Accuracy of clinical diagnosis of dementia with Lewy bodies: a systematic review and meta-analysis

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Introduction

The identification of DLB as a distinct disease is relatively recent. Its diagnosis is based on diagnostic criteria, which were updated over the years. Our aim was to perform a systematic review of the studies on diagnostic accuracy in dementia with Lewy bodies (DLB) and to meta-analyse sensitivity, specificity and accuracy of the used diagnostic criteria, in order to evaluate how they changed over time.

Methods

Systematic review

We performed electronic searches of MEDLINE and SCOPUS databases. We performed the last search on December 2015. We excluded abstracts and chapters of book. We included articles if they reported any of diagnostic parameters or raw data, specifically regarding the clinical diagnosis of DLB. We decided to perform the meta-analysis only on those studies that used pathological examination as gold standard. We excluded the studies not specifying the criteria used or using multiple diagnostic criteria. Two authors (GR and RS) independently performed the literature search, selected all potentially relevant papers, screened the full texts, and extracted data from the eligible studies. Disagreements were resolved by asking the opinion of a third reviewer (GL).

Data preparation

We evaluated the different diagnostic criteria used, and if the criteria were applied in the early (<3 years) or later stage of disease (>3 years). We defined three categories of diagnostic criteria: **"criteria antecedents to those of McKeith 1996", "McKeith criteria 1996"** and **"McKeith criteria 2005".** Some studies reported accuracy based on different diagnostic criteria in the same population and on diagnosis of possible or probable separately. These studies were included in the meta-analysis with more than one record. When the diagnosis was not distinguished between possible and probable, we considered the diagnostic parameters as for a diagnosis of possible DLB (actually possible + probable).

Given that PPV and NPV are more conditioned by the different proportion of patients with DLB or other diseases evaluated in each specific setting, and therefore less generalizable, we only meta-analyzed sensitivity, specificity, and accuracy values.

Statistical analysis

Bayesian meta-analyses of available data were performed. Bayesian methods offer a flexibility, which allows the approach to be extended to consider complex likelihood functions other than Normal. Bayesian methods might also perform better and provide robust credible intervals in applications with a relatively small number of studies.

