A systematic review of prevalence and incidence studies of dementia with Lewy bodies

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Abstract

Background: substantial variation in the prevalence of Dementia with Lewy Bodies (DLB) has been reported with estimates ranging from 0 to 26.3% of all dementia cases, potentially making it the second most common dementia subtype.

Objectives: the aim of this study was to review systematically and critically for the first time previous studies of the clinical prevalence and incidence of DLB in the population.

Methods: a systematic literature search was performed using PubMed. Selected articles had to describe an original study that provided a prevalence and/or incidence number for the whole population for DLB as defined by pre-set clinical criteria and findings.

Results: six studies reporting the prevalence of DLB and one study reporting the incidence of DLB met the inclusion criteria. Prevalence estimates, depending on case criteria, range from 0 to 5% with regard to the general population, and from 0 to 30.5% of all dementia cases. The only estimate for DLB incidence is 0.1% a year for the general population and 3.2% a year for all new dementia cases. The number of available studies was too small to hypothesise on the potential effect of age, sex and genetic background on the results.

Conclusions: although the literature on the prevalence and incidence of DLB is limited, there is a general consensus that DLB must be considered in the range of neurodegenerative conditions in the elderly. The move towards use of consensus criteria facilitates comparison and is welcome. Their application in a more routine way towards rigorously defined and selected study populations will lead to more comparable and generalisable studies in the future.

Keywords: dementia with Lewy bodies, Parkinson’s disease dementia, prevalence, incidence, population, elderly

Introduction

Dementia covers a wide range of symptoms of disease and there has traditionally been an effort to divide it into various subtypes defined by specific criteria and their timing of onset.

The term Dementia with Lewy Bodies (DLB) arose from the 1996 proceedings of the First International Workshop of the Consortium on Dementia with Lewy Bodies [1]. Before this, there were several terms to describe the appearance of Lewy bodies in dementia. Amongst these were diffuse Lewy body disease, Lewy body variant of Alzheimer’s disease, senile dementia of the Lewy body type and Alzheimer disease with concomitant Lewy body disease. It was recognised that they have overlapping clinical and pathological features and debate continues as to whether these represent the same disease approached from different perspectives.

DLB has been suggested to be the second most common type of degenerative dementia in older people [2]. According to previous reports on the frequency of occurrence of DLB in non-population-based studies, estimates for prevalence varied between 3.0% [3] and 26.3% [4] of all demented cases over the age of 65 years. This is similar to estimates from autopsy series, which have ranged between 15 and 25% [5, 6]. Prevalence and incidence studies are important for both health-care planning and epidemiological research as they provide essential knowledge to assess the burden of a condition within a population. This systematic review is the first to be conducted and employs strict methodological inclusion and exclusion criteria of published and available literature on the estimation of population prevalence and incidence of DLB.

Methods

Search strategy

A systematic literature search was performed in December 2004 using the entire time scale of PubMed without using any language restrictions. Mixture of the following key words were used to perform multiple searches: dementia...
(MeSH), Lewy body dementia (MeSH), incidence (MeSH) and prevalence (MeSH). 221 titles and abstracts were read and a preliminary list of papers that could possibly describe prevalence and incidence studies of DLB were selected. If in doubt and if the abstracts were absent, the reference was included. Reference lists of retrieved articles were checked to see if any further articles could be found. The search continued until it was clear that no new references were being retrieved. Seven studies were selected for this review.

**Study inclusion criteria**

Predefined criteria were applied to select the final list of articles to be included in the review. Articles had to describe an original study that provided a prevalence and/or incidence number for the whole population (not restricted by referral patterns or type of residence) for Dementia with Lewy bodies as defined by any pre-set clinical criteria (whether they are based on McKeith 1996 criteria [1] or not). Prevalence is the number of cases existing at a given time in a given population usually expressed as a percentage [7]. Incidence is the number of instances of illness commencing during a given period in a specified population [7].

**Data extraction and validity assessment procedure**

All data about the methodology and results from each study included were extracted using a proforma form for data collection. Information was recorded about the study’s location and population, the sources used to identify possible cases, methods to identify included cases along with the inclusion and exclusion criteria. Decisions to include or exclude a study and the information retrieved were compared between all three authors. Discrepancies were discussed and agreement was achieved by consensus.

**Results**

Two hundred and twenty one articles (221 identified from electronic searches, no additional articles from reviewing reference lists) were examined. Of these 214 were excluded mainly because they were not original descriptions of population prevalence and incidence studies or did not investigate DLB as one of their dementia subtypes.

**Study methodology**

**Methods used to define base population**

By definition, all included studies were population-based. Most of the studies used recent census figures to define their base population. One used a door-to-door survey method [8] (Table 1). Exclusion criteria were based on age, ethnic background and place of residence only. Clinical prevalence was measured in those over 65 in four studies [8–11], those over 70 in one study [12] and those over 75 in one study [13]. Incidence was measured in those over 65 in one study [14].

