NICE National Institute for Health and Care Excellence

Surveillance report 2018 – Epilepsies: diagnosis and management (2012) NICE guideline CG137

Surveillance report

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Surveillance decision

We will plan a full update of the guideline on epilepsies: diagnosis and management. In addition, editorial and factual corrections were identified. Full details of the surveillance review are included in appendix A: summary of evidence from surveillance.

Reason for the decision

There have been repeated warnings about the use of sodium valproate in women and girls of childbearing age because of its association with congenital malformations and developmental delay. NICE guideline CG137 was amended in January 2015 and February 2016 to reflect strengthened safety warnings on sodium valproate from the Medicines and Healthcare products Regulatory Agency (MHRA). Further regulatory action published in early 2018 needs to be reflected in the guideline: in the short-term, safety warnings in NICE guideline CG137 will be further strengthened, but as the guideline contains some recommendations for sodium valproate as a first-line treatment, NICE proposed that these should be reviewed in order to consider any new evidence around the risks and benefits of treatment with sodium valproate. This decision led to the current exceptional surveillance review, which considers evidence relevant to the full guideline.

There is new evidence available that impacts directly on the guideline recommendations:

- 1.3 Information includes broad recommendations on providing tailored information to people with epilepsy, their families and/or carers, on sudden unexpected death in epilepsy (SUDEP), how risks of SUDEP can be minimised, and on contacting families who have experienced SUDEP to offer support. There is new evidence that indicates nocturnal supervision may help to prevent SUDEP and that advice on this would be welcomed by families/carers; the recommendation could be strengthened by specifying the additional information that could be provided on SUDEP.
- 1.5 Diagnosis and 1.7 Classification were developed in 2004, since then the International League against Epilepsy (ILAE) has amended its classification, terminology and definitions of epilepsy and this change should be considered and reflected within these recommendations and in the terminology used throughout the guideline.
- 1.9 Pharmacological treatment:
    - There have been repeated warnings about the use of sodium valproate in women and girls of childbearing age because of its association with congenital malformations and

developmental delay. Regulatory action in early 2018 (comprising a contraindication in pregnancy and women of childbearing potential who are not taking effective contraception and the requirement for a pregnancy prevention plan) will need to be reflected in the guideline. The guideline contains some recommendations for sodium valproate as a first-line treatment, however new evidence suggests that other anti-epileptic drugs (AEDs) are more effective and have better safety profiles and may be alternatives to sodium valproate.

- New evidence demonstrates that new AEDs may be effective as first-line treatment where these are not currently recommended or only recommended as adjunctive treatment; new AEDs may also be effective as adjunctive treatment. This includes the effectiveness of zonisamide, and perampanel as first line treatments for focal seizures; and the use of brivaracetam as an adjunctive treatment for focal seizures.

- There is also evidence that supports the use of established AEDs, such as phenytoin as a first-line treatment for focal and generalised tonic-clonic seizures.

- New evidence supports the current recommendation of offering prednisolone or tetracosactide as a treatment for infantile spasms. Evidence also indicates that the combination of vigabatrin and prednisolone is more effective than either oral prednisolone or intramuscular tetracosactide used alone in short-term suppression of infantile spasms. There is also evidence that indicates sulthiame (which is not currently recommended) may halt seizures when used as an add-on therapy to pyridoxine.

- New evidence supports the use of cannabidiol as an adjuvant treatment of seizures associated with Dravet syndrome. However, this evidence would be reviewed as part of the proposed NICE technology appraisal (TA) on cannabidiol for adjuvant treatment of seizures associated with Dravet syndrome or Lennox-Gastaut syndrome, so will not be considered in the update of NICE guideline CG137, but a reference to the TA would be made if it is produced.

- New evidence indicates that the following pharmacological treatments that are not currently recommended may be effective: clobazam for drop seizures in children with Lennox–Gastaut syndrome and sulthiame as a treatment in children with benign epilepsy with centro temporal spikes.

- New evidence indicates that behavioural interventions such as intensive medication reminders (which are not currently recommended) can be good at improving adherence to treatment with AEDs.

- 1.11 Psychological interventions recommends that psychological interventions may improve quality of life for people with epilepsy, and highlights that they do not impact on seizure frequency. While the new evidence supports the current recommendation, it may also provide additional specific details concerning which psychological interventions can improve quality of life, and for whom.

- 1.13 Vagus nerve stimulation (VNS): new evidence indicates that for focal seizures, VNS stimulation using a high stimulation paradigm is significantly better than low stimulation in reducing frequency of seizures. VNS is recommended in the guideline for people with refractory epilepsy and focal seizures, but low and high stimulation are not differentiated; therefore the evidence on low versus high stimulation VNS should be considered in an update.

- 1.14 Prolonged or repeated seizures and convulsive status epilepticus advises on first-line treatment for children, young people and adults with prolonged or repeated generalised, convulsive seizures in the community that includes providing buccal midazolam or intravenous (IV) lorazepam. New evidence in status epilepticus indicates that intramuscular (IM) administration of midazolam is more effective than lorazepam IV for cessation of seizures, frequency of hospitalisation and intensive care unit admissions, hence evidence concerning midazolam IM should be considered in an update.