Results

Figure 1. Flow-chart of electronic search: selection of included studies

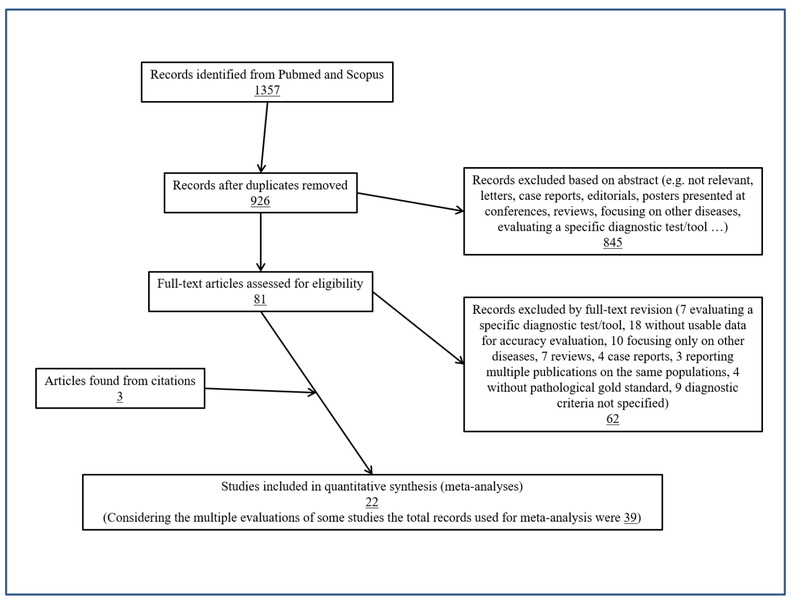
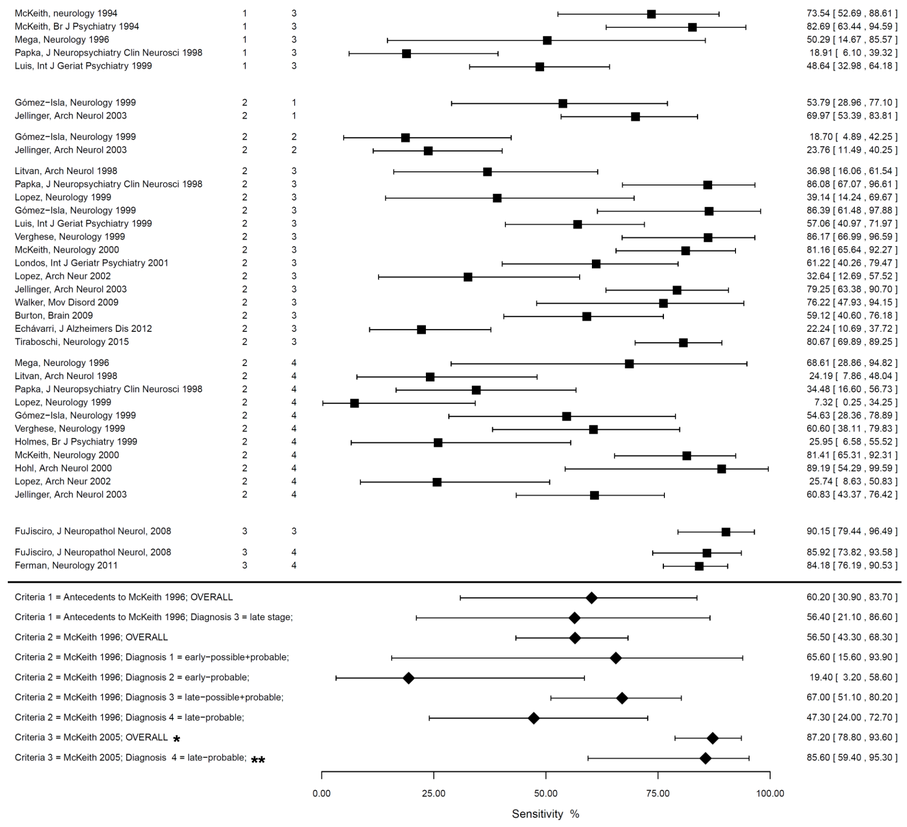


Table 1. Records from the studies included in the meta-analyses.

