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OF SCIENCE, TECHNOLOGY AND MEDICINE

Young Onset Dementia:

Epidemiology, clinical symptoms, family burden, support and outcome.

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Executive Summary

Dementia affecting the under 65 years age group is increasingly recognised as an important medical and social problem. This report is based upon research carried out over a 2½ year period in two London boroughs. A comprehensive methodology was used to attempt to identify every case of dementia which began before the affected person was age 65 years and to establish a specific cause. The study identified 185 cases of young onset dementia, giving a prevalence of 67.2 cases per 100,000 at risk in the 30-64 years age group. Extrapolating these figures suggests that there may be 16,737 (95% CI: 13,975-19,879) people affected in the wider UK population. The prevalence rates for specific dementias included Alzheimer's disease (21.7/100,000 (15.6-29.3)) , Vascular Dementia (10.9/100,000 (6.7-16.5)) and Frontotemporal dementia (9.3/100,000 (5.5-14.7). It was notable that Alzheimer's disease accounted for less than half of the cases of dementia.

Non-cognitive and behavioural symptoms were common in the patients, 53% experiencing delusions, and 44% hallucinations. There were no statistically significant differences between the different dementias. The caregivers experienced high levels of burden with 53% rating as 'cases' on the General Health Questionnaire (GHQ). Female gender, looking after someone with non-cognitive symptoms and poor marital quality prior to onset of the dementia all predicted higher levels of distress and burden.

A 'bottom-up' direct cost-of-illness analysis was carried out on the patient sample. The total cost for the two areas was estimated to be £1.4 million annually, which extrapolates to £132 (£110-£156) million for all young onset dementia in the UK. There were no significant associations with patient or caregiver factors and cost-of-illness. Compared to older people with dementia this group of younger patients appear to use less community resources and more costly institutional care. Over the period of this study, concern about and services for younger people with dementia in both areas increased dramatically.

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Terms and Abbreviations

95% CI	95% Confidence Interval
AD	Alzheimer's Disease
ADS	Alzheimer's Disease Society
ADL	Activities of Daily Living
APP	Amyloid Precursor Protein
ARD	Alcohol Related Dementia
BEHAVE-AD	The Behavioural Pathology in Alzheimer's Disease Scale
BRSD	Behaviour Rating Scale For Dementia (CERAD)
CADASIL	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
CAMCOG	Cambridge Mental Disorders in the Elderly Examination, Cognitive Sub-Section
CERAD	Consortium To Establish A Registry In Alzheimer's Disease
CDR	Clinical Dementia Rating Scale
ChAT	Choline Acetyltransferase
CIA	Confidence Interval Analysis
CJD	Creutzfeldt Jakob Disease
CRAC Dementia	Council of Relatives to Assist the Care of Dementia
CT	Computed Tomography Scan
CVA	Cerebrovascular Accident (Stroke)
CVR	Cardiovascular Reactivity
DLB	Dementia With Lewy Bodies
DRT	Dementia Relief Trust
EE	Expressed Emotion
EEG	Electroencephalogram
EMI	Elderly Mentally Infirm
EPH	Elderly Person's Home
FAD	Familial Alzheimer's Disease
FTD	Frontotemporal Dementia
GHQ-*n*	General Health Questionnaire (-28, -30, -60 item versions)
GP	General Practitioner

HAD	Hospital Anxiety and Depression Scale
HIS	Hachinski ischaemia Scale
IDDD	Interview to Determine Deterioration of Daily Function in Dementia
IT	Information Technology
JCG	Joint Commissioning Group
JPG	Joint Planning Group
KC&W	Kensington, Chelsea and Westminster
MI	Myocardial Infarction
MMSE	Mini Mental State Examination
MOUSEPAD	Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia
MRI	Magnetic Resonance Imaging
NHNN	The National Hospital for Neurology and Neurosurgery
NOS	Not Otherwise Specified
nvCJD	New Variant Creuztfeldt Jakob Disease
OB	Objective Burden
ODBC	Open Database Connectivity
OPCS	Office of Population Census and Surveys
PAS	Patient Administration System

1. Introduction & Review of The Literature

Dementia affecting the under 65 years age group is being increasingly recognised as an important medical and social problem (Alzheimer's Disease Society, 1996; Health Advisory Service, 1997).

A recent UK study (Gray and Fenn, 1993) focused on burden of illness in terms of care provision and cost. The cost for Alzheimer's Disease (AD) was £1,039million in 1990/91, twice the cost of coronary heart disease, and over one third more than stroke care. Residential care for AD alone was estimated to have accounted for £676million, almost two thirds of total costs, dwarfing the cost of day-care (£4m), home care (£26m) and informal care payment (£65m). These figures are based upon care for elderly people with AD, little is known about the cost of care for younger people with AD, and even less about the non-AD dementias.

Accurate epidemiological data is vital for effective service planning. In people aged 60-65 years, the prevalence of AD is approximately 0.7%. However, there are few estimates of the prevalence of other dementias nor of AD in younger age groups; without knowing the prevalence of all causes of dementia in this population, services planned on data relating to AD only may substantially underestimate the need that is present.

The burden of illness in the under 65 years age group is likely to be different, both in terms of the dementias involved and the subsequent effects on the patient, carer and family. A dementia affecting someone in their forties or fifties will have a profound effect on their own and their spouses employment and financial situation, as well as on their family, which is likely to include children still living at home. Moreover, autosomal dominant familial dementias generally, and focal or unusual dementias such as Pick's disease, frontal lobe dementia and prion disease may be more common in the younger patient; these illnesses often have an early onset with a behavioural presentation. There are sparse research data available on the burdens of caring for someone with a non-AD dementia.

1.1 The Concept of Young Onset Dementia: Background and History

The concept of Young Onset Dementia can considered from two perspectives: that of the medical and scientific research findings relating to the disease; and that of the organisation of the health and social services providing care for these patients and their families.

1.1.1 The Medical and Scientific Model of Presenile Dementia

Two major themes can be drawn out from the medical model of dementia that differentiate presenile from senile dementia:

- Senile Alzheimer's Disease and Presenile Alzheimer's Disease

Alzheimer's disease was originally described as a presenile disease (Alzheimer, 1907), yet subsequently shown to be the commonest cause of dementia in older people (Tomlinson et. al., 1968). Since these findings were published, a number of studies have compared, contrasted and attempted to identify differences between younger and older people with AD.

- Senile V. Presenile Dementia: Differential Diagnosis

The second theme arises from the non-Alzheimer dementias - Frontotemporal dementia, Pick's disease, Huntington's disease and prion dementias. Most of these

diseases are characteristically presenile dementias, and are comparatively rare in older people when compared to AD.

Within both themes, the question arises as to whether these are the same biological diseases affecting different age groups, or whether they are similar clinical syndromes which have different pathophysiological causes in older and younger people.

Senile V. Presenile Alzheimer's Disease

The majority of evidence for a medical model of a distinct Young Onset Dementia population comes from Alzheimer's disease. Alzheimer's original descriptions were of a woman who died in her mid fifties with dementia (Alzheimer, 1907). This established the view that Alzheimer's disease was a rare cause of presenile dementia, an opinion that remained prevalent until the careful clinicopathological studies of the 1960s. These studies demonstrated that the histopathological hallmarks of Alzheimer's disease, namely senile plaques and neurofibrillary tangles, were qualitatively the same as those found in the majority of cases of senile dementia (Terry et. al., 1964; Blessed et. al., 1968; Tomlinson et. al., 1968). Following these publications, the term senile dementia of the Alzheimer type (SDAT) became widely used with the term Alzheimer's Disease reserved for presenile cases. However, it was recognised that any distinction between these two would depend upon an arbitrary age (usually 65 years). More recently there has been a tendency to use Alzheimer's disease, regardless of the age of the patient (Terry and Katzman, 1983).

By contrast to this unitary view of Alzheimer's disease, has been the opposing concept separating early and late onset disease with the proposal that Alzheimer's disease type 1 refers to late onset disease and Alzheimer's disease type 2 to early onset (Bondareff, 1983) with each type having subtly different features. This theory of early and late onset disease has contributed to the most recent ICD10 classification: Dementia in Alzheimer's Disease with early onset is said to be characterised by a relatively rapid deterioration and the presence of aphasia, apraxia, alexia and agraphia, whereas dementia in Alzheimer's Disease with late onset is characterised by a slower progression with memory impairment as the prominent feature (World Health Organisation, 1992). However, much of the data on which the distinction between Alzheimer's disease types 1 and 2 is based referred to early and late onset being distinguished by a median age at death of around 70-80 years (see section on neurochemistry below, page 13). Moreover, there remains a major question as to what extent the phenotypic differences between early and late onset disease can be used to argue that these are categorical biological differences or even different diseases, or whether they are merely dimensional changes which show an association with age. Some of the data arguing for phenotypic differences between early and late onset disease are reviewed below.

Clinical

Alzheimer drew attention to the cluster of cortical deficits in his original case with prominent dysphasia, dyslexia, dysgraphia and agnosia in addition to the memory deficit (Alzheimer, 1907). These have since been viewed as clinical characteristics of early onset disease and in particular dysphasia is claimed to be more severe in younger onset cases (Seltzer and Sherwin, 1983). Similarly, a number of studies have suggested that early onset cases have a more rapid progression of their dementia (Heston et. al., 1981; Seltzer and Sherwin, 1983; Reisberg et. al., 1989a) although this has not been confirmed in all studies (Huff et. al., 1987).

Neuroimaging

A number of studies have compared presenile and senile onset AD using neuroimaging techniques. Using a semi-automated technique Sullivan et al (1993)

found significant differences in CSF volumes in young onset AD compared to late onset cases. In particular, patients in the young onset group were quantitatively more abnormal and showed a different pattern of abnormality than the patients in the late onset group. Positron emission tomography (PET) studies have demonstrated different metabolic patterns in the two groups. Predominant metabolic impairment has been demonstrated in the frontal and temporoparietal cortex in presenile AD, with more global hypofunction present in patients with senile onset AD (Koss et. al., 1985; Mielke et. al., 1991). Similarly, single-photon emission computed tomography (SPECT) studies have demonstrated greater regional reduction in blood flow in presenile patients, and have also demonstrated relative left frontal hypoperfusion in presenile-, but not in senile-onset patients (Jagust et. al., 1990).

Neuropathology

As with the proposal that the clinical features are more severe in early onset AD, it has also been suggested that the neuropathological features are more pronounced. Hansen et al (1988) compared young and old Alzheimer cases and found that the only statistically significant difference was a higher tangle count in the younger group. The loss of cells in the cerebral cortex based on automated counting is also greater in younger onset cases (Mountjoy et. al., 1983). The loss of large cortical cells in this study was confined to the temporal lobe in the late onset cases.

Loss of pigmented neurones from the locus coeruleus has also been used to distinguish between early and late onset and, indeed, was the basis of Bondareff's distinction between type 1 and type 2 in that the cell loss from the locus coeruleus was confined to the early onset group (Bondareff, 1983).

Neurochemistry

The pattern of neurochemical deficits identified from post mortem analysis of neurotransmitter markers in AD brain tissue echoes that found from neuropathology and clinical studies, namely more severe deficits in the younger cases. This has been a consistent observation for the cholinergic biosynthetic marker enzyme, choline acetyltransferase (ChAT) (Rossor et. al., 1982; Bird et. al., 1983). However, it is important to recognise that the age at which the groups were distinguished varied between studies. Thus, in the publication of Rossor et al (1982) the analysis was based upon the median age at death for the disease group which happened to be 79 years. Thus the early age at death group includes many patients that would be considered as part of the SDAT group with an onset in their late sixties or early seventies. The difference between these two age groups could partly be attributable to the decline in neurotransmitter markers with age in the control group, such that in the younger group there was no significant difference when compared with elderly controls but only with age matched controls (Rossor and Mountjoy, 1986). Such an analysis would suggest that some of the neurochemical deficits in the disease were identical to those found in the elderly. Nevertheless, a discriminant function analysis involving both neurochemical and neuropathological markers does provide some support for two distinct groups (Bondareff et. al., 1987).

Molecular Genetics

It is the area of genetics that has begun to draw the clearest distinctions between AD in younger people and AD in older people. The discoveries of mutations in the Amyloid Precursor Protein (APP) gene on chromosome 21 (Goate et. al., 1991), and more recently mutations in the presenilin-1 (Sherrington et. al., 1995) (Chromosome 14) and presenilin-2 (Rogaev et. al., 1995) (Chromosome 1) genes have all been in families with autosomal dominant AD where, with a few exceptions, the disease has started before the age of 65 years, and often much younger.

The clinical descriptions of APP mutation pedigrees indicate a relatively constant age at onset of around 50 years. They have the characteristic of early memory impairment shared with sporadic Alzheimer's disease. Myoclonus is quite frequent and one family developed extra-pyramidal features later in the disease; the two members in this family who have come to autopsy both have cortical Lewy bodies (Lantos et. al., 1994). Apart from the presence of Lewy bodies, the neuropathology is otherwise typical of Alzheimer's disease (Lantos et. al., 1992; Mann et. al., 1992; Lantos et. al., 1994; Farlow et. al., 1994). Neuroimaging in APP mutation FAD is not reported to show any differences; Comparison of pedigrees with APP 717 val→ile using PET showed no differences within the broad pattern of bi-parietal, bi-temporal hypometabolism characteristic of Alzheimer's disease (Kennedy et. al., 1995).

The presenilin pedigrees have a more variable age at onset with a range from around 35 years up to the early 60's. The clinical features are similar, although myoclonus is reported to be particularly prominent (Lopera et. al., 1997).

The many phenotype studies ranging from clinical through neuropathology and neuroimaging to neurochemical studies identified differences between a group of earlier and later onset Alzheimer's disease. However, this could not adequately distinguish between a categorical biological difference and a dimensional difference which showed an association with age. The precise biological classification provided by molecular genetic analysis of familial Alzheimer's disease provides a benchmark against which these phenotypic differences can be assessed. However, as yet there are few studies attempting to contrast early onset familial versus late onset familial and early onset familial versus early onset sporadic. It is possible that some of the reports of phenotypic differences within Alzheimer's disease were due to an inclusion of familial Alzheimer's disease within the early onset groups although this remains to be established.

Senile V. Pre Senile Dementia: Differential Diagnosis

By contrast to AD, very few studies have systematically compared younger and older populations with other forms of dementia.

VaD is thought to be the second most common cause of dementia in the elderly after AD. Only one studies has specifically examined the prevalence of presenile vascular dementia (McGonigal et. al., 1993), although most studies describing clinical populations of patients under the age of 65 years with dementia report a sub-group of vascular cases. Newens et al (1993) found 86 cases of presenile VaD compared to 227 cases of presenile AD; however, they were identified in order to be excluded from the remainder of the study. Similarly amongst descriptions of clinical services Ferran et al (1996) reported that 17% of people under 65 years referred for the investigation of suspected dementia eventually received a diagnosis of VaD, while Delaney and Rosenvinge (1995) found that 17/27 people with PSD in the Southampton area were suffering from VaD. These studies all confirm the presence of a presenile VaD population, yet little is known about prevalence, nor how these patients compare with late onset VaD (Rocca et. al., 1991c). There is growing evidence that genetics plays a major part in the aetiology of presenile VaD. CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is a familial form of vascular dementia that has been described in various forms since 1977 (Tournier-Lasserve et. al., 1993). The disease has a mean age at onset of 45 years (range 27-65 years). The strokes usually occur in the absence of hypertension or definable vascular risk factors. The disease is associated with mutations in the *notch3* gene (Joutel et. al., 1996), and have been found in 45 out of 50 screened cases of CADASIL (Joutel et. al., 1997).

Pick's disease and frontal lobe degeneration are also frequently cited as examples of young onset dementias. Compared to AD and VaD there have been no large scale prevalence or incidence studies. For Pick's disease the largest series of cases ever described is 21 (Mendez et. al., 1993). In this study 16/21 had an age of onset

before 65 years, and 19/21 had been mis-diagnosed in life; predominantly being diagnosed as AD. The lack of clinical diagnostic criteria has inhibited epidemiological studies, although Pick's disease is part of the frontotemporal dementia syndrome (The Lund and Manchester Groups, 1994). Similarly with FLD, despite a large number of clinical studies and case series of patients and familial pedigrees, little is known about its epidemiology. The majority of familial forms have an early age at onset (Knopman, 1993; Gustafson, 1993; Brown et. al., 1996). However, the lack of diagnostic criteria and apparent high rates of mis-diagnosis make it difficult to determine whether this group of dementias is more common in younger people.

Other dementias such as the Prion Diseases (Collinge and Palmer, 1993a), Huntington's disease (Jones et. al., 1997), dementia in multiple sclerosis (Rao et. al., 1991) and alcohol related dementias (Smith and Atkinson, 1995) are all more common in younger people.

In summary, the medical and scientific evidence shows that dementias occur at all ages, and for the more common diseases (AD and VaD) there is an age related increase in prevalence, with a nonetheless significant number of people developing the disease before the age of 65 years. For AD, younger people are more likely to have autosomal dominantly inherited forms of disease, although ongoing genetic studies may eventually show similar genetic aetiology in older people. Attempts to compare younger and older populations of patients with AD have generally failed to show substantial differences between the clinical, pathological and biochemical features of the two groups, and any evidence for such a difference has been further obscured by the genetic discoveries with the likelihood that the earlier young onset groups of AD patients were probably a mixture of genetic and sporadic forms of AD.

Thus the diseases causing dementia in this group appear to be the same phenotypic diseases as those affecting older people except that they have started earlier than average and are more likely to have a genetic aetiology. The unusual dementias are more commonly described in younger people, but whether this is due to epidemiological differences, or selection bias is not known.

1.1.2 The Health Service Model of Young Onset Dementia

It is very difficult to identify the origins of young onset dementia as a specific patient group from the health services literature. However, an overview of the changes, particularly in mental health services, over the past 15 years helps to put the appearance of this group into context.

Prior to the early 1980's it is likely that the majority of younger people with dementia would have ended up under the care of a psychiatrist in a large institution. At this stage there were few specially trained old age psychiatrists and most general psychiatrists would have people with dementia of all ages under their care.

During the 1980's two major changes in the health service had an effect on the population of younger people with dementia. First, the move from an asylum or institutional based service to a community service meant that people with dementia were less likely to enter long stay institutions and were more likely to be cared for at home or in their local community. These changes occurred at the same time as the development of specialist Old Age Psychiatry services, with an almost universal cut-off age of 65 years between General Psychiatry and Old Age Psychiatry, based upon the normal male retirement age. Old Age Psychiatrists receive specialist training, and have considerable experience in the investigation and care of people with dementia, but often inflexibility in the organisation of services means that people under 65 years with dementia are excluded from the Old Age Psychiatry services.

Younger people with dementia are generally seen for diagnostic assessment by neurologists, but with the diagnosis having been made, neurologists rarely take a responsibility for long term care.

As the care of people with dementia has shifted from institutions to the community resources such as day care, day hospitals and respite care were developed to support them and their carers. Almost universally these are age specific services catering for older people. Similar models developed in social services departments with teams for older people (over 65 years) and teams for younger people, with similarly strict demarcations. Even if access is granted to day care or respite care the younger person and their family often find it distressing that they have been placed with people who are often 20-30 years older (Quinn, 1996).

The majority of younger people with dementia are cared for by their families in the community (Delaney and Rosvinge, 1995), and receive a relatively low level of services (Baldwin, 1994b; Newens et. al., 1995). Their carers tends to be highly stressed, but uncomplaining (Baldwin, 1994a; Sperlinger and Furst, 1994).

In 1991 a group of carers in Merseyside, supported by the Alzheimer's Disease Society (ADS), published a Declaration of Rights for Younger People with Dementia, subsequently revised as a charter for younger people with dementia and their carers (Table 1) (Alzheimer's Disease Society, 1996).

All younger people with dementia, their families and carers should have access to comprehensive, specialist services from diagnosis to long-term care.

- **Early Diagnosis, assessment and referral**

GP's should have the relevant skills, training and support to recognise the symptoms of dementia in all age groups and refer people to a specialist consultant who can make a diagnosis and provide ongoing medical supervision

- **Access to specialist services**

Younger people with dementia should have access to a full range of specialist services including home, day, respite and continuing care which recognise the different life circumstances and environment of younger people and their carers. Specialist counselling should also be made available.

- **Adequate financial support**

There should be adequate financial support for younger people with dementia and their carers to enable them to meet the extra costs of caring for dementia.

- **Good employment practice**

Employers and the social security system should adopt good employment practices which recognise dementia as grounds for early retirement and which protect a person's entitlement to

services for this group with specific funding; to raise awareness of this group in primary care and to improve the education and training in this area. This theme has also been taken up by the Health Advisory Service in a recent report (Health Advisory Service, 1997).

1.2 Epidemiology

1.2.1 Dementia in The Elderly

The epidemiology of dementia in elderly people (those aged over 65 years) has been extensively studied since the 1960's, both in terms of prevalence (the number of cases within a defined population) and incidence (the number of new cases developing, usually over an annualised period). Accurate data on prevalence and incidence of dementia are essential for issues such as service planning, and scientifically to support decisions on research priorities.

Three particularly important studies on the prevalence of dementia have come from the EURODEM collaboration studies in Europe (Hofman et. al., 1991), the Framingham Study in the USA (Kokmen et. al., 1989), and from a quantitative integration of the dementia prevalence literature from 1945 to 1985 (Jorm et. al., 1987). All three of these studies have confirmed that the prevalence of dementia, after the age of 65 years, broadly doubles with every 5 years increase in age.

	Age Group (Years)						
Study	**65-69**	**70-74**	**75-79**	**80-84**	**85-89**	**90-94**	**95-99**
EURODEM	1.4	4.1	5.7	13.0	21.6	32.2	34.7
Framingham	0.9	2.0	4.3	8.9	---------- 16.3 ----------		
Jorm et al	1.4	2.8	5.6	10.5	20.8	38.6	

Table 2 - Age Specific Prevalence of Dementia (%) in the Elderly

Overall, there is excellent consistency between these reports, particularly those that integrate a number of different studies. Individual studies are more susceptible to methodological differences such as differing criteria for diagnosis, variable thoroughness of case finding and differing definitions of severity required for caseness. Thus although the rates for the Framingham study are lower, the authors make clear that because of their methodology of identification from medical case notes, their figures are likely to be an underestimate, and indeed should be taken as a baseline figure only.

Dementia as a broad syndrome is a useful starting point for understanding the numbers of affected individuals in a population. However, details of the specific diseases present is needed to drive research into the causes of dementia, and for future planning, particularly as treatments for the specific dementias begin to appear.

From autopsy studies, AD is known to be the most common cause of dementia in the elderly, followed by VaD and DLB (Byrne et. al., 1989; Perry et. al., 1989).

The availability of well validated criteria for AD, in particular the NINCDS/ADRDA criteria, allows cases of AD to be identified from the general dementia population with at least 80% sensitivity (Blacker et. al., 1994; Kosunen et. al., 1996). The papers included in Jorm's study were almost all published prior to the publication of the NINCDS/ADRDA criteria and although differentiation of different diseases was attempted it is difficult to compare confidently the results with the EURODEM (Rocca et. al., 1991b) and Framingham studies which

did use the criteria. Table 3 summarises the age specific prevalence of AD from the two major studies using the NINCDS/ADRDA criteria.

	Age Group (Years)						
Study	**65-69**	**70-74**	**75-79**	**80-84**	**85-89**	**90-94**	**95-99**
EURODEM	0.34*	------ 3.2 ------		------ 10.8 ------		---	---
Framingham	0.4	1.1	3.3	6.9		---------- 12.6 ----------	

*60-69 age group

Table 3 - Age Specific Prevalence Rates (%) for AD in the Elderly

The situation for VaD and DLB is more problematic. As will be discussed in more detail in the following section (See pages 22 and 23), consensus criteria for other dementias have only been developed more recently, and their validity, sensitivity and specificity, particularly when they are applied in epidemiological studies are as yet unproved.

Prevalence data on VaD is available from the EURODEM study (Rocca et. al., 1991c), however it is recognised by the authors that these are fragments of data. The study was performed prior to the publication of the NINDS/AIREN criteria for VaD (Roman et. al., 1993), and none of the prevalence studies included involve the use of neuroimaging for diagnosis. The fragments of data available are summarised in table 4.

	Age Group (Years)						
Study	**60-69**	**70-74**	**75-79**	**80-84**	**85-89**	**90-94**	**95-99**
EURODEM	0.7	-------- 2.5 --------		-------- 4.2 --------			

Table 4 - Age Specific Prevalence Rates (%) for VaD in the Elderly

Very little is known about the population epidemiology of DLB. Evidence from autopsy studies suggests that DLB may be the second most common form of dementia (Byrne et. al., 1989). The application of recently published clinical diagnostic criteria in future epidemiological studies will hopefully provide prevalence data on this previously under-recognised disease.

1.2.2 Dementia in Younger People

Dementia in people under the age of 65 years is undoubtedly uncommon when compared to the prevalence in older people, and performing epidemiological studies of rare diseases presents methodological difficulties. In particular, population cohort studies, such as the Gospel Oak study (Livingston et. al., 1990), which are ideal in populations of elderly people where dementia is relatively common are unsuitable for younger populations where prevalence is low, and thus very large populations need to be screened to identify a significant number of cases.

The methodology used by the major studies that have reported data for prevalence of dementia in the younger age group has been identification from medical case note review. These include studies based in the UK Northern Region (Newens et. al., 1993), Scotland (McGonigal et. al., 1993), Framingham (Kokmen et. al., 1989) and Copiah County (Schoenberg et. al., 1985). However, the Northern Region study included only cases of AD while the Scottish study included AD and VaD.

An alternative methodology is a two stage screening process such as part of larger population health studies. This was used by two Nordic studies from Sweden -

The Lundby Study (Rorsman et. al., 1986), and from Finland (Sulkava et. al., 1985).

Some studies of dementia prevalence in the elderly have used a lower cut-off age of 60 years and thus may provide data on prevalence in some younger people; studies of this type have been performed in Appignano, Italy (Rocca et. al., 1991a) and in the Gospel Oak Study, London (Livingston et. al., 1990). However, in the Gospel Oak study, only women were included in the 60-65 year age group.

