Original Research Article

Dementia and Geriatric Cognitive Disorders

Dement Geriatr Cogn Disord 2007;24:220–228
DOI: 10.1159/000107084

Accepted: May 14, 2007
Published online: August 10, 2007

Validity of Dementia Diagnoses in the Danish Hospital Registers

Thien Kieu Thi Phung[a] Birgitte Bo Andersen[a] Peter Høgh[a]
Lars Vedel Kessing[b] Preben Bo Mortensen[c] Gunhild Waldemar[a]

[a]Memory Disorders Research Group, Department of Neurology, [b]Department of Psychiatry, The Centre of Neuroscience, Copenhagen University Hospital Rigshospitalet, Copenhagen, and [c]National Centre of Register-Based Research, Aarhus University Hospital, Aarhus, Denmark

Key Words
ICD-10 · DSM-IV · Dementia diagnosis · Danish register · Validity

Abstract
Background: The validity of dementia diagnoses in the Danish nationwide hospital registers was evaluated to determine the value of these registers in epidemiological research about dementia. ***Methods:*** Two hundred patients were randomly selected from 4,682 patients registered for the first time with a dementia diagnosis in the last 6 months of 2003. The patients' medical journals were reviewed to evaluate if they fulfilled ICD-10 and/or DSM-IV criteria for dementia and specific dementia subtypes. The patients who were still alive in 2006 were invited to an interview. ***Results:*** One hundred and ninety-seven journals were available for review and 51 patients were interviewed. A registered diagnosis of dementia was found to be correct in 169 (85.8%) cases. Regarding dementia subtypes, the degree of agreement between the registers and the results of the validating process was low with a kappa of 0.36 (95% CI 0.24–0.48). ***Conclusion:*** The validity of dementia syndrome in the Danish hospital registers was high and allows for epidemiological studies about dementia. Alzheimer's disease, although underregistered, also had a good validity once the diagnosis was registered. In general, other ICD-10 dementia subtypes in the registers had a low validity and are less suitable for epidemiological research.

Introduction

In recent years, valuable knowledge about the epidemiology of dementia have been elucidated thanks to large longitudinal population-based studies such as The Rotterdam Study [1], The Kungsholmen Project [2], The PAQUID (Personnes Agées QUID) Study [3], The Canadian Study of Health and Aging [4], and The Baltimore Longitudinal Study of Aging [5]. Most of these studies compiled comprehensive health data about thousands of older individuals and followed them over 10–12 years.

For three decades, the Danish national registers have recorded the whole population's demographic, socioeconomic, and health data. Each individual is registered in these databases with a unique national personal identification number (CPR) assigned by The Danish Civil Registration System (DCRS) to all people who have lived in Denmark since 1968. DCRS registers demographic data such as age, gender, birthplace, residence, marital status,

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1420–8008/07/0243–0220$23.50/0

Accessible online at:
www.karger.com/dem

Thien Kieu Thi Phung, MD
Memory Disorders Research Group, Section 6131, Department of Neurology
The Neuroscience Centre, Copenhagen University Hospital Rigshospitalet
9 Blegdamsvej, DK–2100 Copenhagen (Denmark)
Tel. +45 35 45 62 47, Fax +45 35 45 24 46, E-Mail kieu.phung@rh.hosp.dk

citizenship, kinship, profession, emigration, and death (www.cpr.dk). All contacts with somatic and psychiatric hospital departments in the entire country have been recorded in the two hospital registers: The National Patient Register (NPR) since 1977 [6] and the Psychiatric Central Research Register (PCRR) since 1969 [7]. Internationally, the Danish registers are known for having contributed to important knowledge in medical epidemiology. However, they have only been used to a limited extent in dementia research. Danish register-based epidemiological studies have unique advantages, as longitudinal studies including a much younger and larger study population with millions of person-years of follow-up can be carried out using much less resources. Moreover, selection bias due to nonparticipation or loss to follow-up is negligible. The CPR numbers make it is possible to link the registers to study multiple risk factors from early to late life. To date, four Danish registry-based epidemiological studies about dementia have been published, in which patients with mood disorders were found to have increased risk of developing dementia, and vice versa [8–11].

