic evaluations Otherwise this section is clear and excellent.	Amended (now section 4.1.2).
	FB	A worthwhile section.	No action required.
	AJ	this section seems to be addressing two issues 1) Paragraph 1 examines the sensitivity and specificity of ambulatory vs sleep deprived EEG in adults with a clinical diagnosis of epilepsy. It wasn't clear if this was in relation	Now section 4.1.2. This section focuses on the diagnostic utility of various types of EEG for detecting epileptiform discharges when a clinical diagnosis of epilepsy has been made. We

		to classification of the seizure type based on interictal features or an attempt to capture clinical events and confirm a diagnosis. 2) Paragraph 2 - the relative utility of these tests in establishing the nature of events i.e. epileptic vs non-epiletic Doesn't quite make sense and both paragraphs really discuss adult data (although the second systematic review did include 2 studies with children). Not sure what is being evidenced here. Subsequent discussion thus leads to further confusion NS - what does this mean? Not sure the conclusion drawn is valid as the evidence presented is addressing different things helpful to present the +2-3 evidence in relation to melatonin with or without sleep deprivation as this is used in clinical practice Recommendations: f a clinical diagnosis of epilepsy has been made, EEG is required for further classification of epilepsy. If routine EEG is normal, as second line EEG investigation, consider an ambulatory or sleep deprived recording. - why would we not consider a melatonin sleep induced EEG based on the evidence presented. Where an EEG capturing sleep is required as a diagnostic procedure, the administration of melatonin should be considered for sleep induction in young children - the guideline preamble has stated that an EEG is not a diagnostic test so not sure the word 'diagnostic' is correct here.	have made this clearer by changing the structure of this section.
	MO	An ambulatory will capture sleep in addition to an awake study and may be more appropriate for young children Sleep deprivation is difficult in young children and infants	Reference to this has been included in the 'Ambulatory EEG' paragraphs in section 4.1.2.
	KKT	Accepted	No action required.
4.2	TS	Why include this? The guidelines concerns children from one month. And strange to have cEEG in NICU when cEEG in PICU is not mentioned (because status ep is not dealt with)	This section has been removed.
	PB	This guideline stated that it will not look at neonatal seizures- this section therefore not relevant to guideline	This section has been removed.
	MK	This section should be deleted since it refers to neonatal seizures that are specifically outside the remit of this guideline.	Section removed.

	AF	CFAM or CFM? CFAM is the analysing monitor - which I like as well: but CFM perhaps the more general term.....arguable for clarity -might clarify with '(and commonly below 1 month of age) ' after ' We were unable to use any evidence to make recommendations in the use of continuous EEG or cerebral function monitoring (CFAM) for monitoring of epileptic seizures in the neonatal unit. The studies identified related to patients who were at risk of seizures, typically as a result of birth complications' Also end of this section -suggest not relevant to THIS epilepsy guideline. (as it is useful in Neonates for confirming seizures present, and type).	Section removed.
	KKT	Accepted	No action required.
	JC	As previous	No action required.
	IM	Should probably put some practical advice (and cautions) on the use of CFAM	This section has been removed.
	HC	It is unclear why this is mentioned at all as neonatal seizures are outside the scope of this guideline	This section has been removed.
	AJ	Not sure why this is in this guideline at all as the guideline remit expressly excluded neonates and seizures in the first month of life.	This section has been removed.
	MO	not in the guideline remit	This section has been removed.
4.3	TS	Ok	No action required.
	MK	There is a comprehensive account of what is a series of relatively low-level evidence. This section could be usefully shortened.	The section has been edited (now section 4.2).
	AQ	Why no mention of the use of SPECT or PET? - Epilepsia. 2013 Feb;54(2):341-50. Interictal PET and ictal subtraction SPECT: sensitivity in the detection of seizure foci in patients with medically intractable epilepsy. Desai A1, Bekelis K, Thadani VM, Roberts DW, Jobst BC, Duhaime AC, Gilbert K, Darcey TM, Studholme C, Siegel A.	As this is separate and specific to epilepsy surgery, it is outwith the scope of this guideline on the diagnosis and management of epilepsy.
	MO	recommendations for who should be imaged are clear and concise	Thank you.
	KKT	Accepted	No action required.
	FB	No additional comments apart from editing requirement.	The section has been edited (now section 4.2).
	CR	No comments other than it is worth noting that the information from imaging can be used in the presence of a single unprovoked seizure to consider whether diagnosis of epilepsy is met (eg single seizure, TSC on imaging). Refer to section on Definition of Epilepsy above	Agree – no changes to guideline required.
4.3.1	TS	Ok	No action required.
	AQ	No issues with section	No action required.
	AF	-?second paragraph - English/typo??!	Amended (now section 4.2.1).

		Suggest 2nd 'epilepsy' redundant/typo!	
	JC	As previous	No action required.
	MO	Should be emphasised that CT is easily available and useful in emergencies but MR is the method of choice	Now section 4.2.1. Agree; this has been added.
	CR	Typo: of epilepsy in children epilepsy No other comments unless it is worth discussing risk:benefit (radiation risks)	Typo addressed. We are not addressing the radiation risks as CT is for emergency only and there was no evidence for this. Now section 4.2.1.
4.3.2	TS	Magnetic Resonance Imaging (MRI) is the imaging modality of choice and should be performed in all patients with epilepsy except children with idiopathic generalised epilepsy /and BECTS/ who respond to drug treatment	Now section 4.2.2. Agree; amended and table included for reference.
	KKT	Accepted	No action required.
	CR	Should you use idiopathic/genetic generalised epilepsy (current ILAE term) Typo: close bracket after 2012 Typo: affect or effect? I wondered if the Table terminology might be best explained in a legend as 'localisation related' is not consistent with the ILAE definitions provided earlier. This is important also for the later section 4.3.3	Amended (now section 4.2.2). Agree, but this cannot be changed as this is from ILAE recommendations for neurology paper.
	AQ	This guidance must have recommendations regarding sequences to perform. While there are variable protocols used around the world, the guidance must state a bare minimum of sequences to use. A T1-weighted sequence must be used with isotropic voxel size in order to enable the reconstruction of images in any plane: - Gaillard WD, Cross JH, Duncan JS, et al. Epilepsy imaging study guideline criteria: commentary on diagnostic testing study guidelines and practice parameters. Epilepsia. 2011;52(9):1750–1756 - Cendes F. Neuroimaging in investigation of patients with epilepsy. Continuum (Minneap Minn) 623–642;19(3 Epilepsy) - Bastos AC, Comeau R, Andermann F, et al. Diagnosis of subtle focal dysplastic lesions: curvilinear multiplanar reformatting from three dimensional magnetic resonance imaging. Ann Neurol. 1999;46:88–94 - Colombo N, Salamon N, Raybaud C, et al. Imaging of malformations of cortical development. Epileptic Disord. 2009;11:194–205 - Barkovich AJ, Rowley HA, Andermann F. MR in partial epilepsy: value of high-resolution volumetric techniques. AJNR. 1995;16:339–343 FLAIR imaging is mandatory with it being shown to demonstrate an accuracy of 97% for the demonstration of abnormalities with	Now section 4.2.2. There were no comparator studies on different sequences when we reviewed the evidence. This has been highlighted in the commentary paper quoted by the reviewer (Gaillard WD, Cross JH, Duncan JS, et al. Epilepsy imaging study guideline criteria: commentary on diagnostic testing study guidelines and practice parameters. Epilepsia 2011;52(9):1750–1756) However, the guideline development group agree with the reviewer regarding standardised epilepsy imaging protocol. A good practice point has been added: When neuroimaging non-urgent cases of children and young people diagnosed to have epilepsy consider: 1. appropriate clinical information including EEG findings, where possible 2. having standardised epilepsy neuroimaging protocols and sequences.

		hippocampal sclerosis. this paper also shows the need for the inclusion of a inversion recovery sequence. - Kuzniecky RI, Bilir E, Gilliam F, et al. Multimodality MRI in mesial temporal sclerosis: relative sensitivity and specificity. Neurology. 1997;49(3):774–778.	
	JC	As previous	No action required.
	VW	brackets opened but not closed around NICE statement	Now section 4.2.2. Amended.
	AJ	Should there not be a recommendation ? e.g. All children diagnosed with epilepsy (except those with a genetic generalised epilepsy or self limiting focal epilepsy with central temporal spikes) should have a 1.5T MRI at diagnosis and Imaging should be carried by a radiologist with experience in paediatric neuroradiology	This is covered in section 4.3.2. No recommendation is needed.
	MO	Appropriate recommendations	No action required.
	RC	“BECTS”. Define if not used previously	Now section 4.2.2. Amended to BCETS and defined.
4.3.3	TS	A few language errors In the end the dealing with "Magnetic Resonance Imaging (MRI) is the imaging modality of choice and should be performed in all patients with epilepsy except children with idiopathic generalised epilepsy and BECTS who respond to drug treatment" should be added to the recommendations or good practice points	Now section 4.2.3. These errors have been corrected. As per comment above relating to this section.
	PB	This section could be shorter - briefly pointing to 3T improving lesion detection in summary and studies mainly in adults? -'In children with drug resistant focal epilepsy 3T MRI should be considered if 1.5T does not detect and define a lesion.'- levels of evidence at consider level - 'should be considered'- rather replace 'should' to avoid confusion, e.g. with 'need to'?	Now section 4.2.3. ‘Should be considered’ is the correct strength of recommendation because it is extrapolated from adult studies.
	AQ	No issues with section	No action required.
	JC	As previous	No action required.
	VW	specialized should be specialised	Now section 4.2.3. Amended.
	HC	Paragraph 6 - should be consistent in use of terminology focal rather than partial	Now section 4.2.3. Amended.
	AJ	All the evidence presented seems to adult data. Can we extrapolate this to children? Are we more likely to find co-incidental findings of no clinical relevance in children? can we attribute the levels of evidence to children?	Now section 4.2.3. The guideline group considered this and felt the incidental findings would be the same in children as in adults.

	MO	Recommendations for the use of 3T are appropriate but there is a recurring problem with this guideline who is it for? specialist epileptologist or healthcare professionals in primary or secondary care. 3T MRI is a specialist investigation mainly for use in epilepsy surgery programmes	Now section 4.2.3. As per comments in preceding sections.
	KKT	Accepted	No action required.
	CR	Typo: this additional information lead to a change Typo: They found 97(12%) new diagnosis with 3T scan which were not found in previous 1.5T scan. Whilst some of these were incidental findings, and in 37 patients (5%) that affected subsequent management. Typo: frequency of detection of a new lesion by re-imaging at 3.0 T patients with refractory partial epilepsy, candidates for surgery, was found to be low Typo: Another retrospective, database study comparison of 1.5 and 3T, a qualitative comparison of 3-T and 1.5-T MRI Unclear: in all four parameters (the four parameters were not described) Typo/unclear: Studies were mainly in an adult population with only one including adolescents. Although these studies are from adult population, ... Typo: paediatric epilepsy population (populations?) Apart from typos resulting in readability impact, no other comments. All relevant evidence seems included, the recommendation arising is appropriate, for the Scottish context.	Corrected (now section 4.2.3). Thank you.
4.4	TS	In general 4.4 needs more structure, could be shorter without losing content. Some language errors.	Now section 4.3. This has been made more concise and errors have been corrected.
	JC	As previous	No action required.
	MK	Again this is a long section that could be usefully shortened. In the Good Practice Point “genetic testing” could be more explicitly defined (ie gene panel testing and chromosomal micro array).	The guideline group considered being more specific about the type of genetic testing, but as genetic technology is changing rapidly this was not felt to be a useful thing to add to the GPP.
	CR	Typo: Deoxyribonucleic acid (no capital D required?) No other comments, clear text.	Amended during editing.
	IM	It's a bit too "wordy" - could be more succinct.	Now section 4.3. This has been made more concise and errors have been corrected.
	MO	Well written section highlighted the usefulness of genetic testing	No action required.
	FB	The above should be "GENETIC TESTING", as it is in the guideline.	Comment noted, but relates to the peer review feedback form, rather than the

		The second paragraph needs to be rewritten to provide greater clarity. Is there an error in the first sentence of this paragraph?	guideline. Sentence removed.
	KKT	Accepted	No action required.
4.4.1	TS	Prenatal genetic testing and preimplantation genetic diagnosis (PGD) and carrier testing ought to be mentioned	These have been included in paragraph 4 of section 4.3.1.
	AF	? english? -.....Before genetic testing is requested ..... families should be fully informed.....	Amended.
	VW	4th paragraph, concerns should be concern and last sentence, remove the 'be' and replace with to	Now section 4.3.1. Amended.
	MO	Clearly stated and well written A patient leaflet should be produced in addition to one for SUDEP	This will be suggested as a workflow for SPEN to develop a patient-centred guide to all investigations that may be encountered, including imaging, EEG, and genetic testing. SIGN also produce a patient version of the guideline.
	KKT	Accepted	No action required.
	FB	Replace "full informed" with "fully informed". The recommendation of a discussion with an experienced clinician or genetic counsellor is a good one but is it realistic?	Amended. The GPP is for a small, select group of patients who need specific genetic testing. The conditions where it would apply are listed in the GPP. It is not for routine use, so should be feasible.
	RC	“Before genetic testing is requested families should full informed”. Insert ‘be’ after ‘should’.	Now section 4.3.1. Amended.
	CR	Typo: should full informed Typo: and reduces feelings of self-blame73-75 demonstrated that in families (the start of a sentence before the word 'demonstrated' appears missing) No other comments. All relevant benefits are discussed.	Amended to ‘fully informed’. This sentence has been amended.
4.4.2	TS	Mention that "gene panels" could mean that a set of genes are sequenced OR that a set of genes are looked at in whole exome or whole genome data.Since knowledge of genes related to epilepsy is increasing exponentially exome/genome sequencing offers the significant advantage that gene data (from the majority who did not get a diagnosis) can be refiltered after some time when the list of known genes has increased considerably. Should be mentioned I Think even though not generally available today. Good practice Points: why is the need for a Clinical genetecist or pediatriic neurologist with genetic interest more emphasised in the second point? The indication (and yield) is stronger in the second point. If any difference I would say the need for best possible	Now section 4.3.2. This point may be too detailed for this guideline. The guideline is aimed at clinicians managing epilepsy (and deciding when to use genetic testing), not at labs designing panel testing. Owing to the pace of technological advances, technical recommendations could rapidly become outdated. Hence, the general reference to “gene panel testing or whole exome sequencing”. Appropriate counselling is emphasised throughout section 4.3 (for all forms of genetic testing). Owing to higher levels of incomplete penetrance, array CGH testing is being used here to emphasise the point. This is not to say that counselling is not important

		consultation is at least as strong or stronger in the more unspecific epilepsy case which is quite often polygenic and with todays knowledge not that easy to evaluate and with less consequences.	in relation to other forms of genetic testing, as per the first good practice point.
	PB	levels of evidence eluded to in paragraph stated above recommendations but should probably follow same method of nomenclature by putting in to the side	Now section 4.3.2. There was insufficient evidence to cite evidence level in this section, hence they are included as good practice points rather than recommendations.
	CR	Typo: {with drug-resistant seizures Typo: One study by performed Typo: it is important to involve experienced clinician in the counselling of families Typo:epilepsy interns Typo: were all observational studies that did include control groups or assess bias (? did or did not) Typo: describing that clinical features (the rather than that?) Typo: answer the question (?answering the question) Otherwise no comments. Difficult and rapidly changing section as technology rapidly advances.	Thank you. The draft has been edited and typos corrected throughout.
	JC	As previous	No action required.
	FB	The genetic information in this section should be provided in the form of a table, as well as the text	It is unclear what would be added to a table.
	VW	Remove	Now section 4.3.2. This section provides an overview of the current evidence base on genetic testing and the group consider this to be of interest to HCPs.
	HC	Chromosomal microarray, second paragraph the initial sentence does not make sense and needs rewording	Now section 4.3.2. Sentence amended.
	JC	Clearly laid out	No action required.
	AJ	should we be differentiating between patients with epilepsy vs those with epilepsy plus in our genetic approach?	Now section 4.3.2. There is no strong evidence to suggest that this should be done, so we cannot make specific recommendations on this. There is no clear definition as to what is meant by “epilepsy plus”. The second good practice point emphasises that additional features need to be considered when deciding on genetic testing approach.
	MO	Concisely outlined what tests are available and when should they be used. However in	Now section 4.3.2. Agree. We hope the guideline makes it clear