The available data on broad dementia diagnoses in people under the age of 65 years are summarised in table 5.

	Age Group (Years)						
Study	**30-34**	**35-39**	**40-44**	**45-49**	**50-54**	**55-59**	**60-64**
Framingham	---------- 0 ----------			77	40	86	249

** Age group 60-69

Table 6 - Age Specific Prevalence Of Alzheimer's Disease (Per 100,000 population) in Younger People

Immediately evident is the variability in the data, and as with the figures for broad dementia, those studies which screened populations of subjects failed to find cases unless large scale screening was performed.

Identification of possible presenile VaD (Multi-Infarct) patients is included in only two studies (table 7)

	Age Group (Years)						
Study	**30-34**	**35-39**	**40-44**	**45-49**	**50-54**	**55-59**	**60-64**
Scotland	--	--	3.5	5.3	12.9	27.0	52.2
Finland	---------- 80 ----------						
	(5/6120)						

Table 7 - Age Specific Prevalence Of Vascular Dementia (Per 100,000 population) in Younger People

From this review of the literature on the epidemiology of dementia in younger people it is clear that when compared to older population there is relatively limited information available. The available data are derived from studies of differing methodology and consider only the most common dementias as found in the elderly. Notably, none of the studies considers frontotemporal dementia, a disorder known to occur relatively commonly in clinic based samples of younger people with dementia (Neary, 1990; Ferran et. al., 1996; Harvey et. al., 1996).

Epidemiological studies of dementia in younger people need to be based upon very large populations at risk, and thus for practical purposes usually follow a methodology based upon identification of diagnosed cases. Both of the UK based studies (Scotland and Northern Region) primarily identified cases from hospital inpatient notes, although supplementary sources of identification were included in both studies. In the Scottish study the completeness of their data was tested by examining case registers which confirmed that all cases of presenile dementia in Scotland were admitted as inpatients at some time during their illness (McGonigal et. al., 1992). Similarly in the Northern Region study, few cases were referred outside of the catchment area. Both of these studies were therefore confident of the completeness of their case finding, however for current and future investigators the situation may not be so simple. In particular, both of these studies were completed prior to 1988. The NHS reforms that have been occurring during the late 1980's and 1990's are likely to have made this type of case note research much more difficult. The closure of large mental hospitals and the introduction of community care has resulted in the establishment of many small community mental health trusts, each usually has its own case notes, and computerised patient databases. In parallel with this, the number of acute hospital beds has been declining, and increasing amounts of medical investigation is carried out on an outpatient basis. In the new NHS it may be much less likely that every younger patient with dementia will have an inpatient admission for diagnosis. Moreover, the Community Care Act (1990) has changed the organisation of social services, one effect of which has been that rather than being placed in state run residential or nursing homes in their local area, patients may be more likely to be placed in contracted private care outside of their home area. In the design of this study we have attempted to address these issues while taking into account the need to design a research protocol that is methodologically comparable to the existing studies.

1.3 The Diagnosis of Dementia in Younger People

This study is based upon the application of validated clinical diagnostic criteria, which are available for a growing range of diseases. When applied with care, they can provide good sensitivity and specificity of diagnosis. The following is a review of the diseases and diagnostic criteria being considered in this study.

1.3.1 Dementia

Dementia is characterised by the development of deficits in multiple domains of cognition which may be due to a specific aetiology such as AD or VaD, from the effects of a general medical condition, or from the persisting effects of a toxic or intoxicating substance. In order to make a specific diagnosis of one of the dementia syndromes, the first stage is to confirm that a dementia is actually present. The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders version 4 (DSM-IV) (American Psychiatric Association, 1994) provides a concise definition of dementia (Appendix A1.1, page 119). Based upon identification of cases of dementia according to these criteria it is then possible to make more specific diagnoses.

1.3.2 Alzheimer's Disease

Alzheimer's Disease is a neuropathological diagnosis determined by the presence of neurofibrillary tangles and senile plaques in the brain of a patient with dementia (Gearing et. al., 1995) . The disease frequently starts with memory impairment, but is invariably followed by a progressive global cognitive impairment. Neurological examination is often normal early in the disease. Structural neuroimaging may be normal early in the disease, but cerebral atrophy, particularly of the medial temporal lobe structures, is apparent as the disease progresses (Rossor, 1993). Three main sets of diagnostic criteria have become widely accepted; the DSM-IV (American Psychiatric Association, 1994), the World Health Organisation 10th International Classification of Diseases (ICD-10), and the National Institute of Neurological, Communication Disorders and Stroke / Alzheimer's Disease and Associated Disorders Association (NINCDS / ADRDA) research diagnostic criteria for AD (McKhann et. al., 1984):

DSM-IV

A DSM-IV diagnosis of AD requires the patient to have developed deficits in multiple domains of cognitive function which consist of memory impairment, plus one or more impairments in the domains of language (aphasia), motor activities (apraxia), visual perception (agnosia) and executive functioning (frontal lobe function) (American Psychiatric Association, 1994). Furthermore these deficits should be significant enough to impair social and / or occupational function. The development of these symptoms should have been gradual, progressive and not associated with other CNS diseases, systemic disorders known to cause cognitive impairment, or substance abuse. The deficits should not occur exclusively during a delirium, and should not be better accounted for by any other DSM-IV diagnosis, for example a major depressive disorder.

ICD-10

The ICD-10 diagnostic guidelines define dementia as a decline in both memory

There should be an absence of other systemic or brain diseases that could mimic dementia, excluded by clinical examination and special investigations. The symptoms should not have a sudden onset, and there should be no neurological signs to suggest focal brain damage.

The ICD-10 criteria are less specific in the definition of the domains of impairment required for a diagnosis of dementia, but as with the DSM-IV, they focus on the course of the disease, and the absence of other signs of systemic or neurological disease.

NINCDS/ADRDA

The NINCDS/ADRDA provide more comprehensive research diagnostic criteria for AD, and permit levels of certainty (definite, probable, possible) to be assigned to the diagnosis (McKhann et. al., 1984).

A diagnosis of **definite** NINCDS/ADRDA Alzheimer's Disease requires neuropathological confirmation of the disease.

A **probable or possible** diagnosis of AD requires that dementia is established clinically with the cognitive impairment documented using a test such as the Mini Mental State Examination (Folstein et. al., 1975), and confirmed using formal neuropsychological testing. There must be deficits in two or more areas of cognition with progressive worsening of memory and other cognitive functions. Consciousness should be undisturbed and there should be an absence of systemic or other brain disease that could account for the symptoms. Notably, the criteria require an onset of the disease between the ages of 40 and 90 years.

The criteria then provide several sections to enable probable cases to be differentiated from possible cases. Probable AD is supported by progressive deterioration of specific cognitive functions, impaired activities of daily living and altered behaviour. It also recognises that there may be a family history. Specific investigations such as lumbar puncture should be normal, the EEG may show slow wave activity, and structural imaging should show progressive cerebral atrophy.

Other features are recognised as being consistent with probable AD, these include; plateaux in the course of the disease, associated psychiatric and behavioural symptoms, neurological abnormalities such as myoclonus and gait disorders, seizures in advanced disease and the occasional finding of a normal CT scan. Features which make a probable diagnosis of AD unlikely include a sudden or apoplectic onset, focal neurological findings, and seizures or gait disorder early in the disease.

Those patients with typical core features but factors making a probable diagnosis unlikely are defined as having **possible** AD. Reliability and validity studies of the criteria have been carried out and suggest that when diligently applied 80% specificity is possible (Blacker et. al., 1994).

1.3.3 Vascular Dementia (VaD)

Neuropathologically, VaD includes cases of dementia resulting from ischaemic and heamorrhagic brain lesions, and from ischaemic-hypoxic damage such as occurs following cardiac arrest. These pathological changes result from a range of underlying aetiologies complicating accurate diagnosis in life. Diagnosis is also complicated by the uncertainty of ascertaining the temporal relationship between cerebral insults such as strokes, and the onset of the dementia.

Diagnostic criteria for VaD are less well developed (Verhey et. al., 1996) and there is no firm consensus on the most appropriate criteria to use for clinical trials (Antuono et. al., 1997).

DSM-IV criteria (American Psychiatric Association, 1994) are very similar to the criteria for AD, but require the presence of focal neurological symptoms, or neuroimaging signs of multiple infarctions in the cortex. The ICD-10 criteria require a history of transient ischaemic attacks, or a succession of small strokes. The important presence of vascular risk factors is recognised, together with the findings of focal neurological signs and symptoms and neuroimaging confirmation of vascular lesions.

In 1993 a work group of the National Institute of Neurological Disorders and Stroke (NINDS) and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) reported on a workshop held to discuss diagnostic criteria for research in VaD (Roman et. al., 1993). They recognised the difficulties inherent in the diagnosis, and classified VaD syndromes as follows:

1. Multi-Infarct Dementia
2. Strategic Single Infarct Dementia
3. Small Vessel Disease with Dementia
4. Hypoperfusion
5. Haemorrhagic Dementia
6. Other Mechanisms

This classification shows the difficulty of establishing a single set of diagnostic criteria for a disease with at least six discrete aetiologies.

A summary of the criteria is presented in appendix A1.3. The working group recognised that the criteria were not ideal. Clinical application results in the selection of a 'pure' group of vascular dementias, which undoubtedly exclude many patients with a vascular component to their disease.

1.3.4 Dementia with Lewy Bodies (DLB)

The neuropathological hallmark of DLB is the finding of numerous eosinophilic inclusions (Lewy Bodies) in cortical neurones of a patients with dementia. Rarely Lewy bodies are the only pathological changes present, although more commonly there are Alzheimer type senile plaques. Neurofibrillary tangles are usually rare or absent. The dementia often presents in a similar way to AD, however, frontal lobe and visuo-spatial impairments, unlike in AD, usually occur early in the disease. Other features which differentiate DLB from AD include: motor features of Parkinsonism, prominent visual hallucinations, systematised delusions, marked fluctuation, falls and syncopal episodes. The consensus criteria for DLB reflect these features (appendix A1.4) (McKeith et. al., 1996).

1.3.5 Frontotemporal Dementia (FTD)

Frontotemporal Dementia describes a clinical syndrome of behavioural disorder associated with fronto-temporal cerebral atrophy (Gustafson, 1987; The Lund and Manchester Groups, 1994), usually beginning before the age of 65 years. The syndrome has three main pathological substrates: in the frontal lobe degeneration type nerve cell loss and spongiform change is seen; in the Pick's disease type, swollen or 'ballooned' neurones (Pick cells) and intraneuronal inclusion bodies (Pick bodies) are present; and in the third variant of the disease, spinal motor neurone degeneration occurs in association with frontal lobe degeneration type pathology (Neary et. al., 1993).

The core clinical features of these patients are the insidious onset of a selective loss of cognitive abilities, namely language and/or frontal executive function,

with the relative preservation in other domains such as episodic memory, orientation and visuo-perceptual function. Personal and social awareness is lost early, and the disease is associated with disinhibition, mental rigidity and inflexibility in association with maintained general independence.

The diagnostic criteria (appendix A1.5) are useful for identifying groups of patients with this syndrome, however, the disparate pathology underlying the disease means that this will inevitable be a heterogeneous group.

1.3.6 Alcohol Related Dementia

Alcohol-Induced Persisting Dementia (DSM-IV), alcoholic dementia (ICD-10) and alcohol related dementia (ARD) all refer to patients with a history of chronic alcohol abuse presenting with cognitive impairments fitting a picture for dementia. As with primary degenerative dementias the deficits progress with continued drinking, however, there is evidence to suggest that they may become static or even regress if abstinence is attained (Tuck et. al., 1984). In addition to general ARD, there are a number of specific syndromes related to alcohol induced brain damage: Wernicke-Korsakoff syndrome (thiamine deficiency); Marchiafava-Bignami disease; pellagrous encephalopathy (niacin deficiency); and acquired hepatocerebral degeneration (shunting of portal blood to the systemic circulation). Unlike ARD, these syndromes all have distinctive pathology and links to established pathogenesis (Victor, 1994).

Surveys of alcoholics attending from treatment suggest that up to 50% of those over the age of 45 years with a lengthy drinking history will have evidence of cognitive impairment (Edwards, 1982). In surveys of patients being investigated as inpatients for dementia a mean of 10% have been found to have alcohol as the most likely contributing cause (Lishman, 1997).

Neuropsychologically patients have deficits of memory function, speed and attention, visuo-perceptual function and particularly frontal lobe (executive) function (Grant, 1987; Pohl, 1987). Neuropsychological deficits are usually mild to moderate and show slow, but never complete recovery with abstinence. The presence of frontal lobe deficits seems to predict a poor outcome as abstinence is difficult to maintain, resulting in a chronic downwards spiral (Gurling et. al., 1986; Goldman, 1990).

Neuroimaging studies consistently show cerebral atrophy in 50-70% of chronic alcoholics with cortical shrinkage and ventricular enlargement, often particularly affecting the frontal lobes (Gurling et. al., 1986; Smith and Atkinson, 1995; Lishman, 1997).

Neuropathologically, there is considerable heterogeneity. The complicating factor is to identify consistent pathological change that defines a primary alcohol related dementia syndrome. In many cases there is also conflicting evidence of a secondary dementia syndrome related to the effects of alcoholism on nutrition and the systemic systems, such as Wernicke lesions in the base of the brain. The most consistent findings have been cerebral atrophy, a reduction in the amount of white matter and a reduced thickness of the corpus callosum. Microscopically there is nerve cell loss, particularly in the frontal cortex, although without specific pathological hallmarks (Lishman, 1997).

Epidemiologically few studies have attempted to measure the prevalence of an alcoholic dementia syndrome. Copeland et al (1992) in a study based on 1,070 people over the age of 65 years living in Liverpool found a prevalence of 0.3% for alcohol related dementia. In a study of elderly people in institutional care, those patients with ARD were found to be a mean of 10 years younger than subjects with other dementias (Carlen et. al., 1994). Notably, this same group of alcohol related dementia patients had milder cognitive impairments, and also had twice the average length of institutionalisation (Carlen et. al., 1994).

Patients with ARD are likely to be younger and to require long term care, often in institutions, in a study of younger people with dementia it is important to include this group of patients as they are likely to contribute to overall burden of care for younger people with dementia.

The DSM-IV criteria for Alcohol-Induced Persisting Dementia require the criteria for dementia with evidence from the history, physical examination or investigations that the deficits are etiologically related to the persisting effects of alcohol.

1.3.7 Other Degenerative Dementias

Beyond these major causes of dementia there are a large number of diseases that result in cerebral degeneration and dementia. In a study of rare diseases such as the young onset dementias it is important not to exclude any specific diseases that result in syndromes fulfilling the criteria for dementia. For diseases that do not have well validated formal diagnostic criteria clinical judgement based upon research findings and reports of case series form the basis of the clinical diagnosis. Diseases in this group are likely to include HIV/AIDS related dementia (Lipton, 1997), Huntington's disease (Jones et. al., 1997), Multiple Sclerosis (Rao et. al., 1991), Corticobasal degeneration (Schneider et. al., 1997), progressive supranuclear palsy (PSP) (Rossor and Brown, 1995) and the prion diseases (Collinge et. al., 1993b), including New Variant Creutzfeldt Jakob Disease (nvCJD) (Will et. al., 1996).

1.3.8 Other Acquired Causes of Cognitive Impairment

In any population of cognitively impaired younger people, having excluded degenerative dementias there will be a number of cases due to physical causes such as head injury, poisoning and substance misuse. Although the causes of cognitive impairment in this group are different from the degenerative dementias, in many cases the resulting deficits result in all the problems of dependency and need for care as for a patient with degenerative dementia, except that there will often be a need for very long term (life long) care.

1.4 Caregiving in Dementia

Patients with dementia inevitably become incapable of caring for themselves as the disease progresses. The responsibility for their care at this point falls on family members, often the spouse, or on the state for those without relatives.

The impact or burden of caring for a mentally ill relative on family members was first recognised by Grad & Sainsbury in 1963 , and has become a widely recognised and researched issue. The following is a selective review of the very large literature available on caregiving and its effects on the patient and caregiver.

1.4.1 Caregiver Gratification

Before turning to the more commonly studied caregiver burden, or negative aspects of caring for someone with dementia it is important to consider what is known about the gratification and rewards of caregiving. Clearly, if there were no gratification involved there would be little drive for the caregiver to care, yet the majority of care provided to people with dementia is by informal caregivers.

The small amount of formal research in this area suggests that the gratifications of caregiving are derived from the continuity of the marital relationship. In a study of 50 wife caregivers, Motenko (1989) identified four factors which were particularly associated with caregiver gratification:

- Continuity Of Closeness Of The Marital Relationship

- The Meaning Of Caregiving To The Carer
- The Social Support Network
- The Patient Illness Characteristics

The influence of the marital relationship on caregiving is further discussed in section 1.4.4, page 28. Marital closeness, and changes in this facet of the relationship were important. Wives who perceived no change in their degree of marital closeness were those that derived the greatest satisfaction from caregiving. By contrast, those with a distant relationship that became close, or those with a close relationship that become distant with the onset of the disease all reported less satisfaction with their caring role.

In terms of the caregivers views of caring, those wives who provided care to reciprocate past attention and love from their husbands derived the greatest satisfaction, while the wives who provided care out of a sense of duty experienced less gratification. Similarly, it was the continuity of the social support network that provided gratification, this was both in terms of external support, and the support of having a husband at home, rather than living alone (with a husband either dead or in an institution).

In terms of patient characteristics, the longer the person was sick the less frustration the carer experienced. Lack of gratification came from disruptions to the carers life caused by more rapid changes in the patient. A slow illness with minimal behaviour change and thus disruption was associated with higher gratification in caregiving.

This study, although limited by small numbers and the use of exclusively wife caregivers, does provide insights into the caregiving experience and the reasons that caregivers go on caring.

1.4.2 Caregiver Burden

Despite the gratifications that maintain caregivers in the caring role, the experience of a sense of burden is universal amongst carers (Rabins et. al., 1982; Mace and Rabins, 1981). The experience of burden in caregiving is a broad concept that infiltrates many areas of the caregivers life. Caregiver burden has been defined as:

"The physical, psychological or emotional, social, and financial problems .. experienced by family members caring for impaired .... adults" (George and Gwyther, 1986)

This definition has helped to lead to the conceptualisation of caregiver burden in terms of a number of domains: physical health; mental health; social participation and financial resources. Caring for someone with dementia has an influence on all of these caregiver domains.

In terms of physical health caregivers have been shown to have higher blood pressure than non-caregivers (King et. al., 1994), and to have more complaints of physical symptoms than controls (Baumgarten et. al., 1992). Lutzky and Knight (1994) measured cardiovascular reactivity (CVR) in 92 spouse caregivers, and found that increased CVR (an independent measure of stress) was associated with the frequency of problem behaviours and the duration of caregiving. Other studies which have examined overall physical health in caregivers have all confirmed that caregiving has a significant negative effect (Pruchno et. al., 1990; Neundorfer, 1991; Bergman-Evans, 1994).

The psychological effects of caregiver burden include the subjective experience of stress (Eagles et. al., 1987) or distress (Gilleard et. al., 1984), and psychiatric disorders including depression (Russo et. al., 1995; Livingston et. al., 1996) and anxiety (Russo et. al., 1995).

Depression and anxiety disorders are particularly common with up to 45% of women carers of people with dementia being affected by depression (Livingston et. al., 1996). Other studies have founds rates of 27% for Major Depression and 16% for Generalised Anxiety Disorder amongst carers. By contrast to anxiety and depression however, other conditions such as panic disorder, alcohol dependence and psychotic disorders are rare (Russo et. al., 1995).

Caring for someone with dementia requires the caregiver to spend increasing amounts of time with the sufferer, reducing the opportunities for social interaction outside of the home. Moreover, progressive disability and behaviour change may discourage friends and family members from visiting thus further isolating the caregiver (Wenger, 1994). Social support, and particularly the continuation of the social support network help to provide gratifications in caregiving (Suitor and Pillemer, 1993; Carlson and Robertson, 1993; Robinson and Steele, 1995; Haley, 1997).

A further dimension of caregiver burden is financial burden. Caring for someone with dementia, and particularly a younger person places heavy financial burdens

assessments are useful, a range of more specific dementia caregiver burden assessments have been developed.

To conceptualise caregiver burden the determinants are frequently divided into 'objective' and 'subjective' components (Thompson and Doll, 1982). Objective burden (OB) relates to factors in caring that disrupt family life such as changes in finance, role, family life, supervision and support networks. Subjective burden (SB) refers to the caregivers physical and psychological responses, in terms of factors such as stress, overload, embarrassment, resentfulness and unhappiness. Although these concepts appear distinct there is frequently confounding of objective and subjective sources of burden, and the majority of the available scales have been subject to criticism (Vitaliano et. al., 1991b; Donaldson et. al., 1997).

Despite the conceptual and methodological problems (Stephens and Kinney, 1989), a wide range of comprehensive caregiver burden measures have been developed of which 10 were reviewed in detail by Vitaliano et al (1991b). Their recommendations for choosing an appropriate scale for a particular study are summarised as follows:

- Choose a scale specific to the population being studied; e.g. if the sample contains only carers for patients with AD, use a scale designed and validated for AD carers.

- Specific burden measures should always be combined with general measures such as the GHQ or depression/anxiety scales to relate specific burden to more general distress.

- Brief measures are more preferable as they reduce participant fatigue, and reduce the time and costs for administering and scoring.

A final point, rarely made explicit, is that specific caregiver burden measures are only valid in populations of caregivers who are actually caring for someone with dementia. Although an apparently obvious point, this effectively prevents use of the scale in control populations of non-caregivers, or even with caregivers who have stopped caring, such as when the sufferer dies or enters institutional care.

The available evidence supports the need for the assessment of caregivers on a range of assessments that will incorporate both specific and general measures of burden.

1.4.4 The Marital Relationship & Caregiving

The responsibility of caregiving most frequently falls upon the spouse. Amongst older people with dementia it is more likely that a wife will be caring for her husband (Fitting et. al., 1986), and the marital relationship is one of the determinants of caregiver satisfaction. In a study of young onset dementia, caregiving is likely to be more evenly split between husbands and wives. A number of studies that have compared husband and wife caregivers provide insights into the different responses each gender has to the caregiving rôle.

Fitting et al (1986) used a structured interview to assess 54 spouse caregivers (28 men and 26 women), who were caring for a partner diagnosed with a dementing illness. The carers age ranged from 50 years to 90 years with a median age of 67 years. The assessment examined interpersonal relationships, social networks, caregiver burden, caregiver personality and the functional impairment of the demented person. The results showed that husbands and wives experience caregiving in a similar way. Younger wives and older husbands caring for severely demented partners were however, more burdened. Wives tended to rate more deterioration in their marital relationship than husbands, and as a group rated themselves as more distressed than the men. The younger caregivers in the sample also rated themselves as more lonely and more resentful of their caregiving role.

Zarit et al (1986) examining 31 husband and 33 wife caregivers also found that wives initially reported more burden than husbands. However, over a 2 year period in this longitudinal study, the difference disappeared. The sense of burden appeared to correlate with the style of caring; husbands adopted an instrumental approach to caregiving at an early stage, using practical techniques to deal with problems, while wives initially had difficulty coping the with emotional issues involved, but later adopted a more practical approach.

In a study of 92 spouse caregivers (52 wives and 40 husbands), depression, stress, burden, neuroticism, cardiovascular reactivity and coping style were assessed (Lutzky and Knight, 1994). The male and female caregivers were similar in terms of age, income, education and social support, and the severity of the dementia in the patient groups were also similar. As in all of these studies, wives reported greater levels of burden than husbands, and had higher rates of psychological distress and depression. However, the wife caregivers were found to have higher rates of neuroticism, and the authors hypothesise that because of this they tend to report symptoms of distress more readily. Similarly, in terms of coping style, wives tend to use an 'escape/avoidance' style, rather than 'seeking social support'.

Clipp & George (1993), compared 272 spouse caregivers of dementia patients with 30 spouse carers of cancer patients. They found that caring for someone with dementia was more distressing than caring for someone with cancer, moreover, they also identified an effect of age of caregiver, with younger caregivers also reporting a higher level of burden than older carers. Unfortunately, the study did not compare husband and wife caregivers.

A significant part of the marital relationship relates to intimacy and sexual activity. Three studies have attempted to assess the effect of one partner becoming demented on this aspect of marriage. Morris et al (1988) explored the quality of the marital relationship between 13 wives and 7 husbands caring for their demented spouses. A lack of intimacy in the relationship, either before the dementia or since it had developed predicted greater burden in the carer. Those caregivers who experienced a loss of intimacy with the development of the dementia were the most likely to suffer depression.

Assessing sexual activity, Wright (1991) studied 30 couples where one partner had been diagnosed with AD with 17 couples where both partners were healthy. Only 27% of the AD couples were still sexually active compared with 82% of the well couples. This decline in sexual activity is supported by other research which suggests that a combination of stress and concern by the well partner about the demented persons ability to consent to sexual activity are to blame for this difference (Gwyther, 1990). Despite the decline in sexual activity in the majority of cases, wives of 14% of the affected males reported unwelcome sexual overactivity, and notably in half of theses cases the affected person was under the age of 60 years (Wright, 1991).

Overall these data suggest that women experience greater burden and distress than men when caring for a demented spouse. However, coping strategies may differ between the sexes, at least early in the illness. The development of dementia has a profound effect on marital intimacy, which in itself may be an independent vulnerability factor for burden. Younger men with dementia appear to have higher rates of unwanted sexual overactivity placing additional stress on their spouse caregiver.

1.4.5 Non-Spouse Caregivers

By comparison to spouse caregivers, there has been less formal research into the burden experienced by non-spouse caregivers; i.e. other family members, friends, and professional carers.

Several surveys have examined stress symptoms and psychological disturbance amongst professional carers. For nurses in a variety of hospital ward settings, similar levels of stress (measured using the GHQ-60) have been found, although younger, lower-ranking and less experienced nurses who spend more time with patients are more likely to have higher levels of stress (Livingstone and Livingstone, 1984).