Since the hospital registries were established primarily for statistical purposes, the validity of each individual diagnosis registered in the NPR and PCRR has to be evaluated on an ad-hoc basis before being employed in epidemiological research [6]. A number of studies have looked at the general validity of ICD-8 diagnoses [12, 13] as well as the validity of specific ICD-8 diagnoses in the hospital registers such as hypertension [14], myocardial infarction [15], mood disorders [16], etc. These studies have found great variations in the validity of individual diagnoses. The validity of dementia diagnoses registered in the NPR and PCRR has not been adequately evaluated.

In order to avail of the Danish hospital registers as a unique resource for epidemiological studies in dementia, the aim of this study was to systematically evaluate the validity of dementia diagnoses in these registers, both as dementia syndrome and dementia subtypes, through a centralized review of medical journals and clinical assessment of a randomly selected sample of patients from the NPR and PCRR.

Materials and Methods

The Registers

Data from the NPR and PCRR are based on admissions to somatic hospital departments since 1977 [6] and psychiatric hospital departments since 1969 [7], respectively. Since 1995, the NPR and PCRR have also included data from hospital-based outpatient clinics and emergency departments [6]. Diagnoses are registered in the NPR and PCRR by WHO International Classification of Diseases (ICD) codes, ICD-8 [17] from 1970 to 1993 and ICD-10 [18] from 1994 onwards. Due to administrative and research-related reasons, ICD-9 was not introduced in 1978.

Study Population

The Danish National Board of Health was requested to define a patient population from the NPR and PCRR and select a random sample from this population for the study. Data from the NPR and PCRR were pooled to identify all the patients in Denmark registered for the first time with dementia as primary or secondary discharge diagnosis in the period 01.06.2003 to 31.12.2003 (4,682 persons). This population included both inpatients and outpatients from all public hospitals in the entire country. ICD-10 codes for Alzheimer's disease (AD), vascular dementia (VaD), frontotemporal dementia (FTD), and dementia without specification were used (table 1).

A random sample of 200 patients (4.3%) was selected from this patient population via random number generator from the SPSS 6.0 statistical package. The variables for the index contact (i.e. the contact at which dementia diagnosis was registered for the first time) included: patients' CPR numbers, type of register, hospital, department, county, admission date, discharge date, primary diagnoses, secondary diagnoses, type of hospital contact (inpatient, outpatient, or emergency room). To obtain an overview of medical history for each patient, the same variables for all other somatic and psychiatric admissions or ambulatory courses, prior or subsequent to the index admission, were also collected.

Validation

The validating process was carried out in three steps:

A comparison of registered diagnoses in the NPR and PCRR with clinical diagnoses documented by the local physicians in the medical journals.

A comparison of registered diagnoses in the NPR and PCRR with results from our evaluation based on the quality of documentation about dementia work-up in the medical journals.

In a subset of patients who were still alive in 2006 and agreed to participate, clinical diagnoses were established through patient interview. The results were used to supplement those from step 2 to reach a final conclusion.

Validation Step 1 – Review of Medical Journals

Letters were sent to hospital departments to request the 200 medical journals. If dementia diagnoses were made by another department prior to index admission or the patients were subsequently referred to another department for further investigation after index admission, the medical journals from the departments in question were also obtained and used to validate dementia diagnoses. The journals were reviewed and clinical diagnoses documented by local physicians in the medical journals were recorded and compared with registered diagnoses in the NPR and PCRR.

Validation Step 2 – Centralized Rating of Medical Journals

Two physicians – one consulting neurologist (B.B.A.) and one resident (T.K.T.P.) in neurology with respectively 9 and 2 years of experience in working with dementia – at the Copenhagen Memory Clinic, Rigshospitalet, rated the medical journals independently according to a predefined protocol. The results were compared and any disagreement was clarified at consensus meetings

Table 1. ICD-10 codes for dementia and distribution of registered dementia diagnoses among the 197 randomly selected patients

Diagnosis	ICD-10 Code	Cases
AD	F00.0, F00.1, F00.2, F.00.9, G30.0, G30.1, G30.8, G30.9	58 (29.4%)
VaD	F01.0, F01.1, F01.2, F01.3, F01.8, F01.9	27 (13.7%)
FTD	F02.0	3 (1.5%)
Dementia without specification	F03.9	109 (55.3%)

with the professors in clinical neurology (G.W.) and clinical psychiatry (L.V.K.) at the Faculty of Health Sciences, Copenhagen.

