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Review

Mortality in people with intellectual disabilities and epilepsy: A systematic review

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ABSTRACT

Purpose: Epilepsy is highly prevalent in people with intellectual disabilities and mortality is increased in people with epilepsy generally. This review summarises research on the comparative risk of mortality in people with intellectual disabilities and epilepsy compared to the general population, people with intellectual disabilities without epilepsy, and people with epilepsy without intellectual disabilities.
Method: Studies were identified via electronic searches using Medline, Cinahl and PsycINFO and cross-citations. Information extracted from studies was tabulated and reviewed narratively.
Results: Sixteen studies met the inclusion criteria. Epilepsy was associated with increased mortality in people with intellectual disabilities in most studies, particularly in those experiencing recent seizures. Further research is needed to substantiate some of the reported findings.
Conclusion: Services must be equipped with the skills and information needed to manage this condition in order to minimise the risk of death in people with intellectual disabilities and epilepsy.

1. Introduction

Epilepsy is one of the most common serious brain disorders, affecting over 50 million people worldwide [1]. The prevalence of epilepsy has been estimated at approximately 0.5–1.0% of the general population [2–4]. In people with intellectual disabilities, estimates of the prevalence of epilepsy vary due to differences in the methods used and inherent population biases [5]. Despite this variation, it is clear that the prevalence of epilepsy in people with intellectual disabilities is much greater than in the general population [6]. Reported rates range, for example, from 16.1% of 1595 people with intellectual disabilities identified in South Wales [7] to 30.7% in a random sample of 753 people with intellectual disabilities aged 40 or more from Ireland's National Intellectual Disability Database (NIDD) [8]. In a systematic review of the prevalence of chronic health conditions in children with intellectual disabilities, the most common condition was epilepsy [9] with prevalence rates in the 14 studies identified ranging from 5.5% to 35.0%, with an overall weighted mean prevalence rate of 22.0% (95% CI 20.8, 23.2).

Mortality is increased in people with epilepsy, with a recent systematic review and meta-analysis of 38 epilepsy cohorts including over 165,000 patients finding a pooled relative risk of death of 3.3 (95% CI 2.83, 3.92) compared to the general population [10]. Risk of premature death was lowest in idiopathic epilepsy and in people with epilepsy who had attained seizure freedom.

People with epilepsy may have elevated mortality from external causes such as accidents including drowning [11]. However, Sudden Unexpected Death in Epilepsy (SUDEP) is the most important category of epilepsy related death [12]. In the UK it is estimated that 500 deaths per annum are SUDEP [13]. Overall findings regarding the risk of SUDEP in people with intellectual disabilities are inconsistent. One systematic review of risk factors for SUDEP based on 27 studies found that 'mental retardation' was not a risk factor for SUDEP [14]. However, it is not clear how many studies in the review included intellectual disability as a risk factor. A more recent review identified 23 articles which considered intellectual disability and SUDEP of which 14 found intellectual disability to be a risk factor for SUDEP and none found intellectual disability to be a protective factor in SUDEP [15].

For people with intellectual disabilities, epilepsy or convulsions has been identified as an important and to some extent potentially preventable cause of death [16]. The study looked at ages and causes of death recorded on death certificates for people with

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intellectual disabilities, or conditions that can cause intellectual disabilities, who died between 2004 and 2008 in England. Epilepsy or unspecified convulsions were involved in 948 deaths (13% of those identifiable) of people with intellectual disabilities or possibly associated conditions. In other people, they were involved in 0.4%. Based on Standardised Mortality Odds Ratios (an approximation of the Standardised Mortality Ratio), adjusting for ages at death, people where death involved epilepsy or unspecified convulsions were 9.7 times more likely than others to have an intellectual disability-related condition (95% CI 9.1, 10.4).