Macpherson et al (1994) used the GHQ-30 to assess 188 professional carers from four care settings; an EMI (Elderly Mentally Infirm) home, and EPH (Elderly Person's Home), a Hospital ward and a PNH (Private Nursing Home). Their sample was 91% female, and they found a GHQ caseness rate of 26.6%; not significantly different from the general population norm for GHQ caseness in women generally (33%) (Huppert et. al., 1988). There were no differences between any of the care settings. However, there was a strong association between GHQ score and the number of episodes of patient aggression experienced by staff in the preceding week. Moreover, those 'disturbed' staff were more likely to perceive a lack of support at work, and to report 'shouting back' at patients in response to aggression. This association between perceived lack of support and burden appears to be a common factor between spouse and professional carers.

Those patients with dementia not cared for either by a spouse or a professional carer are either living alone, or are cared for by another family members or a friend. Amongst older people with dementia, the most common family member to whom the burden of caregiving falls is the daughter or daughter-in-law.

Expressed emotion (EE) has been examined in daughter carers for its influence on

Coping Style The use of emotion related coping styles predict higher burden ratings in carers. These type of coping styles include escape/avoidance strategies, and the expression of anger and denial. By comparison practical coping styles such as seeking information, seeking social support and problem-focused caring are associated with lower ratings of burden (Forstl and Geiger-Kabisch, 1995; Kramer, 1997).

Family Support The consistency and continuity of family support networks is an important predictor for lower caregiver burden. The distancing and loss of family support predicts higher levels of burden. The presence of social conflict is a particular indicator of burden (MaloneBeach and Zarit, 1995).

Formal Support Formal support networks, in terms of practical assistance appear to have less influence on caregiver burden, and are a less powerful predictor of burden than family support (Vernooij-Dassen et. al., 1996). Other research reviewing the effects of respite care also fail to find any effect on caregiver burden (Colerick and George, 1986; Flint, 1995).

Physical Health Deteriorating physical health was particularly reported by daughters caring for parents as a predictor of burden, however, stressed spouse caregivers also report higher levels of physical symptoms (Pruchno et. al., 1990; Neundorfer, 1991; Baumgarten et. al., 1992; Hooker et. al., 1992; Bergman-Evans, 1994).

Previous Psychiatric Disorder Caregivers who had suffered from a psychiatric disorder prior to becoming a caregiver, are more likely to become stressed and psychiatrically ill when they have to look after someone with dementia (Russo et. al., 1995).

Personality Several studies have examined personality traits in caregivers. The only consistent trait relating to burden to emerge from these studies has been neuroticism (Hooker et. al., 1992; Reis et. al., 1994; Welleford et. al., 1995).

Expressed Emotion High-EE in the caregiver tends to be associated with increased experience of distress and burden, and to be associated with less effective coping styles (Bledin et. al., 1990; Vitaliano et. al., 1993).

Reviewing this list of caregiver factors that predict burden, it is possible to see that many of them are inter-related, e.g. neurotic personality traits and high expressed emotion have a logical association with emotion-focused caring. The surprising finding is that formal support has little effect on burden, suggesting that the types of formal support being provided (usually directed at the patient) are ineffective, and that relieving caregiver burden requires support interventions that focus on the caregiver and their needs, rather than the needs of the patient. However, many of these studies overlap and there is little consistency in the conceptual framework used to define caregiver characteristics.

1.4.6.2 Patient Factors

Personality Change Patients with dementia inevitably undergo personality change. In the two studies that have assessed change in patient personality with caregiver burden, both found a significant correlation (Welleford et. al., 1995; Williams

et. al., 1995).

Intimacy

Intimacy with the caregiver, whether it is the spouse or daughter is associated with reduced burden. A loss or lack of intimacy increases the sense of duty, burden and depression in the carer (Morris et. al., 1988; Wright, 1991; Walker et. al., 1992; Ballard et. al., 1995)

Cognitive Impairment

The relationship of the degree of patient cognitive impairment to caregiver burden is also not straightforward. Donaldson et al (1997) in their systematic review identified ten papers addressing this issue of which three failed to find a significant relationship. A non-linear relationship between cognitive impairment and burden has been suggested; with maximum burden at the point when the cognitive impairment demands that the caregiver seeks outside help, and reducing burden once this point is passed (Pruchno and Resch, 1989).

Functional Disability

The degree of functional disability is only a weak predictor of caregiver burden. The available evidence suggests that the sense of caregiver burden has little relationship with the physical disabilities of the patient. Donaldson et al (1997)found that only 1 of 7 studies examining the effects of ADL impairment on burden found a significant relationship between the two.

Non-Cognitive Symptoms

Non-cognitive symptoms of dementia include mood disturbance, psychotic symptoms (delusions and hallucinations), neurovegetative change and behaviour disturbance in the affected person. Caregivers appear to find this type of symptom particularly burdensome (Donaldson et. al., 1997; Teri, 1997). The non-cognitive symptoms of dementia are usually disturbing, disruptive and emotion generating for the caregiver; all factors which lead to increased burden.

The non-cognitive symptoms emerge as the principal patient predictor of caregiver burden, although their mechanism of inducing burden is likely to be through caregiver factors. As with caregiver factors there is clearly overlap between these different factors; e.g. personality change and non-cognitive symptoms on intimacy and the relationship between the carer and patient.

1.4.7 Predictors of Institutionalisation

Institutionalisation of the person with dementia is often viewed negatively; the caregiver may feel defeated and to have failed, and a major financial burden is shifted to society. Identifying the factors which predict institutionalisation may identify targets for intervention that could reduce the need for institutional care.

In an early study, 209 caregivers were followed longitudinally over a period of one year (Colerick and George, 1986), by which point 63 patients had entered institutional care. Both patient and caregiver characteristics were compared. Those who remained at home were more likely to have an elderly, unemployed spouse as a caregiver. Those who became institutionalised were most likely to be cared for by an employed daughter who was experiencing high levels of burden prior to institutionalisation. Notably they were also making heavy use of community services, which failed to prevent institutionalisation. Patient characteristics failed to predict the need for institutional care.

Gold et al (1995) interviewed 157 caregiver dyads and followed them up over a period of two years. During this period 45 remained at home, 69 entered institutional care and 43 died. In terms of the reasons given for institutionalising the person they were caring for, 81% of the carers cited factors relating to the patient (wandering, incontinence, aggression and the need for constant supervision) while only 52% reported reasons relating to themselves as a caregiver (exhaustion, needs of other family members and physical illness). However, those who institutionalised their relative were more burdened initially, and were looking after someone with more behavioural problems; after the placement they became less burdened. By comparison those who kept their relative at home became more burdened by the second assessment.

In terms of patient factors alone, as with predictors of burden, it is the presence of non-cognitive symptoms that predict institutionalisation (Mortimer et. al., 1992; Lawlor, 1994; Martinson et. al., 1995; Magni et. al., 1996)

Caregiver burden is a complex, multi-factorial concept that encompasses factors involving the patient, the caregiver, the family and external sources of support. Although considerable research has been performed in this area there remain many challenges to be overcome before these interrelationships can be fully understood. The assessments available, and those used in previous studies tend to lack concrete conceptualisation of the factors being assessed making comparisons between studies difficult. The most consistent predictors of burden, and hence outcome appear to be those relating to the caregiver, and non-cognitive symptoms in the patient. Almost all of the available research has focused on populations of older patients and their predominantly female carers.

1.5 The Economics of Dementia

1.5.1 Cost-Of-Illness Methodology

Health care in the developed world is increasingly driven by economic pressures. Decisions regarding the introduction of new treatments and the re-organisation of services are now often based upon analyses of cost effectiveness, efficiency and cost minimisation. Caring for people with dementia is inevitably costly as a result of the need for supervision, support, and in many cases, institutional care.

Cost-of-illness studies attempt to estimate the direct and indirect economic burden of a disease (Robinson, 1993; Rice, 1994; Greenhalgh, 1997). Direct costs relate to costs for which a payment is made and include medical care, investigations, nursing care, home care, drugs, respite care, institutional care, inpatient and outpatient services. Direct costs are usually estimated from the number of services received multiplied by the unit price or charge. For some items, such as drug costs, these are relatively fixed and based upon published 'market' rates. In the United States medical care services are often costed for insurance purposes, providing a reasonably reliable figure upon which to base an economic analysis. It is only more recently that the UK NHS and social service have begun to publish detailed cost breakdowns for health and social service interventions, and these must often be gleaned from multiple sources (Gray and Fenn, 1993).

For most diseases, indirect costs are derived from two sources, morbidity and mortality. Morbidity costs relate to the value of reduced or lost productivity as a result of the disease. Mortality costs relate to shortened life expectancy, and the value of the productive time lost due to premature death (Rice, 1994). Chronic disabling diseases such as dementia, have an additional source of indirect cost related to informal caregiver time, and their own loss of productivity (Weinberger et. al., 1993; Clipp and Moore, 1995).

The majority of cost-of-illness studies in dementia have been prevalence-based studies; the direct and/or indirect economic burden as a result of the prevalence

of the disease, estimated over a period of time (usually 1 year). This type of study identifies the main components of the cost and can identify possible targets for economy or redistribution of resources. Prevalence based costing can be performed by two broad approaches - 'top-down' and 'bottom-up'. In the 'top-down' approach the total cost for utilisation of a resource is calculated (e.g. all nursing home care), and then the proportion of this that relates to a specific disease is estimated by identifying the proportion of cases with the index disease that are making use of the resource. This was the primary methodology used by Gray & Fenn to estimate the cost of AD in England in 1990/91 (Gray and Fenn, 1993). For example, with acute and geriatric hospital care the total number of bed days occupied for mental disorders was obtained from the Hospital Inpatient Enquiry. Published data on prevalence of AD were then used to estimate the proportions of hospital patients in acute and geriatric beds with AD, and this was combined with the cost per bed day to give the cost of inpatient care (Gray and Fenn, 1993). This type of methodology gives a useful indicative estimate of total cost, but it is primarily applicable to large scale studies, and provides little detail on local costs or local cost variation.

A 'bottom-up' analysis is usually based upon a sample of patients identified from a prevalence study or other population cohort. In a 'bottom-up' study, details of direct resource utilisation and/or indirect factors are collected from each subject. These data are then costed to give a monetary value and may be presented in several ways. By summing data from all subjects a total cost-of-illness for the study group can be calculated, and subsequently extrapolated further based upon prevalence data and population figures. However, as other data are often available for the subjects, other imaginative analyses can be performed, for example relating cost to diagnosis, severity of disease and a range of other factors. In an example of this type of study, Livingston et al (1997) sampled a population of 700 older people in a London borough and interviewed them to ascertain individual service usage. Costing of services permitted comparison of service use according to diagnosis (dementia, depression, anxiety, activity limitation and those who were well). In particular this study was able to demonstrate that anxiety and depression, which were often untreated, were associated with significant cost when compared to people who were well.

1.5.2 'Top-Down' Cost-Of-Illness Studies in Dementia

Three major studies of the cost of dementia care using a 'top-down' approach have been published. Two earlier studies were based on US costs and examined the cost of Alzheimer's disease (Hay and Ernst, 1987) and was later updated (Ernst and Hay, 1994), and senile dementia (Huang et. al., 1988). Both of the American studies considered both direct and indirect costs, including mortality and morbidity costs. The third study was based in the UK and estimated the cost burden of illness across all the main areas of provision (hospital and residential care, general practice, day care, home care and informal care). Although the UK study estimated indirect costs, these consisted only of payments to informal carers and did not include morbidity or morbidity costs.

As all three of these studies followed different methodologies for estimating cost it is of interest to compare their results. However, a number of technical problems need to be resolved before a direct comparison can be made. First, the cost-of-illness estimates have been made for different years. The Ernst and Hay study is based upon 1983 costs, although subsequently updated to 1991, the Huang study is based upon 1985 costs, and the UK Gray and Fenn study is based on 1990/91 costs.We have therefore taken the estimates from these studies and corrected them for inflation at the standardised rates of 2% and 4% to 1997 prices. The second problem with comparing these studies is that the cost estimate given is total cost to the country (US or UK). To allow comparison between countries we have therefore calculated a cost per case based upon the number of cases reported by the study. This then allows a direct comparison between studies, however, caution is required in interpreting these comparisons due to the corrections and

assumptions that have been made. In particular, it is difficult to take into account the population demographic changes that will have occurred between the dates of these studies, and that are resulting in rising numbers of people with dementia. Finally, costs have been converted into £ sterling using a dollar exchange rate of £1=$1.66 (December 1997 rate).

The data on cost-of-illness from 'top-down' studies is summarised in table 8. Only cost estimates relating to direct costs and indirect costs from informal care are included. Huang et al made a separate estimate of indirect morbidity and mortality cost which is not shown in this table.

Study	Inflation Rate	1983	1985	1991	1997	Cost Per Case	Cost Per Case (£)	Cost Per Case (Direct Costs Only)
Ernst & Hay	**2%**	$B29.5	$B30.69	$B67.3*	$B75.79	$49,375	£29,044	£6,775
	4%	$B29.5	$B31.91	$B67.3*	$B85.16	$55,476	£32,633	£8,892
Huang et al	**2%**		$B44.72	$B50.36	$B56.72	$36,948	£21,734	£6,444
	4%		$B44.72	$B56.59	$B71.60	$46,644	£27,437	£8,135
Gray & Fenn	**2%**			£B1.04	£B1.17	£2,925	£2,925	£2,745
	4%			£B1.04	£B1.31	£3,287	£3,287	£3,067

$B=Billion Dollars, £B=Billion Pounds
*Updated figures from Ernst and Hay, 1994

Table 8 - 'Top-Down' Cost-of-Illness Studies in Dementia

There is clearly variability between the results of these three studies, with the UK study apparently showing significantly lower costs. The main difference between the UK and US figures relate to the calculation of indirect caregiver costs. Gray and Fenn calculate the indirect costs of informal caregivers from the payments they receive in the form of state benefits (Attendance Allowance etc.), while Ernst & Hay and Huang et al. calculate this indirect cost from the cost that would have been incurred if the care had been provided by nursing aides. By comparison, the Gray and Fenn methodology probably underestimates the economic burden, as benefits tend to be under-claimed, and no account is taken for loss of income or earnings by the informal carer. By removing the more difficult to estimate indirect costs of informal care, as shown in the final column of the table, a potentially more comparable measure of cost-of-illness in dementia is derived - the direct cost. With this correction, the two American studies remain comparable, however, the cost-of -illness for UK patients remains less than half that of the US patients. This cost difference is likely to be due partly to differing methodology in the studies, and more probably to differing health care costs in the two countries. Comparing these three studies provides an indication of the likely range of the real cost of dementia, and also highlights the methodological problems involved in interpreting these data, particularly when comparing studies.

1.5.3 'Bottom-Up' Cost-Of-Illness Studies in Dementia

Only a single major study has reported total cost-of-illness for dementia using a 'bottom-up' approach based upon patient samples from Northern California (Rice et. al., 1993). Ninety three patients with diagnosed AD living in the community were compared with 94 individuals in institutional care. As in the Ernst and Hay study (Ernst and Hay, 1994), the indirect costs were estimated on a replacement

basis, i.e. the cost of providing a formal replacement for the informal care received and excluded morbidity and mortality costs. Based upon 1990 costs, the study found similar annual costs for community care ($47,083 per year) and institutional care ($47,591 per year), although for those cared for in the community 73% of this cost related to unpaid informal care, compared to only 12% in institutionalised patients.

Correcting these costs for inflation and converting the costs into UK sterling is summarised in table 9.

Study	Inflation Rate	1990	1991	1997	Cost Per Case (£)
Rice et al	**2%**	$47,000	$47,940	$53,988	£31,758
	4%	$47,000	$48,880	$61,849	£36,382

Table 9 - 'Bottom-Up' Cost-Of-Illness Studies in Dementia

Comparing the results in table 8 and table 9 shows very close agreement between the cost of care derived from Ernst & Hay's study and that obtained by Rice et al. Both of these studies, although taking a fundamentally different approach to estimating cost-of-illness ('top-down' vs. 'bottom-up'), use similar methods for estimating direct and indirect costs and derive highly comparable per case costs. However, as already discussed, caution is required in interpreting these figures in absolute monetary terms due to the hypothetical nature of the estimates of indirect care costs, these results do, however, suggest that comparisons between studies taking different approaches to estimating cost are possible.

Extracting only the direct costs for comparison is more difficult in 'bottom-up' studies where the population being evaluated is not an epidemiologically valid sample. The Rice et al (1993) study is a comparison of two groups of patients (those in the community and those in residential care), but the proportions of patients in the two groups are not representative of the actual proportions of patients in the two care settings. However, extracting the direct care costs only gives an annual cost of £20,255 for all patients in the study when corrected for inflation by 3% and converted to £ sterling. Taking only those in the community however, the direct care costs are only £9,163, while for the sample in institutional care the annual figure is £31,169. This dramatically demonstrates the influence of institutional care rates on the overall cost of dementia care.

A number of other 'bottom-up' studies have examined the burden related to components of care received, such as the cost of informal unpaid care (Stommel et. al., 1994; Max et. al., 1995; Souetre et. al., 1995), the cost of community care (Souetre et. al., 1995; Livingston et. al., 1997), the cost of institutional care (Welch et. al., 1992) or the relationship between factors in the disease and the cost of care (Souetre et. al., 1995; Ernst et. al., 1997).

1.5.4 The Indirect Costs of Informal Unpaid Care

Estimating the monetary value of informal, unpaid care is probably the most complex and difficult area in cost-of-illness studies in dementia. By definition the carers involved are unpaid and thus a hypothetical estimate must be made of the value of this care input. For community resident patients, informal care is likely to represent the majority of the total cost burden. Three main methods have been used in existing studies, and unfortunately it is very difficult to compare results derived by each method.

The three methods available are, first, to use payments to informal carers as an estimate of the cost to the State of the informal care, and a surrogate maker of informal care costs. This is the method used by Gray and Fenn (1993), and derives the lowest estimated cost for unpaid care of all the published studies.

The second method is to value caregiver time by multiplying the number of hours of care provided by the gross national product per capita per hour. This method has been used in only one study

2. Hypothesis, Aims and Methodology

2.1 Hypothesis

Primary Hypothesis

The primary hypothesis is that dementia occurring in people under the age of 65 years is more heterogeneous than previously recognised, and that focusing only on the common causes of dementia, as defined from data on older populations, substantially underestimates the impact of dementia in this group.

Secondary Hypotheses

Within the young onset dementia group:

1. High levels of caregiver stress and burden are associated with behavioural disturbance and functional impairment in the patient, and with lack of support.

2. High levels of stress and burden result affect the mental health of the caregiver.

3. The level of support interventions, measured using the surrogate marker of cost of care received, has a negative correlation with caregiver stress and burden.

2.2 Aims of the Study

- To measure the prevalence, diagnoses and behavioural syndromes in a population based cohort of patients with young onset dementia, and to assess outcome over a 1 year period.

- To measure the burden in a population based cohort of carers for patients with young onset dementia, in terms of physical health, psychological well-being, and degree of carer burden in the main family caregiver.

- To measure the costs of care received in this cohort.

- Identification of risk factors in a family which should attract increased vigilance by service providers.

- To compare the relative burden and care cost of the particular diagnoses and their behavioural profiles.

- To apply data on the epidemiology and cost-of-illness to National figures to estimate the total UK burden of the dementias in this age group.

- To compare data collected in this younger group of patients with published historical data for older groups.

2.3 Methodology

2.3.1 Overview

	Case Identification	Patient/Caregiver Recruitment (T0)		Follow-up (T0 + > 1 year)
Patient Name	X			
Details of GP	X			
Request Case Notes	X----------	----------	----------	----------X
Request copy of GP Notes	X----------	----------	----------	----------X
GP Permission	X			
Contact Patient	X			
Informed Consent		X		
Patient Assessment		X		
Carer Assessment		X		
Health Economic Evaluation		X		
Outcome				X

2.3.2 Inclusion Criteria

- Diagnosis of possible Dementia according to DSM-IV Criteria (Appendix A1.1)
- Onset of dementia occurred before age 65 years (Current age may be > 65 years)
- Alive and resident within the boroughs of Kensington & Chelsea, Westminster or Hillingdon on the project census day (1st April 1995)

2.3.3 Exclusion Criteria

- Dementia due to the Human Immunodeficiency Virus (HIV) - Due to research in progress at both the Chelsea & Westminster Hospital and St Mary's Hospital it was decided not to include these patients in the study.

2.3.4 Ethical Issues

The major principals of ethical research enshrined in the Nuremberg Code and the Declaration of Helsinki are:

- The minimisation of harm,

- The maximisation of benefit (beneficence)
- Truth telling
- Autonomy and self determination through the process of informed consent.

Truth telling and disclosure can present considerable problems in patients with dementia. In particular, caregivers are often unwilling to allow the patient to be told their diagnosis, and even when told the diagnosis, patients with significant

A number of specific issues were considered:

I. Having identified a patients name as a possible case there was often no easy way of identifying who the primary family caregiver or next of kin would be. We were concerned that writing to a severely demented patient may be misinterpreted by a family member as unsympathetic. However, by contrast, we were also aware that if we wrote only to the caregiver of a mildly demented person this might similarly cause offence.

II. We were also concerned that some patients and caregivers may be unaware of their diagnosis, and would be upset by receiving a letter that mentions dementia or conditions such as Alzheimer's disease.

III. We recognised that there were likely to be more severely demented patients where informed consent would be impossible.

IV. There would be a significant number of patients without a caregiver or family member, and that some of these might also fall into category (III) above; yet excluding subjects in III and IV could bias the results of the study.

V. It was possible, as part of the assessment process, that significant unmet need might be identified. As an aim of the study was to examine the influence of patient, caregiver and support factors on outcome, the intervention of the investigator would be likely to introduce a confounding variable. However, this aspect of avoiding confounding the study had to be balanced with both the ethical and humanitarian issues involved.

To address some of these issues it was decided not to approach any patient or carer without the agreement of their General Practitioner and/or other doctor involved in their care. Whenever possible we asked the person referring the patient to discuss the referral with the patient and carer first, and ideally to introduce me to the family personally.

Initial approaches to patients would refer to dementia only in terms of 'memory problems' until personal contact had been established and the patient and carers understanding of their illness could be explored with them.

The aim was to obtain fully informed consent from all patients and carers. Where this was not possible in the patient due to the severity of the dementia a full discussion was carried out with both family and professional caregivers, and the next of kin was asked to sign to indicate their assent for the patient to be included. As the project was non-invasive and essentially involved no risks this was felt to be an appropriate procedure by all of the 5 ethics committees.

It was decided that should significant unmet need be identified, an outline of the problems would be sent to the GP and/or referrer to allow decisions to be made regarding increased support etc. Careful documentation of all such interventions were carried out.

Patient consent was not sought for access to medical records. Recently proposed legislation will potentially make this a requirement of similar projects in the future. Agreement to access medical records was sought from the doctor in charge of the patient. The need to obtain written consent from patients in order to access medical records would undoubtedly have hindered the progress of the study, particularly in the case of more severely demented subjects and those without caregivers.

2.3.5 Selection of Catchment Areas

In selecting areas to study we decided to use local authority boundaries which in both areas were largely coterminous with health authority boundaries. To obtain a catchment area with at least 0.5 million people, two London boroughs were

sought, ideally where there would be facilitative individuals working within the existing services. To avoid bias, an inner city and a suburban borough were chosen.

The suburban area is the London Borough of Hillingdon. The Dementia Research Group had provided advice on an earlier project (Kirk et. al., 1995) sponsored by the Joint Commissioning Group for Mental Health of Older People within Hillingdon. Work on the needs and service provision for younger people with dementia had been in progress in the borough since 1991, however no specific service provisions had been implemented at the inception of this project, and we were given encouragement to take the previous work forwards and involve Hillingdon as one catchment area.

To identify an inner city catchment area we informally contacted a range of statutory and voluntary services in central London. Through contact with Margaret Butterworth of CRAC Dementia (Council of Relatives to Assist the Care of Dementia) we learnt that the Royal Borough of Kensington and Chelsea (RBK&C) were taking account of the needs of younger people with dementia and were commissioning the Dementia Relief Trust (DRT) to investigate need and service provision (Quinn, 1996). The proposed DRT project would use the KC&W health authority boundaries as a catchment area, which includes both RBK&C and the City of Westminster. RJH was invited to join the steering committee for the DRT project and encouraged to use KC&W as the inner city catchment area.

2.3.6 Case Identification

The project commenced on 1st April 1995 with a recruitment period of 2 years. The primary aim of the project was to identify every case of dementia where the disease began before the age of 65 years in the two catchment areas. The prevalence of young onset dementia is low and with minimal co-ordination of services in the two areas a broad methodology was required. The strategy used was one of enthusiastic personal contact with professionals and others who may have contact with potential subjects, together with gaining access to more formal sources of information on patients, both combined with an awareness campaign for the project.

2.3.6.1 Raising Awareness of the Project

It was vital that as many professionals as possible who were working in the two catchment areas were made aware that a project to identify every case of young onset dementia was in progress.

A computer database was established containing addresses for the following groups:

- All GP's in the two areas - this information was extracted electronically by the Information Services Department of The National Hospital for Neurology and Neurosurgery from the Patient Administration System GP database selecting all records where the postal code was the same as the study area postal codes.

- All Psychiatrists (General Adult and Old Age), Neurologists, Geriatricians and General Physicians. Human Resources departments for all of the hospital trusts in the two areas provided names and contact addresses.

- Social Services, Voluntary Services, Day Centre and Nursing Home team leaders and heads of department/section. This section of the mailing list was developed in collaboration with a wide variety of professionals who suggested contacts that should be informed of the project.

A mail-merged, personalised letter, response card and leaflet describing the project was sent to each person in the contact database.