Based on the Danish and European guidelines for diagnosing and managing dementia [19, 20], a full work-up for dementia was defined as: history of dementia illness, cognitive test, psychiatric evaluation, blood tests (complete blood count, renal function test, liver function test, thyroid function test, calcium, sodium, potassium, cobalamine, folate or methylmalonate, and CRP or SR), ECG, CT/MRI scan of the brain, physical examination including vital signs and neurological examination, and evaluation of activities of daily living. Guided by the quality of clinical information of dementia work-up in the medical journals, the rating physicians determined whether dementia could be diagnosed according to ICD-10 [18] or DSM-IV [21] criteria using 5 rating categories (table 2). Patients who fitted into categories 1, 2, and 3 were considered to have dementia.

The patients concluded to have dementia according to categories 1 and 2 were further classified into subtypes: AD according to ICD-10 and NINCDS-ADRDA for probable AD [22], VaD according to ICD-10 and NINCD-AIREN for probable VaD [23], FTD according to ICD-10 and Work Group on Frontotemporal Dementia and Pick's disease [24], and Lewy body dementia (LBD) according to consensus guidelines for the clinical and pathological diagnosis of dementia with Lewy body [25]. Additionally, the severity of dementia was rated according to ICD-10 criteria.

Table 2. Rating categories for dementia syndrome

(1) Fulfill criteria for dementia, well documented: A full work-up and all criteria for dementia according to ICD-10/DSM-IV were well documented.
(2) Fulfill criteria for dementia, insufficient documentation: Documentation of one or two elements of a full work-up was missing (but not cognitive test), but the whole clinical picture allowed the probable diagnosis of dementia.
(3) Clinical impression of dementia, insufficient documentation: The clinical picture clearly gave a strong impression of dementia, although one or two ICD-10/DSM-IV criteria could not be fulfilled due to lack of documentation (e.g. precise duration of symptoms, behavioral/psychological symptoms, cognitive test).
(4) Unable to conclude, very insufficient documentation.
(5) Did not fulfill criteria for dementia.

Validation Step 3 – Interview of the Patients

Patients who were alive in 2006 were invited by mail to participate in the study. If there was no reply after 2 weeks, they were contacted by telephone. The rating resident (T.K.T.P.) and a research nurse at the Copenhagen Memory Clinic performed the interviews. The face-to-face interview included history of dementia illness, past medical history, past and current medications, Mini-Mental State Examination (MMSE) [26], the short form of Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [27], The Telephone Interview for Cognitive Status (TICS) [28], Instrumental Activity of Daily Living (IADL) [29], the short form (15 items) of Geriatric Depression Scale (GDS) [30], Global Deteriorating Scale (GLDS) [31], Hachinski Ischemic Score [32], and a neurological examination. The research nurse, who was blinded to the results of medical journal review, did the cognitive tests (MMSE, TICS) and GDS. If the patient and caregiver only agreed to a telephone interview, the research nurse did the TICS with the patient and the resident interviewed the caregiver for IQCODE, IADL, GLDS, history of dementia illness, past medical history, and medication history. Duration of cognitive symptoms prior to index admission in 2003 was carefully verified with the patients and caregivers. All the interviews occurred during the first 6 months of 2006, approximately 3 years after dementia diagnoses were registered.

After the interviews, it was concluded whether the patients fulfilled criteria for dementia and specific dementia subtypes based on the synthesis of results from all the assessments. Through consensus meetings, clinical information from the interviews supplemented those from the review of medical journals to reach a final conclusion. When patient interviews were not possible, the conclusions from the review of medical journals would apply.

The Danish Scientific Ethical Committees and the Danish Data Protection Agency approved this study. Informed consents were obtained prior to patient interviews.

Data Analysis

Data analysis was done with SPSS 13.0 statistical package. Normally distributed data were summarized as mean and standard deviation and nonnormally distributed data as median and lower and upper quartiles (25th and 75th percentiles). Kappa statistics were used to estimate overall agreement between the registers and the results of the validating process regarding dementia subtypes for the cases concluded to have dementia in this study.