		view of the issues raised with genetic testing such as VUS and benign copy variant genetic testing should only be carried out when there is the expertise to obtain informed consent and able to deal with results. Again epilepsy genetic is a very specialised field raising once more who is this guideline written for most of it would seem to be written for specialists	that genetic testing should only take place in the context of expertise and detailed counselling.
	KKT	Accepted	No action required.
	RC	Delete superfluous bracket before 'with drug-resistant seizures'. "One study by performed chromosomal microarray in patients with generalised epilepsy and intellectual disability and reported that 22%". Remove 'and' before 'reported'.	Now section 4.3.2. Amended. Amended.
5.1	TS	Some language errors. otherwise ok.	Language errors have been amended.
	PB	Information point -rather should become good practice point? I think it would simplify practical points by putting good practice points, recommendations and information points together. Patient quotes can be left at beginning of section	This has been amended throughout the guideline.
	MK	This section could also be usefully shortened. It repeats some statements already covered earlier in the guideline (e.g. SMC and off-label use). It could perhaps make the point that the evidence for a choice of an anti-epileptic drug in general terms is a challenge for prescribers because of the lack of head-to-head studies in this area of clinical practice.	This section has now been edited to be more concise. A comment on head-to-head studies has been included.
	JC	Section is well laid out and supported by evidence	Thank you.
	FB	This is, of course, a very important section. It requires some editing.	This section has now been edited to be more concise.
	IM	Overly wordy and confusing introduction. Could be tighter.	The introduction has been made more concise.
	VW	antiepileptic and anticonvulsant used interchangeably, should choose one term and stick to it	The draft has been changed to 'antiepileptic drugs' throughout.
	MO	The recommendations are appropiate in this section to the level of evidence But there is nothing on when to start drugs, when drugs levels need to be done and when they shouldnt be done What adverse effects should be monitored When and how AEDS should be stopped In the guideline there are times when the term anti-convulsant drugs is used and this is inappropiate and only the term anti-epileptic drugs should be used.	This is covered in the SPEN pathway and referenced. The evidence is for treatment. This is outwith the scope of this guideline. The draft has been changed to 'antiepileptic drugs' throughout.
	KKT	Accepted	No action required.

	CR	Typo: depending on number of factors Typo: It is important to discuss the options available, potential side effects, treatment response, adherence to treatment, potential length of treatment and likely treatment response. (treatment response mentioned twice) Typo: Adherence to AEDs in paediatric age group (?the paediatric age group) Typo: anticonvulsant drugs (used AEDs elsewhere, use same for consistency?) - also interchanged anticonvulsants and AEDs in other sections eg 5.2.1 (suggest chose one for consistency?) Typo: care of the children (care of children with epilepsy?) Typo: (2012)38, pharmacological treatment Typo: for AEDs, for generalised epilepsies (remove comma) Otherwise no comments on the overview section.	Thank you. The draft has been edited and typos corrected throughout. Anticonvulsant drugs has been changed to AEDs thoughout.
5.2	TS	Presenting references after 2012 is ok but in the recommendations in the end previously reviewed drugs should be at least mentioned in the text (like in the Dravet text) and included (like in the drug Annex), i.e. topiramate, levetiracetam and valproate as monotherapy and lacosamide as add-on. As it is now the whole picture is not conveyed. And it does not feel right that zonisamide is mentioned in a recommendation but not the above...	The advice from NICE and the NICE recommendations have been added to the pharmacology sections.
	MK	This section should be “Focal Seizures”. SANAD was a large head-to-head pragmatic study and has been 1++ but I suggest this is perhaps not correct. There was a very heated paediatric criticism of this study in the peer review journals following its publication. For example. the mean age of the study participants was 38 years± 18, and only 1.4% of the study population had Epilepsy with Centro-Temporal Spikes in further confirmation that children were very poorly represented in this study. There was no sub-group analysis of children in this study. Other criticisms were that the protocols for dosage escalation of medications did not reflect current practice, that dosage regimes were loose and pragmatic, all leading to potential bias.	The term ‘focal epilepsy’ has been used throughout as this is the syndromic diagnosis, whereas focal seizures are a symptom of various epilepsies. SANAD has been removed from this section, however it supports the NICE recommendations cited. While it is mostly an adult study, it is well-conducted therefore merits a 1++ appraisal. It is pragmatic for dosage to be set by clinicians, tailored to individual patients, starting with low dose. Therefore the results of SANAD can be extrapolated to the guideline population.
	AJ	"Oxcarbazepine has a similar efficacy and safety profile to other AED’s, in the treatment	This section has been revised and the NICE

		of children with epilepsy" is this sentence in the correct section as is not evidenced in the review of adjunctive therapy trials in difficult to treat focal epilepsies. Recommendations: Oxcarbazepine, could be considered for the treatment of children (3 years and older) with focal epilepsy. - should this not be in section 5.2.1? Lamotrigine and carbamazepine are both suitable as first line monotherapy for children and young people with focal epilepsy (> than 4 years)- Should this not also be in section 5.2.1? Zonisamide could be considered as adjunctive therapy in children (age 6 years and above) and young people with poorly controlled focal epilepsy. - evidence has also been presented for Perampanel with the same level of evidence as for zonisamide so wondered why a similar recommendation for the former is not forth coming?	recommendations incorporated. Zonisamide evidence is an RCT of 200, with a one-year extension study which showed it was well tolerated. Perampanel evidence is limited to one RCT of 85 participants on perampanel for 19 weeks.
	MO	Recommendations are appropriate.	No action required. Some recommendations have been amended to incorporate the NICE recommendations, and in response to other peer reviewers.
	FB	The term "suffer from" is a value judgement, which should be avoided. It should be replaced with "have". The findings of the SANAD trial and poorly presented.	'Suffer from' has been removed. Trial now removed.
	AF	P22 -5.2 last sentence doesn't 'flow' – presume after 4.3 –half of ep pts have focal epilepsy -: and 4.3.2 –up to 25% of focal have a structural lesion – so do you want to emphasise that its largely focal epilepsies that are drug resistant, or make a more general point??? Maybe its me, but not clear!!!-	Thank you. This section has been edited.
5.2.1	TS	See above	No action required.
	FB	There is a mass of data in this section. It would be much easier to read if the conclusions were presented and the detailed data were relegated to an appendix. The sentence: "Findings from this trial show that lamotrigine was significantly better than carbamazepine..." does not explain what "better" means. In fact, it was not more effective at stopping seizures but the retention rate was much better, probably because it was better tolerated.	It is SIGN style to present the supporting data in beside the recommendation, to demonstrate how the recommendation was derived. The section has been edited for better clarity. This section has been removed.
	PB	-'partial'-should be focal -'(hazard ratio [HR] 0.78 [95%CI0.63-0.97])...' SIGN 81,143 do not mention HR,CI, occasionaly HR/RR in sentences with no CI -'This meta-analysis demonstrated that oxcarbazepine had a similar efficacy and	Now within section 5.2. 'Partial' has been changed to 'focal' throughout. It is SIGN style to state RR and CI where appropriate.

		incidence of adverse events compared to other anti-epileptic drugs'- is this sentence not enough for this paragraph? - similarly one sentence probably enough for zonisamide? 'open label RCT'- rather 1-	
	MO	recommendations appropriate	No action required.
	KKT	Accepted	No action required.
	CR	Guideline advised that this section would use 'focal' throughout and then Carbamazepine is referred to 'as a drug of first choice for partial seizures' in the first paragraph of this section. Typo: 95%CI0.63-0.97 (space after CI) Typo: and a non-significant advantage (had a non-...) Typo: was significant better (was significantly) Typo: carbamazepine again lamotrigine Typo (multiple): CI are variably presented with or without spaces before the [Might be worth emphasising the lack of high quality trials in children does not necessarily mean that other medications are of lower value....	Now incorporated within section 5.2. This has been changed to focal seizure. Thank you. The draft has been edited and typos amended throughout. A sentence has been added to the introduction highlighting that there is a lack of head-to-head trials. We cannot make a statement supporting medications without an evidence base.
5.2.2	TS	See above	No action required.
	PB	-Zonisamide conclusive statements from trials for both paragraphs with percentages perhaps- sum up in 2 sentences? -Perampanel - p values in guideline necessary? Evidence ratings fine	This has been amended (now within section 5.2). See previous response regarding presentation of statistics.
	FB	The statement on perampanel is misleading. It can be associated with considerable behavioural disturbance; this is almost certainly a dose -related effect.	The statement has been removed and information on side effects added (now within section 5.2).
	IM	Could they include when to prescribe adjunctive therapy?	This is a clinical decision and cannot be determined by this guideline.
	HC	Need to consistently use the term focal rather than partial The recommendations all highlight use of medication over 3-6 years - what should be the recommendations for focal onset seizures <3years?	This has been amended throughout. No evidence was found for this age range.
	MO	recommendations appropriate	No action required.
	KKT	Accepted	No action required.
	CR	Typo: (n=: 107 + 100 Typos (3): partial epilepsy' ,'responder rates	Thank you, the draft has been edited and all typos have been amended (now within section 5.2).

		Typos or unclear format for referencing: An extension study, which was non-comparative (n=144) 105, followed the above trial.104. This. Was not sure why some other RCTs were not considered for mention: Levetiracetam Double-blind placebo-controlled trial of adjunctive levetiracetam in pediatric partial seizures. Glauser TA et al. Neurology, 2006, 66(11), 1654-1660	The section has been edited with more detail regarding the advice from NICE. We reviewed evidence post NICE guidelines 2012, so this paper was outside the date range of the SIGN literature review.
5.3	TS	Ok	No action required.
	MK	Reference 109 refers to a Cochrane review on Dravet's syndrome and not childhood absence epilepsy.	Changed to the correct reference.
	CR	Typo: 2012, pharmacological No other comment.	The text has been edited.
	FB	Perhaps the high rate of psychiatric disorder in absence seizures should be highlighted (for example, see the paper by Caplan). No additional comment.	This is a section on drugs we have not looked at the individual syndromes and their psychiatric co-morbidities.
	PB	Here useful to quote recommendations /good practice points from NICE here so clinicians may know what is practically recommended for bilateral tonic clonic/myoclonic/tonic seizures or need to strongly highlight pages in annex for practical management. This section should comment on all types of generalised seizures and recommendations vs just absence epilepsy, so clinicians can find it all in one place.	This has been addressed by including NICE recommendations and references to papers reviewed since 2012 NICE publication. This section includes only absence and other syndromes because of evidence after 2012. This has been clarified.
	SD	I think there should be a caveat to the statement about the use of sodium valproate in girls of reproductive age. This should be along the lines of the importance of recognising the need for good seizure control to avoid injury and death and that not with standing our concerns about the drug it should not be withheld from young women.	MHRA advice has been added.
	MO	recommendations appropriate	No action required.
	KKT	Accepted	No action required.
5.3.1	TS	Ok	No action required.
	CR	Excellent, clear and no other comments.	This section has been edited to be more concise.
	PB	-'An open-label continuation study in...' could this not be shorter and summated without all the detail;leave OR and p-values like SIGN 81. Evidence ratings fine	See previous response regarding presentation of statistics.
	IM	No issues with content Could a separate section be included for MHRA advice and valproate?	It is preferable to refer readers to the MHRA so they can access the most up-to-date MHRA advice.

	AJ	The first study quoted (levetiracetam, ref 107) is ranked as ++1 - not sure this is correct as the study was too brief (14days) to make meaningful conclusions. The cochrane review discussed highlights the difficulties with meta- analysis due varied methodologies and that studies where not placebo controlled, etc - is the level of evidence of ++1 therefore based on the single large randomised trial in which case the cochrane review could be ignored? I found this paragraph comparing Ethosuximide, sodium valproate and lamotrigine as a result confusing. If the evidence suggests that all three drugs are equally effective why is lamotrigine not included in the recommendations?	This paragraph has been reworded and evidence rating downgraded. This has been reworded to state that the CR identified one large RCT, and then reports the results of the RCT. The 1++ demonstrates confidence in the results of the systematic review undertaken by Cochrane, rather than the quality of the trials within in. This relates to treatment failure at 12 months, that sodium valproate is superior to lamotrigine and ethosuximide is superior to lamotrigine. Recommendations and further details from NICE have been added.
	MO	Appropriate	No action required.
	KKT	Accepted	No action required.
5.4	TS	See comments on 5:2. Valproate isn´t even mentioned... The term cannaboid...I haven´t seen it Before. Why not stick to cannabidiol? The CBD dose should be 10 and 20mg per kg!	This section has been edited for clarification and reference to sodium valproate (NICE 2012) has been made. Corrected to cannabiodiol. The doses have been amended to 10 and 20 mg per kg.
	PB	paragraph 1 : summary of LGS not necessary Evidence ratings fine Cannabidiol need to come into recommendation (with inclusion of phrase pointing to possible near future licensing/and/or use)	This has been removed. No action required. Trials on cannabidiol have been added. Advice from SMC is awaited before a recommendation can be made.
	MK	The incidence of up to 10% quoted seems extraordinarily high and not in keeping with my clinical experience. My own very clinical brief review of the literature broadly suggests that it may be rather lower than this. This condition is very much less common than Dravet's syndrome. Cannabidiol - Reference 117 is incorrect – this refers to Dravet's syndrome. There are 2 RCTs of cannabidiol in LGS – (Theile, Lancet 2018 and Devinsky, NEJM 2018). It seems odd that the only level 1++ evidence for LGS does not carry a Recommendation or at least a justification for not doing so. (The earlier Cochrane review is not, in my view, appropriately labelled as 1++ for reasons I have stated earlier and in any event it states that no one drug of the four listed was highly efficacious).	This paragraph has been removed. Amended to Devinsky 2018 and Thiele study added.