Lectures and talks on Young Onset Dementia including a presentation of the research project were given at several sites in the two areas:

- Kensington & Chelsea Mental Health Unit (Psychiatrists)
- Mount Vernon Hospital Post Graduate Medical Centre (GP's and Hospital doctors)
- Hillingdon Hospital Postgraduate Centre (3 annual lectures - 1995, 1996, 1997) (GP's and Hospital Doctors)
- Kensington & Chelsea Dementia Liaison Group (Medical, para-medical, social services and voluntary groups working with people with dementia)
- CRAC Dementia (The Council of Relatives to Assist in the Care of Dementia) 3rd Conference (1995) and 4th Conference (1996) (Butterworth, 1996). (Medical, para-medical, social services, voluntary groups and family caregivers)
- Hillingdon Branch of the Alzheimer's Disease Society Annual General Meeting, 1995.
- Alzheimer's Disease Society 5th National Study day on Dementia in Younger People (Alzheimer's Disease Society, 1995).

As discussed above, RJH was also a steering committee member of a Dementia Relief Trust project sponsored by The Royal Borough of Kensington and Chelsea to investigate caregiving experiences in young onset dementia (Quinn, 1996). This collaboration allowed close inter-working with social services in KC&W with cross-referral of cases.

Personal meetings were held with key contacts within health and social services in the two areas to describe the project and encourage referral and notification of all cases.

2.3.6.2 Hospital Information Systems

Information Services Departments (ISD) of all NHS Trusts within the two areas were contacted and asked to search their Patient Administration Systems (PAS) for ICD9 and ICD10 diagnosis codes (Appendix 4) in patients born after 1920 (to capture patients up to the age of 75 on project census day (1/4/95)). ISD's from The National Hospital for Neurology and Neurosurgery (NHNN), St Mary's Hospital, Hillingdon Hospital and The Chelsea & Westminster Hospital responded. Only the NHNN and St Mary's Hospital were able to complete the request. The PAS at Hillingdon Hospital could not be searched in the way requested, and the PAS at The Chelsea and Westminster Hospital had only been established a short time and had very limited data available. None of the mental health trusts responded, further enquiries revealed that this was because their information systems were unsuitable for this type of searching at the time of the enquiry.

2.3.6.3 Clinicians

Personal contact was made with key neurologists and psychiatrists working in the two areas. Access was requested to any clinical material, departmental databases, patient notes and copies of clinic letters or discharge summaries that would enable identification of cases of young onset dementia.

Three neurologists kept well organised filing systems containing copies of clinic letters and/or discharge summaries. These were hand searched for potential cases. Two neurologists searched their own correspondence and forwarded identified cases. One neurologist maintained a comprehensive database of all

patients seen which was searched electronically using the same protocol as the hospital PAS systems.

Two psychiatrists maintained a departmental electronic database, however, due to technical problems it was not possible to extract data. All of the psychiatrists contacted were positive about the project and agreed to notify names of potential cases.

2.3.6.4 Social Services

To resolve issues of confidentiality, particularly relating to inter-agency working access to social services was made through intermediary facilitators. Within KC&W, Christine Quinn worked closely with social work colleagues in both boroughs to identify cases. All cases identified to her were passed on to this project with the agreement of the social worker or care manager. Where agreement could not be obtained, anonymous data were passed on to provide the date of birth, diagnosis, age at onset and postcode of the patient.

In Hillingdon contact was established with a senior social worker in the People with Disabilities Team (PWD) (Myf Wilson). In Hillingdon a borough-wide information system linked all social services departments. In the second year of the project a list of all identified cases was checked with the social services information system and details of allocated social workers were provided. It was not possible to search this system by diagnosis, but it provided comprehensive information on social work involvement in known cases.

2.3.6.5 Other Professionals

Membership of the Kensington & Chelsea Dementia Liaison Group facilitated personal contact with a range of social and voluntary care organisations in KC&W. In Hillingdon close collaboration with Dr Martin Skelton-Robinson (Psychologist with special responsibility for younger people with dementia) facilitated identification of a large number of the cases. Data from the previous study within Hillingdon (Kirk et. al., 1995) provided a further list of patients.

2.3.7 Patient Recruitment

As each patient was identified information was entered onto the study database. The extent of this initial information ranged from an isolated name without even an address or date of birth, to full medical discharge summaries and copies of case notes.

Details of the patients GP was sought from the referrer or from other sources such as hospital PAS systems. Once identified, a letter was sent to the GP requesting permission to make contact.

In parallel to seeking GP permission, copies of hospital medical records, and where possible, social services case files were requested to provide study data and verification of study inclusion and exclusion criteria.

Once the GP's permission was received a letter was sent, addressed to the patient and carer asking them to make contact by telephone or letter. Once contact was made an initial interview date was arranged, either at the patient/carers home, or at another suitable location (NHNN or Nursing/Residential home etc.). During the initial telephone call and at the first meeting the nature and purpose of the study was explained and the patient and/or carer was asked to sign a consent form.

2.3.8 Patient Assessment

All assessments, interviews and ratings were performed by RJH, except for a small number of CAMCOG assessments on Hillingdon cases carried out by an assistant psychologist attached to the project during 1996 (Jenni Brooks).

A semi-structured interview with the carer alone was used to collect demographic details, history of cognitive impairment, past medical history, drug history, family history. Results of investigations, in particular neuropsychological assessments and neuroimaging, and confirmation of the history were obtained from GP records, hospital notes, and any other available records e.g. computerised records. For those patients not personally assessed, information was collected from the medical and other records only.

Clinical assessment of the patient included a medical, neurological and neuropsychiatric examination. Structured assessments used were as follows:

2.3.8.1 Modified Hachinski Ischaemia Scale

The modified Hachinski Ischaemia Scale (HIS) (Rosen et. al., 1980) is widely used as a guide to distinguishing VaD from AD. The original 'ischaemia index' contained 14 items (Hachinski et. al., 1975) with a score above 7 suggesting vascular dementia, and below 4 being more compatible with a primary degenerative dementia. Factor analysis and review of the original index has reduced the scale to 8 items, which was the version used in this study.

2.3.8.2 Clinical Dementia Rating Scale (CDR)

A global assessment of dementia severity was made using the Clinical Dementia Rating Scale (CDR) (Hughes et. al., 1982). Ratings on the orientation, memory, and judgement and problem solving domains of the CDR were made from the clinical assessment supplemented with the Cambridge Mental Disorders in the Elderly Cognitive Assessment (CAMCOG) (Roth et. al., 1986), which incorporates the Mini Mental State Examination (Folstein et. al., 1975) and the IDDD (Teunisse et. al., 1991). The CDR was completed following the interview with the caregiver, assessment of the patient and review of the medical notes.

2.3.8.3 BEHAVE-AD

Non-cognitive behavioural symptoms were assessed using the Behavioural Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) (Reisberg et. al., 1987). The BEHAVE-AD was completed by interviewing an informant, who was usually the primary caregiver (family or professional), and related to the patients behaviour in the preceding four weeks. The scale has been validated (Reisberg et. al., 1989b; Sclan et. al., 1996) and is widely used, particularly in clinical trials (Weiner et. al., 1996; Harvey, 1997). A criticism of the use of this scale in the present study relates to it specificity for AD. It was anticipated that dementias other than AD would be found in the study sample, and the BEHAVE-AD has had no validation in other types of dementia. Unfortunately however, other, potentially more suitable scales such as the Neuropsychiatric Inventory (NPI) (Cummings et. al., 1994), the CERAD Behaviour Rating Scale for Dementia (BRSD) (Tariot et. al., 1995) and MOUSEPAD (Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia) (Allen et. al., 1996) were not available in published form at the design stage of the study in 1993/1994.

2.3.8.4 Cornell Scale for Depression in Dementia

In addition to the mood related items in the BEHAVE-AD a specific depression score was rated using the Cornell Scale for Depression in Dementia (Alexopoulous et. al., 1988). The Cornell scale is a 19 item instrument designed specifically to rate symptoms of depression in patients with dementia. For each

item in the scale the severity is assessed according to three explicitly defined grades: 0=absent, 1=mild or intermittent, and 3=severe. It was administered in two stages. First, during the caregiver interview each item on the scale was discussed with the carer, with additional descriptions to ensure that the carer understand the symptom. The carer was then asked to rate each item.

In the second stage, during the patient assessment, each item on the scale was covered as part of the mental state examination, with additional probes used as needed. Any discrepancies between the carers and patients report was further clarified with the carer with the rating adjusted based on the clinicians final judgement.

The scale was designed to be administered by clinicians and no specific training is required to use it. A single depression score is generated by adding the scores for each of the 19 items. The ratings refer to patient symptoms in the preceding 2 weeks, except for one item relating to weight loss which is based upon the preceding month.

2.3.8.5 IDDD

Impairment of Activities of Daily Living (ADL) was measured using the caregiver rated IDDD - Interview to Determine Deterioration in Daily functioning in dementia (Teunisse et. al., 1991). Each of the 33 items on the scale was discussed with the caregiver, once the stem was clearly understood, a rating regarding change in the item in the preceding 4 weeks was made. A minimum score, if all items are rated, is 33, and the maximum score is 99.

2.3.9 Neuropathological Follow-up

Diagnostic confirmation is critically dependent on neuropathology, especially in a study such as this where differential diagnosis is of particular interest. Wherever possible, and appropriate, patients and/or caregivers were asked to give a declaration of their intent for post-mortem and brain tissue donation from the affected person. It was recognised that in the 2½ year life of the project, few cases would come to autopsy, these would, however, help to confirm clinical diagnostic accuracy, and subsequent re-analysis of the data could be performed in later years once a larger proportion of the cohort had died. Post mortem arrangements were organised and administered through the established neuropathology collaboration within the Dementia Research Group. The neuropathology examination is undertaken by Professor Peter Lantos at the MRC Neurodegenerative Disease Brain Bank, Institute of Psychiatry. Routine neuropathological examination, in the framework of the general guidelines by the MRC on brain banking, follows a standardised protocol which, with minor modifications, has been in use for more than seven years. Blocks of tissue are taken from standardised areas and the neuropathologccal diagnosis is established by the use of the appropriate neurohistological stains (including Bielschowsky silver impregnation) and immunohistochemical techniques. When required, immunohistochemistry includes Aß protein, ubiquitin, prion protein, and Tau.

2.3.10 Diagnosis

The medical, psychiatric and neuropsychological assessment were reviewed on a case by case basis with as much background information as could be obtained (medical notes, neuroimaging reports and results of other investigations). A consensus diagnosis was established by applying a hierarchical diagnostic algorithm (Appendix 2).

Having excluded cases not fulfilling DSM-IV criteria for dementia or with an age at onset over 65 years, the top of the algorithm filtered cases with findings that could give a conclusive diagnosis. This top level includes those with a defined genetic disorder e.g. Huntington's disease and familial Alzheimer's disease; where a living person with clinical disease was also known to carry a pathological

mutation this was considered a conclusive diagnosis. For those patients with a clear autosomal dominant family history of dementia, but without a known mutation in the family, histopathological confirmation of diagnosis in another affected family member was also considered to diagnostically conclusive.

Histopathological confirmation of diagnosis was available in some cases from the results of a previous cerebral biopsy, or at post mortem for those patients who died after the commencement of the study.

At the second level of the algorithm, well recognised and validated clinical diagnostic criteria were applied to make the diagnoses of Alzheimer's disease (NINCDS/ADRDA criteria (McKhann et. al., 1984), Vascular Dementia (NINDS/AIREN criteria (Roman et. al., 1993)), Dementia with Lewy Bodies (McKeith et. al., 1992; McKeith et. al., 1996), Frontotemporal Dementia (Lund and Manchester Criteria (The Lund and Manchester Groups, 1994)), Alcohol Related Dementia (DSM-IV criteria for Alcohol-Induced Persisting Dementia (American Psychiatric Association, 1994)).

At the third level of the algorithm there remained a group of patients, fulfilling the DSM-IV criteria for dementia, but not fulfilling criteria for one of the above diagnostic categories. These were further assessed clinically and wherever possible a specific disease diagnosis was made, or the case was assigned to a Dementia Not Otherwise Specified (NOS) category.

2.2.11 Age at Onset of Disease

The age at which the dementia commenced is almost impossible to date accurately. By definition most dementias have an insidious onset, and this may be particularly marked in the slowly progressive frontal lobe degenerations.

However, age at onset is an important variable in a study of patients with young onset dementia. Surrogate markers that have been used in other research include age at diagnosis or age at presentation to medical services; both of which are susceptible to bias.

The methodology used in this study to establish age at onset was a pragmatic one. Age at onset of disease was defined as the age of the patient at which the earliest conclusive dementia symptom was noticed by the carer (or patient, if appropriate), or documented in the medical notes and other correspondence.

2.3.12 Caregiver Assessment

The caregiver and patient were interviewed separately as part of the assessment process. The main interview with the caregiver was use to complete collection of the history and demographic data and the patient functional and behavioural assessments.

At the end of the interview it was explained to the caregiver that we also wished to assess how well they were coping by asking them to complete several questionnaires in their own time. The self assessment questionnaires were shown to the caregiver with an explanation on their completion. They were then left with the caregiver to be returned in a stamped addressed envelope. If the assessments were not returned within 10 days RJH contacted the caregiver by phone to remind them to return them.

Five dimensions of care-giver well-being were examined (adapted from Colerick and George (1986)): physical health, mental health, economic status, caregiver burden, and marital quality.

2.3.12.1 Axis I - Physical Health

The caregivers perception of their own physical health was assessed using a 100mm Visual-analogue scale (VAS). The scale was anchored at 0 (My health has significantly deteriorated as a result of caring for someone with dementia) and 100 (My health has significantly improved as a result of caring for someone with dementia). Instructions were given on the completion of the VAS with the advice that the centre of the line represented no change.

2.3.12.2 Axis II - Mental Health

The caregivers mental health was measured using the 28 item General Health Questionnaire (Goldberg and Hillier, 1979) (GHQ), and the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983). These scales were particularly chosen for their ability to rate psychological caseness, together with caseness for anxiety and caseness for depression.

The definition of caseness is that above a particular cut-off score, should the subject be assessed by a psychiatrist they would have a high probability of being diagnosed with a psychiatric disorder.

General Health Questionnaire (GHQ-28)

The GHQ is a self-administered screening questionnaire designed to detect subjects with a diagnosable psychiatric disorder (Goldberg and Hillier, 1979). The questionnaire focuses on two classes of symptoms: the inability of the subject to carry out their normal, healthy functions, and the appearance of new phenomena of a distressing nature. In its original form it consisted of 60 questions and was validated such that above a critical cut-off score a psychiatrist using a standardised assessment interview was likely to make a psychiatric diagnosis (Goldberg and Blackwell, 1970). Factor analysis of the long version of the GHQ (GHQ-60) generated a much shorter version suitable for use in population screening (GHQ-28) (Goldberg and Hillier, 1979).

For each item in the GHQ one of four responses are chosen e.g.:

A1.	**Have you recently been perfectly well and in good health?**	Better than usual	Same as usual	Worse than usual	Much worse than usual

Two methods of scoring are possible and both were used in this study. As a screening test for psychiatric caseness, the 'GHQ scoring method' of 0-0-1-1 respectively for each response, provides a score of 0-28. A threshold score of 5/6 is then used to determine caseness. In the original validation study of the GHQ-28, this gave a sensitivity of 80% and a specificity of 88.8% (Goldberg and Hillier, 1979). A lower cut off of 4/5 may also be used which increases sensitivity, but reduces specificity. For the purposes of this study we wanted higher specificity and therefore the higher cut off was used. Whether the caregiver was rated as a case or not was used as a primary independent variable in the subsequent analysis of the study.

The Lickert scoring method (0-1-2-3) was also used to provide an overall measure of psychological morbidity, deriving a score between 0 and 84.

The GHQ has been widely used in studies of psychological health, including a number of studies of caregivers for people with dementia (Philp and Young, 1988; O'Connor et. al., 1990; Gold et. al., 1995; Livingston et. al., 1996) and stroke (Young and Forster, 1992; Forster and Young, 1996; Logan et. al., 1997).

Hospital Anxiety & Depression Scale (HAD)

The HAD is a 14 item self assessment scale developed for detecting states of depression and anxiety in general medical outpatients (Zigmond and Snaith, 1983). While the GHQ-28 is a useful instrument for detecting 'caseness', the HAD gives more specific information about the presence and degree of anxiety and depression.

For each item in the HAD, the carer selects one of four responses e.g.:

Worrying thoughts go through my mind	A great deal of the time	A lot of the time	From time to time, but not too often	Only occasionally

Seven items on the scale refer to symptoms of anxiety, and seven to symptoms of depression. A Lickert scoring method is used (3-2-1-0), deriving a depression score from 0-21, and an anxiety score from 0-21. The score is validated as a measure of severity of symptoms (Zigmond and Snaith, 1983). As with the GHQ, a cut-off score can be used to determine caseness for anxiety and depression. For studies such as this, where only those patients with a high probability of mood disorder (high specificity) are to be selected then a cut-off score of 10/11 is usually applied (Zigmond and Snaith, 1983).

The HAD has also been widely used in a range of diseases. Although it has mostly been used with patients it has also been applied in other studies of caregivers of people with dementia (Welleford et. al., 1995; Gold et. al., 1995) and stroke (Anderson et. al., 1995)

2.3.11.3 Axis III - Economic Status

Caregiver economic status was assessed as part of the health economic assessment. Caregivers were asked whether either they or the patient had had to reduce their hours of work or give up work entirely. Social security benefits being received were recorded and as part of the questionnaire pack the carer completed a 100mm visual-analogue scale of financial status. The VAS was anchored at 0 (Finances have become significantly more restricted as a result of caring for someone with dementia) and 100 (Finances have become significantly less restricted as a result of caring for someone with dementia).

2.3.11.4 Axis IV - Caregiver Burden

As previously discussed, caregiver burden is usually viewed in a multi-axial variable, and this has been reflected in the structure of the caregiving assessments being used. However, a number of unifying 'caregiver burden' scales have been developed. In the absence of widely accepted scales it was decided to use two caregiver burden measures that had good face validity and had been used in a number of previous studies.

Burden 1 and 2

The Burden 1 and 2 scale was developed for a study of gender comparison in caregiving (Pruchno and Resch, 1989), and was able to identify statistically significant differences in caregiver burden between male and female carers. The Burden 1 measure asks the carer to respond to the question "*When caring for another person, some people experience a sense of burden. Overall, how burdened do you feel in caring for the person you are looking after?"*, with response on 5 point scale. Burden 2 is a 17 item index of burden, with each item describing psychological responses or feelings in the caregiver relating to the caring experience; each item rated as never, sometimes, or often. The items in the scale were drawn from a review of the caregiving literature (Pruchno and Resch, 1989).

The Screen for Caregiver Burden (SCB)

The SCB (Vitaliano et. al., 1991a), is a 25 item burden index which rates the presence of, and amount of distress caused to the carer by a range of objectively burdensome items, and subjectively burdensome caregiver feelings. Two scale scores are derived: Objective Burden (OB) and Subjective Burden (SB).

The SCB has been more widely applied in caregiving studies of Alzheimer's disease (Vitaliano et. al., 1993; Welleford et. al., 1995), the frail elderly (Thompson et. al., 1993) and in multiple sclerosis (Knight et. al., 1997).

2.3.11.5 Axis V - Marital Quality

The final axis of the caregiver assessment is that of marital quality. This assessment was only used with spouse (married or equivalent) caregivers. The Locke-Wallace Marital Adjustment Scale was chosen as it is a short, but reliable, well validated assessment of marital quality (Locke and Wallace, 1959). The questionnaire has 23 items, twelve items have a multiple choice response, nine items ask the extent of agreement or disagreement on marital issues, one item presents a checklist of 22 areas of potential difficulty within marriage of which the subject circles as many as apply. The final item provides a seven point scale of degree of happiness in marriage. The responses on the questionnaire are scored according to a weighting derived from factor analysis of the scale (Kimmel and Van der Veen, 1974). Scores range from 48 to 138, with a higher score representing better 'marital adjustment'.

Two specific problems were identified with the use of this scale. First, it is usually completed by both husband and wife with a comparison of the two scores providing a measure of compatibility. This was not felt to be possible with demented subjects and therefore only the non-demented partners marital adjustment was measured. Secondly, the dementia itself may alter marital adjustment, either in a positive or negative way. Clearly this is an important concept, but it was felt to be difficult to measure in a valid way in this study. The index point for marital quality was decided to be the period of marriage shortly before the dementia began. This was made clear in the printed instructions, and was reinforced when the questionnaire pack was handed to the caregiver.

2.3.13 Health Economic Assessment

The aim of the health economic assessment was to collect 'bottom-up' data on the direct cost-of-illness for the patients in the study. Because of the methodological problems associated with estimating indirect cost-of-illness as discussed in section 1.5.4, it was decided to focus this study on direct costs only. To collect data for this analysis carers were asked about the involvement of a range of health, community care and social services in the preceding 12 months:

GP Consultation

Out Patient Appointments

CPN

Admiral Nurse

Social Worker

Psychologist

Meals on Wheels

Home Help

Domicilliary/Home Care

Day Care

Respite Care

Residential/Nursing/Long Term Care

Data on the costs and average use per annum of these services were collected principally from previous research publications (Philp and Young, 1988; Gray and Fenn, 1993; Philp et. al., 1995; Livingston et. al., 1997) to allow direct comparison with other studies. However, for some interventions information on cost was obtained directly from service providers within the catchment area. This was the case where cost data on the service were not available in published sources (e.g. Admiral Nurses in KC&W and Psychologists in Hillingdon).

For those patients not living at home, their place of resident was recorded.

Residential Care

Nursing Home Care

Long Stay Hospital Care

Acute Hospital (Medical or Psychiatric) Ward

Average cost per annum for residential care were obtained by reference to available sources of published figures (Gray and Fenn, 1993; Kirk et. al., 1995).

Health economic studies of the dementias are in their infancy and there is as yet little agreement about the most appropriate methodology to be used. To provide transparency in the data collected for this study the costings and calculation methods used for this study are fully presented in the results section. This will allow other investigators to apply their own values to the data and allow more accurate comparison between studies. This openness is intended to be in-line with the published recommendations on cost-of-illness studies (Rice, 1994).

2.3.14 Data Management and Statistical Analysis

Data were initially collected onto paper forms in sets of research case notes. After being reviewed and supplemented with information from hospital and GP notes the data were entered into a database under Microsoft Access 7.0 (Microsoft Corporation, 1995). A range of data validation rules were built into the database to ensure correct coding. The database automated the process of case identification by generating standardised letters, and providing summaries of rates of recruitment, and progress reports on patient contact and assessment.

Data analysis was performed using SPSS version 7.5 (SPSS Inc, 1996) via Open Database Connectivity (ODBC) links to the main data tables within the Access database.

Statistical analyses were performed according to the statistical guidelines for contributors to medical journals (Altman et. al., 1989) and guidelines for the documentation of epidemiological studies (Epidemiology Work Group of the Interagency Regulatory Liaison Group, 1981).

In the presentation and analysis of the data, 95% confidence intervals are presented for all means, medians and rates, and are displayed as error bars on charts. Confidence intervals are particularly important as a study aim is to apply results on the epidemiology of young onset dementia to the wider population. The range of values provided by the confidence interval will allow more objective application of the study data. Confidence intervals were calculated using SPSS 7.5 (SPSS Inc, 1996) and CIA (Confidence Interval Analysis) (Gardner et. al., 1992)

The study is a cross-sectional survey with a primary aim of describing the prevalence of dementia in people under 65 years of age with the hypothesis that the diagnoses will be more heterogeneous that that found in other studies of older populations. The secondary hypotheses to be tested are comparisons of sub-groups within the study population - these comparisons, by definition, will be exploratory analyses only. For this reason we have tried to avoid direct significance (hypothesis) testing of differences between groups (p values), but rather focused on determining the size of difference between sub-groups using confidence intervals (Gardner and Altman, 1989). P values have been inferred from confidence intervals; where the 95% confidence interval of the difference between two means does not cross 0, or where the 95% confidence intervals for two means do not overlap, then p is inferred to be <0.05.

Categorical data, not suitable for confidence interval analysis were analysed using Chi squared. Exact p values and degrees of freedom used are quoted for accuracy.

Pearson's product moment correlation coefficients were calculated to evaluate the association between variables, with Spearman's rank correlation coefficients calculated for data with a distribution significantly different from normal. The 95% confidence intervals of the correlation coefficients were calculated using the CIA program.

3. Population Studies of Young Onset Dementia

3.1 Introduction

The primary aim of this study is to identify, with a high degree of accuracy, the prevalence of specific clinical dementia syndromes within a geographically defined population of patients with young onset dementia.

3.2 Overview of Catchment Areas

3.2.1 The Royal Borough of Kensington & Chelsea and The City of Westminster

The Royal Borough of Kensington & Chelsea and the City of Westminster (KC&W) are situated in the centre of London and contain the UK parliament and the majority of government departments. The two boroughs have a combined area of approximately 25 Km^2, with a total population of 335,500 people of which 112,309 are aged between 30 and 64 years. The Jarman Underprivileged Area Score for KCW, based on 1991 census data is 21 with a range between 8 and 48 for individual wards (Personal Communication - Professor Jarman). The population is ethnically diverse, and it has been estimated that for Kensington & Chelsea alone, borough residents come from nearly 100 different ethnic backgrounds (Quinn, 1996). From UK Census figures approximately one fifth of people in the catchment area are from black and ethnic minority communities (The National Monitor, 1991). The boroughs also contain some of the richest and poorest areas of the country, yet despite this Westminster is the eighth most deprived area in the country (by Jarman index). The main areas of deprivation are in the Golborne (Jarman UPA91:49), St Charles (39) and Avondale (38) wards in the North, and South Stanley (34), Earls Court (26) and Kelfield (24) wards in the South.

KC&W is a single health authority commissioning area, but consists of two local authority boroughs, and consequently two social services organisations. Health services are provided by a number of Trusts. The main community trusts are Parkside Community Health (NHS) Trust in the North of the catchment area and Riverside Community Health (NHS) Trust in the South of the borough. However, North West London Mental Health (NHS) Trust provides mental health care for people under the age of 65 years in North Westminster, and for people over the age of 65 years in North East Westminster.

Community mental health care is provided at 6 main units: The Paterson Centre for Mental Health (Under 65 years), St Charles Hospital Mental Health Unit (all ages), South Kensington & Chelsea Mental health Unit (all ages), The Gordon Hospital (Under 65 years), Latimer House Day Hospital (Over 65's) and St Pancras Hospital (Over 65 years). Throughout Westminster, the care of people under 65 years with mental health problems including dementia, is provided in different hospitals to that of older people.