Table 3. Medical chart review - registered diagnoses in the NPR and PCRR versus clinical diagnoses documented in the medical journals

Registered diagnoses	Clinical diagnoses						
	dementia without specification	AD	VaD	FTD	LBD	no dementia	total
Dementia without specification	**88**	12	2	1	1	5	109 (55.3%)
AD	0	**56**	1	0	0	1	58 (29.4%)
VaD	1	0	**26**	0	0	0	27 (13.7%)
FTD	0	0	0	**3**	0	0	3 (1.5%)
Total	89 (45.2%)	68 (34.5 %)	29 (14.7%)	4 (2.0%)	1 (0.5%)	6 (3.0%)	197 (100%)

Figures in bold indicate full agreement.

Table 4. Dementia syndrome according to centralized rating of medical journals

	Dementia syndrome according to DSM-IV and ICD-10	DSM-IV	ICD-10	DSM-IV or ICD-10
(1)	Fulfill criteria, well documented	101	98	114
(2)	Fulfill criteria, sufficient documentation	13	16	
(3)	Clinical impression of dementia, insufficient documentation	49	49	49
(4)	Unable to conclude, insufficient documentation	28	28	34
(5)	Did not fulfill criteria for dementia	6	6	
	Total	197	197	197

Results

Background Information

Medical journals from 197 (98.5%) patients, 71 (36%) male and 126 (64%) female, were obtained. The patients' mean age at the 1st day of index contact was 81 ± 9 (SD) years. The 3 patients for whom no medical journals were available were excluded from the analysis.

The patients were from 45 public hospitals located in 15 counties representing all hospital capture areas in Denmark. The distribution of registered dementia diagnoses for the 197 cases were: 109 (55.3%) dementia without specification, 58 (29.4%) AD, 27 (13.7%) VaD, and 3 (1.5%) FTD (table 1).

Validation Step 1 – Medical Chart Review

The clinical diagnoses documented in the medical journals were: 89 (45.2%) with dementia without specification, 68 (34.5%) AD, 29 (14.7%) VaD, 4 (2.0%) FTD, 1 (0.5%) LBD, and 6 (3.0%) without dementia. In 24 (12.2%) cases, the clinical diagnoses differed from the registered diagnoses in the NPR and PCR in which 16 additional cases had specific subtypes (12 AD, 2 VaD, 1 FTD, and 1 LBD instead of dementia without specification), 1 case had VaD instead of AD, 1 case had dementia without specification instead of VaD, and 6 cases had no dementia (4 with dementia ruled out, and 2 with no certain conclusion; table 3). The majority of discrepancies occurred in the registered diagnosis of dementia without specification (21 out of 24 cases).

Validation Step 2 – Centralized Rating of Medical Journals

The rating physicians then reviewed the clinical information about dementia work-up and concluded whether criteria for dementia have been met according to the 5 categories described above (table 2). In total, 163 patients (82.7%) belonged to categories 1, 2, or 3 by either DSM-IV or ICD-10 and were concluded to have dementia (table 4). Two thirds of the cases (114) belonged to categories 1 or 2

Table 5. Registered diagnosis in the NPR and PCR versus raters' diagnosis

Registered diagnoses	Raters' diagnoses						
	dementia without specification	AD	VAD	FTD	LBD	no dementia	total
Dementia without specification	**51**	30	0	0	1	27	109
AD	5	**46**	1	0	1	5	58
VAD	17	4	**4**	0	0	2	27
FTD	2	0	0	**1**	0	0	3
Total	75	80	5	1	2	34	197

Figures in bold indicate full agreement.

Table 6. Registered diagnosis in the NPR and PCR versus combined results of medical chart review and interview

Registered diagnosis	Combined results						
	dementia without specification	AD	VAD	FTD	LBD	no dementia	total
Dementia without specification	**49**	36	0	0	1	23	109
AD	5	**47**	2	0	1	3	58
VAD	13	6	**5**	1	0	2	27
FTD	2	0	0	**1**	0	0	3
Total	69	89	7	2	2	28	197
Dementia present					**169**		

Figures in bold indicate full agreement.

and one third (49) to category 3. It was possible to classify 88 (44.7%) patients from categories 1 and 2 into dementia subtypes. Eighty cases (40.6%) fulfilled both sets of criteria for AD, 5 cases (2.5 %) fulfilled criteria for VAD, 1 case (0.5%) fulfilled criteria for FTD, and 2 cases (1%) fulfilled criteria for LBD (table 5). Thirty-four cases were classified as 'no dementia' by the raters (6 did not fulfill criteria for dementia, and 28 cases did not have sufficient clinical information to conclude). These 34 cases included the 6 cases also classified as 'no dementia' by clinical diagnoses in the medical journals. The overall agreement between the results of the centralized rating of medical journals and the registered diagnoses regarding dementia subtypes for the cases concluded to have dementia by the raters was low with a kappa of 0.38 (95% CI 0.26–0.5).