Response rates in the studies assessing the prevalence of DLB were reasonable to excellent and ranged from 78 to 100% with a resulting group size ranging from 157 to 3715 participants.

**Method of recruitment**

The method of choice to study the prevalence and incidence of dementia and its subtypes is using a two-phase design where the total population or a random sample is screened for the presence of dementia followed by clinical assessment of positively screened cases [15]. This design eliminates reliance on referral cases within a health care system. This method of recruitment was used in all retained studies here (Table 1).

**Diagnostic criteria for case inclusion**

**Dementia diagnosis**

All studies used the DSM-III-R or DSM-IV criteria to diagnose dementia.

**Diagnosing DLB**

Five prevalence studies reported using the McKeith 1996 criteria [1, 8, 10–13] while one used a modified McKeith 1995 criteria [16] with no restriction on duration of Parkinson’s disease (PD) [9]. The Cache County study did not give an account of the methods used for differential diagnosis within the existing published papers but contact with the investigators has provided confirmation that the McKeith 96 guidelines were used. Authors were contacted as the study was the only true existing population-based study of the DLB incidence identified from the literature.

**Study results**

Prevalence estimates for clinical DLB range from 0 to 5% with regard to the general population, and from 0 to 30.5% of all dementia cases. The Cache County study provides the only incidence report, estimated at 0.1% a year for the general population and 3.2% a year for all new dementia cases (Table 2). Six studies did not report on the sex of those diagnosed while one reported that they were all men [8]. Further collected information on the retrieved studies can be found in Tables 1 and 2.

**Discussion**

This is the first systematic review of all population prevalence and incidence studies of clinically diagnosed DLB. There are six population-based studies of prevalence of DLB and one population-based study of the incidence of DLB included. Prevalence estimates for clinical DLB, depending on case criteria, range from 0 to 5% in regards to the general population, and from 0 to 30.5% of all dementia cases. According to the Cache County study, the estimate for DLB incidence is 0.1% a year for the general population and 3.2% a year for all new dementia cases.

**Studied populations**

The estimates for DLB prevalence reported for true population-based studies are generally lower than those from other types of samples (as described in the Introduction). This is particularly marked if the estimates based on the McKeith 96 criteria are compared. Prevalence estimates for DLB then drop to 0–5% of the general population and 0–21.9% of all dementia cases.
Table 1. Description of population-based studies reporting the prevalence or incidence of DLB

<table>
<thead>
<tr>
<th>Study</th>
<th>Base population (size of eligible population)</th>
<th>Method of recruitment</th>
<th>Size of contacted population (no. recruited)</th>
<th>Age group</th>
<th>Diagnosis personnel</th>
<th>Dementia criteria</th>
<th>DLB criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herrera (2002)</td>
<td>Urban Catanolava, Brazil (6624)</td>
<td>Random sample in defined geographical area</td>
<td>1681 (1656)</td>
<td>&gt;65</td>
<td>Neurologists</td>
<td>DSM-IV ADRDA AIREN</td>
<td>McKeith 96</td>
</tr>
<tr>
<td>Rahkonen (2003)</td>
<td>Urban Kuopio, Finland (4518)</td>
<td>Random sample in defined geographical area</td>
<td>703 (601)</td>
<td>&gt;75</td>
<td>Neurogeriatrists</td>
<td>DSM-III-R DMS-IV</td>
<td>Mc Keith 96</td>
</tr>
<tr>
<td>Stevens (2002)</td>
<td>Urban North London, UK (1276)</td>
<td>Random sample in defined geographical area</td>
<td>1276 (1085)</td>
<td>&gt;65</td>
<td>Medical doctors and psychiatrists</td>
<td>ICD 10 DSM-IV ADRDA AIREN</td>
<td>McKeith 95 with no restriction of duration of PD</td>
</tr>
<tr>
<td>Yamada (2002)</td>
<td>Japanese Brazilian residents of Campo Grande, members of the Okinawa Kenjinkai association, Brazil (200)</td>
<td>Random sample contacted by mail</td>
<td>– (157)</td>
<td>&gt;70</td>
<td>Neurologists</td>
<td>DSM-III-R ADRDA AIREN</td>
<td>McKeith 96</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miech (2002)</td>
<td>Cache County, Utah US (5677)</td>
<td>Whole community</td>
<td>5677 (5092)</td>
<td>&gt;65</td>
<td>Neuropsychologists, geriatric psychiatrists, research nurse and psychogeriatrician</td>
<td>DSM-III-R</td>
<td>McKeith 96 (personal communication)</td>
</tr>
</tbody>
</table>
Table 2. Prevalence and incidence of DLB in population-based studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Numbers screened</th>
<th>Age</th>
<th>Dementia/population</th>
<th>DLB/population</th>
<th>DLB/dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Silva (2003)</td>
<td>703</td>
<td>&gt;65</td>
<td>4.0% (28/703)</td>
<td>0.1% (1/703)</td>
<td>3.6% (1/28)</td>
</tr>
<tr>
<td>Herrera (2002)</td>
<td>1656</td>
<td>&gt;65</td>
<td>7.1% (118/1656)</td>
<td>0.1% (2/1656)</td>
<td>1.7% (2/118)</td>
</tr>
<tr>
<td>Rahkonen (2003)</td>
<td>601</td>
<td>&gt;75</td>
<td>22.8% (137/601)</td>
<td>5.0% (30/601)</td>
<td>21.9% (30/137)</td>
</tr>
<tr>
<td>Stevens (2002)</td>
<td>1085</td>
<td>&gt;65</td>
<td>6.6% (72/1085)</td>
<td>2.0% (22/1085)</td>
<td>30.5% (22/72)</td>
</tr>
<tr>
<td>Yamada (2001)</td>
<td>3715</td>
<td>&gt;65</td>
<td>3.8% (142/3715)</td>
<td>0.1% (4/3715)</td>
<td>2.8% (4/142)</td>
</tr>
<tr>
<td>Yamada (2002)</td>
<td>157</td>
<td>&gt;70</td>
<td>12.1% (19/157)</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Incidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miech (2002)</td>
<td>5092</td>
<td>&gt;65</td>
<td>3.6% a year (185/5092)</td>
<td>0.1% a year (6/5092)</td>
<td>3.2% a year (6/185)</td>
</tr>
</tbody>
</table>