General medical and neurological services are also widely distributed across the catchment area. There are two main acute units are St Mary's Hospital and The Chelsea and Westminster Hospital, however patients with neurological problems from KC&W are also seen at St Charles Hospital, Charing Cross Hospital, The Hammersmith Hospital, The Middlesex Hospital (University College London Hospitals NHS Trust), St Thomas's Hospital and The National Hospital for Neurology and Neurosurgery; all of which are either within or very close to the

3.2.2 The London Borough of Hillingdon

The London Borough of Hillingdon is situated approximately 24 Km West of London. It is bordered to the South by Heathrow airport, a major source of employment in the area, and to the West by the M25 motorway. The total area of the borough is more than 4 times that of KC&W at approximately 110 Km^2. The borough has a population of 232,000 people of which 81,184 are between the age of 30 and 64 years. The majority of the population live in the South and East of the borough, with the North West area around Harefield being mostly rural and semi-rural.

The Jarman UPA91 index for Hillingdon is 8 with a range from -14 to 26 (Personal Communication - Professor Jarman). The ethnic diversity is also less than KC&W with 88% of the population being white. There is less differentiation between the poorest and wealthiest parts of the borough, although there are still areas of significant deprivation in Crane (UPA91:26), Botwell (25), Barnhill (20) and Yiewsley (21) Wards.

Mental health care is provided to the whole of the borough by a single provider (Hillingdon Hospital (NHS) Trust) with inpatient facilities at Hillingdon Hospital, and a community mental health resource centre for people under 65 years in Ruislip Manor, to the North of the borough. People over the age of 65 years have inpatient, outpatient, day hospital and community services provided by the Woodland unit at Hillingdon hospital.

Acute medicine and neurology are provided at Hillingdon Hospital in the South of the Borough and Mount Vernon Hospital in the North. Each hospital has one neurologist, although a number of patients may be referred elsewhere, principally including Northwick Park Hospital, Charing Cross Hospital (Regional Neurosciences Centre) and The National Hospital for Neurology and Neurosurgery.

3.3 Study Population Socio-demographics

3.3.1 Case Identification

The names of 227 people were referred to the project. The primary source of identification as known for 100% of cases and is summarised in table 11.

	Study Area		
Primary Source	**Hillingdon**	**KC&W**	**Total**
	n (%)	**n (%)**	**n(%)**
Psychologist	47 (46.1%)	0	47 (20.7%)
Hospital IT Systems	9 (8.8%)	37 (29.6%)	46 (20.3%)
Neurologist	17 (16.7%)	22 (17.6%)	39 (17.2%)
Psychiatrist	5 (4.9%)	27 (21.6%)	32 (14.1%)
Social Worker	0	21 (16.8%)	21 (9.3%)
General Practitioner	8 (7.8%)	6 (4.8%)	14 (6.2%)
Physician (Non-neurologist)	12 (11.8%)	2 (1.6%)	14 (6.2%)
Admiral Nurse	0	9 (7.2%)	9 (4.0%)
Other	4 (3.9%)	1 (0.8%)	5 (2.2%)
Total	**102**	**125**	**227**

Distribution of Source of Referral - Hillingdon vs. KC&W: χ^2= 117, df=8, p=0.000

Table 11 - Primary Sources of Case Identification

'Other' sources of referral included self referral (1), Crossroads care (2) and the Alzheimer's Disease Society (2). It is important to note that this table represents the 'primary' source of identification of cases - i.e. the source from which the case was first identified. In many cases several sources referred the same case.

It is immediately apparent from the table that there are significant differences in the source of identification between the two areas. In Hillingdon, 46% of the cases were identified through the psychology services, while there were no primary referrals from psychologists in KC&W. This bias is likely to be due to three factors. First, an earlier project to identify cases of young onset dementia was lead by the psychology service in Hillingdon, and this list of names was passed on at start of the study (Kirk et. al., 1995). Secondly, as a result of the earlier project, the head of psychology and collaborator for this project (MS-R) was appointed as lead clinician for young onset dementia, and many cases were referred through him. Finally, MS-R had a close working relationship with the neurologist in the South of Hillingdon and most cases of dementia seen in the neurology clinic were routinely referred for psychological assessment.

Within KC&W a high percentage of cases was identified from hospital IT systems, unlike Hillingdon where, due to technical problems, we were unable to search the IT systems.

Close collaboration with social services in KC&W produced 21 cases, however, although there were no primary identifications from social services in Hillingdon, considerable data were provided later in the project. Admiral nurses only exist within KC&W, hence there were no referrals from them for Hillingdon.

These data seem to show that either close collaboration with individuals involved with the care of younger people with dementia, or effective searching of hospital IT systems are the best source of identification of cases. It was disappointing that

despite a leaflet and personalised mail-shot campaign backed up by lectures at meetings there was only a 6% response from GP's.

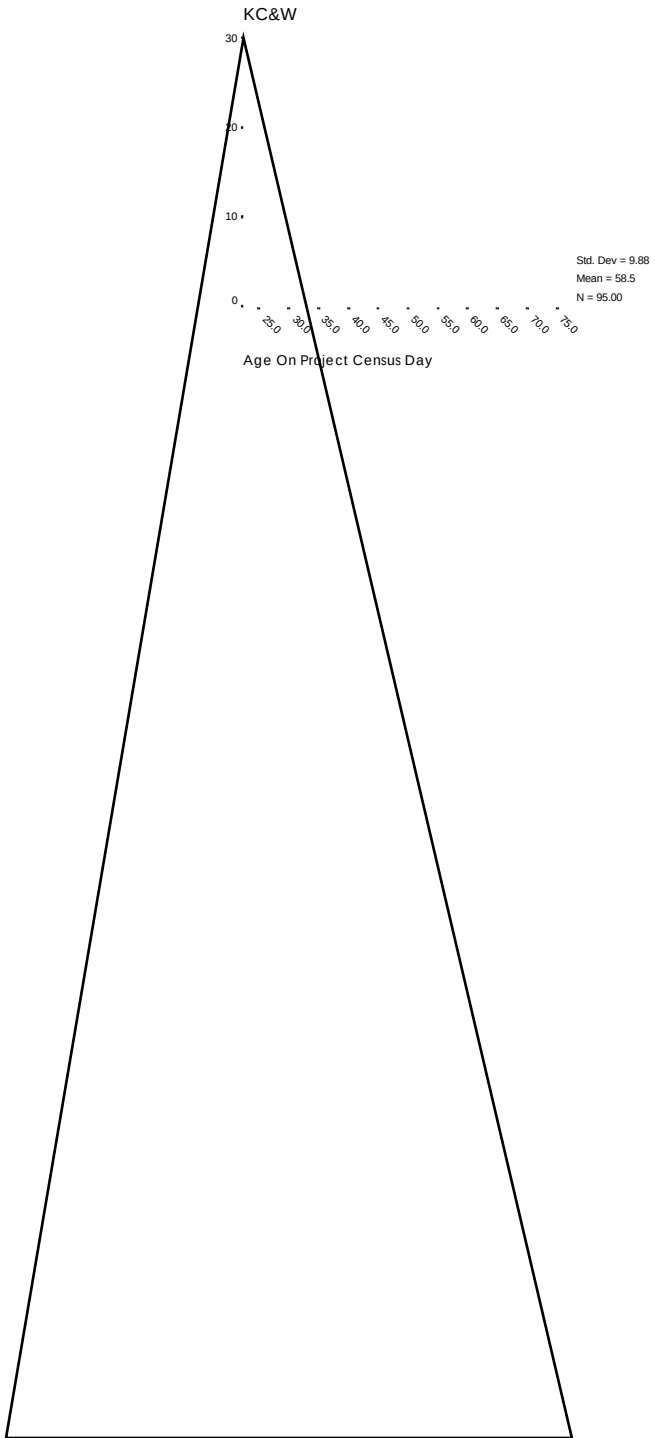
Of the 227 cases 19 were excluded by not fulfilling DSM-IV criteria for dementia (6 were 'worried well', 7 traumatic brain injury, 2 chronic schizophrenia, and a 4 further cases were identified from hospital IT systems who had no evidence of cognitive impairment from review of their case notes and were considered to be mis-codings)

In 23 of the remaining 208 cases, the dementia had started after the patients 65th birthday, and these cases were also excluded from further analysis.

This gave a study population of 185 cases (Appendix 3).

3.3.2 Age

The age of the patient on the study census day (1/1/95) was calculated from the date of birth for each patient. Details of date of birth were missing for 26 cases. The mean age of the population was 58.7 years (95%CI: 57.4 - 60.1 years). Figure 1 shows the frequency distribution of age in the two study areas.



There was no difference between the gender distributions in the two study areas (Table 12), (95% CI of difference in proportions of male cases in KC&W and Hillingdon Populations: -15% to +13%), there was however a significantly greater number of male than female cases (95% CI inferred $P<0.05$) in the study sample.

3.3.4 Marital Status

Information on the marital status of the patients were available in 155 (83%) of cases and is summarised in table 13.

	Study Area		
Primary Source	**Hillingdon (n=77)**	**KC&W (n=108)**	**Total (n=185)**
	%	**%**	**%**
Married/Co-Habiting	58.3%	56.3%	57.4%
Single/Never Married	15.5%	21.1%	18.1%
Separated/Divorced	19.0%	19.7%	19.4%
Widowed	7.1%	2.8%	5.2%

Marital Status Distribution, Hillingdon V. KC&W: $\chi^2=2.11$, df=3, p=0.55

Table 13 - Marital Status In The Two Study Areas

There was no significant differences in the distribution of marital status between KC&W and Hillingdon.

3.3.5 Socio-Economic Class

The patient's occupation was coded according to the Registrar Generals Classification of Occupations (Office of Population Censuses and Surveys, 1980) from which socio-economic class for each subject was derived. In addition to the six standard classes, an additional Economically Inactive (E) group was included as these data are also available from census figures. The economically inactive group include the long term unemployed, and people who have taken early retirement.

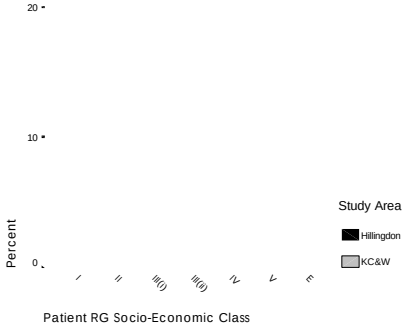
It should be noted that this coding of occupation was made on the basis of occupation prior to the onset of the dementia. For married housewives, the occupation of the husband was coded. To be classified as Economically Inactive, the person was required to have been unemployed or retired for at least 1 year prior to the first symptom of dementia.

Information was available for 96 (51.9%) cases and is summarised in tabular and graphic from in figure 2.

% within Study Area

		Study Area		
		Hillingdon	KC&W	Total
Patient RG Socio-Economic Class	E	9.1%	7.7%	8.3%
	I		11.5%	6.3%
	II	25.0%	17.3%	20.8%
	III(i)	38.6%	11.5%	24.0%
	III(ii)	9.1%	17.3%	13.5%
	IV	13.6%	19.2%	16.7%
	V	4.5%	15.4%	10.4%

SEC Hillingdon V. KC&W: χ^2=17.4, df=6, p=0.008



An issue arose with the analysis of these data. It was apparent from the age distribution of the study population that a significant number of cases where the disease had started prior to age 65 years, had 'graduated' beyond 65 years by the date of the project census. However, only a minority were beyond the age of 70 and therefore OPCS figures used refer to people aged 30-69 years (35-69 years for marital status).

3.4.1 Gender

Data on gender distribution in the two catchment areas were extracted from published OPCS census data. The gender distribution for people aged between 30 years and 64 years was calculated together with 95% confidence intervals for each proportion. Table 15 tabulates these data and compares the study populations, with the total population.

	Hillingdon		KC&W		Total Population*	
	Observed	OPCS[1]	Observed	OPCS[1]	Observed	OPCS[1]
Male	57.8% (46.9-68.1)	49.8% (49.5-50.1)	58.9% (48.4-68.9)	49.2% (49.0-49.5)	58.4% (50.9-65.6)	49.5% (49.3-49.7)
Female	42.2% (31.9-53.1)	50.2% (49.9-50.5)	41.1% (31.1-51.6)	50.8% (50.5-51.0)	41.6% (34.4-49.1)	50.5% (50.3-50.7)

* Male V. Female: $p<0.05$ inferred from 95% Confidence Intervals
1. 30-69 years age group

Table 15 - Gender Distribution Compared With OPCS Data

In neither individual area was there a significant difference in gender distribution from the OPCS figures. However, when both areas are combined there was a greater number of male than female cases identified, and this is significantly different, at the 5% level, from the OPCS figures.

3.4.2 Marital Status

Data on marital status in the populations of the two study areas between the ages of 35 and 69 years were extracted from OPCS census figures. A higher age cut-off of 35 years was chosen as below this age there is a bias in the normal population towards being single, and only a small proportion of the study population is below the age of 35 years.

As can be seen from table 16 the distribution of marital status was highly representative of the total population.

	Hillingdon		KC&W	
	Observed	OPCS	Observed	OPCS
	n=84	n=91,393	n=71	n=125,399
Married	58%	77%	56%	56%
Single	16%	9%	21%	26%
Divorced	19%	5%	20%	13%
Widowed	7%	9%	3%	5%
	$\chi 2=0.0004$, df=3, p=0.99		$\chi 2=0.14$, df=3, p=0.95	

Table 16 - Marital Status Compared to OPCS Figures

3.4.3 Socio-Economic Class

OPCS census figures provide a distribution of socio-economic class based upon a 10% sample of the total population. There was no statistically significant difference between the study population and OPCS figures (table 17).

SEC	Hillingdon		KC&W	
	Observed	OPCS	Observed	OPCS
	n=87	n=16,957	n=76	n=18,039
I	0%	6%	12%	9%
II	25%	24%	17%	31%
III(i)	39%	12%	12%	10%
III(ii)	9%	22%	17%	9%
IV	14%	8%	19%	6%
V	5%	3%	15%	3%
E	9%	25%	8%	32%
	χ^2<0.0001, 6df, p=0.99		χ^2<0.0001, 6df, p=0.99	

Table 17 - Socio-Economic Class Compared to OPCS Figures

Despite their being no overall differences between the distribution of social class in the two populations there do appear to be differences between observed and known numbers of people in particular classes. In particular class E (The economically inactive) appear under-represented in the study populations. This is likely to be a coding effect. In the study occupation was recorded as the best level achieved, while the census recorded occupation on the day of the census. The majority of patients in the study were economically inactive as a result of their illness, but were actually coded according to their previous occupation. Those patients coded as E were people who were retired from work, or long term unemployed prior to the onset of their illness.

The lack of patients in SEC I in the Hillingdon area may be explained by the differences in source of identification between the two areas. The six cases in SEC I in the KC&W area were all identified from either neurologists (2 cases) or the hospital IT systems (4 cases). Five of the 6 cases had no contact with statutory services and were paying for private care - and hence would not otherwise have been identified for the study. In the Hillingdon area we were unable to search hospital systems due to technical problems and thus potentially a small number of cases who have had only fleeting contact with statutory health or social services care may have been missed.

3.4.4 Ethnic Group

Data on ethnicity for people aged 30-69 years were extracted from OPCS census figures. To simplify the analysis, groups with small numbers (Indian, Pakistani and Bangladeshi) were aggregated. As can be seen in Table 18 the study groups were highly representative of the actual population.

Ethnic Group[1]	Hillingdon		KC&W	
	Observed	OPCS	Observed	OPCS
	n=90	n=91,393	n=95	n=125,399
White	97.8%	88%	87.4%	83%
Black Caribbean	0%	1%	3.2%	3%
Black African	0%	0%	1.1%	2%
Indian	2.2%	8%	4.2%	4%
Other Asian	0%	1%	4.2%	3%
	$\chi 2$=0.453, 4df, p=0.99		$\chi 2$=0.308, 4df, p=0.99	

1. Groups not represented in either study population not shown for clarity.

Table 18 - Ethnic Group Compared To OPCS Figures

3.5 Overview of Demographic Data

The data presented in sections 3.3 and 3.4 have provided an overview of demographics of the populations of cases identified in Hillingdon and KC&W. The numbers of cases identified, as would be expected from the few prevalence studies performed to date, are small by comparison to the total population. Only minor differences in the gender and SEC distributions were identified between the study population and the general population. By comparison the ethnic mix in the study populations reflected the underlying population, which was particularly important in the KC&W area with its broad range of ethnicity. As already discussed, some of the variance in the SEC distribution may be a result of bias due to difference sources of case attainment in the two areas.

The difference found in the gender distribution (more males than females) in the total population does require some further consideration. The variation found was just significant according to 95% confidence intervals and it is thus possible that this was a chance finding. However, this is unlikely given that in the total population the difference in gender distribution is in the opposite direction (more females than males). It is possible that the prevalence of dementia in males under 65 years is greater than that of females, however, this would be at variance with previous studies which have variously shown that females are at greater risk (McGonigal et. al., 1993) or that there is no difference in risk (Newens et. al., 1993).

Overall, with certain cautions outlined above, the study population is a representative sample of the total population, and extrapolation of these data to wider populations is justified.

As the total number of cases is small and there were no major differences between the two study areas, the two populations were then combined into a single group for further analysis.

3.6 The Prevalence of Dementia in the Population

The next phase of data analysis was to examine the age-specific prevalence of dementia and then the prevalence of the specific clinical dementia syndromes.

3.6.1 All Causes Of Dementia

From the original population of 227 referred cases, 185 were included in the study on the basis of a diagnosis of dementia according to DSM-IV (Appendix A1.1)

with an age at onset below 65 years (Appendix 3, page 126). The prevalence of dementia, with their Confidence Intervals, by 5 year age groups from 30 years to 64 years was calculated by reference to OPCS census data. Summaries for the ranges 30-64 and 45-64 years were also calculated to allow comparison with published studies (table 19).

The number of cases of young onset dementia where the affected person had 'graduated' beyond the age of 65 years at the project census day are also shown, for information only.

			All Causes of Dementia						
Population[1]			All		Male		Female		
Age Range	Male (N)	Female (N)	N	Rate[2]	N	Rate	N	Rate	Significance[3]
30-34	23898	23375	6	12.7	3	12.6	3	12.8	NS
			(4.7-26.7)[4]		*(2.6-36.7)*		*(2.7-37.5)*		
35-39	18526	19106	3	8.0	1	5.4	2	10.5	NS
			(1.6-23.3)		*(0.1-30.1)*		*(1.3-37.8)*		
40-44	18982	19643	6	15.5	1	5.3	5	25.5	NS
			(5.7-33.8)		*(01.-29.4)*		*(8.3-59.4)*		
45-49	16549	16799	11	33.0	6	36.3	5	29.8	NS
			(16.5-59.0)		*(13.3-78.9)*		*(9.7-69.5)*		
50-54	15185	15237	19	62.5	10	65.9	9	59.1	NS
			(37.6-97.5)		*(31.6-121)*		*(27-112)*		
55-59	13983	13626	42	152.1	28	200.2	14	102.7	NS
			(110-206)		*(133-289)*		*(56.2-172)*		
60-64	12716	13141	43	166.3	26	204.5	17	129.4	NS
			(120-224)		*(134-300)*		*(75.4-207)*		
30-64	95941	97552	**130**	**67.2**	**75**	**78.2**	**55**	**56.4**	**NS**
			(56.1-79.8)		***(61.5-98)***		***(42.5-73.4)***		
45-64	58433	58803	**115**	**98.1**	**70**	**119.8**	**45**	**76.5**	**NS**
			(81.1-118)		*(93.4-151)*		*(55.8-102)*		
Over 65[5]			**55**		**33**		**22**		

1. Combined populations of KC&W and Hillingdon
2. Rate per 100,000 people at risk
3. Significance of difference between genders by inference from 95% CI.

4. 95% Confidence Interval for the prevalence rate
5. Prevalence rate not calculated

Table 19 - Age & Gender Specific Prevalence Rates in The Study Population

The data for total prevalence with 95% confidence intervals is displayed graphically in figure 3.

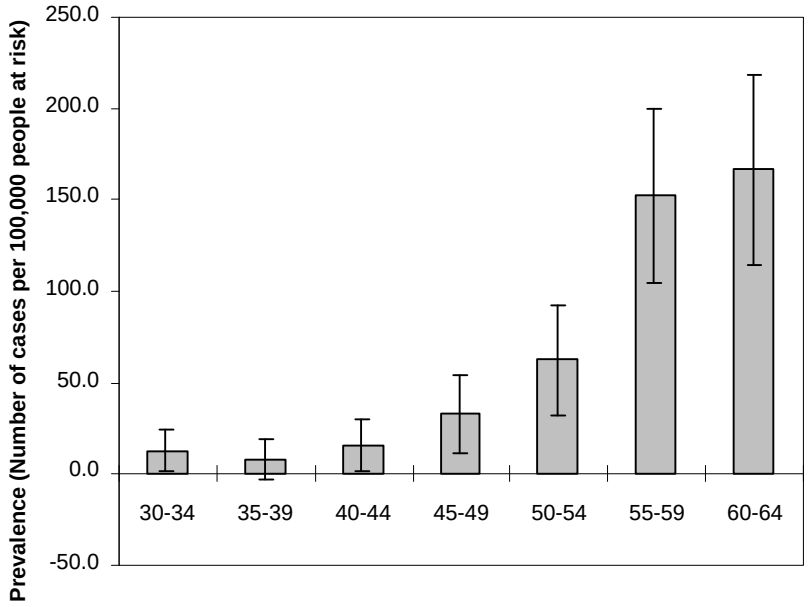


Figure 3 - Prevalence of Dementia by 5 Year Age Groups

As can be seen from the graph, below the age of 45 years the prevalence of dementia is low and constant. Between age 45 and 60 years the prevalence of all dementias follows the pattern of near exponential increase, with an approximate doubling of the prevalence for each 5 year age group. The prevalence in the 60-64 years age group is then similar to the 55-69 years group. As the prevalence of dementia continues to rise with doubling prevalence for each 5 year age group after the age of 65 years (Jorm et. al., 1987), it is likely that the plateau seen here is a result incomplete case identification of cases who were close to age 65 years.

3.6.2 Differential Diagnosis

Using the methodology described in section 2.3. differential clinical dementia diagnoses were made as shown in table 20.

The Other Dementias group consisted of Huntington's Disease (9 cases), Dementia in Multiple Sclerosis (8 cases), Corticobasal Degeneration (2), Prion Dementia (CJD) (2), Dementia due to Carbon Monoxide Poisoning (1), Dementia and Down's Syndrome (3), Dementia in Parkinson's disease (2) and Pre-senile dementia NOS (8).

Clinical Diagnosis	Hillingdon n(%)	KC&W n(%)	Total (%)
Alzheimer's Disease	27 (30%)	35 (37%)	62 (34%)
Vascular Dementia	21 (23%)	13 (14%)	34 (18%)
Frontotemporal Dementia	10 (11%)	13 (14%)	23 (12%)
Alcohol Related Dementia	4 (4%)	15 (16%)	19 (10%)
Dementia with Lewy Bodies	8 (9%)	4 (4%)	12 (7%)
Other Dementias	20 (22%)	15 (16%)	35 (19%)

Table 20 - Differential Diagnosis

For dementias that accounted for at least 10% of the study population, age specific prevalence rates, with 95% confidence intervals were calculated.

3.6.3 Alzheimer's Disease

For AD, a diagnosis of probable AD according to NINCDS/ADRDA criteria was used. It should be noted that NINCDS/ADRDA criteria require the disease to start after the age of 40 years. However, this requirement was waived for the purpose of this study; one case had an age at onset of 38 years. Table 21 displays the age specific prevalence rates for AD.

Age Range	N	**Rate[1]**	*95% CI*
30-34	0		*NA*
35-39	0		*NA*
40-44	1	**2.6**	*(0.7-14.4)*
45-49	2	**6.0**	*(0.7-21.7)*
50-54	5	**16.4**	*(5.3-38.4)*
55-59	14	**50.7**	*(27.7-85.1)*
60-64	20	**77.3**	*(47.2-119)*
30-64	**42**	**21.7**	***(15.6-29.3)***
45-64	**41**	**35.0**	***(25.1-47.4)***
Over 65	**20**	**-**	**-**

1.Rate per 100,000 people at risk

Table 21 - Age Specific Prevalence Rates for Alzheimer's Disease

3.6.4 Vascular Dementia

The age specific prevalence rates for VaD are shown in table 22. Diagnoses were made according to NINDS/AIREN criteria for probable VaD.

Age Range	N	**Rate[1]**	*95% CI*
<49	0	**0.0**	
50-54	2	**6.6**	*(0.8-24.4)*
55-59	9	**32.6**	*(14.9-67.9)*
60-64	10	**38.7**	*(18.5-71.1)*
30-64	**21**	**10.9**	***(6.7-16.5)***
45-64	**21**	**17.9**	***(11.1-27.4)***
Over 65	**13**	**-**	**-**

1.Rate per 100,000 people at risk

Table 22 - Age Specific Prevalence Rates for Vascular Dementia

3.6.5 Frontotemporal Dementia

FTD was diagnosed according to the Manchester/Lund criteria. Although numbers were small, age specific prevalence rates and their confidence intervals are shown in table 23.

Age Range	N	**Rate[1]**	*95% CI*
<44	0	**0.0**	
45-49	4	**12.0**	*(3.3-30.7)*
50-54	1	**3.3**	*(0.8-18.3)*
55-59	7	**25.4**	*(10.2-52.2)*
60-64	6	**23.2**	*(8.5-50.5)*
30-64	**18**	**9.3**	***(5.5-14.7)***
45-64	**18**	**15.4**	***(9.1-24.3)***
Over 65	**5**	**-**	**-**

1.Rate per 100,000 people at risk

Table 23 - Age Specific Prevalence Rates for Frontotemporal Dementia

3.6.6 Alcohol Related Dementia

The age specific prevalence rates for Alcohol Related Amnestic Syndrome are shown in table 24.