The high prevalence of epilepsy in people with intellectual disabilities, combined with the increased risk of mortality in people with epilepsy, makes the topic of mortality in people with intellectual disabilities and epilepsy a pertinent one. This review aims to summarise studies on mortality in the general population of people with intellectual disabilities and epilepsy and as such it excludes studies on specific syndromes associated with intellectual disabilities. However, the review does include information relating to people with Down syndrome which is by far the most common chromosomal disorder associated with intellectual disability with a prevalence of approximately 1 in 700 live births [17]. Most early studies of mortality in people with intellectual disabilities and epilepsy were hospital based, with an early search of the literature finding no population-based studies including all types of intellectual disabilities on the influence of epilepsy on mortality [18]. Since that time, further studies have been conducted, including population-based studies. In this review, we summarise existing research published from 1990 that quantifies the mortality of people with intellectual disabilities and epilepsy using a comparative statistic relative to either the general population, people with intellectual disabilities who do not have epilepsy, or people with epilepsy who do not have intellectual disabilities. The statistics reported are defined in Table 1. For all of these, a value of one implies no difference between the two groups, a value of more than one indicates that the risk is greater in the target group, and a value of less than one indicates that the risk is less in the target group. For example, a hazard ratio of two implies double the risk of dying in the target group than in the comparison group. If the hazard ratio is 0.5 then the relative risk of dying in the target group is half the risk of dying in the comparison group. For all of these statistics, the value can be considered statistically significant at $p < .05$ if the 95% confidence interval does not include one.

2. Method

Electronic literature database searches were conducted in Medline, Cinahl and PsycINFO on EBSCO. In addition, the reference lists of articles meeting the inclusion criteria were searched and articles from authors' personal collections included. The reference lists of key book chapters were also searched [19–21]). Searches were completed on 19 June 2014. Searches included terms relating to both mortality and prevalence to create a pool of articles on mortality or prevalence, with articles on prevalence being retained for a separate review. Searches combined terms for epilepsy, intellectual disabilities, and mortality/prevalence with the Boolean operator 'AND'. Full details of the search terms are given in Appendix One.

Table 1
Definitions for statistics reported.

Term	Definition
Standardised mortality ratio (SMR)	Number of observed deaths in the target population divided by the number of deaths that would be expected based on death rates of a chosen standard population
Relative risk or risk ratio	The risk of an event (e.g. death) in the target population divided by the risk in the comparison group
Hazard ratio	A specific type of relative risk which is obtained using the Cox Proportional Hazards Model, a regression model that takes into account time until the event occurs
Odds ratio	The odds (number of times an event happens divided by the number of times it does not happen) of an event occurring in one group divided by the odds of the same event in another group

2.1. Inclusion criteria

- Peer reviewed.
- English language full text.
- Published from 1990; articles published before this date were excluded as they predate both improvements in epilepsy treatment and major changes in service provision for people with intellectual disabilities [22].
- Primary research.
- Presents a comparative statistic (e.g. relative risk, standardised mortality ratio (SMR), hazard ratio) on mortality in adults or children with intellectual disability and epilepsy compared to the general population, people with intellectual disability without epilepsy, or people with epilepsy without intellectual disability.
- Samples of adults or children with intellectual disabilities or samples where 50% or more have intellectual disabilities or mixed samples where results are disaggregated for people with intellectual disabilities.

2.2. Exclusion criteria

- Case studies.
- Case series.
- Narrative reviews.
- Studies based on neonates (new born infants up to 28 days after birth), all other age groups were included.
- Studies on conditions where intellectual disabilities cannot be assumed (e.g. cerebral palsy, autistic spectrum disorder (ASD)) where results were not disaggregated for people with intellectual disabilities.
- Studies on specific syndromes associated with intellectual disabilities with the exception of Down syndrome. Less common syndromes were excluded, such as Fragile X syndrome which has a prevalence of 1 in 4000 males and 1 in 8000 females [23] and is not always associated with intellectual disabilities [17].
- Does not present a comparative statistic approximating relative risk (e.g. presents only descriptive statistics, presents chi-squared analysis).

Initially, titles and abstracts were used to exclude those studies which were obviously not within the scope of reviews on prevalence or mortality. Those retained for further screening were those for which relevance could not be assessed without accessing full text, or those that were chosen as potentially within scope. These studies were screened by the first and second author and discussed until consensus was reached on whether or not they met the inclusion criteria in relation to mortality in people with intellectual disabilities and epilepsy.

Where multiple articles used the same sample or samples were likely to have considerable overlap (e.g. [24,25]), only the most recent study was included unless the studies were looking at different topics within the same sample (e.g. [29,25] are based on