Prevalence and incidence can only be estimated from cases derived from defined populations. Within a defined population, there are two main options for case finding. The first is by relying on referrals from various health care services and patients' groups that serve this known population. The second is direct examination of the whole population sample. The latter is particularly valuable for direct generalisation of findings for two main reasons. Firstly, it is already acknowledged that the total dementia ‘burden’ in most populations is not identified. Many dementia cases go unnoticed by the health care system since there is no organised population-based effort directed at the early detection of dementia [17]. Secondly, selection bias caused by the referral of patients from primary to secondary or tertiary care centres can directly affect results of clinical or epidemiological studies [18]. Thus despite the rapid progression of DLB along with the visual hallucinations and parkinsonism commonly found in this disorder, it is not known whether the prevalence of DLB is truly lower in the general population than in a referred group as these are groups with different denominators.

Many of the retrieved studies looking at the burden of DLB based their analysis on groups already referred to the health care system and thus were not retained for analysis in this systematic review [4, 19–21]. In all retained studies, base-populations were defined using census data [9–11, 13, 14, 22] or by a door-to-door survey [8]. In the chosen studies, there were no selection criteria apart from age, ethnic background and place of residence. This offers the best guarantee that the results from the studied cohort will reflect occurrence in the population. The Cache County Study illustrates the necessary attention to the population base with high basic response and follow-up rates [14]. By definition, all selected studies have also screened participants who live in institutions. This is because DLB has unknown prevalence in both community and institutional settings. Studies such as the community-based SALSA study were not selected here. The SALSA study included 1789 self-designated Latino residents, including from assisted care facilities, of Sacramento but did not include nursing homes [22]. Its estimate for DLB prevalence using the McKeith 1996 criteria is 0.05% with a dementia prevalence estimate of 4%.

**Findings according to case criteria**

ICD and DSM have not incorporated diagnostic criteria for DLB, which has hampered attempts to identify it in population-based epidemiological studies of dementia subtypes. For example, no separate category of cortical Lewy body disease was made in the Honolulu Asia Aging Study because White and co-workers felt it was too difficult to make a valid diagnosis without the benefit of autopsy findings [23]. The advent of diagnostic guidelines, such as the 1996 Consensus criteria [1], has allowed its inclusion in more recently initiated epidemiological surveys with assessment by clinicians. Five prevalence studies used the McKeith 1996 criteria [8, 10, 11, 13, 22] while one used a modified McKeith 1995 criteria with no restriction on duration of PD [9]. The McKeith 1996 criteria are considered to be specific for the diagnosis of DLB although not particularly sensitive [24]. The Stevens (2002) study used rigorous methodology and diagnostic criteria and explored the relationships between the application of those criteria on the 107 people they found to be demented, 22 of whom with a diagnosis of DLB (21%) (7 probable, 15 possible). Application of DSM IV to the seven probable cases resulted in a diagnosis of four people with Alzheimer’s disease (AD), one with vascular dementia, one with Parkinson disease dementia (PDD) and one unspecified (similarly with ICD-10). This suggests that in studies using only the main psychiatric diagnostic criteria that do not include DLB, cases will be forced into an AD diagnosis.