Age Range	N	**Rate**	*95% CI*
<44	0	**0.0**	
45-49	2	**6.0**	*(0.7-21.7)*
50-54	6	**19.7**	*(7.2-42.9)*
55-59	5	**18.1**	*(5.9-42.3)*
60-64	3	**11.6**	*(2.4-33.9)*

30-64	16	**8.3**	*(4.7-13.4)*
45-64	16	**13.6**	*(7.8-22.2)*
Over 65	3	**-**	-

Table 24 - Age Specific Prevalence Rates for Alcohol Related Dementia

3.6.7 Other Causes of Dementia

Although the numbers of cases are small, table summarises the estimated prevalence of the other rare causes of dementia in the study population:

Disease	Number of Cases	Rate per 100,000 at risk
Huntington's Disease	9	4.7
Dementia in Multiple Sclerosis	8	4.1
Dementia in Down's Syndrome	3	1.6
Corticobasal Degeneration	2	1.0
Prion Disease	2	1.0
Dementia in Parkinson's Disease	2	1.0
Dementia Due To Carbon Monoxide Poisoning	1	0.5
Presenile Dementia NOS	8	4.1

Table 25 - Prevalence of Rare Causes of Dementia in the 30-64 Years Age Group

3.7 Distribution of Cases By Age at Onset of Disease

Considering prevalence of dementia only in terms of the current age of the patient will tend to bias the results towards an older mean age, as most patients will have had their illness for up to several years before diagnosis. Indeed, 55 of the cases that were referred or identified for this study fulfilled the criteria by having an age at onset below 65 years, but by the date of study census day were older then 65. The prevalence data were therefore reanalysed based upon age at onset of disease.

3.7.1 All Causes Of Dementia

Figure 4 shows the distribution of all cases of dementia by age at onset of disease.

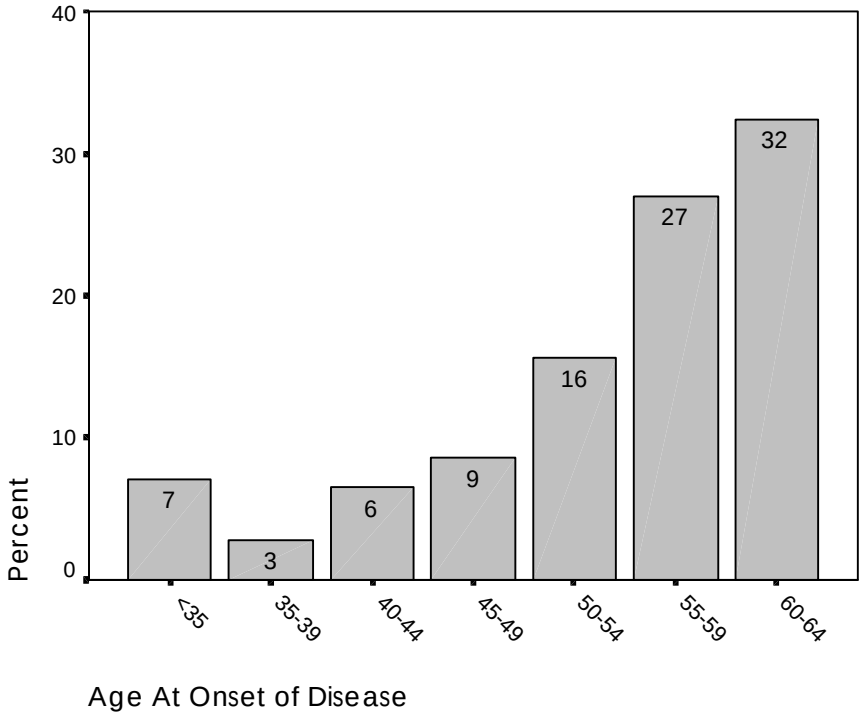
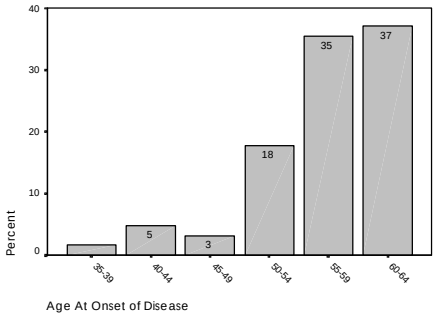
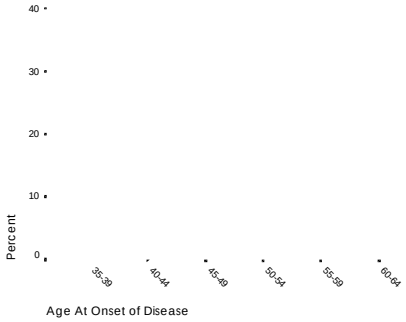


Figure 4 - Distribution of Dementia by Age At Onset of Disease

3.7.2 Specific Causes Of Dementia

Figure 5 is a composite of graphs showing the distribution of specific clinical dementia diagnoses by age at onset of disease.





Alzheimer's Disease *(n=62)*

	UK Population		Estimated Number of Cases Based Upon Current Study (95% CI)		
	Female	***Male***	***All***	***Female***	***Male***
30-34	2171400	2224900	558	279	279
			(205-1213)	*(58-814)*	*(58-817)*
35-39	1922800	1937700	308	201	105
			(63-899)	*(24-727)*	*(3-583)*
40-44	1976800	1978600	614	503	104
			(225-1337)	*(163-1174)*	*(3-582)*
45-49	1904700	1905800	1257	567	691
			(629-2248)	*(184-1324)*	*(253-1504)*
50-54	1545700	1535700	1924	913	1011
			(1159-3004)	*(417-1731)*	*(485-1858)*
55-59	1473400	1466700	4473	1514	2937
			(3234-6057)	*(828-2534)*	*(1951-4239)*
60-64	1483400	1383600	4768	1919	2829
			(3440-6422)	*(1118-3071)*	*(1854-4151)*
30-64	**12478200**	**12433000**	**16737**	**7035**	**9719**
			(13975-19879)	*(5303-9159)*	*(7646-12184)*
45-64	**6407200**	**6291800**	**12457**	**4903**	**7537**
			(1029-14985)	*(3575-6535)*	*(5877-9501)*

Table 26 - Estimated Number of Cases (95% CI) of Young Onset Dementia in the UK by Age and Gender

3.8.2 Specific Dementia Diagnoses

Although it was recognised the numbers of cases of specific dementias identified in this study was small, the use of confidence intervals for the rates allows an estimate of the magnitude of the true numbers of each dementia to be estimated by application to UK figures. These data are summarised in table 27

	UK Population	***AD***	***VaD***	***FTD***	***DLB***	***ARD***	***Other***
30-34	4396300						558
							(205-1213)
35-39	3860500						308
							(63-899)
40-44	3955400	102			102		410
		(26-570)			*(26-570)*		*(112-1048)*
45-49	3810500	229		457	114	229	229
		(27-827)		*(125-1170)*	*(29-636)*	*(27-827)*	*(27-827)*
50-54	3081400	506	203	101	101	608	405
		(165-1183)	*(24-73)*	*(26-564)*	*(26-564)*	*(223-1322)*	*(110-1038)*
55-59	2940100	1491	958	745	213	532	532
		(814-2502)	*(438-1996)*	*(300-1535)*	*(26-770)*	*(173-1244)*	*(173-1244)*
60-64	2867000	2218	1109	665	111	333	333
		(1353-3412)	*(530-2038)*	*(244-1448)*	*(28-616)*	*(69-972)*	*(69-972)*
30-64	**24911200**	**5407**	**2704**	**2317**	**772**	**2060**	**3476**
		(3886-7299)	*(1674-4135)*	*(1373-3662)*	*(284-1682)*	*(1178-3338)*	*(2292-5057)*
45-64	**12699000**	**4441**	**2275**	**1950**	**542**	**1733**	**1516**

(3187-2275) (1410-3480) (1156-3086) (175-1264) (991-2819) (829-2540)

Table 27 - Estimated Numbers Cases (95% CI) of Specific Young Onset Dementias in the UK by Age and Gender

3.9 Autopsy Confirmation of Diagnosis

As of December 1997, 4 cases from the study have undergone autopsy. In all cases the clinical diagnosis was confirmed at autopsy (Alzheimer's disease - 2, FTD -1 (Pick's disease), Dementia due to Carbon Monoxide Poisoning - 1).

3.10 Discussion

The study was based upon the identification of diagnosed dementia in two catchment areas using a broad and pragmatic methodology in an attempt to ensure as complete case identification as possible. The sample of patients identified appears to be representative in terms of major demographic features from the total population from which it was drawn.

The prevalence of dementia for people aged between 30 and 64 years as ascertained by this study was 67.2 per 100,000 people. If the age specific prevalence rates from this study (table Table 19 - Age & Gender Specific Prevalence Rates in The Study Population, page 64) are compared with other studies (table 5, page 19), they can be seen to be similar. The results from this study are very similar to those from the Framingham study (Kokmen et. al., 1989), although their rates for the 45-49 and 60-64 years age group were marginally higher. It is only Jorm et al's (1987) figures for the 60-64 year age group that are substantially higher, and this is likely to be due to his methodology of deriving the figures by extrapolated estimates based upon a quantitative integration of a number of epidemiological studies.

This study derives detailed prevalence data for dementia in patients as young as 30 years; data that have not previously been available. It is clear that at the lower end of the age range, dementia is very rare, nevertheless this group of patients are likely to require very specific and specialist services.

Given the low prevalence in people under the age of 50 years, specific local service provision is unlikely to be cost effective or practical; much larger catchment areas are needed to generate a significant population of patients. Data from this study can be used to estimate that there are approximately 2700 people under 50 years of age with dementia in the UK. This number of cases is likely to be adequately cared for, particularly in terms of assessment and diagnosis, by 3 or 4 specialist units; essentially the number that are already in existence (London, Manchester, Liverpool & Cambridge). However, approximately 11,000 people between 50 and 64 years old in the UK are affected by dementia, a more substantial number of cases, but still small in terms of planning local provision of care.

The data relating to specific dementia diagnosis are of particular interest, as previous studies have tended to focus on either a broad dementia syndrome, or a specific type of dementia such as AD.

This study identified a rate of 35 cases of AD per 100,000 people aged 45-64 years. This is almost identical to the prevalence rates identified by Newens et al (1993) (34.6/100,00) and McGonigal et al (1993) (38 (male)-42 (female)/100,000). The data from this study are also consistent with the findings of the Framingham study (Kokmen et. al., 1989) (table 6, page 19). This study, as with Newens et al's (1993) study, failed to replicate McGonigal et al's (1993) finding of a significantly higher rate of dementia in females. The consistency of the findings related to AD from this study when compared to other studies is reassuring and allows fairly confident predictions to be made of the prevalence of AD in other similar populations.

It can therefore be estimated that there are approximately 5,500 people under the age of 64 years suffering from AD in the UK. This represents less than one third of the estimated number of cases of all forms of dementia (16,700); an important finding which has implication both for clinicians and care planners. Amongst elderly people with dementia, the majority of patients will be suffering from AD; conversely amongst younger people with dementia, the majority of patients will not have AD. If clinicians are aware that they are less likely to be dealing with AD when assessing a younger person with dementia this will help to guide appropriate investigation. Moreover, for care planners designing services for younger people with dementia, a design based upon experience with older populations of patients, who will predominantly have AD, is unlikely to be appropriate in a younger population with a variety of dementia diagnoses and a much lower rate of AD.

The third most common diagnosis identified in this population is VaD. The age specific rates identified in this study were highly consistent with those found by McGonigal et al (1993), although in their study they also found small numbers of cases below the age of 50 years.

Having established that the findings from this study for Dementia, AD and VaD are consistent with other similar studies, it is reasonable to view the prevalence data that has been derived for other forms of dementia with some confidence.

This is the first epidemiological study to have identified prevalence rates for FTD based upon an epidemiological cohort. The data show that this is the third commonest cause of dementia in people under 65 years, with a rate approximately half that for AD, and similar to the rate for VaD. Patients diagnosed with FTD according to the Manchester/Lund criteria are a mixed population of cases of Pick's disease, Frontal Lobe Degeneration (FLD) and FLD with motor neurone disease. According to these data, 1 in 7 cases of dementia in people under the age of 65 years is likely to be due to FTD. Hopefully, better awareness and understanding of the disease, together with emerging diagnostic criteria will improve the recognition of this population of patients.

In a study comparing young onset dementia patients referred to a psychiatry service and a neurology service, 100% of the FTD cases were initially referred to the psychiatrist; probably reflecting the frequent behavioural presentation. Once a diagnosis of FTD is established, specific support can be provided to carers, such as through the Pick's Disease Support Group (The Pick's Disease Support Group, 1998). Epidemiological studies of older patients have failed to identify FTD as a significant cause of dementia; this study supports our previous hypothesis that FTD is a more prevalent disease amongst younger people (Harvey et. al., 1996).

By comparison with AD, VaD and FTD, Dementia with Lewy Bodies was much rarer amongst this population of younger dementia patients. Only 1 in 21 cases of dementia were due to DLB; with such low numbers of cases it was not possible to estimate prevalence figures confidently as very large confidence intervals were generated. It has been suggested that DLB accounts for up to 20% of dementia in older people (Byrne et. al., 1989; Perry et. al., 1989); the data from this study suggest it is a rare cause of dementia in younger people.

The prevalence rates for Alcohol Related Dementia were similar to those for VaD and FTD, although showing a different age distribution with a peak in the 50-59 year age group, and declining rates over the age of 60. Extrapolating these figures suggests that approximately 2000 people are affected by Alcohol Related Dementia in the UK, 12.5% of all causes of young onset dementia. Although these are not very large numbers, unlike the degenerative dementias this is a preventable cause of morbidity, usually related to the end stages of chronic alcoholism. Improved recognition of and services for chronic alcoholics in their 30's and 40's might reduce the rates of this disease. Very little is known about this population of patients who are usually excluded from epidemiological studies. Having demonstrated that they represent a significantly proportion of the young

onset dementia population it is hoped that this will encourage further research into the longitudinal course, aetiology and prevention of ARD.

The remaining 20% of the patients with dementia in this study were grouped together as 'Other Causes of Dementia'. Of these cases, a quarter were below the age of 35 years, with an age distribution significantly different to that for the primary degenerative dementia groups (figure 5, page 70). The most common cause of dementia in this group was Huntington's disease (8 cases), with a prevalence rate of approximately 4.7/100,000 which is consistent with European rates of 0.5-7.8/100,000 and US rates of 5-7/100,000 (Chiu, 1994). The remaining cases had dementia in Multiple Sclerosis (Rao et. al., 1991), corticobasal degeneration, prion dementia, and dementia in Parkinson's disease. These are all rare diseases, most often managed by neurologists. Only three cases of dementia associated with Down's syndrome were identified. This was lower than had been anticipated. Despite ensuring that learning disability consultants in the two catchment areas were aware of the study, no referrals were received from doctors or social works from learning disability teams.

The final 8 cases identified were classified as Presenile Dementia NOS. In these cases there was clear evidence of a degenerative dementia as defined by DSM-IV, but often due to the severity of the disease, and/or the lack of medical information it was not possible to assign a more specific diagnosis.

Overall the study has provided detailed information on the prevalence of dementia in younger people. By reference to other similar studies these data appear robust and reliable and it is hoped that it will be useful for service and research planning.

3.10.1 Limitations

The study includes only patients identified through clinical services. The numbers of missed cases would, however, be expected to be low as dementia in someone under the age of 65 years is unlikely to escape medical attention. From the prevalence results for all causes of dementia it seems that cases who were close to age 65 years were the most likely to be missed. Although the study specifically sought to recruit patients with an **age at onset** below 65 years, with no upper current age limit, some older patients, who nevertheless had an onset before the age of 65 years, may not have been referred to the study.

No referrals were received from learning disability teams, and thus the rate of dementia among people with Down's syndrome and other learning disabilities is likely to be an under-estimate.

Diagnoses are based upon clinical criteria, which are recognised to have a sensitivity of 80%. On-going follow-up of the cohort to autopsy will help to confirm diagnosis and prevalence, however, at least 20% of families refuse permission for autopsy and thus a potential selection bias will be present even in a pathologically confirmed series.

3.10.2 Clinical Implications

- Alzheimer's disease accounts for less than one third of cases of dementia in people under the age of 65 years. Clinicians should be aware that they should be diagnosing AD in younger patients much less frequently than in older people.

- Dementia under the age of 50 years is very rare, given the small numbers, and wide variety of diagnoses, clinicians should strongly consider referring these very young people to a specialist unit, at least for an initial diagnostic assessment.

- One in 7 cases of young onset dementia are due to FTD. Clinicians should be vigilant for this diagnosis. Patients frequently have a marked behavioural syndrome. Once a diagnosis has been made specific support is available to caregivers through organisations such as the Pick's Disease Support Group.

- Alcohol Related Dementia accounts for 12.5% of dementias in people under the age of 65 years. The peak prevalence is in people in their 50's. As this is a preventable disease, better recognition, services and research aimed at understanding the aetiology and developing preventative strategies would be valuable.

4. Clinical and Behavioural Features of the Young Onset Dementias

4.1 Representativeness of the Assessed Population

Of the 185 cases of young onset dementia, 87 consecutively recruited patients were assessed in detail with the full research protocol (47%). The assessed and non-assessed patients were of similar age distribution, and had similar age at onset of disease and length of illness (Table 28). The proportion of male to female patients was however, significantly greater in the assessed group.

Parameter	Assessed Cases (n=87)	Non-Assessed Cases (n=98)	p
Age (Years)	59.6 *(58.2-61.0)*[1]	59.6 *(55.3-59.9)*	NS
Gender	60M:38F	48M:39F	0.456[2]
Age at Onset of Disease (Years)	53.3 *(50.7-55.9)*	54.2 *(52.5-55.9)*	NS
Length of Illness (Years)	6.47 *(5.03-7.91)*	5.46 *(4.48-6.44)*	NS

1. Mean (95%CI) 2. Fishers Exact Test

Table 28 - Comparison Of Detailed Assessment Group To Full Population

The distribution of marital status, ethnic group and residence of patient on study census day are shown in tables 29, 30 and 31 respectively. The small numbers in some of the cells precluded formal statistical comparisons of the groups. However, a simple comparison of the two groups shows that the non-assessed cases were more likely to be single, and less likely to be divorced. For the non-assessed cases data were not always available, the number of valid cases is shown in brackets (*n=*).

	Single	Married	Divorced	Widowed
Assessed Cases *(n=87)*	12 *(13.8%)*	49 *(56.3)*	20 *(23.0%)*	6 *(6.9%)*
Non-Assessed Cases *(n=68)*	16 *(23.5%)*	40 *(58.8%)*	10 *(14.7%)*	2 *(2.9%)*

*Unsuitable for analysis >20% of cells with expected count <5.

Table 29 - Representativeness by Marital Status

	White	Back Caribbean	Black African	Indian	Other Asian
Assessed Cases *(n=87)*	82 (94.3%)	3 (1.6%)	1 (0.59%)	6 (3.2%)	4 (2.2%)
Non-Assessed Cases *(n=98)*	89 (90.8%)	1 (1%)	1 (1%)	4 (4.1%)	3 (3.1%)

*Unsuitable for analysis >20% of cells with expected count <5.

Table 30 - Representativeness by Ethnic Grouping

	Own Home	Nursing Home	Residential Care	Psychiatry Ward (Adult)	Acute Ward	Long Stay Hospital	Psychiatry Ward (Old Age)
Assessed Cases *(n=87)*	61 (70.1%)	10 (11.5%)	4 (4.6%)	5 (5.7%)	2 (2.3%)	4 (4.6%)	1 (1.1%)
Non-Assessed cases *(n=87)*	57 (65.5%)	13 (14.9%)	6 (6.9%)	4 (4.6%)	4 (4.6%)	2 (2.3%)	1 (1.1%)

*Unsuitable for analysis >20% of cells with expected count <5.

Table 31 - Representativeness by Residential Location

Due to the method of evaluation of SEC using occupation, data were available for only 21% of non-assessed patients and therefore, formal statistical comparison

Comparing the assessed group of patients with those who were not assessed by diagnosis revealed a significantly different distribution of diagnoses between the two groups (Table 32). However, the majority of the variance is a result of a greater frequency of other causes of dementia (28%) in the non-assessed group; this is likely to reflect a tendency to avoid assigning a specific disease diagnosis where inadequate information was available from the clinical records.

	AD	VaD	FTD	DLB	ARD	Other
Assessed Cases *(n=87)*	32 (36.8%)	18 (20.7%)	16 (18.4%)	6 (6.9%)	7 (8%)	8 (9.2%)
Non-Assessed cases *(n=98)*	30 (30.6%)	16 (16.3%)	7 (7.1%)	6 (6.1%)	12 (12.2%)	27 (27.6%)

$\chi 2=14.7$, df=5, p=0.012

Table 32 - Distribution of Diagnoses In The Population

Although the numbers of cases in some of the groups are small, the patient sub-population studied appears to be adequately representative of the total patient population.

4.2 Clinical Features

4.2.1 Risk Factors for Dementia

Past Medical History

The frequency of a range of medical conditions is reported in table 33 . For each disease the number of patients in each diagnosis group with the condition is reported, together with this figure as the percentage of all patients with that diagnosis.

	AD (n=32)	VaD (n=18)	FTD (n=16)	DLB (n=6)	Alcohol (n=7)	Other (n=8)
MI	5 (15.6%)	4 (22.2%)	-	3 (50%)	-	2 (24%)

in the alcohol related amnestic syndrome group, although the numbers here are small.

Hachinski Ischaemic Score

The modified Hachinski ischaemia score was used to assist differential diagnosis. Figure 7 displays the mean and 95% confidence intervals for the HIS in each diagnosis group. It is interesting to note that both the AD and Alcohol Related Dementia groups have significantly lower HIS scores than the vascular group, the FTD group has higher mean score which overlaps with both the AD and VaD groups.

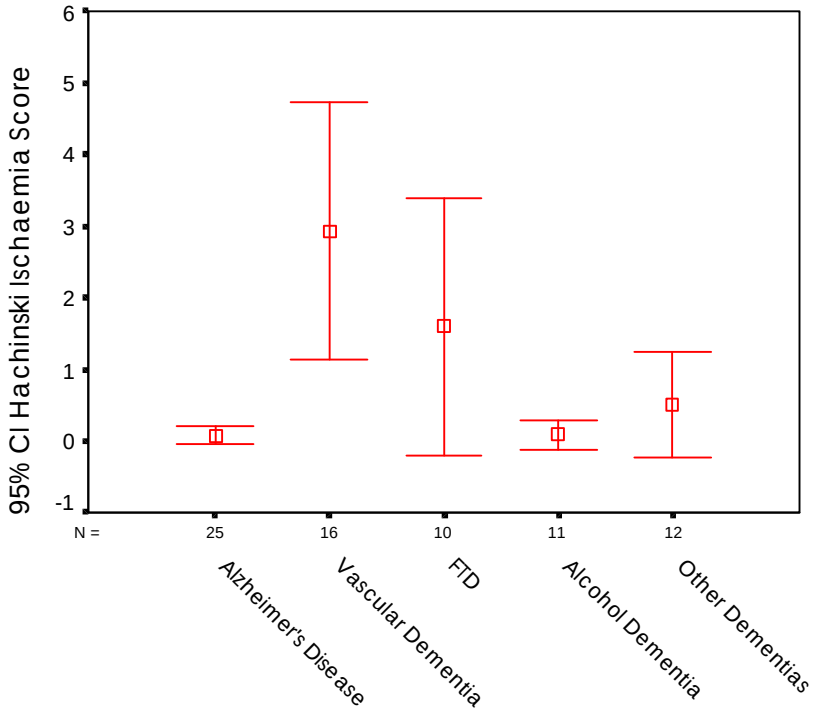


Figure 7 - Modified Hachinski ischaemia Score By Diagnosis

Family History

The proportions of cases in each diagnosis group reporting at least one first degree family member with a similar illness are shown in figure 8. Among the AD cases there was one family with a known presenilin 1 mutation. The likely reason for the high rate of a family history in the other dementia groups were the 9 cases of Huntington's disease. In 8 of the 9 cases, the patient had undergone genetic testing, all of which had been positive for the Huntington's mutation. Twenty five percent of the FTD group also had a family history, more than double that of the AD patients.

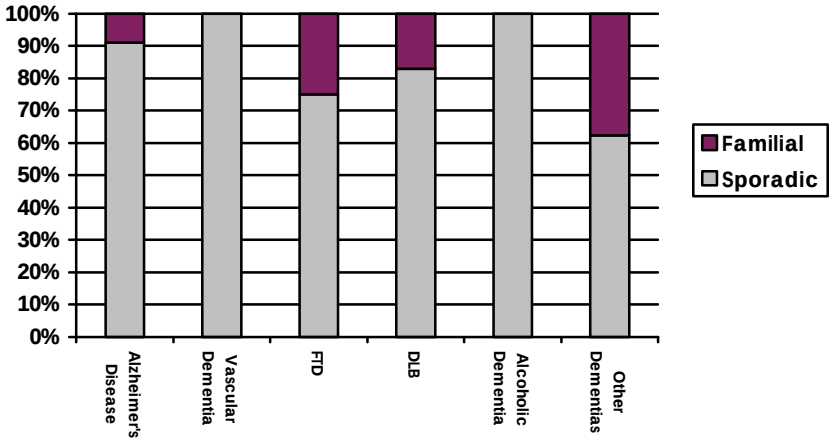


Figure 8 - Presence of Probable Familial Dementia By Diagnosis

Education

Figure 9 shows the mean length of education for each diagnosis group. There were no differences between the groups, although the Alcohol Related Dementia group showed a slight trend towards having received less education.

