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Prognosis following a first unprovoked seizure

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Question

What is the risk of further unprovoked seizures and the risk of premature death in people presenting with a first unprovoked seizure?

Context

Approximately one in 25 people will have at least one unprovoked seizure during their life,. A single unprovoked seizure does not signify one has epilepsy as such diagnosis requires two or more unprovoked seizures, usually more than 24 hours apart. However, since a single unprovoked seizure is such a common event, it is important that clinicians can effectively counsel patients and their family on the risk of further unprovoked seizures (and therefore an epilepsy diagnosis) and the risk of premature mortality following their first seizure.

This Cochrane review therefore aimed to provide accurate estimates of the number of individuals going on to have further unprovoked epileptic seizures at certain timepoints following a first unprovoked seizure of any seizure type (or a cluster of epileptic seizures within a 24-hour period or a first episode of status epilepticus). Additionally, it also aimed to provide accurate information on the risk of premature death.

Criteria for study selection

The review included both retrospective and prospective studies of people of all age groups (except neonates) with a single unprovoked seizure of any type who were followed up for at least 6 months. Studies had to include at least 30 participants. Moreover, studies on mortality had to report a proportional mortality ratio (PMR) or a standardized mortality ratio (SMR) at a specific timepoint to be included.

As unprovoked seizures are the focus of this review, studies on people who had seizures that occurred due to precipitant or provoking factors, or in close proximity to a neurological insult were excluded. Studies on situational seizures such as febrile convulsions were also excluded.

Summary of the results

The authors identified 58 studies with a total of 12,160 participants (median 147, range 31 to 1443) of which 26 studies were pediatric studies, 16 were adult and the remaining 16 combined pediatric and adult populations.

In this Cochrane Corner we will focus on the results of the pediatric population and the mixed (children and adults) populations and less on the adult-only population.

Only studies that reported seizure recurrence data at 6, 12 and or 24 months were included in meta-analysis. This was the case for 46 studies of which 23 were pediatric, 13 adult and 10 had a combined population. Seizure recurrence estimates for time points beyond two years could not be provided as most studies had short follow-ups and too few reported data at a single time point after two years.

At six months the estimated overall seizure recurrence for the whole population (mix of adult and children) is 27% (95% CI*: 24% to 31%; 27 studies, 7111 participants, moderate-certainty evidence). At one year the recurrence is 36% (95% CI: 33% to 40%; 34 studies, 6843 participants, moderate-certainty evidence) and it is 43% at two years (95% CI: 39% to 47%; 27 studies, 6908 participants, moderate-certainty evidence).

In the children subgroup analysis, the seizure recurrence estimates are slightly higher: 30% at six months (95% CI: 23% to 37%; 14 studies, 2232 participants, moderate-certainty evidence), 38% at one year (95% CI: 31% to 44%; 16 studies, 2313 participants, moderate-certainty evidence) and 45% at two years (95% CI: 36% to 54%; 12 studies, 2172 participants, moderate-certainty evidence). In the adult subgroup the recurrence estimates were slightly lower than the mixed population.

The included evidence was of moderate certainty. The main limitation was the clinical and methodological heterogeneity caused by some studies that had quite extreme results compared to others. The clinical heterogeneity was somewhat expected as there was variation in the age groups that were included in the studies and treated and untreated individuals were usually combined. However, most studies did show consistent results and the review authors thought the heterogeneity did not impact on the overall results too much.

Results relating to mortality following a first unprovoked seizure were reported in nine studies including 2373 participants, but the data could not be combined in a meta-analysis due to the variability in the reported results. The data did seem to support the consensus that the underlying etiology is the main driver determining the risk of mortality with a first unprovoked seizure, however the authors did not undertake any formal assessment of prognostic factors for mortality in this review.

Conclusion and implications for practice

Seize recurrence estimates after one unprovoked seizure ranged from 30% at 6 months, 38% at 1 year to 45% at 2 years in children. Clinicians can use this information when counselling patients and their families. However, long-term recurrence data, especially beyond 10 years, is still lacking.

REFERENCE:

Neligan A, Adan G, Nevitt SJ, Pullen A, Sander JW, Bonnett L, Marson AG. Prognosis of adults and children following a first unprovoked seizure. Cochrane Database of Systematic Reviews 2023, Issue 1. Art. No.: CD013847. DOI: 10.1002/14651858.CD013847.pub2.

Access the full text of this review via the Cebam Digital Library for Health (www.cebam.be/nl/cdlh or www.cebam.be/fr/cdlh).