		I would suggest that stating that the use of cannabidiol is “controversial” does not really have a place in an evidence-based guideline. It is not clear in the last paragraph why Lennox-Gastaut syndrome should be picked out as needing expert input over and above other complex conditions discussed.	Removed. A new GPP has been added at the introduction to the section stating all children with complex epilepsy syndromes need specialist referral.
	HC	There is an incorrect spelling of cannabidiol (written as cannaboid when presenting evidence of RCT) A comment is made that treatment with cannabidiol is controversial - I would challenge that treatment with cannabinoids is controversial. Although cannabidiol is not yet licensed should there not be a comment as to where it may lie in treatment option for LGS or Dravet as add on therapy should license be granted.?	Spelling corrected to ‘cannabiodiol’. Licensing and SMC advice is now available.
	CR	Typo? and partial seizures (use of focal ?) Typo: evidence, for improved seizure Typo: clobazam, from post hoc Typo: results,(n=267 Typo: n=59,4-30 Typo: RCT,(n=54 Typo: drop seizures in the LGS Typos (multiple): 20-mg (should be 20mg), also 10-mg No other comments, recommendations arising are reasonable.	Thank you, the draft has been edited and all typos have been amended.
	FB	Perhaps this section should begin with a comment on the major effect that this syndrome can have on the life of the child and their family. Replace "cannaboid" with "cannabidiol"	These sections focus purely on drug efficacy. Amended.
	MO	This is a difficult syndrome to treat and should be managed by paediatric neurologist with an interest in epilepsy why include this in a guideline whose target audience is the primary and secondary healthcare professionals The recommendations are appropriate	This has been clarified in the second paragraph of section 5.4.
5.5	TS	Some language errors. Content ok but not easy to read because of	Language errors have been corrected. See also previous response regarding presentation of statistics.

		the way references are presented.	
	CR	Typo: spasms with Hormonal (no H required), this repeated later in the same section, also Prednisolone (appears with or without a P/p) in this section Typo: had sown higher spasm Typo: compared to lowed Typo: p=0,002 (change comma) Typo: with in this review Typo: single-blind study by evaluated Typo: in 221 children under 2 years of age, patients with newly diagnosed infantile spasms No other comments, all evidence included seemed reasonable.	Thank you, the draft has been edited and all typos have been amended.
	PB	Necessary to define? -'There are two systematic reviews ...' ; '...methodology poor...'- 1- rather -'A Cochrane Review looked the treatment of infantile spasms...' ; '... high risk of bias...'- 1- rather - one or two sentences on steroid /Vigabatrin efficacy indications probably enough as SIGN 81 summated in brief-p17-18. The sentence on other drugs could be kept. Combination therapy useful to mention and could be 'consider' level in the recommendation.	The evidence levels are linked to the quality of the way the systematic review was carried out rather than the quality of studies within it. Combination therapy was not considered. This study considers long-term developmental outcomes. Combination therapy is superior at treating spasms alone. Although there are more side effects, it achieves a higher rate of spasm cessation.
	HC	I am surprised the recommendation is that hormonal treatment only should be considered as the first line treatment for infantile spasms? The most recent large RCT as quoted is VGB with steroids, vs steroids alone? Showing superiority? (ref 133, O'Callaghan et al) - there is no explanation as to why this has not been considered as part of the recommendation?	No recommendation could be made on the basis of this single study.
	AJ	paragraph 3 - 2 systematic review are discussed for the treatment of epileptic infantile spasms . the quality of studies in the review are described as poor and yet the level of evidence attributed is 1++. Is this correct? This is again the case in paragraph 5 which summarises the two reviews and recommendations and ranks the evidence again as 1++ The cochrane review in paragraph 12 highlighted the high risk of bias and yet level of evidence is again 1++? subsequent studies and review are not ranked?	This is a well conducted systematic review of poor studies, so the systematic review level of evidence is presented. We are unable to give an evidence level to studies within the Cochrane review that SIGN did not critically appraise. Low quality and poor methodology of studies, as described by Cochrane, are highlighted in the text. The guideline group presented the terminology as per the studies and feel this is appropriate. This study was published after the literature

		should we be either using the term epileptic infantile spasm or West's syndrome throughout as non-epileptic infantile spasms may also occur? I wondered why the ICISS study was not discussed?i.e. combination therapy vs steroids or vigabatrin alone Lancet Child Adolesc Health. 2018 Oct;2(10):715-725. doi: 10.1016/S2352-4642(18)30244-X. Epub 2018 Aug 29. Vigabatrin with hormonal treatment versus hormonal treatment alone (ICISS) for infantile spasms: 18-month outcomes of an open-label, randomised controlled trial. O'Callaghan FJK1, Edwards SW2, Alber FD3, Cortina Borja M4, Hancock E5, Johnson AL6, Kennedy CR7, Likeman M8, Lux AL9, Mackay MT10, Mallick AA9, Newton RW11, Nolan M12, Pressler R13, Rating D14, Schmitt B15, Verity CM16, Osborne JP2; International Collaborative Infantile Spasms Study (ICISS) investigators.	search, but has. now been included.
	MO	appropriate recommendations	No action required.
	MK	This should refer to “Epileptic Spasms” and not “Infantile Spasms”. This section is another example of where high grading of evidence level is being applied when it is explicitly noted in the text that the methodology of the studies is poor. Similarly, it is not appropriate to assign a 1++ recommendation to a NICE guideline. In the recommendation on the use of Vigabatrin it is noted that children should be closely monitored for adverse effects. I suggest this needs to be more specific around the risk of permanent visual damage and that the evidence around this is reviewed in more detail. This is an important clinical safety issue.	The term infantile spasms is most commonly used in the trials. The NICE guideline is graded as level 4. There is no new evidence of visual field damage. Other adverse events are reported with this drug and hence the need for monitoring for adverse events overall.
	FB	There seem to be increasing evidence for the value of combination treatment but this is not particularly emphasised.	The recommendation is not based on a single paper. The rate of response was similar to the rate of spasm response in previous single treatment. There were no significant differences between combination and single therapy.
	KKT	Accepted	No action required.
5.6	TS	The whole Picture not conveyed. Everolimus only drug mentioned. At least refer to other AEDs ("standard treatment" as mentioned in the everolimus recommendation) depending on seizure type In the paragraph just above the recommendation. First sufficient evidence, the insufficient...?	A search was conducted for a range of AEDs. This is reporting those in which evidence was identified. This sentence has been removed.
	MK	Tuberous sclerosis – This might be better titled “Seizures in Tuberous Sclerosis”. However the reality of this is that it is a	For internal consistency the terminology has been left as it is. The advice from NICE has now been added in more detail along with the

		review of the evidence around Everolimus rather than the evidence for the treatment of epileptic seizures in tuberous sclerosis – though I appreciate the focus of the key question was on new AEDs.	more recent evidence for newer AEDs.
	CR	Typo: 5.5).Early Typo: mean age 4.1.4 No comments, excellent summary of evidence.	Thank you, the draft has been edited and all typos have been amended. The section has been edited slightly to make it more concise.
	PB	-summary of condition in guideline necessary? -'There is one phase 3, randomised, double-blind...' Probably only first and last sentences of paragraph necessary? -'There is one small, underpowered RCT ...'- as study underpowered and not able to come to conclusion should this even be rated?	Summary of condition has been removed. This paragraph has been amended. This study is rated 1+. No recommendation can be made because of selection bias, which is acknowledged by the authors.
	AJ	In paragraph 2 the last sentence reads: Adjunctive everolimus treatment significantly reduced seizure frequency in patients with TSC and intractable epilepsy however the percentage reduction in seizure frequency or further stats are not provided to support this statement. As this is the only study referenced. I am uncertain the level of evidence is correct as everolimus has potential to harm	Further detail has been added. The evidence levels are for how well the study was conducted. Potential harms are discussed, along with consideration of balancing harms versus benefit.
	MO	appropriate recommendations but need to state that everolimus should only be administered in specialist centres	This has been included as a good practice point for Dravet syndrome, Lennox–Gastaut syndrome and tuberous sclerosis in the introduction to Section 5.
	KKT	Accepted	No action required.
5.7	TS	SMEI not used by the ILAE now. And usually not in publications. Do not use or write "previously entitled"	Reference to SMEI has been removed.
	CR	Typo: international league against epilepsy (capitals) Typo: partial or focal? Typo: 50%>seizure reduction Typo: placebo verses Comment: the difference between CBD and placebo was not significant (p=0.08) therefore why is this non-significant result included? My read was that it failed to reach statistically significant differences for 50% seizure reductions. Worth checking of the fenfluramine RCT (119 patients) for DS is published before the SIGN guideline goes live as this data is in prep for publication at this time and shows superior	Thank you. The draft has been edited and typos amended throughout. Agree; we are not recommending. Thank you, this has been added.

		response rates.	
	PB	-Paragraph one and two in this guideline necessary? -'A Cochrane review was originally carried ...';'The Cochrane review rated the quality of the evidence as low to moderate.'-1++- 1- rather?	Paragraphs one and two have been removed from this section. This is a well-conducted systematic review of low/moderate studies, so the systematic review level of evidence is presented. We are unable to give an evidence level to studies within the Cochrane review that SIGN did not critically appraise. Low quality and poor methodology of studies, as described by Cochrane, are highlighted in the text.
	HC	A comment is made that treatment with cannabidiol is controversial - I would challenge that treatment with cannabinoids is controversial. Although cannabidiol is not yet licensed should there not be a comment as to where it may lie in treatment option for LGS or Dravet as add on therapy should license be granted.?	Removed from all sections. Cannabidiol is now licensed and the text updated accordingly.
	MK	Dravet's syndrome – evidence is labelled as 1++ in a Cochrane review rating the quality of evidence as "low to moderate". Regarding cannabidiol, my comment is similar to 5.4 on LGS: The cannabidiol RCT trial is evidenced as a 1++ study and yet no Recommendation follows from this or an alternative reason. Again cannabis based 5 medicinal products are indeed controversial but I suggest that is not justification for not considering the implications for the evidence.	1++ denotes the quality of how the systematic review was conducted. The quality of the studies identified is highlighted in the text. Evidence for cannabidiol in LGS has been added.
	FB	The expression in the first paragraph is poor. The reviewer recommends: "it is defined as follows. (This should then be followed by a clear definition). The possible relevance of drug interaction should be emphasised.	This paragraph has been removed. We would expect any prescriber to consider drug interactions so it would not be specific to this section.
	AJ	paragraph 5: the cochrane review rates the quality of evidence as low and yet the evidence is ranked as ++1?	This is a well-conducted systematic review of low/moderate studies, so the systematic review level of evidence is presented. We are unable to give an evidence level to studies within the Cochrane review that SIGN did not critically appraise. Low quality and poor methodology of studies, as described by Cochrane, are highlighted in the text.
	MO	Again a syndrome that should be managed by Paediatric Neurologists with an interest in epilepsy but recommendations are appropriate	As above; a good practice point has been included.
	KKT	Accepted	No action required.
5.8.1	TS	A few language errors	Amended (now section 5.8).
	CR	No further comments on this section, it is rather vague....	Unfortunately there is a lack of evidence to provide further clarity.
	MO	appropriate recommendations again these treatments are used in specialist centres and in autoimmune epilepsies not appropriate for	As above; a good practice point has been included (now section 5.8).

		a guideline with a target audience of primary and secondary healthcare professionals	
	FB	Still an area where data is lacking.	Agree
	KKT	Accepted	No action required.
General	MK	6.1.1 – 6.1.6 Ketogenic diets - This amounts to some six pages reviewing the evidence for ketogenic diet in a variety of circumstances. As I have noted before there needs to be consistency within the recommendations – if it should be used in children with drug resistant epilepsy then it "should" be used in other specific circumstances where there is drug resistant epilepsy. In general terms I think this whole section could be usefully shortened and the reader would probably be less interested in the description of the studies than in the recommendations themselves. I have already commented on the consistency of the Recommendations from section to section.	The terminology has changed to 'should be offered' and the section has been edited.
6.1	KKT	Accepted	No action required.
	TS	Well written and structured. Could serve as a model for other chapters (like investigative procedures and pharmacological treatment. Even though references are presented in the text it's easy to read and follow. I think the introduction/summary of present knowledge and practices (based on evidence presented later) followed by subchapters with references and recommendations in the end, is a good structure if one wants to have the references in the text.	Thank you. The other sections have been edited.
	PB	information point should rather be good practice point? Can the paragraphs not be summarised more?	The group discussed this and felt that it should remain as an information point. The formatting of this throughout the guideline will be considered once the content is finalised.
	JC	Interesting section which considers patient opinion as well as evidence whether this approach works, an important consideration	Thank you.
	NS	Paragraph commencing: 'There has been an assumption that the KD can promote improved cognitive outcome…' – some rewording needed. Would be beneficial to cite Epilepsy Behav. 2016 Jul;60:153-157. doi: 10.1016/j.yebeh.2016.04.033. Epub 2016 May 18 (RCT of cognition/behaviour and KD in children). See Epilepsy Behav. 2018 Oct;87:69-77. doi: 10.1016/j.yebeh.2018.06.004. Epub 2018 Aug 31 for a further overview. Can continue to emphasise that cognitive parameters beneficial to measure alongside seizure control in future studies. - May wish to say that in certain patient groups other than metabolic disorders (e.g. infantile spasms), <3 months may be needed to determine efficacy. Or, in some cases, longer, particularly if the patient has cluster	The first reference (Ijiff) is included in the drug resistant section of the ketogenic diet section as part of the Cochrane review. Van Berkel reference has now been included. 3 months is a clinical rule of thumb only. Subsequently, it is a clinical decision. This section has been re-worded following your suggestion.

		seizures. - Rather than stating 'consideration should be taken to stopping the KD after 2 years', it may be better to reword to reflect the following from the consensus statement (subtle change in meaning): 'There is no maximum duration for KDT. The consensus group recommends that KDT risks and benefits be reconsidered, however, at each clinic visit and certainly after ~2 years of continuous use.'	
	CS	Really interesting and helpful to see consideration of social impact and considerations around this	Thank you.
	VW	Introduction should mention the the aim of the diet is to induce ketosis	Inducing ketosis has been added, but the aim is seizure reduction.
	HC	Throughout the evidence base and recommendations, there is no mention with regard to the types of diets to be used	This is a clinical decision and is outwith the scope of this guideline.
	MO	Useful treatment but difficult to adhere to and needs intensive input from dieticians recommendations appropriate Many of the recommendations made in this section are appropriate but are mainly dealing with the epilepsies that are almost exclusively managed by tertiary centres and it seems that this guideline is written for tertiary specialists and not primary and secondary care health professionals	The pros and cons are presented. The guideline is written for primary through to tertiary care. Some of the recommendations are for specialists. This can inform primary and secondary care physicians of what options are available, and when referral is appropriate.
6.1.1	TS	See above. Last two sentences in the second paragraph are repeated	This has been amended.
	CR	Typo: potential positives effects of quality of life (positive, effect on) Typo: studies,(3 Typo: reported efficacy, 20.4-56%. (? efficacy in 20.4-56%?) Typo: TThe severity of seizures was also considered.152 In the KD group, seizure severity was significantly reduced compared to the control group (p=0.07). (these two sentences seem a repeat of the last sentence before this) Typo: a problem with the forms of the KD, (? with some forms??) Typo: related to the shorter duration of trial period on patients (? remove 'period', and change on to in?) Typo: suggested attrition rate were higher (?rates)	All amended.

		No other comments, evidence is reasonable.	
	PB	-'The first Cochrane review...'; '...number of studies and sample size was small.'- rather level 1-? -'The efficacy of the KD is commonly...' -this paragraph refers to different kinds of studies which may have different evidence levels;the review vs the single RCT quoted. p-values are not given in SIGN 81 nor 143. -'A ketogenic diet should be used, as a treatment...' - this statement needs qualifying as 'should' is too strong as will not apply to all patients, e.g not suitable practically in some patients with picky eating. Rather , in rightly selected patients ..... Even with 1++ studies the word 'should' vs 'could' is inflexible in this particular regard or need some careful qualifying wording. Recommendation OK	We are unable to give an evidence level to studies within the Cochrane review that SIGN did not critically appraise. Low quality and poor methodology of studies, as described by Cochrane, are highlighted in the text. Statistics are given as some readers like to see the extent of the effect size. The wording of this has been changed to 'offered'. No action required.
	NS	- Is it worth summarising the first Cochrane review of the KD ,when there are numerous subsequent reviews? - RCTs, not RCT's - 'potential positives effects' not 'positives' - 'This latest review supported the earlier review's conclusion150 that the KD is a valid treatment for medically intractable epilepsy.147'. References a little confused here. Should cite 148 and ?be placed earlier on in sentence. - ≥50% seizure reduction more appropriate than >50% seizure reduction - 'The severity of seizures was also considered.152. In the KD group, seizure severity was significantly reduced compared to the control group (p=0.07).' Repetition from previous couple of sentences. - 'The 2018 Cochrane review 148 highlighted that attrition rates were a problem with the forms of the KD, this may be related to the shorter duration of trial period on patients enrolled in RCTs.' Grammar needs amending – semicolon or separate sentences? - Best to have separate paragraphs on attrition rates and adverse effects? - Amend wording – confusing! 'A follow-on study from an RCT153, within an RCT,…' - Rather than stating 'with consideration of stopping the ketogenic diet after 2 years', it may be better to reword to reflect the	The latest review has less evidence from a paediatric population. The second review looked at RCTs only, while the first review was a larger group of studies. These errors have been corrected. Amended. This section has been removed. Amended.

		following from the consensus statement (subtle change in meaning): 'There is no maximum duration for KDT. The consensus group recommends that KDT risks and benefits be reconsidered, however, at each clinic visit and certainly after ~2 years of continuous use.'	Amended.
	VW	ref 148 is not complete cochrane review is not the most recent Needs proof reading, a number of gramatical errors	References will be checked prior to publication.
	FB	The prevalence of the very serious adverse effects listed should be stated. No additional comment.	Added
	PG	'A ketogenic diet should be considered after a child has failed 2 anti-epileptic drugs.' Please add 'and is not a candidate for epilepsy surgery'. This point is already made in the pathway in the annex at the end but should form part of key recommendation.	The advice is based on the SPEN pathway which offers KD to all with a confirmed diagnosis of drug-resistant epilepsy.
	MO	appropriate recommendations	No action required.
	KKT	Accepted	No action required.
6.1.2	TS	See above	No action required.
	CR	Typo? where KD was used, 82% (64/78); 67% (41/61) were seizure-free (which of the two figures provided is correct) Typo: and 68% of seizure-free patients (28/41) resolved in <1 week and 76% (31/41) in <1 month (? should (28/41) be after 68%, and when you say 'resolved' I presume you mean 'had seizure remission') Typo: compliance was an issue (Compliance? ie this is the start of a new sentence) Typos: function: improved alertness (should be function,) Typo: physical health: physical endurance (should be physical health,) These two sentences at the end appear redundant? Two studies reporting on reduction in seizures in patients with clinical diagnosis of Glut 1DS, 2 small studies on the positive impact on cognition for individuals with this condition after starting the KD. I think the recommendation by the International Ketogenic Diet Study Group that KD should be commenced early is of very high significance and warrants being one of the final recommendations at the end, as outcomes are better with early access to this treatment as first line therapy.	Amended. Amended. Amended. Section removed. Section removed. Removed. Added.