Validation Step 3 – Interview of the Patients

In 2006, 103 were still alive and 51 agreed to participate in the interviews (3 face-to-face interviews of the patients alone, 34 face-to-face interviews of the patients and their caregivers, 2 telephone interviews of the patients alone, and 12 telephone interviews of caregivers alone).

For all the patients who were interviewed and confirmed to have dementia, onset of cognitive symptoms was confirmed to be at least 6 months prior to dates of index contact. Using the results from medical journals rating as the starting points, this group of 51 patients consisted of 15 dementia without specification, 21 AD, 1 VaD, 3 with dementia ruled out, and 11 with insufficient clinical information to conclude. Through the interviews, it was possible to clarify 9 cases out of 15 with dementia

without specification: 8 were assigned specific subtypes (5 AD, 2 VaD, 1 FTD), and one did not fulfill criteria for dementia. Twenty-one AD cases were all confirmed, the only VaD case was also confirmed. The 3 cases with dementia ruled out by rating of medical charts were confirmed as not having dementia through interview. Among 11 cases judged inconclusive by rating, 3 were found to have dementia without specification, 4 with AD, 3 did not fulfill criteria for dementia, and 1 remained inconclusive after interview.

Combined Results of Review of Medical Charts and Patient Interview

Dementia syndrome was concluded to be present in 169 (85.8%) patients based on combined results of medical chart rating and patient interview (table 5) with the following subtypes: 69 (35.0%) had dementia without specification, 89 (45.2%) had AD, 7 (3.6%) had VaD, 2 had FTD (1.0%), and 2 (1.0%) had LBD. The remaining 28 (14.2%) patients were classified as no dementia: in 10 patients, dementia was ruled out and 18 had insufficient clinical information for conclusion (table 6). Among the 18 patients with insufficient clinical information, 14 were admitted due to acute somatic illness where delirium could not be ruled out and 4 were assessed in outpatient clinics with psychiatric conditions as differential diagnoses.

Regarding dementia subtypes for the 169 cases concluded to have dementia in this study, the degree of overall agreement between the registers and the final results of the validating process remained low with a kappa of 0.36 (95% CI 0.24–0.48). A substantial number of registered dementias without specification (36 out of 109) were concluded as AD. The majority of registered AD cases (47 out of 58 or 81.0%) but only few of VaD (5 out of 27 or 18.5%) and FTD cases (1 out of 3 or 33.3%) were confirmed through the validating process.

Among the 169 patients concluded to have dementia, information about duration of cognitive symptoms up to the admission date of the index contact was available for 124 patients with a median of 24 months and upper and lower quartiles of 12 and 36 months. In all 169 patients, there was sufficient documented clinical information in the medical journals to rate dementia severity according to ICD-10 criteria, yielding 20 (11.8%) patients with severe dementia, 134 (79.3%) with moderate dementia, and 15 (8.9%) with mild dementia.

Discussion

In general, dementia diagnoses may be underregistered as well as overregistered in hospital registers. This study was not designed to investigate to which extent dementia may be underregistered in the registers. Overregistration may occur when less experienced physicians establish dementia diagnosis without appropriate work-up for hospitalized patients with cognitive problems. However, overregistration is not a major problem in the Danish hospital registers, as 85.8% of the dementia diagnoses were actually found to be correct.