The Finnish study undertaken in the city of Kuopio reported the highest prevalence of DLB using the McKeith 96 criteria, at 21.9% [13]. It was specifically designed to estimate the prevalence of DLB in a general population of older people (75 years and older). The major source of diagnostic difficulty was reported to be the reliable identification of fluctuating cognition despite lengthy examination and proxy interviews. The authors also note that the DLB cases were at a less severe stage of dementia and that the greater the severity the more AD and DLB became similar. The five remaining studies of DLB prevalence measured with the McKeith 96 guidelines had similar low levels of DLB as a percentage of the whole population (0–0.1%) and of all dementias (0–3.6%). Only the Cache County incidence study and the study by Stevens et al. reported whether participants were probable or possible DLB cases [9, 14, 22]. Prevalence rates reported in studies led by neurologists (0–2.8%) are different from those reported by other specialists, such as psychiatrists and geriatricians (3.6–30.5%). A systematic comparison will have to be made of diagnostic practices across specialties to understand their potential impact on differential diagnosis. It may be due to a different emphasis on clinical phenotypes with psychiatrists asking about and detecting psychiatric symptoms (diagnosing DLB) and
neurologists about neurological and neuropsychological profiles (e.g. diagnosing frontotemporal dementia).

**Chances of misdiagnosis**

As in DLB, PDD is characterised by dementia and parkinsonism. The clinical profile of DLB and PDD is similar [25, 26] and the nosological relationship between DLB and PDD is not yet clear [27]. Thus, it would not be surprising if some patients with PDD were diagnosed as DLB, and vice versa [28]. At present for the subgroup of DLB cases which have motor symptoms, DLB is diagnosed if dementia occurs before or within 1 year after onset of parkinsonism, whereas PDD is diagnosed if dementia occurs more than one year after onset of parkinsonism [1]. A recent systematic review of PDD has reported its prevalence in the general population aged 65 and over as 0.2–0.5% [29], which is within the range reported here for DLB. However, in all the studies included in this review the study by Stevens and co-workers, the issue of DLB or the timing of onset of parkinsonism and cognitive impairment was not reported. PDD was not even considered as a possible diagnosis. It is possible that some DLB patients should in fact have been diagnosed as PDD. On the other hand, the same Stevens et al. study could have over diagnosed DLB by using this diagnosis regardless of the duration of parkinsonism before dementia [9].

During the systematic search for this review, only one study (the Hisayama study) was found to report neuropathological information from a population-based cohort in relation to the clinical diagnosis of DLB. DLB autopsy prevalence rates depend not only on the prevalence or incidence of DLB in the living population but also on the mortality associated with the DLB condition. In this study, 11.7% of the 105 coming to autopsy were clinically diagnosed with DLB using the McKeith 96 guidelines (equal to 17.4% of all dementia cases) [30]. Until further population based autopsy studies report in this way, it is uncertain what this suggests about rates of clinical diagnosis of DLB in other studies.

**Investigation of potential risk factors**

No relationship between sex and DLB prevalence emerged from the included studies. The only study which reported results by sex has too few to draw any conclusion with four men diagnosed with DLB and no women [8]. Case series have reported DLB to be more common in men than women suggesting a similar pathogenesis to Parkinson’s disease [31]. No prevalence estimates were broken down by age group although there seems to be a link between the two, with an increase in reported prevalence of clinical DLB with age (see Figures 1 and 2). Studies using the same diagnostic criteria for DLB (McKeith 96) and focusing on cohorts aged 65 and over were located in a city in Brazil [11], an urban area in Sri Lanka [10] and a rural town in Japan [8]. Each showed similar prevalence of DLB (0.1%) which does not indicate dramatic environmental factors that may affect participants differently depending on their place of residence.

**Conclusion**

Although the literature on the prevalence and incidence of DLB is limited, there is a general consensus that DLB must be considered in the range of neurodegenerative conditions in the elderly. There are so few true population-based studies that it would be valuable for all seven population-based prevalence and incidence studies included here to report their findings by age group. Varying prevalence rates could give vital clues to aetiology, especially given their wide geographical and potentially genetic spread. The move towards use of consensus criteria facilitates comparison and is welcome. Their application in a more routine way towards rigorously defined and selected study populations will lead to more comparable and generalisable studies in the future.

**Key points**

- This is the first systematic review of population-based estimates for prevalence and incidence studies of DLB.
- Estimates for DLB prevalence range from 0 to 5% with regard to the general population, and from 0 to 30.5% of all dementia cases.
- Only estimate for DLB incidence is 0.1% a year for the general population and 3.2% a year for all new dementia cases.
- The move towards use of consensus criteria facilitates comparison and is welcome.
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References


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