	FB	Again, editing is required. No additional comment.	This section has been edited.
	PG	Ketogenic diet should be recommended in children with glucose transporter 1 deficiency (Glut 1D).' We should add 'including infants'- especially given the cognitive improvements	The evidence is in older children, however the terminology 'children' does not preclude the use in infants. It is stated in the introduction to the guideline that the definition of children, for the purpose of the guideline, is age from one month to 19 years.
	PB	-Paragraph Summary of condition necessary in this guideline? -Summary paragraph of effect not enough with levels of evidence alongside that? Perhaps just needing to quote study percentages from one or two studies regarding seizures? Levels of evidence seems fine Recommendation fine	This paragraph explains why the ketogenic diet is the treatment of choice and why an RCT is not possible. This has been made slightly more concise. It was considered important to retain this to demonstrate how the recommendation was reached.
	NS	- GLUT 1D – more commonly shortened to GLUT1-DS (from 'deficiency syndrome) - 'thus treating the symptoms of Glut 1D' – suggest rewording to 'thus overcoming the energy deficit encountered in GLUT 1D' - 'as a condition where the KD should be considered earlier in a child's epilepsy management' – better: 'should be considered very early in the course of treatment' (from Consensus guidelines).	This has been amended to reflect the Global Consensus Group for Glut 1 and the related consensus paper, ie glucose transporter protein type 1 deficiency syndrome (Glut 1 DS) on first use, followed by Glut 1 DS.
	VW	Used Glut 1D consistently throughout	As per comment above.
	MO	appropriate recommendations	No action required. Some amendments have been made in response to other peer review comments.
	KKT	Accepted	No action required.
6.1.3	TS	See above. Saliva (not salvia).	Amended.
	CR	No comment, the recommendation re early use used here would also be good to have for Glut1D.	Agree – early use is essential for Glut 1, as soon as the diagnosis is made the patient should be put straight onto the diet. This has been added.
	FB	Again, further comment should be made on the serious adverse effect of pancreatitis.	This is a very rare adverse effect, so the group do not feel it needs to be highlighted.
	PB	Summary of condition necessary in guideline? Recommendation fine	This has been made more concise.
6.1.4	TS	Some language errors. Replace astatic with atonic (according to ILEA).	Language errors have been amended. 'Astatic' has been replaced with 'atonic' throughout.
	CR	This is now (ILAE) called: Epilepsy with Myoclonic Atonic Seizures (and the seizures are myoclonic atonic seizures), see https://www.epilepsydiagnosis.org/syndrome/epilepsy-myoclonic-atonic-overview.html This would change the abbreviation of MAE throughout Typo: One was non-comparative study	Amended.

		(delete was) Typo: and seizure freedom in 18%. (was seen in 18%) Typo: AET - there is no real need to abbreviate this as it is used only here (and a second time in the same paragraph where the word treatment could be used) Sentence readability - this sentence is very hard to understand, can you reword?: Seizure freedom occurred spontaneously in three subjects, with ethosuximide and levetiracetam in one each, valproate and lamotrigine in two each, topiramate in three and the ketogenic diet (KD) in five subjects. Typo: this positive outcome (? benefit of the diet in this syndrome) Typo: for MAE and (delete and) Typo: this includes, MAE (delete comma) Recommendations, either use capitals for MAE or otherwise (both are used in different recommendations) The early use of KD is important and warrants consideration in the recommendations.	Amended. Amended. Amended. Amended. Amended. Removed. Removed. Removed. Amended. There is not enough evidence to support a recommendation. It has added as a GPP.
	FB	The definition fails to describe what the seizures look like. It should do so.	This section has been removed.
	PB	Could the studies not be summated in one paragraph? Levels evidence seem mostly fine, but what level does the International Ketogenic Diet base their recommendation on- could actually be 3? Recommendation fine.	The studies are too heterogeneic to summarise in one paragraph. The section has been edited, however, to make it more concise. As this is a guideline, SIGN rates this evidence as level 4.
	NS	- MAE: more appropriate to refer to this as ‘epilepsy with myoclonic-atonic seizures’? - ‘One was [DELETE] non-comparative study’ - AEDs, not AED’s	Refer to generalised epilepsies or first line treatment. Sentence edited for clarity. Amended throughout.
	MO	appropriate recommendations	No action required.
	KKT	Accepted	No action required.

6.1.5	TS	MAD used without explanation.	Expanded to 'modified Atkins diet' and clarified.
	CR	Typo: quality.This Typo: No/low/adverse (no/low adverse...) (also occurs later in this section) Typo: constipation(7) Typo: haematuria(3)diarrhoea Typo: dyslipidaemia was identified (Dyslipidemia - start of new sentence) Typo: within3 months No other comments Recommendations are appropriate, evidence is well laid out	Amended. Amended. Amended. Amended.
	PB	-'Another systematic review concluded...'- levels 1- and 2-? -'A prospective study of infants...'-level actually 2-? -'A systematic review stated that epileptic spasms...'- within this review KD classed as having level 3/4 evidence. The studies could be summated within one paragraph ? Recommendation fine	The gradings have been revised. This section has been edited to be more succinct.
	NS	- Reference earlier on in paragraph (confusing to read) - Why is this a separate paragraph from the summary of article 172? 'A prospective study concluded that the KD should be considered in these groups as a 2nd or 3rd line treatment due to low adverse effects and improvements in development.172' - This paragraph is best place further towards the end of this section 'A systematic review stated that epileptic spasms are the most common sub-group of seizures occurring in the first 2 years of life and recommended that further studies should be performed in this group regarding the efficacy of the KD and other treatment options.174' - In the summary paragraph (commencing with 'In summary, all studies…'), emphasise that observational studies show high efficacy for IS, but that reviews thus far are of low quality. - Include this reference? Epilepsy Res. 2013 Jul;105(1-2):189-94. doi: 10.1016/j.eplepsyres.2012.11.009. Epub 2013 Jan 26. - Also this reference to justify possible short-term use of KD in this cohort? Epilepsia. 2011 Apr;52(4):781-7. doi: 10.1111/j.1528-	These paragraphs have been linked. Thank you for the suggestions. The first reference is a small, low quality study, so it is similar to those already cited in the systematic reviews. The other reference has not been included, as we have not recommended different lengths of time on diet for different diagnoses except for Glut 1DS. This evidence alone would not be sufficient to support a

		1167.2010.02940.x. Epub 2011 Jan 26.	recommendation.
	AJ	Recommendation "Ketogenic diet could be considered as a treatment option for infants and children with infantile spasms."should this not specify failing standard treatment or are we implying this can be used as first line too?	Amended for clarity: those who have not responded to standard treatment.
6.1.6	PB	-'A single non-comparative retrospective study of 32...'- necessary to quote p values? - Could the studies not be summated in a short paragraph ,e.g only overall paragraph with evidence levels alongside that? Levels of evidence and recommendation fine.	SIGN style is to state CI where cited and *P*-values if not. This section has been edited to be more succinct. No action required.
	NS	[Following comments relevant to overall KD section, not specific to Dravet Syndrome] Overall recommendations in each section: The Ketogenic diet could be considered as a treatment option . Possibly better: 'should be considered' or 'may be considered' ? Perhaps add another paragraph mentioning other conditions where the KD is thought to be particularly effective? Can take from Table 1 in 2018 Consensus guidelines.	This links to the levels of evidence and has been changed to 'offered' in some sections. We did not search and review the evidence for all the other conditions, so we are unable to add this.
	FB	The first sentence is repetition. Again, considerable editing is required in this section.	Removed.
	CR	Typo: partial or focal seizures? Typo: where overall response was 70% seizure (change where to the??) Typo: Toperimate This section may need re-wording for clarity: KD was similar to the current gold standard triple combination of AED's (Stiripentol, Valproate and Clobazam, at 89%, Bromides (78%), Valproate alone (48%), Toperimate (35%) and VNS (37%) and significantly more effective than Levetiracetam (30%: p=0.037, Pearson's Chi-square). Typo: ((SE) - I do not think you need a definition of SE in here as it is not relevant to the data being presented Typo: did not occurs No other comments Recommendations are appropriate, evidence is well laid out	Section removed. Amended. Amended and reworded for clarity. Amended to similar to current gold standard of AEDs. Removed. Amended.
	KKT	Accepted	No action required.
	PG	Can the recommendation portray that the proven efficacy of KD in DS is quite low. The clinical discussion tries to say it but in a rather off hand way. For eg: KD in DS is shown to be effective yet only in a small	This would not be appropriate for the recommendation. The paucity of supporting evidence is reflected in the wording: 'could be considered'. The rationale for making a recommendation based on a small evidence

		percentage of the patient population studied. Also the last sentence in the text is not referenced.	base is explained in the text. This is an introductory sentence, rather than evidence.
6.2	TS	Well written and structured.	Thank you.
	MK	Surgery - My comments around the suggestion to limit the description of the studies themselves apply to this section too. Once again there are a variety of 1++ evidence presented where either the outcomes do not apply to children or it is acknowledged there is moderate or low quality evidence.	As previous comments, the 1++ relates to the systematic review and the quality of the included studies is described in the text.
	CR	No comments Well laid out section. The data presented here is very important as it emphasises the rationale for surgery not just for immediate seizure control in young children but for their long term cognitive outcomes. It is of excellent value for clinicians who talk to families about epilepsy surgery and its rationale.	No action required.
	HC	There is now an RCT of surgery vs medical therapy with outcome at 12m - Dwivedi et al NEJM 2017;377:1639-1647, although this will not change the recommendation	This reference has been amended.
	AF	Cost effectiveness mentioned with 2 refs- suggest this be further studied to help maintain funding in difficult financial times.	The two studies have been removed as they do not relate to the NHS. No further studies were identified. Future studies could be considered in the next update of the guideline.
	MO	studies mostly consist of adult patients Level of evidence in children is low very difficult to make sense of due to different procedures, different aetiologies etc	This is commented on in the text. We agree, and this is why individual studies are commented on. There is a large body of lower quality evidence from observational studies and this has been extrapolated from adult studies also.
	FB	A reference is required at the end of the second sentence.	A reference has been added.
	PG	Should we mention newer methodologies such as LITT/ RFA are being investigated.	This would be too detailed. The section is on surgery in general.
	KKT	Accepted	No action required.
6.2.1	PB	Levels evidence fine. Summary of studies rather in a one paragraph; p values necessary?	Now section 6.2. No action required. This section has been edited to be more succinct. It is SIGN style to include these statistics.
	CR	No other comments Well laid out section. Excellent section.	The section has been edited to make more concise (now within section 6.2).
	MO	See above	As per comment above.
	FB	Again some editing is required. No additional comment.	The section has been edited to make more concise (now within section 6.2).

	KKT	Accepted	No action required.
	DS	https://www.ncbi.nlm.nih.gov/pubmed/22905787 - this paper is interesting in regards of long term outcome of epilepsy although it is aimed specifically on more challenging group of patients requiring invasive monitoring. From same author another paper on outcome: https://www.ncbi.nlm.nih.gov/pubmed/21904264 These papers are important due to large amount of patients.	This is an interesting paper but this is going into specifics of invasive patients. This is out of scope for this guideline. This is very selective treatment and such decisions are made by the epilepsy surgery team. Agree this is a large sample, but a retrospective single centre study. This point is made well in the surgery section.
6.2.2	PB	Levels of evidence seem fine. Summary of studies rather just in a one or perhaps two paragraphs similar to summary paragraph with summary ranges of percentages?; p values necessary?	Now section 6.2. As per comments on section 6.2.1.
	MO	low level of evidence	Noted.
	CR	No other comments Well laid out section. Excellent section.	The section has been edited to make more concise (now within section 6.2).
	FB	The guideline should comment on any differences between short-term followup and longer-term follow up.	Length of follow up is included where possible, however the studies are heterogeneic.
	LD	Several studies on post surgical IQ/DQ outcomes are described. Did these studies provide Effect sizes - these would be more informative than P values in giving a sense of the magnitude of change or impact from surgery on cognitive development. I appreciate ES reporting are not always provided. I note the following sentence- "There was significantly different developmental trajectories witnessed at a 2 year follow up in operated versus non-operated children with improved IQ/General Developmental Quotient scores in operated children only (p=0.028)". Can i suggest restructuring this sentence, "Children receiving surgery had higher IQ/Developmental quotient at two-year follow-up than children not receiving surgery (p=0.028)". I note the following sentence- "Follow-up of 2–3 years showed 29 (72.5%) of 40 children had stable developmental velocity relative to preoperative level". I think the term stable trajectories is used to signify different things in this section e.g. one study is presented as "Follow-up of 2–3 years showed 29 (72.5%) of 40 children had stable developmental velocity relative to preoperative level", another is stated as "A retrospective cohort review in children, (n=30) showed developmental progress in	Now section 6.2. For consistency, CI and *P*-values are provided. This sentence has been amended as suggested. This has been clarified for both studies.

		the form of stabilised trajectories in 93% of patients post surgery". Does stabilised trajectory mean that children had a low IQ and this didn't change, or that there was no discernible change in developmental status following surgery i.e. lack of any positive effect? I think this section is important but perhaps could be reorganised and stated with more conceptual clarity.	
	KKT	Accepted	No action required.
6.2.3	PB	-'There are no RCTs measuring QOL in children. An adult RCT reported that patients...'- as adult only should probably not be rated; p values necessary?	Now section 6.2. The adult RCT has been included to give context to the child cohort studies. It is SIGN style is to state CI where cited and *p*-values if not.
	CS	NB - should this be referenced in all sections re treatment options and considerations	Now section 6.2. The guideline group feel this is adequately highlighted in the relevant sections, eg psychology sections.
	CR	No other comments Well laid out section. Excellent section.	This section has been edited to make it more concise, and consistent with the layout of other sections of the guideline (now within section 6.2).
	FB	A reference should appear at the end of the first sentence. Perhaps some comment on the high frequency of psychiatric and cognitive comorbidities affecting quality-of-life should appear in this section.	We have tried to address psychiatric co-morbidities throughout the guideline. QoL pre- and post-surgery was the focus. Heterogeneity of the studies made it difficult to unpick these specific issues.
	MO	no studies in children	Cohort studies in children.
	LD	I would recommend removing the word 'scores' after QoL in second sentence. You could substitute 'ratings' or else leave as QoL. Second paragraph- the sentence "all three monthly intervals measured during the first year" seems unclear. Can you check the meaning and grammar? I note the following- "An adult cohort study (n=575) with 28 surgical participants and 20 medical participants reported higher QOL scores in the surgical group at a QOL follow up study 8 years following surgery (p=0.038) and declining cognitive distress scores (p=0.045) in the medical group". Perhaps restate as, "An adult cohort study (n=575) with 28 surgical participants and 20 medical participants reported higher QOL scores in the surgical group at 8-year follow-up (p=0.038). They also reported declining cognitive distress scores in the medical group (p=0.045)". I don't know what cognitive distress scores are and similarly i'm not sure what is added by a P value in this context.	Now section 6.2. This has been amended. This has been amended. This section has been edited. This has been clarified to state that, as reported by the study, cognitive distress scores are within the Quality of Life in Epilepsy Inventory-89 questionnaire.