Dementia syndrome was concluded to be present if either DSM-IV or ICD-10 criteria for dementia were fulfilled. Two of the items in the ICD-10 criteria made it difficult to rate the medical journals. One ICD-10 criterion is duration of cognitive symptoms for at least 6 months. This arbitrary cut-off for duration has been a subject of debate. Symptom duration was not always specified in the medical journals, being often described as 'lately' or 'during the last months'. Another ICD-10 criterion is the presence of apathy, irritability, emotional lability, or coarsening of social behavior. These symptoms are not always present at the onset of dementia. If present, their documentation might have been omitted in the medical journals. The DSM-IV criteria for dementia syndrome have been validated and routinely used in clinical practice and research in Denmark. They were therefore used simultaneously with ICD-10 during rating in order to increase the sensitivity of diagnosing dementia syndrome based on medical journals' documentation. However, this approach did not make any difference in the total number of patients concluded to have dementia syndrome, either by DSM-IV or ICD-10 criteria or both.

Duration of cognitive symptoms prior to the 1st day of the index contact was found to have a median of 2 years. Other studies have found a mean delay of 1 year before family members recognized cognitive problems and sought physician consultation [33]. The majority (91%) of the 169 patients concluded to have dementia in this study were moderately or severely demented. Probably, mild dementia cases were less likely to be detected during hospital contacts, especially in an acute setting.

The validity of registered dementia subtype diagnoses was less reliable. Firstly, the majority (55.3%) of the cases were registered as dementia without specification. Secondly, the validating process revealed that many AD cases were misclassified as dementia without specification in the registers (33%). However, once AD diagnosis was entered in the registers, it was correct in 81% of cases. Third-

ly, another area of uncertainty was VaD. Due to lack of documented neuroimaging and neurological examination, it was impossible to verify 13 (48.1%) registered VaD cases according to ICD-10 or NINCD-AIREN criteria. Only 5 (18.5%) cases were confirmed as VaD, and 6 (22%) registered VaD cases were found to be AD. FTD and LBD cases were too few to make any conclusion about their validity. One FTD case was confirmed out of the three registered cases. Although documented as a clinical diagnosis in the medical journals, LBD has no ICD-10 code. There were only two LBD cases identified by the validating process, one was documented as clinical diagnosis in the medical journal but registered as dementia without specification, and the other was registered as AD. When LBD cases were classified as AD, the results of statistical analysis were practically unchanged.

In a previous study, it has been estimated that there was 10% of technical errors during registration of operation codes in the NPR [34]. In our study, there were discrepancies between clinical diagnoses written in the medical journals and the registered diagnoses in 24 (12.2%) cases. Six among these 24 cases were registered with dementia in the NPR and PCRR without a definite clinical diagnosis of dementia (2 cases) or despite the fact that dementia diagnoses were already ruled out (4 cases). These could simply be registration mistakes. However, in the 2 cases without a definite conclusion of dementia, it cannot be excluded that the diagnoses were correct and the clinicians who made them had a good knowledge of the patients' cognitive symptoms and history of dementia illness without clearly expressing their clinical judgment in the medical journals.

As the patients in this study were registered with a dementia diagnosis for the first time during the last 6 months of 2003, the generalization of the study results to the whole time span of the NPR and PCRR is limited. When data were collected in 2005, registration of hospital contacts was only complete for the year 2003. If the inclusion period had been extended to prior to 2003, medical journals could have risked being removed from the archives, as they are not required to be kept after 3 years of inactivity. Mortality among patients with dementia is known to be high and disease progression over a longer period of time could make the patients ineligible for interview, and our intention was to interview as many patients and as close to the time of diagnoses as possible. Therefore, it was not possible to adequately validate the information in the NPR and PCRR registered prior to 2003.

The introduction of dementia ICD-10 codes in 1995 coincided with the period of increasing awareness about dementia and more widespread availability of investigations and treatments, marked by the founding of dementia clinics all over the country. Patients with dementia have to be seen by a physician from one of the three specialties – psychiatry, geriatrics, or neurology – in order to receive government subsidies for cognition-enhancing medications. In this study, 66.5% of patients got their first dementia diagnosis from one of these 3 specialties, and 70–80% of these dementia diagnoses were made in outpatient clinics, with dementia being the reason of referral and the primary discharge diagnosis. Dementia work-up and treatment became more standardized and accessible after 1995, resulting in improved accuracy in making dementia diagnoses. Therefore, the results from this study can most likely be generalized to ICD-10 dementia diagnoses registered after 1995.

