Brief: systematic literature review on epilepsy related deaths

Background
Epilepsy Action is a national charity. One of our key goals is to reduce the number of premature deaths from epilepsy. We will do this by:

- Providing advice and information about epilepsy.
- Raising awareness about epilepsy.
- Educating people about epilepsy.
- Providing a voice for epilepsy.

We have launched this project to investigate epilepsy related deaths. This will enable Epilepsy Action to produce resources and materials that will better inform people with epilepsy, their families and clinicians about epilepsy related death and ways to address risks.

Aim and motivation of the systematic review
Epilepsy Action is seeking an experienced researcher(s) to complete a systematic review of the evidence relating to epilepsy related death. Our motivation is to resolve conflicting evidence as to the usefulness of interventions in reducing risks, and highlight where future research is needed to improve current practice.

Epilepsy Action will seek to have the systematic review published in a relevant medical journal. This is because the completed review should help clinicians to quickly and easily understand the current evidence relating to epilepsy related deaths, and make practical decisions about potential interventions and how and when to discuss epilepsy related deaths.

The review will also highlight to Epilepsy Action where further qualitative research would be useful in answering concerns regarding raising awareness of, and discussing, epilepsy related deaths.

Topic and scope
Objectives
Provide Epilepsy Action and its members a comprehensive review of all the evidence relating to epilepsy related deaths. To include where appropriate to the research questions:

- SUDEP
- Status epilepticus
- Maternal deaths from epilepsy
- Comorbid depression and suicide
- Death of an adult or child from an accident that occurred during a seizure (for example a death from drowning, falling, road accident)

To assess the extent of benefits and harms of interventions used by healthcare professionals to reduce the risk of death associated with epilepsy. Including adult and child deaths from epilepsy related accidents, status epilepticus and SUDEP.

Selection criteria and search protocols
Selection of studies for the review and exclusions:
Evidence selection criteria will be finalised between the Reviewer, Epilepsy Action and our research review group prior to the review starting.

Selection criteria includes all relevant studies and evidence.

Eligible study designs (subject to agreement) might include all randomized controlled comparisons, anecdotal evidence, case reports and cross over trials – using such evidence will need to be justified in the methodology.

Exclusions include studies or evidence with a suspected of a high risk of bias.

**Resources and search engines for evidence search**

It will be necessary to use the following methods to search for relevant evidence:

- Grey literature – for example internal reports, conference presentations, posters
- Handsearching – of published journal articles and reports
- Reference lists – Epilepsy Action’s, advisors and Reviewer’s own collections of evidence
- Correspondence – contacts from other researchers, organisations, charities, epilepsy specialist.
- Electronic searches – to include trials registers and trials results registers, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE (if access is available to the Reviewer or their institution).
- Searching other resources – To include national and regional bibliographic databases, citation indexes, dissertations
- Any other sources suggested by the reviewer (to be agreed prior to the review starting).

**Methodology**

The appointed researcher must agree the research methodology to be used, including basis upon which cases will be selected for inclusion in the review, with Epilepsy Action and its chosen advisors BEFORE work commences. In line with normal protocol, the methodology will be included in the write up of the final review.

The method used to extract or obtain evidence and data for review will be agreed by Epilepsy Action and the Reviewer, prior to the review starting.

The method used to assess the risk of bias / methodological quality in included evidence and studies must also be agreed between Epilepsy Action and the Reviewer prior to starting the review.

The tools and statistical package used to complete any meta-analysis, results summary and interpretation of the results must also be agreed with Epilepsy Action.

**Tasks required to complete the review**

- Agree and complete protocol prior to starting the review including analysis framework
- Agree the statistical, bias and search methods that will be used
- Agree efforts to obtain unpublished information
- Gather evidence, studies, citations and reports
- Review gathered evidence, studies, citations and reports to decide which meet inclusion criteria
• Asses the quality if each piece of evidence, studies, citations and reports that meet inclusion criteria
• Identify and comment on the flaws in the evidence
• Compile analysis and review of the data (including following up missing data)
• Complete meta-analysis where able / relevant
• Interpret the results
  o Identify similarities and differences in the individual studies, and extent of benefits and harms of interventions
  o Identify where findings support each other, and conduct meta-analysis to draw useful conclusions
• Develop conclusions
• Develop discussion of areas for further research
• Suggest areas of further research to counteract some of the main flaws in existing evidence
• Write review using format agreed with Epilepsy Action, to produce a non-biased relevant and rigorous review of the literature that Epilepsy Action can seek to have published in a relevant medical journal.
• Submit to Epilepsy Action for peer review and feedback
• Update draft following peer review
• Second and third peer review if required
• Finalise the review
• Attend regular monthly review and update meetings (Skype, Google hangout or similar programme can be used to increase access and reduce travel burden).