		I note the following- "Non-comparative studies in children have addressed QOL post surgery. One study followed 206 children 2 years post epilepsy surgery and reported a 65.5% improvement in QOL scores, unchanged in 29.6% and lower scores in 4.9%". Do you mean 65% of participants reported improved QoL? You can't increase subjective QoL by a percentage. I note the summary- "In summary a positive effect on QOL is reported following epilepsy surgery". This appears to be stated on the basis of a single cohort study where 2/3 reported improved QoL. I wonder if a more provisional statement such as, "There is some limited evidence to suggest the majority of children experience improved QoL following surgery".	This has been clarified. Agree; this has been amended and a statement added that this is similar to improvements in QoL seen in the adult studies.
6.2.4	PB	Levels of evidence seem fine Recommendation: nil to add. Evidence could just be the summary paragraph with summated percentage ranges of mortality/other with levels on there at right side?	Now section 6.2. The guideline group felt that mortality was a specific concern, and therefore needed due consideration and presentation of the evidence.
	KKT	Accepted	No action required.
	CR	No other comments Well laid out section. Excellent section.	This section has been edited to make it more concise, and consistent with the layout of other sections of the guideline (now within section 6.2).
	FB	A balanced statement about cognitive and psychiatric benefits and adverse effects should be made.	Due to the heterogeneity of the studies outcomes it was not possible to make specific statements on psychiatric outcomes. Cognitive outcomes have been included.
	DS	It should be noted that often time in these surgeries adverse events are expected as for example in hemispherectomies hemiplegia and hemianopia.	Now section 6.2 The guidance reflects the available evidence base and adverse events were not so specifically reported.
6.3	TS	Could be shortened and more clearly structured.	This section has been edited.
	FB	Is the section unnecessarily long? No additional comment.	The section has been edited.
	CR	The guideline uses both partial and focal in this section - ? chose focal Typo/meaning: as part of Handforth203) Typo: reporting no significant (? reported) Typo: as part of VNS Study Group (? as part of the VNS Study Group) Typo: no statically significant Typo (this sentence is not properly laid out, and would benefit from less commas): The	Thank you, the guideline has been edited and typos amended throughout.

		exclusively paediatric, high quality paper, (age 4-18 years, mean age 10-11 years Pls check the way referencing is done in this section as its different to elsewhere, eg: (Chambers, 2013)208 Typo (remove brackets): which included (4 RCTs in adults and one RCT in children) Typo: were voice alteration (?extra spacing) Typo: occurred in 0.6% (close the bracket) Typo: Families should discuss the pros and cons (do you mean Clinicians should....) Typo (in Recommendation): who are not candidates for epilepsy surgery evaluation (delete the word evaluation, as someone might be evaluated for surgery and then not suitable, and would have VNS recommended) Readability was a little challenging here, because of typos, use of different referencing as noted above. There is data that early VNS implant in childhood may have better outcomes than late: Improved quality of life and cognition after early vagal nerve stimulator implantation in children. Epilepsy & Behavior 88 (2018) 139–14. Soleman et al. This is similar to studies showing better outcome for all children from earlier seizure improvements (seen in your sections on KD and epilepsy surgery) so I thought it was important to address in this section? Thoughts?	Thank you we have looked at this paper but based on the small number we have decided not to include. Also once the procedure is done, ie VNS implanted it has limitations on other interventions, eg you cannot image children and this is standard practice in Scotland.
	PB	Evidence levels seems fine except: NICE level 4 but observational studies and systematic reviews puts this above level 4 at least. SIGN 143 quite short comments on VNS and should this not follow suit with evidence summated more? Recommendation fine	NICE is level 4 because it is citing NICE recommendations which are derived using expert opinion combined with supporting evidence. This leads to a recommendation, whereas SIGN 143 does not.
	MO	appropiate recommendations Interestingly this recommendations states that VNS can only be inserted on advice of paediatric neurologist there are many other recommendations in this guideline that could do with this statement	Agree, this has been addressed in other sections.
	KKT	Accepted	No action required.

6.4	MK	DBS - Again there are five 1++ evidence levels and yet the conclusion is that because of the “lack of evidence the effect of DBS in the paediatric population is unclear”.	Although the reviews/studies are of high quality, as explained in the text the studies in children are poor and thus the conclusion.
6.4.1	PB	Rating in adults not necessarily applicable and should not be done? This section probably only needs a brief paragraph?	Now section 6.4. Ratings in children and adult extrapolations are given to allow sensible conclusions for the guideline. This section has been edited, as no recommendation is made.
	MO	Recommendations appropriate	No action required.
	KKT	Accepted	No action required.
	AF	Agree with whats there: the new area is the 'brain defibrillator' Neuropace approach - permitting stimulation in eloquent areas eg wernicke's: suggest a watching brief with close assessment of any published cases for reconsideration at next review?	Outwith scope, but could be considered for the next update.
	CR	Typo: epilepsy.This Typo: font colour not black Typo: Surgical adverse effects were reported however (remove 'however') Typo: epilepsy related inquires	All typos amended.
	FB	There is a large amount of text for the procedure for which there is very little data in children and is unlikely to be available to many children in the immediate future.	This section has been edited.
	DS	It should be noted that further treatments as responsive brain stimulation are now available although only in USA with evidence for adults only so far. While currently only FDA approved for adults, the NeuroPace system may have a role in the treatment of children who are not candidates for or who have failed other surgical treatments. To date, there have been no reports of the use of NeuroPace to treat patients younger than 18 years of age; however, a number of features of NeuroPace may appeal for use in a pediatric population. https://www.neuropace.com/manuals/Scientific_Publications_QRCodes1.pdf https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855197/	These interventions are not licensed in the EU, but may potentially be something to consider in a future iteration of the guideline.
General	MK	I suggest that the Psychology title of this section does not describe fully what this section is describing; it clearly includes cognition and neurodevelopment.	This title was initially suggested based on discussions regarding the key questions and the type of assessments/ input required. The group have now updated the title to read psychiatric and neurodevelopment factors in epilepsy.
7.1.1	JC	This section is not particularly my area but it was appeared comprehensive and supported by evidence	Thank you.
	MO	not uncommon in children with epilepsy	No action required.

	CR	No comments, clear to read.	Thank you.
	FB	Why are the numbers not presented? They are available in good epidemiological studies.	Prevalence rates/ epidemiological factors have been included in the sections for each condition.
	LD	I found the first sentence rather poorly constructed, "Young people discussed how they feel down some days because of epilepsy". Which young people, discussed with whom? If you want to use this 'informal' style to start off this section, which i am not taken with, can we use more formal grammar? What about 'Young people discussed feeling low in mood at times because of their epilepsy'. Who is the information point for? 7.1.1 is well written	Reworded as suggested, as this is paraphrased.
	KKT	Accepted	No action required.
7.1.2	PB	Levels of evidence fine	No action required.
	MO	Are not uncommon in children with epilepsy	No action required.
	FB	The importance of psychoeducation for families, carers and teachers should be emphasised. The management of autism is not intuitive. Correct management is, however, very important.	Indeed – we would agree. The draft refers to the SIGN guideline on ASD which provides further advice on management.
	CR	No comments, clear to read. Autistic spectrum Disorder (ASD) - the use of ASD occurs earlier in the guideline and it should be explained there first rather than in this paragraph.	Addressed.
	MK	a “high quality meta-analysis” is assigned only a 2+ level of evidence. The Recommendation discusses the “optimum approach for individuals suspected of having ASD”. This then raises the question as to what “suspected” means and if it is to be encompassed within a recommendation then there needs to be a description to accompany this.	The 2+ is because it includes observational studies. ’High quality’ has been removed. Regarding the wording of the recommendation – this was taken from the SIGN guideline 145 for ASD in children and young people, the wording had to be the same as the recommendation for screening of ASD in a non-epilepsy population, Readers are directed to the 145 guideline for more information about ASD. The screening methods have been discussed in section 7.1.3, with reference to SIGN 143.
7.1.3	PB	Recommendations and levels of evidence fine	No action required.
	MO	same as with children without epilepsy and dealt with in another guideline	No action required.
	CR	No comments, clear to read.	Thank you. Some editing has been undertaken to make the section briefer.
	LD	Sentence- "This review of the literature did not recommend any one secondary screening tools and indicated that.." seems poorly constructed. What about, "However, the review stated that "a single specific instrument..."? Otherwise, reasonable summation.	This has been restructured.
	KKT	Accepted	No action required.

7.1.4	PB	Levels of evidence fine 'peri-natal'- rather perinatal	No action required. Amended.
	MO	Appropriate recommendations	No action required.
	FB	Should the above be "attention deficit hyperactivity disorder"?	Amended.
	LD	Good	No action required.
	KKT	Accepted	No action required.
	CR	ADHD - the use of ADHD as an abbreviation occurs earlier in the guideline and it should be explained there first rather than in this paragraph. No other comments, clear to read.	Addressed.
7.1.5	PB	Looks fine	No action required.
	MO	Same as in children that don't have epilepsy	It was felt that it should be included here due to the high prevalence of epilepsy/ADHD comorbidity.
	FB	There are simple and widely-accepted screening instruments for ADHD, notably the SNAP-IV. The recommendation for specialist assessment might be laudable. In practice, ADHD is so common in children with epilepsy, if this recommendation is to be followed result might be that many children are left untreated.	There was insufficient evidence to recommend the SNAP-IV about other screening measures (this does not mean it is not an effective measure that is widely used). A similar pattern was identified in the NICE guideline on ADHD (NG 87). As there is not additional evidence for the use of specific ADHD screening tools for an epilepsy population we have cited the ADHD NICE guideline.
	LD	Fine	No action required.
	KKT	Accepted	No action required.
	CR	No comments, clear to read. Typo in recommendation: to identify at risk (to identify those) T ypo: as those used with (delete those from here) Define: HKD	Reworded.
7.1.6	CS	Other factors will also impact on this	No action required.
	FB	Important to emphasise these aspects.	No action required.
	CR	No comment other than: Epilepsy with Centro-temporal Spikes (ECTS) (use of capitals is not consistent with other syndromes mentioned in this section, and this is CECTS?) ECTS is used throughout, ILAE use CECTS https://www.epilepsydiagnosis.org/syndrome/ects-overview.html	Now section 7.2.
7.1.7	PB	Levels of evidence look appropriate Recommendations nothing concerning.	No action required.

	FB	This section could be much more specific.	Clarified (now section 7.2.1).
	MO	this is a very important point and it highlighted	No action required.
	LD	typo in first sentence, extra word? "out by with". There have been several matched cohort studies showing that accelerated forgetting is a signature cognitive deficit in children with GGE and average IQ, it seems a likely reason of poor academic attainment and it seems a pity not to reference these studies in this context. Davidson, M., Dorris, L., O'Regan, M., and Zuberi, S. M. (2007) Memory consolidation and accelerated forgetting in children with idiopathic generalized epilepsy. Epilepsy and Behavior, 11(3), pp. 394-400. (doi:10.1016/j.yebeh.2007.05.004) (PMID:17715001)	Now section 7.2.1. Amended. We agree that this literature is relevant to the neuropsychological understanding of the impact of epilepsy. However, it is beyond the scope of this guideline to review the hypothetical mechanisms behind certain cognitive/learning impairments. The key question related not to why such impairments occur/the pathological mechanisms, but to whether there was evidence of impairments/need for particular assessments.
	KKT	Accepted	No action required.
	CR	Typo: carried out by (carried out with) Typo: indicated that children with and young people Typo: (Total participants (no capital?) Typo (in recommendation): those with considered more benign (?remove considered) Typo: attainment. at regular intervals	Amended (now section 7.2.1).
	RC	"Where there is evidence of more complex or severe impairments in cognitive functioning". More details/specifics are needed on this as the statement is unclear.	Now section 7.2.1. Amended for clarity to 'Where there is evidence of more severe and persistent impairments in cognitive functioning'.
7.1.8	TS	The last long sentence is already stated in the beginning of the paragraph. Very long...divide into two sentences?	Now section 7.3. This section has been amended.
	CR	No comments, clear overview.	This section has been edited to be more concise (now section 7.3).
	PB	Depression and anxiety paragraphs level of evidence at least 3	Now section 7.3. SIGN ratings for general reviews are level 4.
	FB	These conditions are almost certainly under-recognised, under-diagnosed and under-treated.	This section has been edited to be more concise (now section 7.3).
	IM	Should probably include tools to identify suicide risk	Now section 7.3. We do not use specific tools for this in child/adolescent services. There is not the same evidence base. Instead, this is done as part of a clinical interview (asking tailored questions). Each child service will have its own means of assessing clinical risk of suicide/self-harm in young people.
	CS	Helpful reference to research	No action required.
	MO	Recommendations appropriate needs to be	Now section 7.3. The recommendation states

		flagged at every visit	“should routinely enquire”. The role of the guideline is to raise awareness among healthcare professionals and for them then to use their professional judgement.
	KKT	Accepted	No action required.
7.1.9	TS	The two sentences in the second last part already stated in the beginning.	This section has been amended. Now section 7.3.1.
	CR	No comments, clear overview.	Thank you
	MK	The Recommendation states that professionals should “routinely enquire” on the basis of the evidence presented. Yet this section is about screening tools. If the Recommendation is to use screening tools then should be explicit in the Recommendation. This issue is then covered in the subsequent GPPs but the Recommendation and the GPPs do not easily fit together.	Rephrased/formatted to make a clearer link between sections recommendations and GGP (now section 7.3.1).
	PB	-'One case control study compared three commonly...'- level 2 evidence -'While screening measures can be used...' - study 240= case control study ,so level evidence 2 Recommendations sounds reasonable.	Now section 7.3.1. Amended.
	IM	As 7.1.8	See above.
	MO	Recommendations appropriate.	No action required.
7.2.1	PB	Studies within reviews mentioned individually should be rated. Recommendation needs adding '...with epilepsy and depression'?	Now section 7.4.1. Studies within a systematic review are not rated by SIGN. This has been reworded.
	HC	Recommendations suggest 'could' rather than 'should' - would recommend the latter	Now section 7.4.1. The use of could/should is dependent on the reliability of the evidence and the balance between the potential benefit and harm. It was felt appropriate to use ‘should’ for this recommendation.
	MO	Recommendations appropriate	No action required.
	FB	There is a relative lack of evidence but the recommendation for CBT appears to be reasonable in the circumstances.	No action required.
	LB	The PIE study was an multi-centre RCT group intervention that managed anxiety and seems ideal for reference in a paediatric epilepsy guideline? Dorris, L., Broome, H., Wilson, M., Grant, C., Young, D., et al (2017) A randomised controlled trial of a manual-based Psychosocial group Intervention for young people with Epilepsy. Epilepsy & Behavior (72), pp 89-98. (doi.org/10.1016/j.yebeh.2017.04.007)	Now section 7.4.1. Agree, this is a very well-designed study looking at psychosocial interventions for young people with epilepsy. The key question was looking at whether interventions were effective in managing anxiety/depression and/or quality of life. The PIE study is a very well-designed study but the groups excluded those with identified clinically significant levels of anxiety/depression and did not use standardised anxiety/depression measures as outcomes. The study did not find any significant improvements in quality of life at follow-up.