The review of medical journals was based on well-validated research criteria and evidence-based national and international clinical guidelines. It took place in a multidisciplinary memory clinic and was done by experienced clinicians. Two physicians rated the medical journals independently, and consensus meetings were held together with two professors in clinical neurology and psychiatry in order to improve the accuracy of making dementia diagnoses. There was a high response rate of 98.5% (197 out of 200 medical journals were obtained). Furthermore, records were obtained for relevant admissions prior and subsequent to the index admission when dementia diagnosis was registered for the first time. Therefore, dementia could be confirmed when the whole clinical picture illustrated a patient with declining cognitive function and gradual functional impairment over time in the absence of other somatic and psychiatric conditions that could lead to cognitive problems. In order to further validate the dementia diagnoses, interview of patients was carried out with comprehensive objective assessments combined with interview of caregivers.

As mentioned above, we designed the study to facilitate clinical evaluation of as many patients as possible by taking the random sample of patients at the latest date when data registration was considered complete at the start of the study. However, the 3-year time interval between initial diagnosis and post-hoc diagnosis could not be avoided. High mortality and low participation rate made it possible to interview only 25% of the patients. Given such constraints, a validation study mainly based on post-hoc centralized review of medical journals was the best possible to carry out. The validity of dementia diagnosis could thus be overestimated as well as underestimated. Because inadequate documentation of clinical

information in the medical journals is not uncommon, the true validity of the registered dementia syndrome diagnosis was likely to be underestimated in this study. However, cases with incomplete clinical information were taken into consideration (categories 2 and 3, table 2) and interview of the patients did partially correct for underestimation. Overestimation of the validity of dementia diagnosis was believed to be negligible. The interviews confirmed 36 out of 37 cases concluded to have dementia by reviewing of medical journals. Although it was only possible to interview 51 out of 103 patients who were still alive, the patients interviewed were considered to be the most important cases to clarify, as most of them were less cognitively and functionally impaired. We contacted by phone the patients who did not reply to our letters and learned that many were too cognitively impaired to participate. As the interviewed patients were a selective group, the results of their interviews were only applied to them and not extrapolated to the whole random sample. As the same patients could have developed dementia in the previous 3 years before the interviews without having dementia at the time the diagnosis was registered in the NPR or PCRR, time of onset of cognitive symptoms was carefully verified with caregivers. The trigger event bringing cognitive symptoms to attention was always decline in function.

In conclusion, a diagnosis of dementia registered in the NPR and PCRR was found to have high validity and is suitable for use in register-based epidemiological studies about dementia. AD, although underdiagnosed and underregistered, had a good validity once the diagnosis was entered in the registers. In general, other ICD-10 dementia subtypes registered in the NPR and PCRR had a low validity and are less suitable for epidemiological research.

Acknowledgements

The authors thank H. Lundbeck for an unrestricted grant and The Danish Alzheimer Research Foundation for financial support of this study. The sponsors were not involved in the design of the study, the analysis of data, or the preparation of the article.