- 1.15 Women and girls with epilepsy advises on the information and advice that should be given to women and girls with epilepsy concerning AEDs and contraception, conception, pregnancy, caring for children, breastfeeding and menopause. As described previously, evidence indicates that using sodium valproate during pregnancy carries the highest risk of foetal malformation but there is also evidence indicating that other AEDs also have increased risks although some AEDs may be associated with no increased risk. Therefore, evidence concerning the use of AEDs in women and girls should be considered during an update.

- The new evidence described above is also relevant to the research recommendations on:
    - newly diagnosed seizures (focal and generalised) – monotherapy
    - epilepsy syndromes
    - treatment of convulsive status epilepticus (that is, not just refractory)
    - AEDs and pregnancy.

It is expected that the evidence relevant to these research recommendations will be considered as part of the guideline update process and research recommendations may change accordingly.

While for some sections of the guideline there was either no evidence identified or the evidence supported current recommendations, due to the proportion of the guideline affected by new evidence, we are proposing a full update.

We found new evidence that supports current recommendations on:

- 1.2 Coping with epilepsy
- 1.6 Investigations
- 1.8 Management
- 1.9.18 Withdrawal of pharmacological treatment
- 1.10 Referral for complex or refractory epilepsy
- 1.12 Ketogenic diet
- 1.16 Children, young people and adults with learning disabilities
- 1.18 Older people with epilepsy

We did not find any new evidence related to the following recommendations:

- 1.1 Principles of decision making
- 1.4 Following a first seizure
- 1.9.2 Initiation of pharmacological treatment and 1.9.16 Other epilepsy syndromes
- 1.17 Young people with epilepsy
- 1.19 Children, young people and adults from black and minority ethnic groups
- 1.20 Review

Nor did we identify any evidence that was relevant to the research recommendation on infantile spasms.

Overall decision

After considering the guideline content, all the evidence and views of topic experts, the surveillance team recommend that NICE guideline CG137 on epilepsies: diagnosis and management requires a full update.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 6 years after the publication of NICE guideline CG137 on epilepsies: diagnosis and management.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Previous surveillance update decisions for the guideline are on our website.

Evidence

We undertook a search for Cochrane reviews published between 11 September 2013 and 19 December 2017 that focused on diagnosing, treating and managing epilepsy and seizures in children, young people and adults in primary and secondary care. This identified 51 Cochrane reviews directly relevant to the majority of recommendation areas within the guideline, in particular in relation to pharmacological treatment.

However, as there was an absence of evidence concerning diagnosis, investigation and classification of epilepsy, we also undertook a focused literature search for quantitative studies published between 11 September 2013 and 23 January 2018 that focused on investigations and diagnosis of the epilepsies. This identified 67 relevant studies. Topic experts were also contacted for their views on the recommendations on diagnosis, investigation and classification of epilepsy.

A previous surveillance review decision in 2014 decided not to update the guideline as there was insufficient new evidence to invalidate the majority of the guideline recommendations.

We also checked for relevant ongoing research (6 studies identified), National Institute for Health Research (NIHR) signals (2 studies identified) and policy and guidance documents (3 documents identified).

We reviewed studies highlighted by topic experts for any potential impact on the guideline scope and remit, with 13 studies and 4 pieces of ongoing research meeting inclusion criteria.

All relevant abstracts were assessed for their impact on the recommendations within NICE guideline CG137. See appendix A for details of all evidence considered and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Five experts responded about NICE guideline CG137. They all indicated that the guideline should be updated. They highlighted that recommendations concerning pharmacological treatment require updating due to:

- New advice from the MHRA around the use of sodium valproate for management of epilepsy, particularly in girls and women of childbearing age.
- The availability of several new AEDs since the last revision of the guideline, including perampanel, and eslicarbazine.
- New research suggesting that the combination of vigabatrin and prednisolone is more effective than either oral prednisolone or intramuscular tetracosactide used alone in completely suppressing infantile spasms (West syndrome).
- Changes in the pricing of levetiracetam.
- The use of cannabidiol in children with refractory epilepsy (potentially from parents independently obtaining it), and a lack of information concerning its use, legality, safety and efficacy.
- Ongoing research in the area of the emergency management of acute tonic-clonic convulsions (and convulsive status epilepticus) in children in hospital.

Topic experts also suggested that a number of other areas should be updated:

- Treatment of epilepsy in the elderly, including atypical seizures in the very elderly, anti-epileptic drug use in patients with dementia.
- Access to specialist services and specialist nursing support for patients with learning disabilities in rural areas.
- Information on SUDEP and nocturnal supervision.
- The benefit of ketogenic diet in adults with severe refractory epilepsy.

Three experts responded concerning the additional request for their views on the diagnosis, investigation and classification of epilepsy recommendations. All topic experts indicated that the

recommendation on diagnosis should be updated and 2 indicated that the recommendations on investigation and classification should be updated. The new ILAE guidelines on diagnosis and classification of epilepsy, the potential role of genetic testing in diagnosing the underlying cause of seizures, and the ability to get useful information from functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scanning were cited as reasons for updating these recommendations.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because the decision was to update, we did not consult on the decision.

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