			Although it documented improvements in epilepsy knowledge (compared with controls) and confidence in discussing epilepsy with others, this was not within the scope of our key question. We do highlight the need for further evaluation of such studies.
	KKT	Accepted	No action required.
	CR	Typo: randomised controlled trial (RCT is already used extensively elsewhere)(also occurs later same section) Typo: improvements on (improvements in?) Otherwise no further comments, clear and all relevant information included.	Now section 7.4.1. Typos amended.
7.2.2	PB	par. 1-'... antedepressant medication...'-antidepressant -quality of studies rated as moderate for RCT's (1-?)and low for the cohort studies(2-).This needs to be in the evidence rating columns.	Now section 7.4.2. Amended. Studies within a systematic review are not rated by SIGN.
	HC	As above	No action required.
	MK	This whole section presumably makes an assumption that this is around the use of other medication in combination with anti-epileptic medication. This could perhaps be clearer. In practical terms this is very common clinical scenario when there is concern about drug interactions and potential deterioration in seizure control. Evidence based recommendations would be of great value in this area.	Now 7.4.2. No evidence was identified but the following statement has been added: Consideration should also be given to interactions between AED and antidepressant medication.
	FB	The recommendation is very questionable. The evidence for the efficacy of antidepressant medication in young people is generally poor but the best evidence is probably for fluoxetine. Venlafaxine is not usually recommended.	Now section 7.4.2. The recommendation has been amended to SSRI's in general. As the evidence base is poor it is worded as 'could be considered'.
	MO	recommendations appropriate	No action required.
	KKT	Accepted	No action required.
	CR	Typo: P value (p value) Typos (serial); use of capitals for names of some medications or families (eg Selective Serotonin Reuptake Inhibitors) but not throughout the entire guideline consistently, probably no capitals?? Typo: adverse symptoms are common to those reported in (?? use of the word common) Otherwise no further comments, clear and all relevant information included.	Now section 7.4.2. Typos amended.
7.2.3	TS	The publication by Wiggs 2018 in Neurology should be added. And after this study it should be more clearly stated that ADHD medications do not generally worsen seizures but on the contrary could improve	Now section 7.5. This study was not included in the initial search as it did not evaluate effectiveness/efficacy of medication on ADHD symptoms (in addition to risk). There

		seizure control. This paragraph is a bit difficult to read, shorten and improve structure? Separate amphetamine and atomoxetine.	are also significant methodological weaknesses in the study, which prevent firm conclusions being drawn [i.e. it does not separately evaluate individual medications, cases include anyone who has had a single seizure (not diagnosed epilepsy condition) and means of measuring seizure events may not have captured all seizure events]. We have made reference to the study in our text but are cautious about drawing firm conclusions given the above weaknesses. This paragraph has been restructured for readability, but not separated
	PB	Evidence ratings and recommendations reasonable.	No action required.
	IM	Could this be broken down into sub-headings? It's quite lengthy otherwise.	This has been divided into subsections within what is now section 7.5.
	HC	As above	No action required.
	MK	The same applies to this section, i.e is this about distinguishing between a direct effect of medication on seizures or about drug interactions and a potential deleterious effect on seizure control. The section on adverse effects needs to have evidence levels attached. My understanding is that there is significant amassed evidence on the use of stimulant medication in the management of ADHD and yet this appears to be a relatively weak recommendation.	Now section 7.5. This was not identified in the evidence, however, we have added the sentence: Consideration also needs to be given to potential adverse interactions between AED and ADHD medication.
	MO	Appropriate recommendation Needs to be highlighted that Epilepsy is not an contra-indication to stimulant medication	See response above to TS comment on section 7.2.3.
	FB	There is much better evidence from a recent (2019) study, to which reference should be made.	This was not identified in our update search.
	KKT	Accepted	No action required.
	RC	Excellent section.	Thank you.
	CR	Typos (multiple): pain (1/100, myoclonus (1/100, facial rash (1/36, and Typo: RCT with in Typo: range age (?age range) Typo: large space before QoL section Typo: Methylphenidate}, Consistency: referencing not following a standard elsewhere in the document: Fosi et al. (2013)255 The sentence regarding the Park et al (2018) study appears to have redundant text at the end: 'compared to those who did not experience a change in seizure frequency' Typo??: worsening of seizure activity in 17%	This section has been edited significantly (now section 7.5).

		(3/36) (three of 36 is not 17%) This text is difficult to read: and five out of seven of the studies in the Ravi et al., 2016 review)253; headache251, 252 and three of the studies in the Ravi et al review253); insomnia251 (Park et al., 2018 and five of the Ravi et al. studies253) and emotional / behavioural changes251 255, 256 and five studies in the Ravi et al., 2016253). Typo (remove brackets or commas):effects, (unrelated to seizure activity), are The layout of this section was confusing, headers did not follow a logical order (unless Methylpheniate / Amphetamine and Atomoxetine were higher order headers to other sections, but then subsections should follow a similar order and the first paragraph of the Amphetamine and Atomoxetine would be best not discussing Methylphenidate). This would improve readability Typo: amphetamine (24%;256 and atomoxetine. (37%; 258 Otherwise no further comments, all relevant information was included.	
8.1	KKT	Accepted	No action required.
	CR	Clear, no comments	No action required.
	MK	Describing the situation of childhood chronic conditions surviving into adulthood may not be appropriate to the situation of young people with epilepsy. Children have capacity and can provide informed consent under that age of 16 years in Scotland.	Agree. This has been removed. Agree. The sentence on consent has been amended, to state 'where necessary'.
	TS	Ok	No action required.
	PB	Looks reasonable	No action required.
	JC	Good to see this section was informed by a wide range of evidence. This is a particularly important time for young people and provides valuable information for clinicians. I have not commented on each individual section.	Thank you.
	CS	really useful section referencing potential concerns, importance of information provision etc	Thank you.
	HC	This is important, and commendable that a section has been dedicated to this topic, with wide ranging recommendations	Thank you.
	MO	This is well laid out and explained very important to young people with epilepsy	Thank you.
	FB	It is important to emphasise the necessity for well-managed transition. Some families find the transition from paediatric to adult services quite traumatic.	Agree. It is hoped the inclusion of this section in the guideline can help support well-managed transition.
8.2	TS	Ok	No action required.

	CR	Typo: (for that study type).Due Clear no comments	Thank you, typos have been amended.
	PB	-'This review included 4 small RCT's..."...Due to the small number of studies, the review authors concluded that the certainty of the evidence was low and they could not make any firm conclusions regarding effectiveness of the limited number of interventions studied.'- 1- rather	The grading is for the quality of the way the review was conducted, rather than the studies within it.
	MO	Unfortunately there is very little evidence in this area	Agree; however, it is hoped that the qualitative review provides useful information.
	KKT	Accepted	No action required.
8.3	TS	Ok	No action required.
	CR	Clear no comments As noted above, recommendations statement: direction to web based resources following a 1:1 (1:1 should be explained as it is inferred, but does not lead to a clear recommendation understanding when these are read as stand alone, as often happens in guidelines this long)	Expanded to 'one-to-one conversation'.
	PB	-In the recommendation 'Paediatric services providing care to children and young people should consider'- the word 'should' needs to be replaced probably due to being reserved for strong recommendations (here not having the level of evidence?) e.g. 'need to consider'?	The use of could/should is dependent on the reliability of the evidence and the balance between the potential benefit and harm. It was felt appropriate to use 'should' for this recommendation because of the good-quality qualitative/mixed-methods evidence.
	IM	I don't think this is particularly helpful, especially the recommendations and this could be improved with more definitive guidance.	This is based on the evidence available, including qualitative research.
	MK	Same comment on Cochrane 1++ grading as in previous sections; there were no young people in the studies reviewed. The recommendation arising from this section would appropriately be termed "could" consider rather than should consider given the acknowledgement of the difficulty in grading evidence. I would of course acknowledge that the intervention itself may cause more good than harm but please note my general comment above on the weighting of this. This broad issue needs to be addressed across the whole guideline so as to achieve internal consistency - as also discussed above.	The 1++ rating is correct as it is a well conducted systematic review. It is an appropriate age group, and while it is not specifically on children with epilepsies it is combined with the qualitative review, and the group felt that the body of evidence as a whole supported a stronger recommendation, given the benefit over potential harm.
	SD	uncontroversial -beyond the fact that these clinics give an opportunity to re-evaluate the persons epilepsy and thus should be physician led	Clarified in text: handover clinic is clinician led and transition clinic is HCP led.
	MO	good practise points comprehensive	No action required.
	KKT	Accepted	No action required.
	RC	"...some young people were more ready to transition and were more knowledgeable	Statement 'more ready to transition' has been removed.

		regarding self-care...There was little or no effect" Please double check this. This is from the Review article, which suggests that there was no increase in the transition readiness score ie not more ready to transition? "The interventions tested in the studies included in this review were very different, so it was not possible to draw conclusions from pooled estimate of effects. There were positive outcomes in the patients' knowledge of their condition following a nurse-led, one-on-one intervention. It was impossible to elicit from this study whether extending this intervention would increase its effectiveness, or to what extent the outcome would be reproducible in other contexts. The study did not find any improvement in the participants' transition-readiness scores (as assessed by the TRAQ), which may indicate that simply increasing disease knowledge is insufficient to improve their readiness for transition. It may also indicate the difficulty in using measurement scales to capture complex attitudes and behaviours. The results also suggested that interventions that use technology may have a beneficial effect on participants' self-efficacy and confidence in managing their own health and health care. Once again, improvements in this measurement were not reflected in a significant improvement in TRAQ scores. Limited evidence suggested that workshop-based interventions did not lead to beneficial outcomes or have a good uptake in patients with spina bifida."	
General	TS	Ok	No action required.
	MK	9.1 and 9.2 I have considerable reservations about this section and in particular its balance. Achieving that balance requires an appropriate description of the mortality risks, including discussion on when, how and where but many of those risks are significantly greater risk than that of SUDEP. The whole tenor of this section and the way the section is set out appears to be strongly orientated towards SUDEP and more strongly still towards the issue around discussing SUDEP principally at the time of diagnosis. It is not that I disagree with the principle of the latter but there are, I believe, multiple other issues to be addressed and not to do so results in a section that lacks appropriate balance and is misleading of the true picture of risk of premature death in children and young people. Indeed the Key Question itself confuses the issues of SUDEP and premature mortality in epilepsy but latter issue is addressed in only a limited way.	Thank you for these comments. The KQ for this was patient led, this has now been clarified in the guideline and thus looked at this in more detail. The introduction now provides details on other causes of mortality and risks. SUDEP is not the greatest risk as opposed to other causes. This is what families are concerned about.

		I suggest there needs to be review of the epidemiology of mortality in children and young people and putting SUDEP into an appropriate context in that regard. Secondly, adopting a blanket approach to the issue of SUDEP runs counter to whole tenor of the guideline where the issues around diagnosis, investigation and treatment are, and should be, tailored to the individual child or young person. There is an abundance of literature that allows the stratification of mortality risk, SUDEP or otherwise, to be determined so that discussion can be tailored to the individual. It is however rarely possible to provide that stratification at the time of diagnosis since the course of that individual's epilepsy cannot be known at the point. As I have stated I do not disagree that a "SUDEP discussion" should take place at diagnosis but the informed value of that is extremely limited and may be considerably misleading in both directions. In relative terms there is only passing reference to the need to have an ongoing discussion about all risks of premature death that is not simply confined to an arguably poorly informed discussion at the time of diagnosis. The Recommendation that follows the evidence in this section appears to be in the strong category using the word "should" and this is perhaps not in keeping relative to other recommendations contained within the guideline. The first Good Practice Point then discusses information on the risks and safety issues associated with a diagnosis. This is an important but far broader statement and this whole issue risks being conflated with SUDEP, which is but only one risk. The second GPP also discusses wider risks again conflating this the sole risk of SUDEP. Again in a brief review of my own there may be some important references missing here (though they may of course have been excluded in the sifting processes). I hesitate to provide a review in support of my general comments on this issue but I am enclosing it with this and hope it may of assistance in striking an appropriate balance to this section. It's author, Prof Richard Appleton has been a previous SIGN guideline	As above, within the limitation of the key questions. This has now been balanced with the introduction including mortality statistics. This is based on high quality qualitative evidence. Thank you a GPP has been made on mortality in this section. Thank you, this was general review and outside the date parameters so we have not included it.

		reviewer.	
	CR	Overall excellent section with current data Typo: (missing a comma) seizure) status Typo: associated with a child or young person (the risks are associated with seizures in a child...) Typo: (remove bracket) much higher. (The risk	Thank you. Typos amended.
	JC	I was particularly interested in this section due to the use of the mixed methods review to support the recommendations made	No action required.
	IM	Very focussed on SUDEP. Section should include other causes of death.	SUDEP, and whether/when to discuss it, was the most important issue for patient and carer representatives. It is not possible to cover every aspect of epilepsy in the guideline.
	SD	I commend the team for calling the section mortality = see my comments above under recommendations. It is important to explain that epilepsy can cause premature death from a variety of causes. I wonder if the team should not consider mentioning the importance of preventable deaths to communicate the fact that some deaths can be prevented by good seizure control, lifestyle choices etc	This has now been added in paragraphs 2 and 3 of section 9.
	MO	Well written section	Thank you.
	FB	The mortality quoted should make it clear that this is not the figure for SUDEP in children, which is much lower. It is an overall mortality you rate.	The section has been revised and different mortality rates quoted.
	KKT	Accepted	No action required.
9.1	PB	Necessary to quote statistical values such standard deviation and confidence intervals? Information point - sufficient time- can this not be included simply in the recommendatons or good practice points?	SIGN style is to state CI where cited and *P*-values if not. We have reviewed where the information points best sit and edited accordingly.
	CR	?? Typo: being at higher risk 270and age range (what does 'and age range' mean in this sentence?) ?? Typo: 1:45 per 1,000 children Typo: confidence interval [CI] (CI is used frequently previously) Typo: (moderate confidence in evidence Typo (no space): 276.In a Swedish Typo (no comma): All SUDEP cases, <16 years Typo: at ages ,16, 16–50, and .50 years	Amended to remove mention of age. Corrected to CI only. Removed through editing. Amended. Removed during editing.

		(presume you mean at ages <16, 16–50, and >50 years) I was not sure of the relevance of presenting adult data here, its important to emphasise paediatric and separately adolescent data (as risk increases in adults and it is then that the male predominance appears). It was harder to read due to frequent typos I thought it was important to emphasise that data is limited by studies relying on diagnosis of SUDEP and postmortem. This limits correct diagnosis of SUDEP particularly in children. We had this issue particularly in QLD, when we had to directly search all postmortem reports for all children who had PM's who had seizures/epilepsy to directly determine SUDEP deaths confirmed by autopsy for QLD, even this would be an under-estimate as not all SUDEP's in children with epilepsy are put forward to post-mortem as most coroners consider the fact that they had epilepsy an indicator that death was 'natural' and not requiring PM. J Clin Neurosci. 2016 Jan;23:58-62. doi: 10.1016/j.jocn.2015.04.027. Epub 2015 Sep 19. A population-based post mortem study of sudden unexpected death in epilepsy. Clark D, Riney K. Typo: repeat visits. Ideally as (does not read as if this is the start of a new sentence) Typo: parents/family /carers (space or no space after /)	Corrected to <16, 16–50 and >50 years. This was included to show that risk increased with age. It was also necessary as some patients remain in paediatric care until the age of 18, which is covered by the adult data. The guideline has been edited before publication. Agree. There is variation in the identification and SUDEP as in some cases there may not be a post mortem to diagnose all possible causes. We have added to the SUDEP introduction that diagnosis of SUDEP is difficult, as not everyone has a post mortem. This reference is now added, thank you. Sentence removed during editing. Sentence removed during editing.
	CS	important to assess family's understanding of information - I am not sure where any reference to need to consider social work involvement may be best placed in this context - would need to be sensitively handled - I am not best placed to comment on this given my background in adult care	We have referred to the multidisciplinary team (to include social work) throughout the guideline.
	SD	I am flattered that the first sentence in this section is a verbatim copy of the opening sentence in adult guideline in epilepsy(written by me!) This section covers all the relevant data . I would be tempted to put in a sentence about the importance of the correct drug for the correct epilepsy syndrome as one way of avoiding SUDEP/premature death - in particular the fact that a dogmatic avoidance of valproate in young women might put them at danger	The sentence has been amended slightly, and therefore does not reference the adult guideline, which was indeed the source. This is a good point for women with increased risks of seizures/mortality. However, there is currently no evidence on avoidance of valproate so we are unable to add this.
	MO	again well written and comprehensive	Thank you.
	FB	One important epidemiological study in the UK appears to be missing. This confirmed a low overall instance in children.	We did not identify any further studies.