References

1 Hofman A, Grobbee DE, de Jong PT, et al: Determinants of disease and disability in the elderly: the Rotterdam Elderly Study. Eur J Epidemiol 1991;7:403–422.
2 Fratiglioni L, Viitanen M, Backman L, et al: Occurrence of dementia in advanced age: the study design of the Kungsholmen Project. Neuroepidemiology 1992;11(suppl 1):29–36.
3 Barberger-Gateau P, Fabrigoule C, Helmer C, et al: Functional impairment in instrumental activities of daily living: an early clinical sign of dementia? J Am Geriatr Soc 1999; 47:456–462.
4 McDowell I, Hill G, Lindsay J: An overview of the Canadian Study of Health and Aging. Int Psychogeriatr 2001;13(suppl 1):7–18.
5 Shock NW, Greulich RC, Andres RA, Arenberg D, Costa PT, Lakatta EW, et al: Normal Human Aging: The Baltimore Longitudinal Study of Aging. Washington, US Government Printing Office, 1984.
6 Andersen TF, Madsen M, Jorgensen J, et al: The Danish National Hospital Register. A valuable source of data for modern health sciences. Dan Med Bull 1999;46:263–268.
7 Munk-Jorgensen P, Mortensen PB: The Danish Psychiatric Central Register. Dan Med Bull 1997;44:82–84.
8 Kessing LV, Olsen EW, Mortensen PB, et al: Dementia in affective disorder: a case-register study. Acta Psychiatr Scand 1999;100: 176–185.
9 Kessing LV, Nilsson FM: Increased risk of developing dementia in patients with major affective disorders compared to patients with other medical illnesses. J Affect Disord 2003;73:261–269.
10 Kessing LV, Andersen PK: Does the risk of developing dementia increase with the number of episodes in patients with depressive disorder and in patients with bipolar disorder? J Neurol Neurosurg Psychiatry 2004;75: 1662–1666.
11 Nilsson FM, Kessing LV, Sorensen TM, et al: Enduring increased risk of developing depression and mania in patients with dementia. J Neurol Neurosurg Psychiatry 2002;73: 40–44.
12 Jurgensen HJ, Frolund C, Gustafsen J, et al: Registration of diagnoses in the Danish National Registry of Patients. Methods Inf Med 1986;25:158–164.
13 Mosbech J, Jorgensen J, Madsen M, et al: The national patient registry. Evaluation of data quality. Ugeskr Laeger 1995;157:3741–3745.
14 Nielsen HW, Tuchsen F, Jensen MV: Validity of the diagnosis 'essential hypertension' in the National Patient Registry. Ugeskr Laeger 1996;158:163–167.
15 Madsen M, Balling H, Eriksen LS: The validity of the diagnosis of acute myocardial infarction in 2 registries: the Heart Registry compared to the National Patient Registry. Ugeskr Laeger 1990;152:308–314.
16 Kessing LV: Validity of diagnoses and other clinical register data in patients with affective disorder. Eur Psychiatry 1998;13:392–398.
17 Danish National Board of Health: Classification of diseases. The Danish edition of ICD 8. Copenhagen, Danish National Board of Health, 1971.
18 World Health Organization: The ICD-10 classification of mental and behavioral disorders: diagnostic criteria for research. Geneva, World Health Organization, 1993.
19 Rubak JM, Bro F, Dinesen O, Rytter L, Vass M, Bisgaard AT: Identifikation og udredning af demens og demenslignende tilstande i almen praksis, ed 1. Aalborg, Dansk selskab for almen medicin, 1999.
20 Waldemar G, Dubois B, Emre M, et al: Diagnosis and management of Alzheimer's disease and other disorders associated with dementia. The role of neurologists in Europe. European Federation of Neurological Societies. Eur J Neurol 2000;7:133–144.

21 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4, Text Revision. Washington, American Psychiatric Association, 2000.
22 McKhann G, Drachman D, Folstein M, et al: Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939–944.
23 Roman GC, Tatemichi TK, Erkinjuntti T, et al: Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 1993;43:250–260.
24 McKhann GM, Albert MS, Grossman M, et al: Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. Arch Neurol 2001;58:1803–1809.
25 McKeith IG, Galasko D, Kosaka K, et al: Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1113–1124.
26 Folstein MF, Folstein SE, McHugh PR: 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
27 Jorm AF: A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. Psychol Med 1994;24:145–153.
28 Desmond DW, Tatemichi TK, Hanzawa L: The telephone interview for cognitive status (TICS): reliability and validity in a stroke sample. Int J Geriatr Psychiatry 1994;9:803–807.
29 Lawton MP, Brody EM: Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969; 9:179–186.
30 van Marwijk HW, Wallace P, de Bock GH, et al: Evaluation of the feasibility, reliability and diagnostic value of shortened versions of the geriatric depression scale. Br J Gen Pract 1995;45:195–199.
31 Reisberg B, Ferris SH, de Leon MJ, et al: Global Deterioration Scale (GDS). Psychopharmacol Bull 1988;24:661–663.
32 Moroney JT, Bagiella E, Desmond DW, et al: Meta-analysis of the Hachinski Ischemic Score in pathologically verified dementias. Neurology 1997;49:1096–1105.
33 Waldemar G, Phung KT, Burns A, et al: Access to diagnostic evaluation and treatment for dementia in Europe. Int J Geriatr Psychiatry 2007;22:47–54.
34 Wille-Jorgensen PA, Meisner S: The validity of data in registration of operations. A quality analysis. Ugeskr Laeger 1997;159:7328–7330.