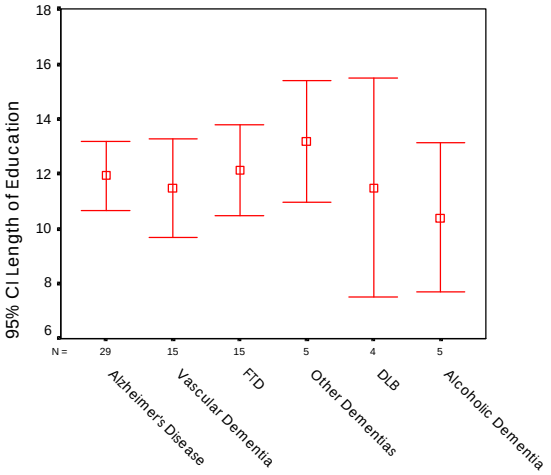


Figure 9 - Length of Education By Diagnosis Group

4.2.2 Clinical Investigation

Patients and carers were asked whether a CT scan, MRI scan or EEG had been performed at any time during the illness. This was further supplemented from information contained in the medical notes and is summarised in table 34.

	AD	VaD	FTD	DLB	ARD	Other
No Imaging	5	3	1	2	2	5
	(15.6%)	(16.7%)	(6.3%)	(33.3%)	(28.6%)	(62.5%)
CT or MRI Alone	17	13	9	4	5	3
	(53.1%)	(72.2%)	(56.3%)	(66.7%)	(71.4%)	(37.5%)
CT and MRI	10	2	6	-	-	-
	(31.3%)	(11.1%)	(37.5%)			
EEG	9	3	7	1	1	0
	(28.1%)	(16.7%)	(43.8%)	(16.7%)	(14.3%)	

Table 34 - Clinical Investigation by Diagnosis

4.2.3 Dementia Severity

Dementia severity was rated using the CDR scale utilising information from the patient and caregiver interview and scores on the MMSE, CAMCOG and IDDD assessments. Figure 10 shows the distribution of dementia severity in the population; (a) shows the whole assessed population (n=87), while (b) breaks severity down by diagnosis, but excludes profound and terminal severities (fig. a) and data for DLB and Alcohol Related dementia (fig. b) to improve clarity as these are small groups.

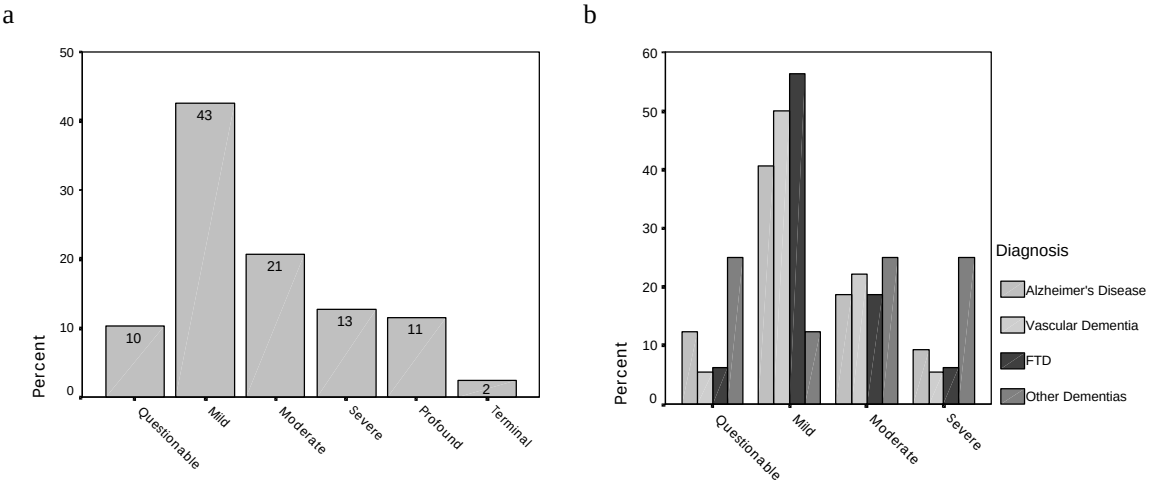
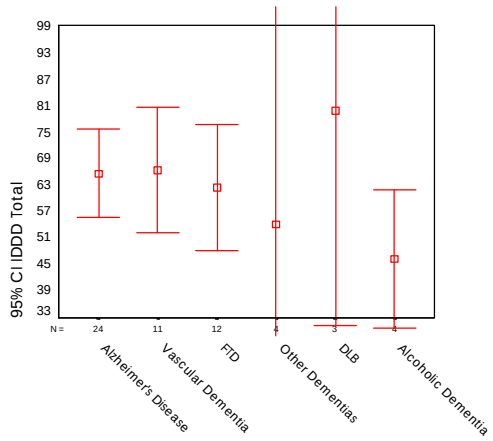


Figure 10 - Distribution of Dementia Severity in Whole Population (a) and By Diagnosis (b)

4.2.4 Functional Impairment

Functional impairment was assessed using the IDDD. There was great variability in the rating which precluded comparison of some of the groups using confidence intervals. There were no significant differences in functional impairment between the three main diagnostic groups (figure 11a), however, as might be anticipated, functional impairment was greater in those in nursing home and residential care when compared to those living at home (figure 11b).

a



b

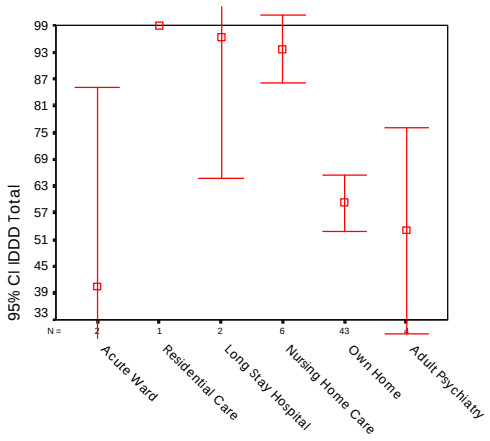


Figure 11 - Functional Impairment by Diagnosis (a) and by Residence (b)

4.2.5

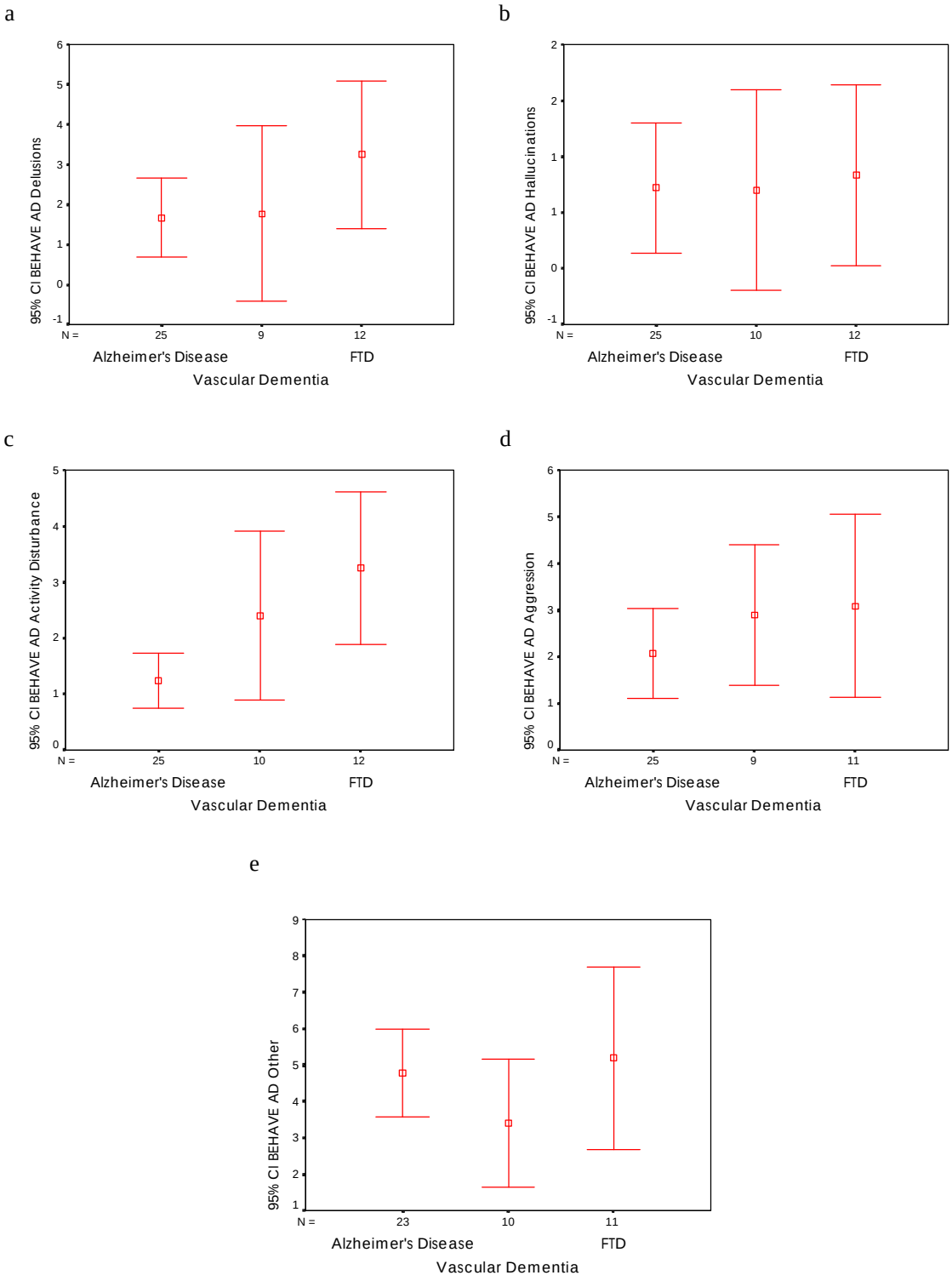


Figure 13 - BEHAVE-AD Sub-Scores for AD, VaD and FTD: Delusions (a), Hallucinations (b), Activity Disturbance (c), Aggression (d), Other symptoms (e)

To compare rates of non-cognitive symptoms between diagnoses, cases rating more than 2 points on the delusions, hallucinations and aggression subscales of the BEHAVE-AD were considered to have the presence of these symptoms. The following summarises the prevalence of hallucinations, delusions, aggression by diagnosis (table 35)

a

	Presence of Delusions		
	Absent	Present	Total
Alzheimer's Disease	20 62.5%	12 37.5%	32
Vascular Dementia	7 38.9%	11 61.1%	18
Frontotemporal Dementia	6 37.5%	10 62.5%	16
Other Dementias		5 62.5%	8
Dementia With Lewy Bodies	3 50.0%	3 50.0%	6
Alcohol Related Dementia	2 28.6%	5 71.4%	7
Total	41 47.1%	46 52.9%	87

b

	Presence of Hallucinations		
	Absent	Present	Total
Alzheimer's Disease	23 71.9%	9 28.1%	32
Vascular Dementia	8 44.4%	10 55.6%	18
Frontotemporal Dementia	10 62.5%	6 37.5%	16
Other Dementias	3 37.5%	5 62.5%	8
Dementia With Lewy Bodies	2 33.3%	4 66.7%	6
Alcohol Related Dementia	3 42.9%	4 57.1%	7
Total	49 56.3%	38 43.7%	87

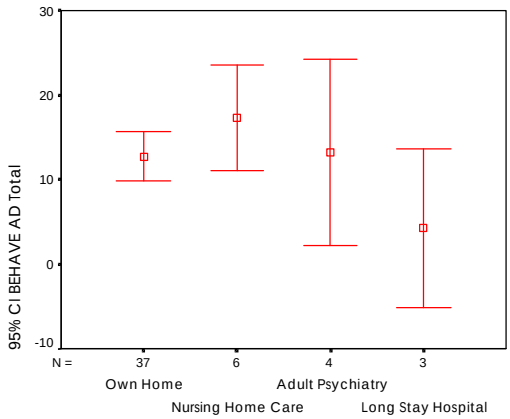
c

	Presence of Aggression		
	Absent	Present	Total
Alzheimer's Disease	17 53.1%	15 46.9%	32
Vascular Dementia	5 27.8%	13 72.2%	18
Frontotemporal Dementia	6 37.5%	10 62.5%	16
Other Dementias	3 37.5%	5 62.5%	8
Dementia With Lewy Bodies	1 16.7%	5 83.3%	6
Alcohol Related Dementia	2 28.6%	5 71.4%	7
Total	34 39.1%	53 60.9%	87

Table 35 - Prevalence of Delusions (a), Hallucinations (b) and Aggression (c) by Diagnosis

Figure 14 shows the mean scores on the BEHAVE-AD by residential location of the patient.

A



b

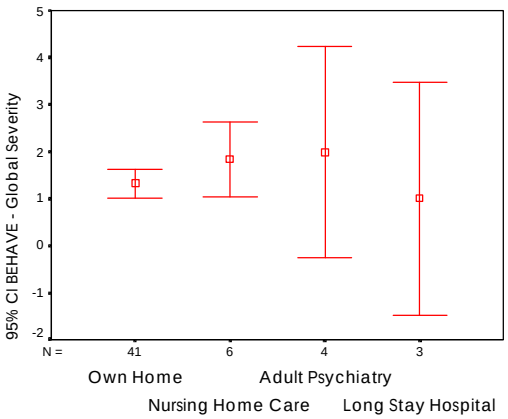


Figure 14 - BEHAVE-AD Scores by Residential Location (a-Total Score, b-Global Rating)

4.2.6 Affective Symptoms

The presence of affective symptoms were measured in the patients using the Cornell Scale for Depression in Dementia. Mean scores with 95% CI's are shown in figure 15.

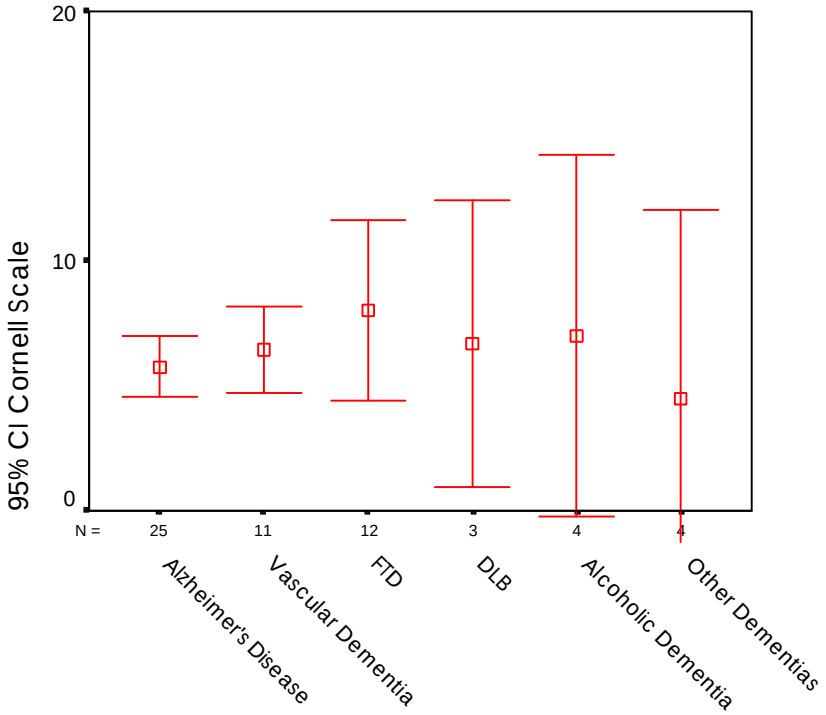


Figure 15 - Cornell Scale For Depression Scores by Diagnosis

4.3 Outcome

At the time of analysis, one year follow-up outcome data was available for 86 patients. In 54 cases (63%) there had been no change in where they were living; 36 were living at home, 5 were psychiatric inpatients, 1 was in Local Authority residential care, 3 were in long stay hospital care and 9 were in nursing homes.

In 14 cases (16%) there was a move to care setting of higher dependency. Of these were 13 people moving from their own home to nursing, hospital or residential care, and 1 person who moved from an acute psychiatry ward to a nursing home.

Eighteen people (21%) died over the 1 year follow-up period. Of these 8 had previously been living at home, 7 were in nursing home care, 2 were in long stay hospital care and 1 had been on an acute psychiatry ward.

4.4 Discussion

4.4.1 Clinical Features & Investigation

The clinical and behavioural features of young onset dementia were assessed in approximately half of the cases identified from the catchment areas. In terms of major demographic features, the assessed cases did not differ significantly from those that were not assessed, and are therefore likely to be a representative sample.

This study was not designed to assess risk factors for dementia, although basic information on past medical history, family history and education were collected. No control group was available to compare with patient groups, and therefore observations of inter-group differences are all that is possible. In terms of past medical history, heart disease, hypertension and stroke were all common in patients with VaD (Hebert and Brayne, 1995), which is as would be expected. It is

notable that there was no history of stroke amongst any of the AD cases. Stroke has been suggested as a possible risk factor for late onset AD (Skoog, 1994), but from this sample appears rare in younger patients. Head injury, a known risk factor for AD (Henderson et. al., 1992), was equally common amongst the other dementias.

Seizures are reported, from autopsy based studies, in between 10% and 60% of AD patients, and in up to 17% of non-AD patients (Hauser et. al., 1986; Risse et. al., 1990; Forstl et. al., 1992). Seizures are known to become more frequent as the disease progresses, and thus our finding of a rate of approximately 10% across all of the major diagnosis groups is consistent with previous studies.

The Hachinski ischaemia score can be used alone as a diagnostic instrument for VaD, however, this results in high sensitivity and low specificity (Verhey et. al., 1996). The HIS has particularly good discriminating power between AD and VaD (Rosen et. al., 1980), which is confirmed in this younger group of patients. In this study the HIS was also able to distinguish VaD from Alcohol related dementia, but was not able to discriminate FTD from either VaD or AD.

Family history is known to be a risk factor for AD, and a number of autosomal dominant genetic mutations that cause AD have been discovered, and indeed, in the study population there was a patient with a known presenilin 1 mutation. It is surprising then that the rate of a positive family history is only 9% amongst the AD cases. This compares with a rate of up to 50% in some other studies (Henderson et. al., 1992), who used a similar method of defining familiarity; i.e. one other affected first degree relative in the family. No cases of familial VaD were identified, which is also surprising given that there are genetic links related to hypertension and hyperlipdaemia, and that CADASIL is an increasingly recognised familial VaD associated with mutations in the *Notch3* gene (Joutel et. al., 1997).

By contrast a quarter of the FTD patients had a positive family history, which is consistent with the increasing evidence for linkage of Frontal Lobe Degeneration to chromosome 17 (Foster et. al., 1997) and chromosome 3 (Ashworth et. al., 1995; Brown et. al., 1995; Wilhelmsen, 1997). A high number of Huntington's patients amongst the 'other dementias' group accounted for the 38% rate of a positive family history in this group.

The extent of clinical investigation that patients received appeared to vary according to their diagnosis. The rate of neuroimaging varied between only 37% of cases in the 'other dementias' and 94% in the FTD group. The low rate of imaging in the 'other dementias' group may again be explained by the presence of a high proportion of HD cases. Diagnosis was often established on the basis of family history, symptoms and a positive genetic test; in this situation clinicians may have been reluctant to expend further resources on neuroimaging. Other studies have examined the rates of neuroimaging for younger people with dementia. The involvement of a neurologist significantly predicts whether neuroimaging will be performed. Newens et al (1994) in their epidemiological sample found a rate of 82.8% for neuroimaging, although this varied between 99.2% for patients diagnosed by a neurologist to only 53% for patients diagnosed by a psychiatrist. In a comparison of a neurology and a psychiatry service diagnosing presenile dementia patients, Allen & Baldwin (1995) found that 71% of patients diagnosed by the neurology service and only 37% of those diagnosed by the psychiatry service underwent neuroimaging. Similarly, in a multi-disciplinary setting involving both psychiatry and neurology, such as in Mersey region, 96% of patients had neuroimaging, including 9% who underwent both CT and MRI. Less data are available on rates of EEG examination, however, in the Northern region 53% of diagnosed presenile AD patients had undergone an EEG (Newens et. al., 1994); approximately twice the rate for AD patients in this study.

Given the relatively low cost of a CT or MRI scan compared to the economic costs of caring for a demented person it would seem that neuroimaging should be

available to all younger patients with dementia, which appears to be the case if a neurologist is involved in the diagnosis. The low rates of scanning performed by psychiatrists may represent either a lack of understanding about how the scan can aid diagnosis and assessment, or that psychiatrists have restricted access to neuroimaging facilities. In this study psychiatrists were usually based in community Trusts without advanced investigational facilities, arranging a scan usually involved a cost from purchasing the scan from a neighbouring acute Trust.

The distribution of dementia severity across the population was not constant. The majority of patients were in the mild and moderate stages of the disease with reducing numbers of the profound and terminal stages. Similar rates of functional impairment were found across the main diagnostic groups, with the highest disability among those in institutional care.

4.4.2 Non-Cognitive Symptoms

Non-cognitive symptoms in this study were assessed using the BEHAVE-AD and the Cornell Scale for Depression in Dementia.

Delusions were present in 53% of this sample of younger people with dementia. This is rather higher than found in the majority of studies which have reported delusions in 25-35% of patients, though with upper and lower limits of 10% and 70% (Allen and Burns, 1995). Amongst the AD patients, delusions were present in 38% of patients which is close to the weighted mean rate of 26.9% (range 10.5%-46%) calculated by Allen & Burns (1995) for 2,787 AD patients diagnosed according to NINCDS/ADRDA criteria.

In this sample of younger patients, delusions were more common in VaD (61%) than in the AD patients (38%). Other studies comparing AD and VaD have usually found delusions more commonly in AD patients, although Cummings et al (1987) found a rate of 47% , and Flynn et al (1991) a rate of 50% in Multi-Infarct Dementia.

Half of the DLB patients had delusions which is also consistent with previous findings (McKeith et. al., 1992). Within the FTD group, a surprisingly high prevalence of delusions was found (63%), which is at variance with studies of Pick's disease, where very low rates of psychosis are reported (Mendez et. al., 1993; Jung and Solomon, 1993). The diagnostic criteria used to define the FTD group, however, do not include any reference to psychotic symptoms, either as a supporting feature, or a feature that makes the diagnosis unlikely. This may, however, be a real finding, since there have been no previous studies of epidemiologically defined populations of FTD patients.

Hallucinations were present in 44% of the sample which is closer to the range of 18%-34% identified in Allen & Burns (1995) comprehensive review. They found a weighted mean rate for hallucinations of 18.6% in NINCDS/ADRDA diagnosed AD cases which is lower than the rate of 28% found in this study. Hallucinations were more common in the VaD cases (55.6%) than in AD, which is consistent with the findings of other studies, although the rates identified in this study were very much higher than these other two studies (16% (Cohen et. al., 1993) and 13%-20% (Cummings et. al., 1987)). The high rate found in this study is likely to relate to the cut-off score method used with the BEHAVE-AD to define hallucinations. High rates of hallucinations were present in the DLB group (66%), a reflection of the prominence of hallucination in the diagnostic criteria.

Aggressive behaviour was present in 61% of patients which has been a commonly identified feature of dementia from other studies of general dementia patients with rates of 45% (Patel and Hope, 1993) to 50% (Rabins et. al., 1982). The rate of aggression in AD patients in this study was 46% which is at the upper limit of the weighted mean of 27.6% (range 11%-51%) for AD patients found by Allen & Burns

(1995). AD patients had the lowest aggression rating of all the groups in the study. The highest aggression rating was for the DLB patients (83%).

Depression was a feature of all of the diagnostic groups, with no difference in the severity of dementia in any of the specific diagnoses. Caution is required in assigning a depression diagnosis on the basis of a rating scale and, indeed, the Cornell scale is not designed for this purpose.

4.4.3 Outcome & Institutional Care

In terms of outcome, the limited data that we were able to collect over a 1 year follow-up period suggests that approximately 15% of YOD patients in any area will move from their own home into institutional care, but that this will be balanced by an equivalent number of deaths.

In this sample 30% of patients were not resident in their own home. For health care planning, based upon these data, approximately 5 Local Authority Residential Care, and 10 Nursing Home/Long Stay Hospital beds will be required for YOD patients for each 100,000 people at risk.

Ongoing follow-up of this cohort, particularly through the KC&W co-ordinated care programme (See section 7.2.2) will provide further data on incidence and outcome in this population.

4.4.4 Limitations

The low rate of familial disease, particularly AD and VaD suggests the possibility of bias in this sample. Higher rates than those found would be expected based upon knowledge of the genetics of these diseases and from previous epidemiological studies. This is a small sample of patients; when divided into comparative groups, such as by diagnosis or residential placement, the numbers in many groups become too small to allow formal comparisons.

As this is a cross-sectional study it is not possible to draw conclusions relating to causality, such as the association between functional impairment and residence. On-going longitudinal follow-up of this cohort may be able to provide more detailed data on these types of association.

The presence of delusions, hallucinations and aggression were assessed using cut-off scores on sub-scales of the BEHAVE-AD. This is likely to have lead to higher sensitivity and lower specificity than the use of either a specialised psychiatric interview or a clinical assessment. This is likely to be most problematic with hallucinations where more than 2 ratings of “Vague: not clearly defined” response would give a positive score for presence of hallucinations.

The presence of depressive symptoms was assessed using a rating scale and not a diagnostic instrument. As a result is it not possible to determine the number of cases of clinical depression among the patients, only to comment on their degree of depression, and use the rating for correlation with other patient and caregiver factors.

For outcome, the number of person years of follow-up is too small to provide detailed analysis of the relationship between specific patient, carer and economic factors and outcome.

4.4.5 Clinical Implications

- Neuroimaging as part of the diagnostic process should be equally available to patients whether they are diagnosed by a neurologist or a psychiatrist. This study suggests that psychiatrists are either more reluctant or have less access to CT and MRI scans than their neurology colleagues.

- High rates of non-cognitive features of dementia were found in this sample. These types of symptoms are known to correlate with caregiver burden. Carers looking after someone with delusions, hallucinations or aggression should be assessed for the need for additional support. Better recognition and treatment of non-cognitive symptoms may have an effect on caregiver burden.

- Service planners can base estimates of need for institutional care in YOD on this population. These data suggest that 5 residential care place and 10 nursing home places will be needed for YOD patients for each 100,000 people aged 30-64 years in the population.

5. Caregiving in Young Onset Dementia

5.1 Definition of Caregiver

For the purpose of the study the term caregiver was defined as a non-statutory professional carer who could be a partner, family member, friend, neighbour, or paid private individual.