	KKT	Accepted	No action required.
	RC	Excellent section. "1.45 per 1000 children"?	Thank you. Removed during editing.
9.2	PB	-'All three studies were rated as moderate...'- the word 'should' in recommendation needs to be 'consider' based on this level of evidence?	The use of consider/should is dependent on the reliability of the evidence and the balance between the potential benefit and harm. It was felt appropriate to use 'should' for this recommendation because it is based on three moderate-rated studies and the mixed-methods review.
	CR	Clarification, meaning of text: (submitted)? Font colour: Ramachandrannair et al (2016) Typo: Families & friends (and friends) Typo: support.(see Typo: people and carers, on the No other comments, section is clear	'Submitted' changed to 'conducted'. Spelling checked and amended. Formatting issues will be addressed at layout. Typos amended.
	JC	The recommendations in this section are made from a mixed methods systematic review using conqual resulting in evaluated guidance that considers users perspectives. It so good to see these types of studies used in SIGN guidance as they present a. More comprehensive overview of what service users find valuable and appropriate.	Thank you.
	SD	Uncontroversial	No action required.
	FB	The importance of providing accurate information, which emphasises the very low risk in children, should be highlighted. It should be explained to families that the reason for providing the information is so that they can understand the low risk but also understand what factors, for example seizure freedom, might make it even lower.	We have added references on the number of mortality causes from SUDEP versus other causes of death. Following feedback from the parent representative on the group, the term 'low risk' has been avoided. This is because it is not helpful for families who have lost a child to hear this described as 'low risk'.
	MO	Appropriate recommendations good evidence levels	No action required.
	KKT	Accepted	No action required.
9.3	TS	Some language errors.	Language errors have been corrected.
	MK	This section begins with an information point on discussion about listening devices/nocturnal supervision/sharing the same bedroom "*if* (my italics) a child is at risk of SUDEP". This has the potential to be significantly misleading since it clearly implies that these are in some way protective. The evidence does not support this in any robust way. This case control study (reference 295) contains no children but is rated as 2+. The absolute risk and factors affecting SUDEP risk are well recognised to be different in children compared to adults. I suggest this	Removed. The evidence level is appropriate to the way the study has been conducted, not the study population. The extrapolation from the study population is reflected in the strength of the evidence.

		should be downgraded. In this paragraph on the same paper it is also stated that "the author suggests that because most deaths are unwitnessed, supervision and attention to recovery after a seizure may be important in SUDEP prevention". I am not sure that that is appropriate for an evidence-based clinical guideline.	
		In the paediatric cohort study (ref 296) the authors clearly stated in their paper that the difference between the results did not reach statistical significance.	This was an old study and it has been removed.
		At a later point there is discussion about the fact that monitoring devices may not *totally* (my italics) eradicate the chances of SUDEP suggesting that controlled studies are required. I believe this too has the potential to be misleading. I suggest that is re-phrased: There is no evidence that the use of monitoring devices can reduce the risk of SUDEP. I am not suggesting that night time supervision or other monitoring does not have a role to play in alerting a carer to a seizure so that appropriate first aid such as positioning can be undertaken, but this issue and the potential to prevent SUDEP occurring must not be conflated.	Agree, hence no recommendation made.
	CR	Typo: pro's and cons	Amended to 'pros and cons'.
		Typo (not a full sentence): Alarm fatigue caused by false alarms. (the sentence that follows this is also not a full sentence)	These sentences have been deleted during editing.
		Typo: Efficacy and of bed alarms and seizure detection monitors	Sentence removed during editing.
		Typo: or when using special precautions such as a listening device were used	Sentence removed during editing.
		Typo: years.Supervision	Removed during editing.
		Typo: children (This entire paragraph needs checking for errors: A cohort study in children (296 (n=310) with learning disabilities, in a residential school who were closely supervised at night, when an alarm went off alerting the staff to the fact a pupil was having a seizure, a member of staff attended straight away and stayed with the pupil until they had recovered found. There....	This was a poor study so has been removed.
		Typo: would need to be taken as there	Amended during editing.
		Typo: their degree of concern of undetected seizures	Amended to 'degree of concern for undetected seizures'.

		Typo: some level comfort having done Question: what does 'motor disturbance' mean? Typo: disturbance.297. It I think this is a difficult section to strike the right balance with limited available evidence. It would be fairly impossible to ever have good studies that can demonstrate an intervention prevents SUDEP. Given the low incidence of SUDEP in childhood (or in non refractory adult populations) you would need a large population study where thousands of individuals were studied with one group having an intervention (such as a defined type of seizure surveillance) and one not, to ever be able to prove that the intervention prevented SUDEP through comparing the two groups. This is unlikely to ever be possible. I There is, however, reasonable data that may be important to emphasise in this section, that the majority (though not all) SUDEP's are overnight, unattended seizure-related events. Only 10% are witnessed events. It is also logical that one would not permit a seizure to occur in hospital and leave the patient unattended. Therefore there is a lot of basic common sense in focussing information with parents not on what we cannot prove (that an intervention cannot prevent SUDEP), but on (when needed, for example if the risk is temporarily higher eg with accidental medication omission/illness/sleep deprivation) how we can reduce the risk of an unattended nocturnal unsafe seizure (e.g. with loss of consciousness), where strategies such as co-sleeping, seizure mattresses, audio/video monitoring all are logically sensible (and some with some evidence on sensitivity/specificity) though with the noted risks mentioned in this section (alarm fatigue, loss of independence). This different emphasis might be best at the end of the section as the last paragraph does not help clinicians focus on reducing unattended tonic clonic seizures overnight with families in their discussion on minimising risk of SUDEP.	Amended to 'some level of comfort'. Amended for clarity to 'motor manifestations'. Amended during editing. Agree, we have clarified in the text why the focus was on SUDEP, ie patient perspective. Sentence added: 'Healthcare professionals should support the individual family's approach to alleviate their anxiety.'
	FB	There is a recent discussion in the journal "Neurology" that might be worth mentioning.	This was not picked up in the literature search. If it is a discussion piece it cannot be cited as evidence.
	PB	-'Negative outcomes to consider...A study of night time...'- needs evidence level. Odds ratio's and CI necessary to quote in this guideline? -'A cohort study in children ...' - evidence 2-	This section has been revised, ratings reconsidered, and good practise points added.

		rather? -/A survey of patient and caregivers views on...'- level 3 evidence The last 2 paragraphs sounds like recommendations/good practice points and need lifting out as such.	
	IM	Would benefit from recommendations that no reliable tool is available. Perhaps too strong on co-sharing a room or listening devices when the evidence for these is weak.	A good practice point has been added to discuss pros and cons so parents can make an informed decision.
	SD	there is little evidence for this I would make a stronger statement to the effect that monitors/seizure alarms and not letting someone sleep alone are unproven, and may cause more anxiety that they are worth	See response above to IM.
	MO	Sensitively written and states quite clearly that monitoring devices do not prevent SUDEP	Thank you.
	KKT	Accepted	No action required.
General	KKT	All sections accepted	No action required.
10.1	FB	Good aims.	No action required.
	CR	No comments, clear.	No action required.
10.2	PB	-'Almost as important as...' paragraph needs right side column line for levels of evidence -'Where appropriate, information about bilingual, and culturally'- missing words in this practice point	Evidence levels have been added. The wording of this sentence has been amended.
	CR	No comments, clear.	No action required.
	FB	Because most people refer to the Internet, the reliable websites for epilepsy information, together with helplines, should be highlighted.	This is incorporated in 'contact details of voluntary organisations', and websites are provided in section 10.4
	MO	useful and appropriate	Thank you.
10.3	PB	How much time needs to given in clinics for this?	These are suggestions for good practice and pointers for the kind of information people need. It is up to clinics how it is delivered (verbal, leaflets, etc.).
	MK	There seems to be no note of water safety in this – a significant risk of unexpected death. If SUDEP is to be included under general information then this would be better addressed as premature death – as I have argued above.	Water safety has been added to this table.
	CR	No comments, clear. Typo: at appropriate, e.g. Typo: keteogenic diet Typo (error paragraph/space): with female adolescents Needs bullet point: pregnancy and	Thank you. Corrected. Corrected. Corrected. Corrected.

		breastfeeding Space before (error): efficacy Typo (no capital required): Relationships Error incorrect paragraph/space: aware of the following:	Corrected. Corrected. Corrected, and will be further addressed during layout.
	MO	Well done and useful	Thank you.
	AF	Could add information here from EEG depts on what the investigations involve - leaflets available on this (Sleep deprivation/melatonin as well as routine tests) to minimise patient concern - similarly for other investigations	This is covered under 'investigative procedures' (general epilepsy information).
	FB	This seems rather formidable in the amount of information that should be provided. Again, would it not be a good idea to highlight the reputable websites and helplines?	This is a list of points it is good practise to provide. It can be part of a discussion, a leaflet or signposting to websites. Sources of further information are listed in section 10.4.
10.4	PB	-'SUDEP Action'- needs gap above	Amended.
	CR	No comments, clear. Have not checked through in detail for typos/paragraphing etc	Thank you.
	NS	'The Daisy Garland', not 'The Daisy's Garland'	Amended.
	FB	This seems to be presented in a random order. Would it not be better to list the more helpful, relevant and user-friendly sources first?	Presented in alphabetical order, as listing what is most helpful etc is subjective and dependent on the individual.
	VW	Correction - The Daisy Garland	Amended.
	HC	An extensive list of places to seek further information - I note all major charities are listed, but Young Epilepsy, a charity dedicated to children and young people with a wide range of resources has been omitted? www.youngepilepsy.org,uk	We have listed the main umbrealla organisations. We cannot list all charities, however we have included NHS Inform which has a directory of local organisations and support groups.
	MO	Comprehensive	No action required.
General	KKT	All sections accepted	No action required.
	MK	I suggest there are clear resource implications for Health Boards in these statements.	The guideline outlines best practice. There may be resource implications for individual boards. The recommendations and the resource implications will be considered by SPEN. This section has been revised to provide more detail.
11.1	JC	Good to see that implementation strategies have been considered rather than just the evidence alone	No action required.
	FB	In this section, the mismatch between ideal recommendations and practical implementation seems to become evident.	The guideline provides recommendations for best practice. This section has been revised to provide more detail regarding resource implications.
11.1.1	AQ	No issues	No action required.
	FB	It appears that work is still required to implement this fully.	Noted

	IM	Is Edinburgh "national epilepsy surgery site"? I thought Glasgow does some operations and Tayside also does non-resective epilepsy surgery.	This has been amended to four centres (now in section 11.3).
	MO	This is a specialist service used in epilepsy surgery services for this children with focal drug resistant epilepsy whose 1.5 t mri is negative There will need to be an increase in GA facilities	This section has been revised (now in section 11.3).
11.1.2	PB	-'This is carried out by a taking a detailed account of presentation and use of standardised screening tools which could indicate raised levels of psychological distress.'- use of such tools is unrealistic time wise and may require further appointments/longer appointments/CAMHS referral. This would be difficult to achieve in within current resources in most centres.	This section has been revised and takes note of the need for more time and access to CAMHS. Now section 11.3.
	CR	No comments (Educational Psychologists ? need capitals or not)	Section replaced with 11.3. Sentence removed.
	IM	Not particularly clear - implementation strategy not entirely clear	This section has been revised with more detail within section 11.3.
	FB	The recommendations are basically good but will appropriately trained, skilled and motivated personnel be available to put them into practice?	The section has been revised to provide more detail on resource implications and support from SPEN.
11.2.1	FB	I have already questioned whether the EEG is required for further classification. Should the word not be "recommended" rather than "required"? Otherwise, the recommendations for implementation appear good.	This has been changed to 'recommended' (now within section 11.3).
	AF	full stop not comma bullet point 2 before ' Ideally' Content - sounds right to me: If cerebral function monitoring included as it has at various points the possible costs of remote access for expert interpretation: training junior to interpret in NNU etc could be added here: I have personally trained many NNU juniors in basics of interpretation (3x/day - every nurse/junior Drt shift change when cases critical!!)	Now within section 11.3. The audit points focus on audit of the implementation of the guideline recommendations. There is no recommendation specifically for cerebral function monitoring.
11.2.2	FB	As already stated, this appears to be work in progress.	This section has been replaced by section 11.3 which is more detailed.
	CR	Typo: there are no additional resource requirements are required No other comments	This section has been replaced by section 11.3.
11.2.3	NS	'dietitian', not 'dietician'	Amended throughout.
	MO	Will need an increase in dietetic services, clinics and specialist paediatric time	This section has been revised and the increase to services discussed within section 11.3.
	FB	It is not clear whether the required number of trained, enthusiastic and committed dieticians would be available to implement the recommendations.	This is now part of section 11.3, which includes a section on resource needs. The lack of dietitians is noted there.
	CR	Typo: and they take require more monitoring due to them growing rapidly at this age therefore more changes are usually required	Section replaced with Section 11.3 and errors amended.

		Typo:epilepsy. Typo: Could this be re-worded to: Sustained funding (charities/partnership/) is required to maintain this service, to implement the SIGN guidelines (agree this is good rewording!) Typo: the feasibility of working work healthcare professionals/health boards/charities other stakeholders locally No other comments	
11.2.4	FB	Again, the recommendations are good but the feasibility, in terms of the workforce required, is questionable.	This is now part of section 11.3, which includes a section on resource needs.
	CR	Typo: More families could be wanting this treatment Typo: national paediatric epilepsy surgery service is nationally Typo: (NSD).NSD as No other comments	Now in section 11.3. Removed during editing. Corrected to 'national'.
11.2.5	MO	provision and access to service needs to be addressed	This section has been revised and the increase to services discussed within section 11.3.
	FB	Comment has already been made on the likely lack of appropriately trained staff to assess and implement the recommendations.	This is now part of section 11.3, which includes a section on resource needs. The lack of dietitians is noted there.
	CR	Typo: with knowledge of epilepsy condition Typo: Equity of service psychological service provision Typo: with healthcare professional and Clarify (explain): epilepsy consortium Explain: NES Typo: will explore the feasibility work with healthcare No other comments	Now in section 11.3. 'Condition' deleted. Removed during editing. Corrected to 'professionals'. Removed during editing. Removed during editing. Amended to 'feasibility of working with'.
11.3	MO	a little bit of realistic editing would not be unreasonable and priority should be given to topics where there is no evidence in children such as in EEG modalities Also need to audit referrals to ketogenic diet service, adherence rates to diet referrals to SESS and outcomes	This section has been revised and is now part of section 11.3.
	FB	Auditing is important. Would it not be possible to provide more robust audit guidelines?	The section has been revised and is now in 11.3. The purpose is to provide a check on whether the guideline recommendations are implemented. More detailed audit tools are outwith the

			remit. However, audit and implementation is being considered by SPEN.
11.3.1	IM	Under-emphasises staffing and equipment costs to expand local services. Doesn't recognise heavy focus of EEG in Glasgow and not in other centres.	This section has been revised and is now part of section 11.3.
	CR	Re text: a diagnosis of epilepsy / assisting with syndromic diagnosis The interictal EEG primarily assists with clues towards aetiology diagnosis (eg focal, genetic, other aetiology patterns), syndromes also reflecting aetiologies (eg Dravet = SCN1A, genetic generalised epilepsies, West = structural>genetic etc).	This is discussed in section 4.1.
	FB	This audit would be difficult to implement without a close working relationship with a clinician skilled in the diagnosis of epilepsy; again, this would be ideal but perhaps not always practicable	SPEN will consider what resource is needed to conduct the audit. This has been added (new section 11.3).
	AF	Though excellent as a guideline I suspect though sample audits possible full audit may take resource currently not available in some depts	SPEN will consider what resource is needed to conduct the audit. This has been added (new section 11.3).
11.3.2	MO	Only available in one centre on a clinical basis	This section has been revised and is now part of section 11.3.
	CR	Typo???? 3T MRI EEG investigation (MR-EEG is not in the guideline!) No other comments	Amended to '3T MRI' (now in section 11.3).
	AF	I think to audit the increased lesion pickup which we believe is obtained with 3T compared to 1.5 T scans would be worth assessing: (ideally long term in terms of outcome, though that would be a major project). Probably not required within a guideline...	The purpose of these audit suggestions is to check if the recommendations are being implemented.
11.3.3	FB	The use of the ketogenic diet has increased over recent years and different diets are now available. Because specialist dietetic services are generally recommended, would it not be better to carry out a more extensive audit in this specialist area? This would include the type of diet, the type of epilepsy, the response and any adverse effects. It will also include data on the duration over which the diet was implemented and any evidence of tolerance.	This has been added (new section 11.3).
11.3.4	FB	Because quite limited data are available on the psychiatric and cognitive outcome of surgery in children (as opposed to adults), should this "audit" not form part of data collection that could be used for subsequent research?	This is something for SPEN to consider.
	AF	All entirely laudable! also?- audit of long term costs compared to equivalent controls if possible - aim cost benefit analysis	This is something to be picked up by the commissioners (NHS NSD).
	CR	No comments other than typos: Typo: QoI	Corrected.