**The maximum timeline that will be considered for this literature review:**

<table>
<thead>
<tr>
<th>Month</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Preparation of protocol.</td>
</tr>
<tr>
<td>2 – 5</td>
<td>Searches for published and unpublished studies.</td>
</tr>
<tr>
<td>2 – 3</td>
<td>Pilot test of eligibility criteria.</td>
</tr>
<tr>
<td>3</td>
<td>Pilot test of ‘Risk of bias’ assessment.</td>
</tr>
<tr>
<td>3</td>
<td>Pilot test of data collection.</td>
</tr>
<tr>
<td>3 – 5</td>
<td>Data collection.</td>
</tr>
<tr>
<td>4 – 5</td>
<td>Inclusion assessments.</td>
</tr>
<tr>
<td>4 – 6</td>
<td>Validity assessments.</td>
</tr>
<tr>
<td>4 – 6</td>
<td>Data entry.</td>
</tr>
<tr>
<td>6</td>
<td>Follow up of missing information.</td>
</tr>
<tr>
<td>6 – 8</td>
<td>Analysis.</td>
</tr>
<tr>
<td>8 – 9</td>
<td>Preparation of review report.</td>
</tr>
</tbody>
</table>

Please note that the above timeline represents the maximum timeframe that we will consider. This is not the desired timescale and Epilepsy Action welcomes applications that are based upon shorter timescales.

**Advice and information for interested reviewers.**

**Researcher / reviewer specifications**
Epilepsy Action is looking to work with a reviewer or researcher with:
• Previous experience of compiling systematic reviews
• Knowledge of completing meta-analysis across multiple studies
• Statistical expertise and access to statistical software - or access to free statistical expertise (for example fixed-effect, random-effects model)
• Experience of, and access too, tools or frameworks used to assess bias (for example, funnel plots, statistical tests, imputation)
• Knowledge of epidemiology and qualitative research methods in addition to statistical methods
• In-depth subject knowledge of epilepsy related deaths and/or SUDEP is not essential but might be advantageous
• Hold a research passport and/or access to a university library.

**Support available from Epilepsy Action**

• Epilepsy Action wishes to contract a researcher or research team to complete this systematic review. The maximum budget for this work is £6,000 - £9,000.
• The budget is payable at specific points throughout the contract. This will be discussed in further detail with the appointed researcher/research team.
• Ongoing support will be provided by Epilepsy Action’s Campaigns team and review group.
  o This includes agreeing the research protocol and selection criteria.
  o Reviewer is expected to pull evidence, articles and citations through journals and databases that they have access too through their academies, institutions or affiliations.
• Epilepsy Action will have the literature review peer reviewed by a panel of our clinical advisors and people with epilepsy, to ensure that the finished product is relevant to the healthcare and advice delivered to people with epilepsy and their families.
• Epilepsy Action will seek publication of the review. However, the reviewer must ensure that they are available to answer questions and complete additional enquiries raised by the peer review team at selected journals in connection with publication.
• Epilepsy Action will also seek to disseminate the important findings of this literature review through as many outlets as possible. This includes representation at public and professional conferences, wider publication of the whole or elements of the review in Epilepsy Action’s own publications Epilepsy Today, Epilepsy professional and website, and external consumer and trade publications.

**Notes for applicants**

Interested in working with us on this systematic review? Then please complete the interest form attached or online at epilepsy.org.uk/EDRreview. Applications close at 3pm on Monday 2 June 2014.

If you would like to ask a question about the review or the application process, please use the comments box facility at epilepsy.org.uk/EDRreview. Our answers to any questions asked will be posted on that page. This is to ensure that all potential candidates have access to the same information.
To ensure that all applicants are treated fairly, Epilepsy Action won’t provide additional information about the work to any interested parties.

**What will happen next?**
Epilepsy Action will discuss each application with a small advisory group made up of external and internal advisors.

**Funding**
This project is made possible by a grant from the Octavia Morris Memorial Fund. For more information about the fund please use the following web address:
octavia.morris.muchloved.com/

Please note applications close at 3pm on Monday 2 June 2014.