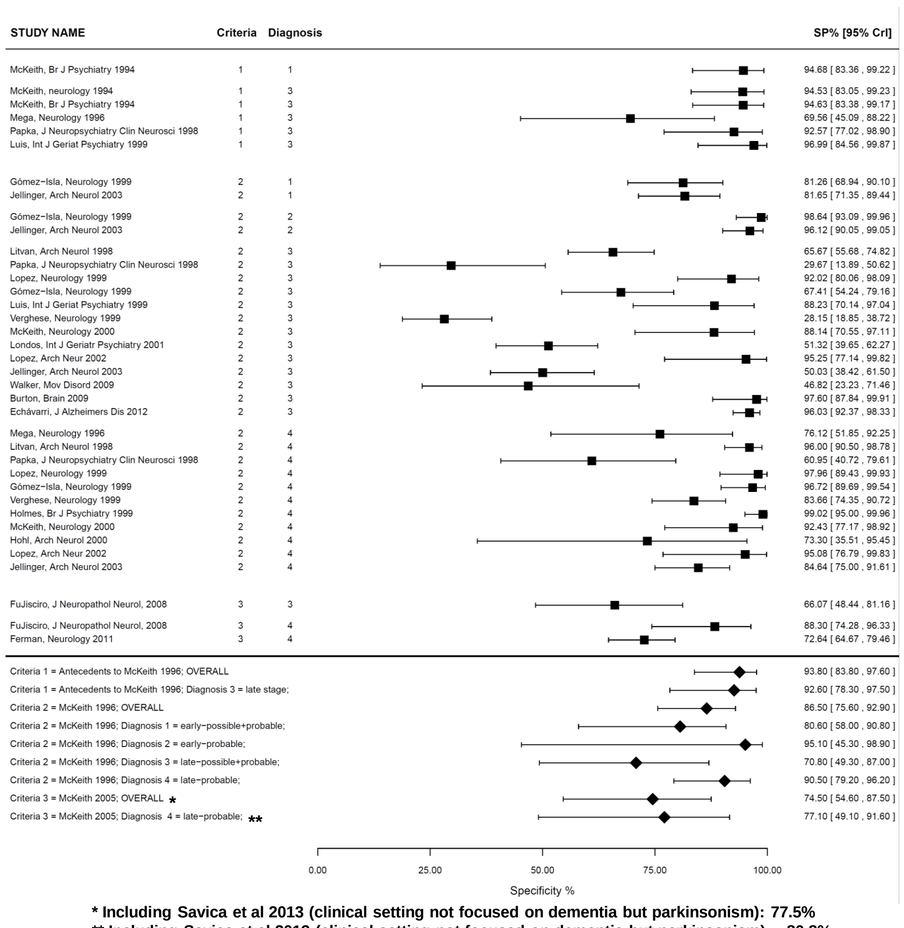
Studies	Sample (N)	In vivo diagnosis	Sens. (%)	Spec. (%)	Acc. (%)	Misdiagnoses
McKeith et al, Neurology 1994	50	Antecedents to McKeith 1996 (Late stage)	73,75	95	86,5	4 raters: 1-3 FP (AD and VaE) and 2-9 FN (mainly AD)
McKeith et al, Br J Psychiatry 1994	50	Antecedents to McKeith 1996 (Early stage)	75	97	88,2	1 FP (organic mood syndr.) and 5 FN (1 Stroke, 2 PD, 1 delusional depression, 1 Unspecified dementia)
McKeith et al, Br J Psychiatry 1994	50	Antecedents to McKeith 1996 (Late stage)	85	97	92,2	1 FP (organic mood syndrome) and 3 FN (1 Stroke, 1 delusional depression, 1 Unspecified dementia)
Mega et al, Neurology 1996	18	Antecedents to McKeith 1996 (Late stage)	50	71	66,33	4 FP (AD) and 2 FN (1 AD e 1 AD+PD)
Papka et al, J Neuropsychiatry Clin Neurosci 1998	39	Antecedents to McKeith 1996 (Late stage)	16,67	95,24	58,98	1 FP (AD) and 15 FN (AD)
Luis et al, Int J Geriat Psychiatry 1999	56	Antecedents to McKeith 1996 (Late stage)	49	100	68,13	0 FP and 18 FN (AD)
Mega et al, Neurology 1996	18	McKeith 1996-probable (Late stage)	75	79	78,11	3 FP (AD) and 1 FN (AD)
Litvan et al, Arch Neurol 1998	105	McKeith 1996-possible (Late stage)	35,7	65,93	61,9	31 FP (mainly PD) and 9 FN (mainly AD and PD)
Litvan et al, Arch Neurol 1998	105	McKeith 1996-probable (Late stage)	17,9	97,24	86,66	3 FP (mainly PD) and 11 FN (mainly AD and PD)
Papka et al, J Neuropsychiatry Clin Neurosci 1998	39	McKeith 1996-possible (Late stage)	88,89	28,57	56,41	15 FP (AD)m and 2 FN (AD)
Papka et al, J Neuropsychiatry Clin Neurosci 1998	39	McKeith 1996-probable (Late stage)	33,33	71,43	53,85	8 FP (AD) and 10 FN (AD)
Lopez et al, Neurology 1999	40	McKeith 1996-possible (Late stage)	34	94	82	4 raters: 1-3 FP (PD/AD/PSP) and 3-7 FN (mainly AD)
Lopez et al, Neurology 1999	40	McKeith 1996-probable (Late stage)	0	100	80	4 raters: 0 FP and 8 FN (AD or possible DLB)
Gómez-Isla et al, Neurology 1999	63	McKeith 1996-possible (Early stage)	53	83	76,81	9 FP (AD) and 6 FN (AD)
Gómez-Isla et al, Neurology 1999	63	McKeith 1996-probable (Early stage)	15,38	100	82,54	0 FP and 11 FN (AD)
Gómez-Isla et al, Neurology 1999	61	McKeith 1996-possible (Late stage)	90	68	71,97	16 FP (AD) and 1 FN (AD)
Gómez-Isla et al, Neurology 1999	61	McKeith 1996-probable (Late stage)	54,55	98	90,16	1 FP (AD) and 5 FN (AD)
Luis et al, Int J Geriat Psychiatry 1999	56	McKeith 1996-possible (Late stage)	57	90	69,38	2 FP (AD) and 15 FN (AD)
Verghese et al, Neurology 1999	94	McKeith 1996-possible (Late stage)	89	28	39,68	55 FP and 2 FN (mainly AD and VaD)