		Typo: reduction/reduced costs (chose one!) Typo: (NSD).NSD	Amended to 'reduced costs' only. Defined as 'National Services Scotland'.
11.3.5	FB	Again, this seems to be a missed opportunity. Since ADHD is so common in children with epilepsy and since there are reputable questionnaires that are very easy to complete that can be used to follow response to treatment, notably the SNAP-IV, should this monitoring not be recommended as routine? It should provide very good evidence for future funding of such services.	There was insufficient evidence to recommend a specific screening tool for ADHD and epilepsy so cannot recommend it for monitoring.
	CR	Typo/clarify: Staffing capacity (wte) No other comments	Amended during editing.
11.3.6	IM	Very weak. Needs more robust assessments, including benefits	This section has been revised and is now part of section 11.3.
	MO	need to work closely with adult services to try and ensure that young people with epilepsy receive the transition care they have described so eloquently requested	This has been expanded and is now part of section 11.3.
	FB	What is missing here is the opportunity for families to comment on the quality of the transition. This should be included.	This has now been included (new section 11.3).
	CR	No comments, Typo: There are currently 8 board that have Capital: drop out/deterioration (presume deterioration means deterioration in seizure control???)	Now in section 11.3. Amended to 'currently eight boards'. Changed to capital. Added 'in seizure control' for clarification.
11.3.7	IM	Very weak - audit of SUDEP deaths - what does this include?	This has been expanded and is now part of section 11.3.
	SD	Agree - Scotland has a very good infrastructure to audit SUDEP deaths	This has been included in section 11.3.
	CR	As the guideline has not been clear about any preventative measure, is the intent to monitor SUDEP death rates in Scotland before/after the guideline? What about auditing families satisfaction with information provision, or the compliance with information provision at/near the time of diagnosis?	There are ongoing discussions with SPEN to address this with studies in Scotland. This is a good idea for qualitative feedback, but not an audit point.
	MO	An ideal topic to be audited by SPEN	This is an issue for SPEN – comments will be noted by SPEN.
	FB	Deaths are not going to be great in number. Again, it would be a shame to miss the opportunity of collecting further relevant data. The type of data can be determined from recent publications.	The suggestion to audit deaths has been removed. The recommendations is based around provision of information and the purpose of this section is to audit whether the recommendations are being implemented.
11.4	PB	Cannabinoids and practical implementation needs attention	Cannabidiol is awaiting assessment by SMC.
	IM	Need to invest in neurophysiology outwith Glasgow.	This is a decision to be made outwith SIGN.
	FB	I always welcome the SIGN guidelines because they are full of common sense. This guideline is no exception but it could be made more readable. I look forward to seeing the version intended for patients and their families.	Thank you. The guideline has been edited before publication.

	MO	A database of all children and young people with epilepsy is needed if there is ever going to be a realistic hope of performing meaningful audit these need to be able to upload data from systems in the individual health boards and it is not reasonable to expect clinical staff to be responsibe for all data input	This is an issue for SPEN – comments will be noted by SPEN.
	KKT	SPEN WILL REQUIRE THEIR SUPPORT TO IMPLEMENT THIS	This is an issue for SPEN – comments will be noted by SPEN.
	CR	No comments to add. I do not work in Scotland/UK therefore I do not have insight into what is included here/excluded. I wondered why no data on Levetiracetam, or more recently Lacosamide is available in the guideline. FDA submission for fenfluramine which appears to have high efficacy in refractory Dravet Syndrome is underway, it is worth keeping this on the radar if there is progress with its availability before this guideline is finalised from draft, as it has high efficacy (>75% responder rates).	SMC advice for levetiracetam and lacosamide included.
General	KKT	All accepted	No action required.
12.1	JC	Conducted comprehensively and in a way to minimize bias	No action required.
	FB	Systematic reviews are always to be recommended but depend on adequate data being available, which is not always the case with regard to child with epilepsy.	This section describes the literature review conducted to inform the guideline. The search covered systematic reviews and primary quantitative and qualitative studies.
	CR	No comments, clear.	No action required.
12.1.1	JC	Databases and keywords outlined indicating a comprehensive search strategy was employed	No action required.
	FB	This appears to be consistent with fairly standard practice.	No action required.
	CR	No comments, clear.	No action required.
12.1.2	FB	I was pleased to see that quality of life featured in this section, although only at the end. Should it be emphasised to a greater extent?	This is the standard outcome used for cost-effectiveness data in all SIGN guidelines. Quality of life was also considered and reported, when included in trial data, for the review of clinical evidence.
12.2	PB	-'What is the most cost-effective way to interpret continuous EEG data in newborn infants? What are the training implications if neonatologists are to interpret? Economic and feasibility analyses are necessary'; What is the most cost-effective way to interpret continuous EEG data in newborn infants? Economic and feasibility analyses are necessary'- why guideline if neonatal seizures were not to be addressed? good questions for a neonatal seizure guideline/pathway.	A health economist was involved throughout the guideline development process. The scope of this guideline is children and young people aged from 1 month to 19 years.
	MK	How these recommendations were arrived at is not immediately apparent and could usefully be cross referenced against the key questions. The list is extremely long and risks coming across as a large “shopping list”. It may be better to focus down on some key questions that are likely to be realistic and to	The list of recommendations has been edited.

		be taken forward.	
	PG	As said earlier: In SUDEP: develop an 'at high risk' checklist where its absolutely essential to talk about SUDEP early on in consultation process.	This is covered in the recommendations in section 9.
	CR	No comments, clear.	No action required.
	JC	Appropriate based on existing literature	No action required.
	NS	To add: 'Further research into predicting response to ketogenic diets (which syndromes or seizure types are particularly likely to respond; possible biomarkers of response) in order to appropriately streamline resources.	The recommendations for research have been rationalised and includes a recommendation for long-term studies of the tolerability and adverse effects of the ketogenic diet.
	FB	This statement in this section is very consistent with my comment above. May I also for attention to the opportunities provided by extending the audit (see audit section) to provide valuable data for research that might affect future practice significantly. Since the psychiatric aspects affect quality of life to such a major degree, should research into these areas of childhood epilepsy not be highlighted at the beginning? In particular, treatment of ADHD is relatively simple, safe and often life-changing. There would be plenty of opportunity to carry out research into this area and the protocols would be quite easy to design. The list of areas requiring further research is extensive. Perhaps some further prioritisation would be worthwhile.	Recommendations are listed in the order of each guideline section. The list of recommendations has been edited.
	AF	-further 2nd line EEG study idea -would clarify -Newborn infants? A laudable aim: Full EEG and CFAM/CFM type monitoring are established methods, and I agree if no Neurophysiologist accessibe there are real training implications - from what has been said is it appropriate this be included here? Age >1 month very relevant: less so after 1 month of age -other neonate suggestion re interpretation of continuous EEG data in newborn infants- agreed: again in part younger age groups, but a needed study -including remote reporting/expert access, now used for other urgent EEG situations -'Role of MRI scans....'-Tesla misspelt -no r I think! -other proposed projects - all look good to me: nowadays the costs, and long term cost benefit analysis of epilepsy surgery should perhaps be included (a personal hatred - ethics should come before cost - but if it can be demonstrated as I suspect that long term COSTS drop with improved seizure control from surgery funds to improve patients seizure freedom and quality of life may be	The list of recommendations has been edited. The recommendation for newborns has been removed as it is outside the remit of the guideline. Typo amended, thank you.

		more forthcoming)	
12.3	PB	Cannabinoids and practical recommendations for use in Scotland	Cannabidiol is awaiting assessment by SMC.
	FB	Wise to review regularly, particularly in changing field such as epilepsy management.	No action required.
	CR	No comments, clear.	No action required.
13.4.2	TS	Ok	No action required.
	PB	-'Mr Philippus Brink'-Dr , not Mr Consultant Paediatric Neurologist, Ninewells Hospital, Dundee'-please replace' Ninewells Hospital' with 'Tayside Children's hospital	Amended.
	MK	Finally my acknowldgement in this section should be: Consultant Paediatric Neurologist and Honorary Professor, Tayside Children's Hospital, Dundee.	Amended.
	CR	My affiliations are: Associate Professor Catherine (Kate) Riney, Paediatric Neurologist & Epileptologist, Queensland Children's Hospital/University of Queensland School of Clinical Medicine, Brisbane, Australia	Amended.
	JC	Dr Judith Carrier Reader Primary Care/ Public Health Nursing School of Healthcare Sciences Cardiff University	Amended.
	FB	Professor Frank MC Besag FRCP FRCPsych FRCPCH Consultant Neuropsychiatrist East London Foundation NHS Trust, Bedfordshire and University College London & King's College London.	Amended.
	NS	Please amend: Dr Natasha Schoeler Ketogenic Research Dietitian, UCL Great Ormond Street Institute of Child Health, London	Amended.
	PG	2 changes in Job title - Dr instead of professor and add 'consultant paediatric neurologist' So it should read as- Dr Pradnya Gadgil Consultant Pediatric Neurologist Kokilaben Dhirubhai Ambani Hospital, Mumbai; Associate Professor Grant Medical College and Sir JJ Group of Hospitals, Mumbai	Amended.
	HC	My title and affiliation should read The Prince of Wales's Chair of Childhood Epilepsy & Honorary Consultant in Paediatric Neurology, UCL Great Ormond Street Institute of Child Health, Great Ormond Street Hospital for Children, London & You g Epilepsy, Lingfield.	Amended.
	LD	Dr Liam Dorris Consultant Paediatric Neuropsychologist, Royal Hospital for Children, Glasgow and Honorary Associate Professor, University of	Amended.

		Glasgow.	
	AF	Fine as is	No action required.
	KKT	As the Clinical Lead for SPEN, I helped set up the team with Carsten Mandt. Would it be possible for this to be acknowledged please? SPEN is the parent body which managed to have SIGN guidelines for Epilepsy come into existence and was the platform on which the entire premise was set up. Dr Krishnaraya Kamath Tallur Consultant Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh Honorary Senior Lecturer, University of Edinburgh Clinical Lead, Scottish Paediatric Epilepsy Network (SPEN)	This has been addressed.
General	KKT	All annexes accepted	No action required.
	JC	Comprehensive and good to see the inclusion of qualitative questions within the review	Thank you.
	MO	not really for me to comment on as they were chosen by stakeholders but the key questions were quite eclectic	No action required.
	FB	These appear to be good questions but there is a lack of questions relating to the management of autism spectrum disorder in children with epilepsy.	ASD is covered in KQs 9 and 10.
	JC	Appears appropriate	No action required.
	MO	useful information	No action required.
	IM	Outwith my expertise	No action required.
	FB	This statement appears to be reasonable. There is a formatting problem at the end of the information box with an inappropriate bullet point.	Formatting issues will be addressed by the graphic designer.
	JC	Please avoid the term ‘ epileptic’ This should say instead suspected epilepsy and unconfirmed epilepsy rather than non-epileptic. Surprised to see these labeling terms still in use.	This is part of SPEN algorithm, so we are unable to make these changes. This comment has been referred to SPEN.
	FB	Again, this pathway appears to be sound, apart from the apparent (perhaps not intended) emphasis on discharge for the patient with non-epileptic attacks instead of referral to appropriate psychology/psychiatry services to address the issue.	This is taken direct from SPEN, so SIGN cannot amend it.
	HC	Useful	No action required.
	JC	See previous comment about non-epileptic	As per comment on Annex 3.
	HC	Useful	No action required.
	FB	This pathway also appears to be sensible. It is probably too early to recommend deep brain stimulation as an option in the second-last box on the left.	This is taken direct from SPEN, so SIGN cannot amend it.
	PB	This annex needs to be highlighted strongly as the source to go to for practical	The advice from NICE has been incorporated directly into each relevant section, and Annex

		considerations in the treatment section; otherwise needs to come into the recommendations in relevant sections	5 cross-referenced in the introduction to section 5.
	JC	Clear and easy to follow	No action required.
	PG	Recommendation says 1st line carbamazepine for generalised tonic clonic seizures instead of sodium valproate as per NICE 2012. The order needs to be VPA Then LTG/ may consider OXZ / CBZ but beware of exacerbating absence/myoclonic. Similarly for Epilepsy with GTCs only.	This is a summary from the NICE guideline. They are listed in alphabetical order, not in order of which should be used first. This has been made clearer in the table.
	HC	It is unclear whether this has been updated from NICE, or whether as is?	The advice from NICE has been incorporated into each section, and an explanation that the SIGN searches were conducted from the time since the publication of NICE, has been added to the introduction to section 5.
	FB	I have some problems with these recommendations. Carbamazepine is an excellent antiseizure drug but it is an enzyme inducer and probably should not be first-line in the twenty-first century because of this. There is, in my opinion, inadequate information on adverse effects that might influence the choice of medication profoundly. This information could be added as a footnote. There is considerable evidence for adverse effects of some of the drugs listed in this table.	This table is a summary of the recommendations in the NICE guideline, and the new evidence base, in this SIGN guideline, and cannot be changed. Carbamazepine is one option, but there are other therapies also listed.
	JC	Quite complex to follow but probably appropriate for clinicians	No action required.
	IM	Not familiar with pathway – can't comment	No action required.
	HC	Useful	No action required.
	FB	This appears to be sound.	No action required.
	HC	Useful	No action required.
	FB	Again, this appears to be sound but has resource implications.	No action required.
	SD	Excellent - but SUDEP action's website was missing	This annex has been removed.
	HC	Useful	This annex has been removed.
	FB	It is good that this emphasises that SUDEP is rare in children. Should it be placed in context with other causes of death in children?	This annex has been removed.
	CR	It's not SUDDEN UNEXPLAINED - its SUDDEN UNEXPECTED (title)! Typo: but for a small number the risk (but for a small number of individuals....) Also being male at/after adolescence is a clearly demonstrated higher risk (vs female)	This annex has been removed.

		This bullet point does not make sense: Discussion with your child's doctor or nurse first. When you say: There is no evidence to support this. (to support monitoring devices reducing SUDEP), it may be important to emphasise why (as it may read that there is evidence that is negative - that disproves that these reduce SUDEP, this is not the case). There is no evidence to support these devices preventing SUDEP as such evidence would largely be impossible to obtain - a large population of people with epilepsy would have to be tracked for several years with half given a seizure alarm device and half not so that a difference in SUDEP outcomes could be proven (because the background rate of SUDEP is low at 1,4500/yr). This is impossible to ever prove. The absence of evidence does not mean that these do not help, it just means we can't prove it. We cannot prove that a parachute saves the lives of those jumping out of planes (as we would have to have people jump with and without one to study this) but we would not write 'There is no evidence to support this' for parachutes. Or to put it another way: has anyone ever done a study of not monitoring patients in hospital vs monitoring them and looked at outcomes, or not attending a seizure in hospital when alerted to one in a group of patients and studying their outcome vs those that were attended? We would not countenance this in a hospital setting, but we countenance that this can occur at home (that a child can be unattended in a tonic-clonic seizure overnight), because we have no population evidence that tells us that SUDEP is prevented by attending to this patient. It might be reasonable to re-word the sentence: There is no evidence to support this. -> There is evidence to support that co-sleeping can reduce the risk of SUDEP. It has not yet been possible to do studies to assess whether a range of other seizure detecting technologies can reduce SUDEP but they may reduce the risk of your child having an unattended seizure overnight. This would then allow you to attend to them more quickly, and be able to call for medical help if needed. The evidence for co-sleeping >10yo is presented earlier in the guideline and this is good evidence (and the only evidence) for surveillance (as the co-sleeper is a surveillance method) preventing SUDEP.	