Verghese et al, Neurology 1999	94	McKeith 1996-probable (Late stage)	61	84	79,6	12 FP and 7 FN (mainly AD and VaD)
Holmes et al, Br J Psychiatry 1999	80	McKeith 1996-probable (Late stage)	22	100	91,23	0 FP and 7 FN (AD)
McKeith et al, Neurology 2000	50	McKeith 1996-possible (Late stage)	83	91	86,36	2 FP (1 AD and 1 PSP) and 5 FN (3 AD and 2 VaD)
McKeith et al, Neurology 2000	50	McKeith 1996-probable (Late stage)	83	95	88,04	1 FP (AD) and 5 FN (3 AD and 2 VaD)
Londos et al, Int J Geriatr Psychiatry 2001	93	McKeith 1996-possible (Late stage)	61,9	51,39	53,76	35 FP (AD) and 8 FN (AD)
Hohl et al, Arch Neurol 2000	10	McKeith 1996-probable (Late stage)	100	80	90	1 FP (AD) and 0 FN
Lopez et al, Arch Neur 2002	26	McKeith 1996-possible (Late stage)	30	100	65	0 FP and 9 FN (AD)
Lopez et al, Arch Neur 2002	26	McKeith 1996-probable (Late stage)	23,08	100	61,54	0 FP and 10 FN (AD)
Jellinger et al, Arch Neurol 2003	99	McKeith 1996-possible (Early stage)	70	82	78,24	12 FP and 9 FN (AD and PD)
Jellinger et al, Arch Neurol 2003	99	McKeith 1996-probable (Early stage)	22	97	73,52	2 FP and 24 FN (AD and PD)
Jellinger et al, Arch Neurol 2003	99	McKeith 1996-possible (Late stage)	81	50	59,71	34 FP and 6 FN (AD and PD)
Jellinger et al, Arch Neurol 2003	99	McKeith 1996-probable (Late stage)	60	85	77,17	10 FP and 12 FN (AD and PD)
Walker et al, Mov Disord 2009	23	McKeith 1996-possible (Late stage)	80	46,15	60,87	7 FP (5 AD, 1 FTD e 1 CBD) and 2 FN (1 AD e 1 CBD)
Burton et al, Brain 2009	52	McKeith 1996-possible (Late stage)	60	100	80,77	9 FP (PDD) and 1 FN (AD)
Echávarri et al, J Alzheimers Dis 2012	200	McKeith 1996-possible (Late stage)	21,21	96,41	84	6 FP (2 AD+TDP43, 1 AD+prion disease, 2 AD+VaD, 1 VaD) and 26 FN (17 AD, 4 mixed dem., 1 PSP, 4 PD)
Tiraboschi et al, Neurology 2015	64	McKeith 1996- possible (Late stage)	81,25	/	/	12 FN (AD)
FuJisciro et al, J Neuropathol Neurol, 2008	76	McKeith 2005-possible (Late stage)	91,3	66,67	81,58	10 FP (1 PSP+AD pathology, 2 CDLB low+Braak stage V-VI, 7 AD) and 4 FN (AD)
FuJisciro et al, J Neuropathol Neurol, 2008	76	McKeith 2005-probable (Late stage)	86,96	90	88,16	3 FP (1 PSP+AD pathology, 2 CDLB low+Braak stage V-VI) and 6 FN (4 AD, 2 poss. DLB)
Ferman et al, Neurology 2011	234	McKeith 2005-probable (Late stage)	85	73	78,03	37 FP (7 TLBD and Braak > 4, 9 AD, 6 AD and amygdala LBs, 4 AD+CVD, 1 CVD, 1 CBD, 2 PSP, 4 FTLD, 2 CJD, 1 other) and 15 FN (not specified)
Savica et al, JAMA Neurol 2013	65	McKeith 2005-probable (Late stage)	100	97,96	98,46	1 FP (AD) and 0 FN

Figure 2. Forest plot: Pooled sensitivity of studies



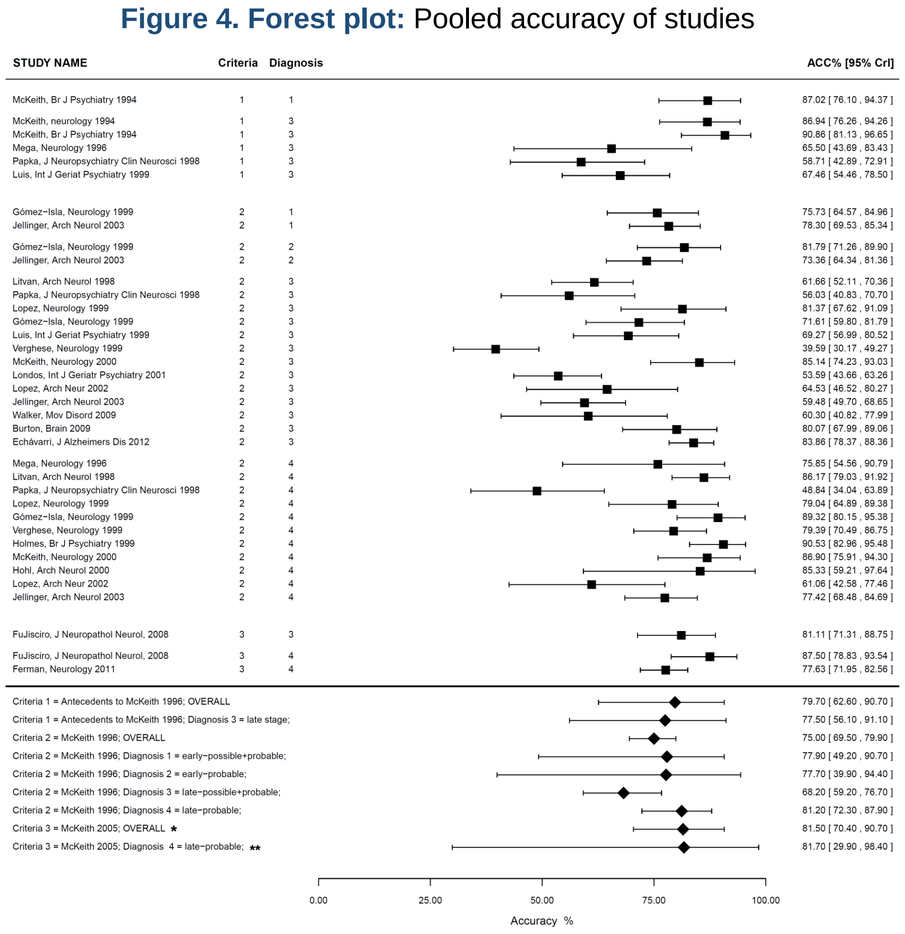
*** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): 88.8%**
**** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): : 88.3%**

Figure 3. Forest plot: Pooled specificity of studies



*** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): 77.5%**
**** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): : 80.8%**

Figure 4. Forest plot: Pooled accuracy of studies



*** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): 88.4%**
**** Including Savica et al 2013 (clinical setting not focused on dementia but parkinsonism): : 90.7%**

Conclusions

One out five patients with DLB has a misdiagnosis. DLB diagnostic criteria have become more sensitive and less specific over time. Diagnostic accuracy did not substantially changed in the last years, and is influenced by the different clinical setting. Further improvement is needed to optimize the clinical diagnosis of DLB, eventually using biomarkers.

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