Patients were defined as having no caregiver if no-one in the above category saw the person or was involved in their care less than once every 3 months.

A primary caregiver saw the patients or was involved in their care daily, or at least 5 times per week.

Secondary caregivers were involved with the patient more than once every 3 months, but less than 5 times per week.

Only the principal caregiver (i.e. the caregiver most involved with the persons care) was invited to participate in the study.

5.2 Presence of Caregiver

Eighty two percent of patients had a primary or secondary caregiver involved in their care (figure 16a), the distribution of relationships of the caregiver to the patient are shown in figure 16b.

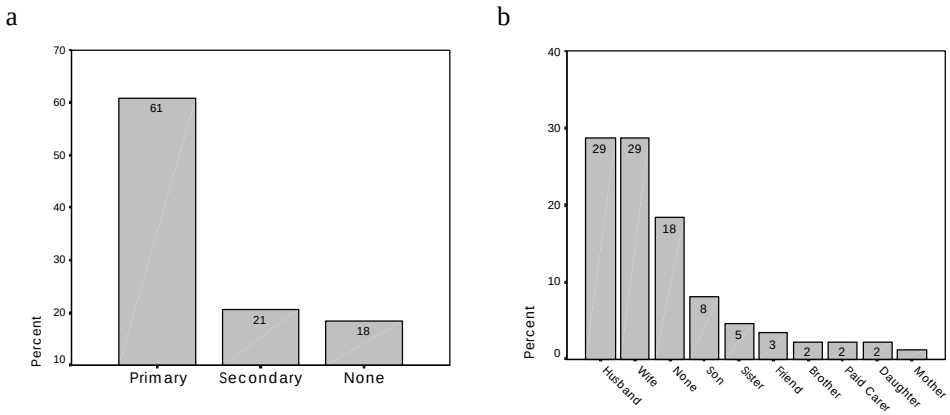


Figure 16 - Presence of a Caregiver (a) and Relationship to Patient (b)

5.3 Population of Caregivers Studied

The 87 patients who underwent comprehensive assessment were being cared for by 71 primary or secondary family caregivers. Of the 71 carers, 40 (56%) agreed to participate in the caregiver component of the study. The mean age of the carers participating in the study was 50 years (S.D. 7.7, range 30-59 years). There were 17 male caregivers (mean age 52 years) and 23 female carers (mean age 50 years).

5.4 Psychological Well-being

Caregiver psychological well-being was measured using the 28 item version of the General Health Questionnaire (GHQ) (Goldberg and Hillier, 1979) as a general measure of distress and as a screen for 'caseness'. The Hospital Anxiety and Depression Scale (HAD) (Zigmond and Snaith, 1983) was used to provide a

measure of the more specific type of psychological caseness (anxiety and/or depression).

5.4.2 General Psychological Well-being and Distress

The "GHQ Scoring Method" for screening tests (0-0-1-1) was used as described by Goldberg and Hillier (1979), with a threshold score of 5/6 indicating caseness. All 40 carers completed the GHQ with 19 (47.5%) rating as non-cases and 21 (52.5%) achieving caseness. GHQ scores were also calculated using the standard Lickert scoring (0-1-2-3); those rating as cases had a mean score of 40 while the mean score for the non cases was 17. There was highly significant separation between the two groups (figure 17)

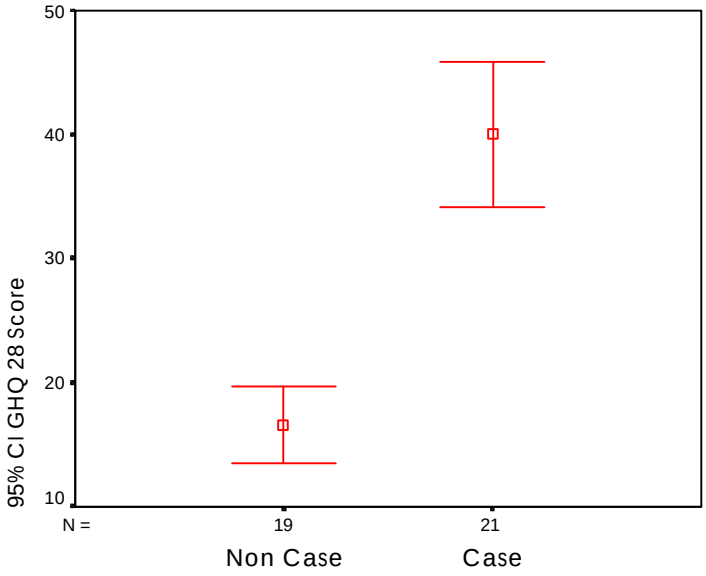


Figure 17 - Full Scale GHQ 28 Scores for Cases and Non-Cases

Comparing male and female caregivers, female caregivers had a trend for higher GHQ scores (figure 18), although comparing the rates of caseness in men (7 cases vs. 10 non-cases) and women (14 cases vs. 9 non-cases) there were no significant differences (Fishers exact test: p=0.3). All of the carers in the study were looking after someone of the opposite gender.

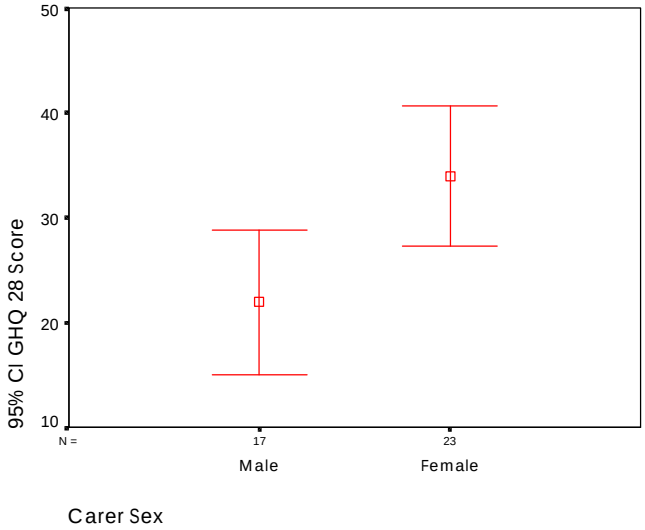


Figure 18 - GHQ Scores in Male and Female Carers

Comparing GHQ scores by study catchment area showed that there was no difference in the degree of caregiver distress between Hillingdon and KC&W (Figure 19)

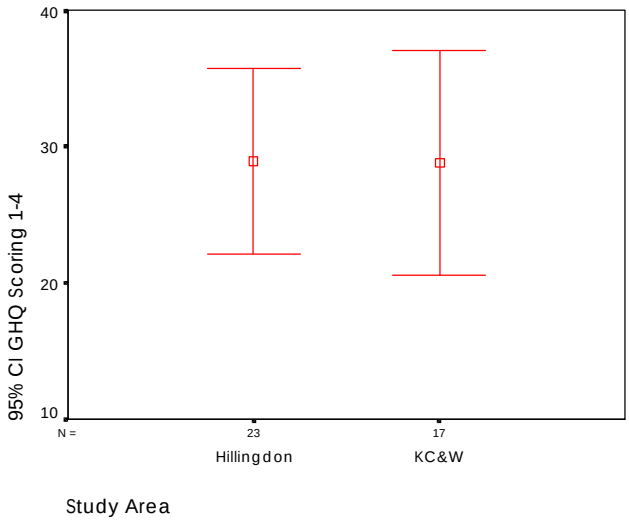


Figure 19 - GHQ Scores For Hillingdon and KC&W

5.4.3 Anxiety & Depression

All 40 carers also completed the HAD. A threshold score of 10/11 on both anxiety and depression scales was used to define caseness. On the anxiety scale 16 (40%) of carers reached caseness, while on the depression scale 5 (12.5%) reached the threshold for caseness. The rates of caseness on the HAD are compared with GHQ caseness in Tables 36a and 36b.

a

		Caseness by GHQ		
		Non Case	Case	Total
HAD Caseness for Anxiety	Non Case	15	9	24
	Case	4	12	16
Total		19	21	40

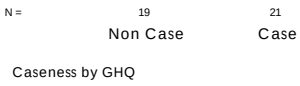
b

		Caseness by GHQ		
		Non Case	Case	Total
HAD Caseness for Depression	Non Case	19	16	35
	Case		5	5
Total		19	21	40

Table 36 - GHQ Caseness Compared To HAD Caseness (a - Anxiety, b - Depression)

Comparing scores on the HAD scales by caseness reveals a trend for higher anxiety scores (figure 20a) and significantly higher depression scores in the GHQ Case group (figure 20b).

a



	CDR	BEHAVE-AD Total	BEHAVE-AD Global	IDDD	Cornell
GHQ 28					
Pearson Coefficient *(n, valid cases)*	-0.149 *(40)*	0.440***(37)*	0.333* *(37)*	-0.106 *(38)*	0.236 *(38)*
95% Confidence Interval	(-0.44 - 0.17)	(0.14 - 0.67)	(0.01 - 0.59)	(-0.42 - 0.23)	(-0.09 - 0.517)
p value	0.358	0.006	0.05	0.526	0.153

Table 37 - Correlation Between GHQ 28 and Patient Variables

5.6 Physical Health

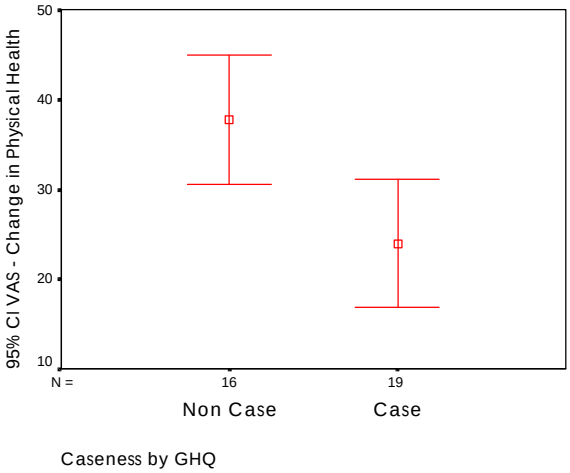


Figure 23 - Change in Physical Health for Cases and Non-Cases

5.7 Caregiver Burden

Two caregiver burden scales were employed in the study to capture a range of burden indicators. Burden 1 and 2 provides a direct measure of the caregivers sense of burden on a 5 item Lickert scale ranging from 'Not at all burdened' to 'Very greatly burdened'. Burden 2 was a composite index of subjective feelings that related to caregiver burden. The screen for caregiver burden (SCB) sought responses on the degree of distress caused to the caregiver by a range of items that related to objective burden and subjective burden.

5.7.1 Burden 1 & 2

On the burden 1 scale 90% of carers indicated that they experienced burden in caring for the person with dementia. The distribution of ratings of subjective burden is displayed in figure 24.

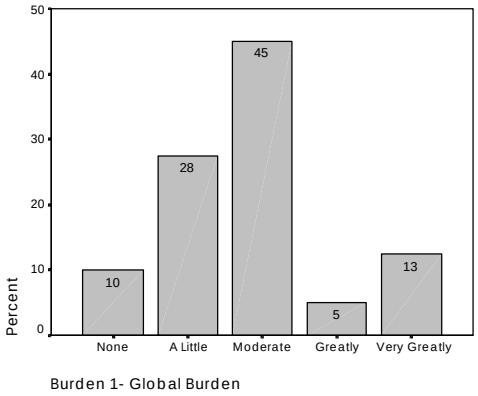


Figure 24 - Distribution of Burden 1 Scores

The effect of patient diagnosis, caregiver GHQ caseness and gender of carer on Burden 1 score is explored in Figure 25a-c respectively. There were no significant differences in Burden 1 scores between the different diagnoses, though there was a trend for higher scores in the FTD caregivers. There was also a trend for higher burden 1 scores in those carers rated as cases by their GHQ score. Female and male caregivers rated very similar burden 1 scores.

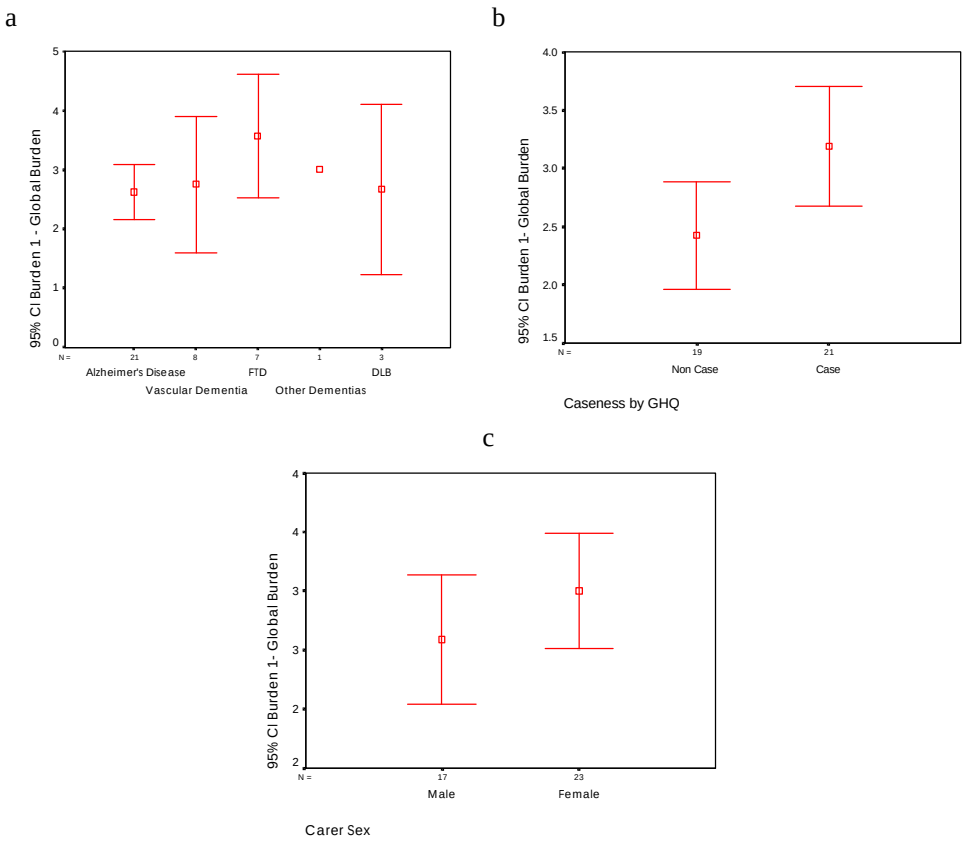


Figure 25 - Burden 1 Score by Diagnosis (a), Caregiver Caseness (b), and Gender of Carer (c)

On the burden 2 scale, there was no difference in levels of burden by diagnosis (figure 26

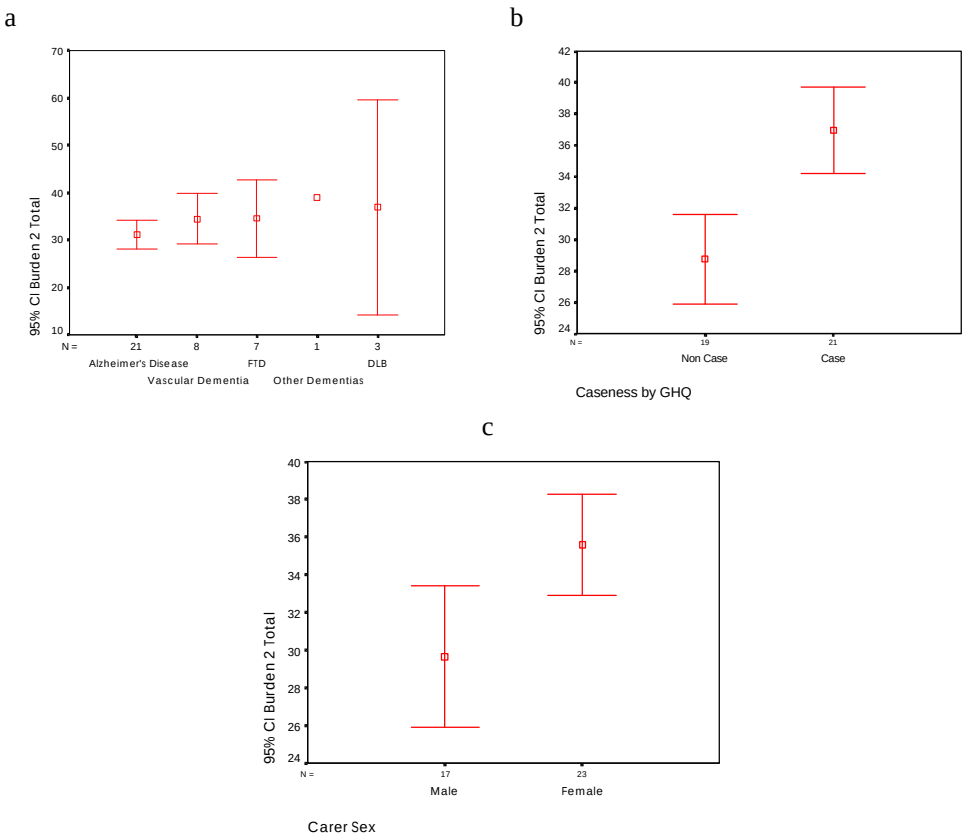


Figure 26 - Burden 2 Score by Diagnosis (a), Caregiver Caseness (b) and Gender of Carer (c)

5.7.2 Screen for Caregiver Burden

The SCB provides two scale scores; subjective burden (SB) and objective burden (OB). As for Burden 1 and 2 the effect of the major patient independent variable (diagnosis) and caregiver independent variable (GHQ caseness) was explored. For both objective and subjective burden there was no significant difference between the different diagnosis groups (figure 27)

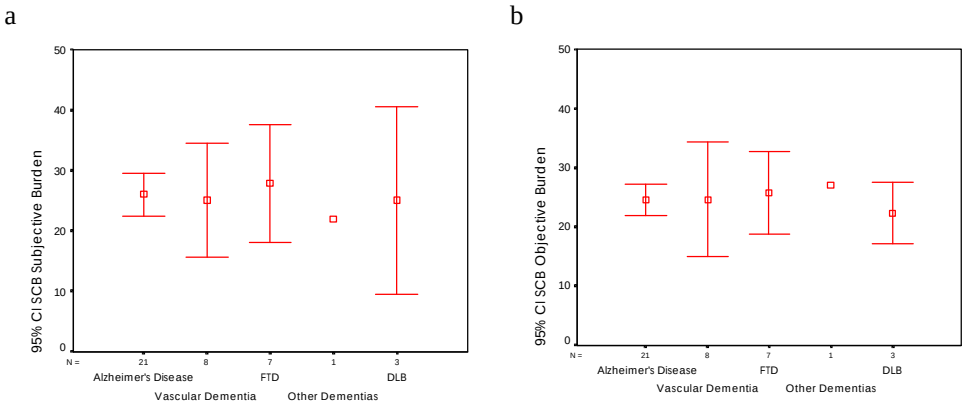


Figure 27 - Subjective (a) and Objective (b) Burden by Diagnosis

By comparison GHQ caseness had an observable relationship with SB and OB. There was a marked, but non-significant trend for higher subjective burden scores, and a significant trend for objective burden to be higher in the GHQ Case group.

a b

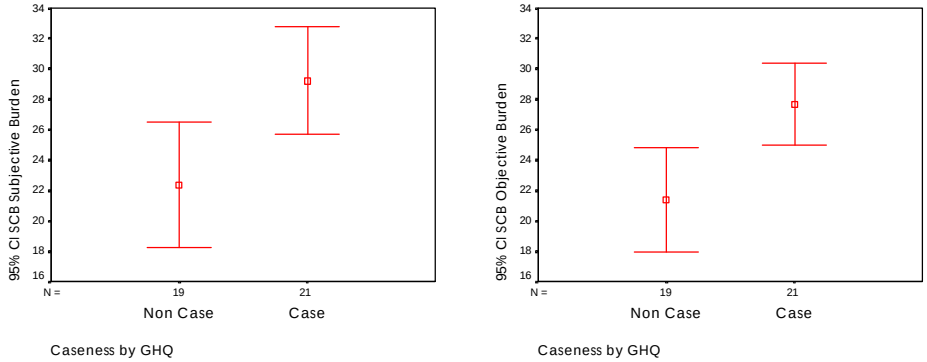


Figure 28 - Subjective (a) and Objective (b) Burden by GHQ Caseness

Female caregivers also tended to give higher ratings for subjective and objective burden (figure 29)

a b

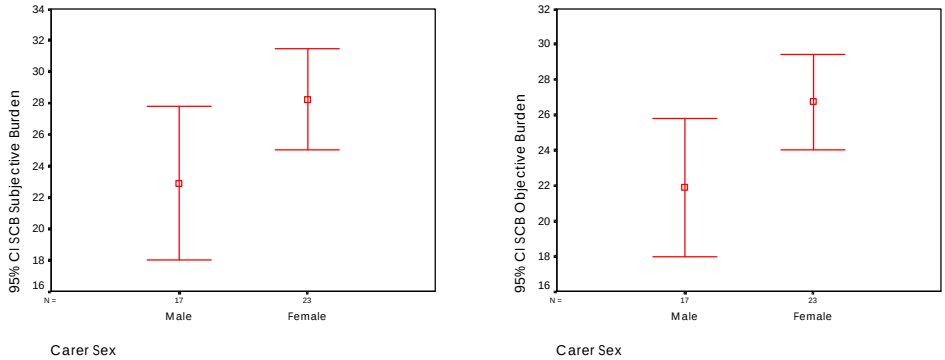


Figure 29 - Subjective (a) and Objective (b) Burden by Carer Gender

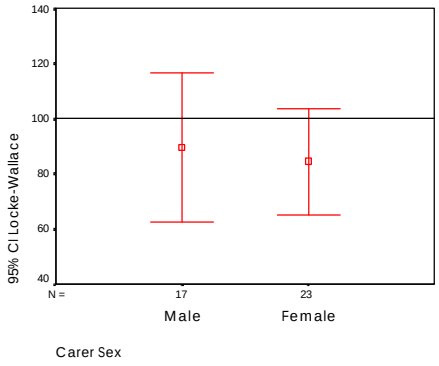
The influence of patient factors were explored by correlating the four burden indicators with the five principal patient severity and behaviour indices (table 38).

	CDR	BEHAVE-AD Total	BEHAVE-AD Global	IDDD	Cornell
Burden 1*(n)*	0.025 *(40)*	0.341* *(37)*	**0.423**** *(37)*	0.074 *(38)*	0.292 *(38)*
95% CI	*(-0.29 - 0.33)*	*(0.02 - 0.59)*	*(0.12 - 0.66)*	*(-0.25 - 0.39)*	*((-0.03 - 0.56)*
p value	0.876	0.045	0.009	0.660	0.075
Burden 2	0.114 *(40)*	**0.482**** *(37)*	**0.582**** *(37)*	0.190 *(38)*	**0.413**** *(38)*
95% CI	*(-0.20 - 0.41)*	*(0.19 - 0.70)*	*(0.32 - 0.76)*	*(-0.14 - 0.48)*	*(0.11 - 0.65)*
p value	0.483	0.003	0.000	0.252	0.010
Subjective Burden	0.082 *(40)*	**0.591**** *(37)*	**0.672**** *(37)*	0.101 *(38)*	0.292 *(38)*
95% CI	*(-0.24 - 0.38)*	*(0.33 - 0.77)*	*(0.45 - 0.82)*	*(-0.23 - 0.41)*	*(-0.03 - 0.56)*
p value	0.617	0.000	0.000	0.546	0.076
Objective Burden	-0.021 *(40)*	0.389* *(37)*	**0.430**** *(37)*	-0.057 *(38)*	0.105 *(38)*
95% CI	*(-0.33 - 0.29)*	*(0.07 - 0.63)*	*(0.12 - 0.66)*	*(-0.37 - 0.27)*	*(-0.22 - 0.41)*
p value	0.898	0.021	0.008	0.732	0.531

Table 38 - Correlations Between Burden Scores with Patient Severity and Behaviour Indices

Burden on all four scales was significantly associated with the severity of non-cognitive symptoms. Burden 2 alone correlated significantly with depression in

a



b

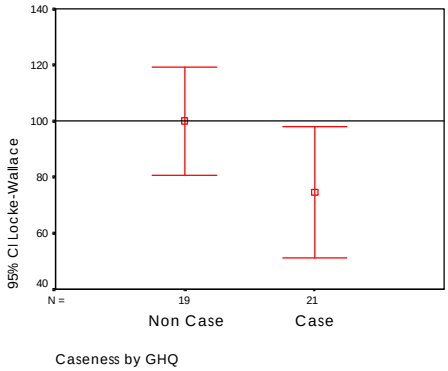


Figure 30 - The Relationships Between Carer Gender (a) and Carer GHQ Caseness With Marital Quality

5.9 Discussion

These results represent the first cross-sectional study of the experiences of caregiving in an epidemiologically defined population of carers for younger people with dementia. This is a true population of younger caregivers, with a mean age in the 50's and no carers above the age of 60 years.

Although the numbers are small, consistent themes do appear from the data. In general, when compared with studies of older carers, this group of younger cares show remarkable similarities.

Firstly, female gender appears to be consistently related to general psychological distress, anxiety, depression and feelings of burden. Unlike the majority of studies of older people, this sample of carers is not predominantly women, but is evenly split between the two genders, providing the opportunity to directly compare male and female carers.

In terms of the GHQ, more than half (52%) of this sample of caregivers rate as 'cases'. This is significantly higher than population norms, which for women are approximately 33%, and men 25% (Huppert et. al., 1988; Buck et. al., 1997). Similiar rates of GHQ caseness have been found in other surveys of presenile dementia carers from the Southampton area (50% caseness) (Delaney and Rosvinge, 1995) and Manchester (58% caseness) (Baldwin, 1994a). This high rate of caseness is similar to that found amongst carers of EMI patients in general (Gilleard et. al., 1984) (57-75% caseness), and is significantly higher than the rates seen among professional carers (27%) (Macpherson et. al., 1994) and carers for frail elderly people (39%) (Buck et. al., 1997). Unlike Eagles et al (1987), however, there was no association between dementia severity and carer GHQ score.

In terms of psychiatric illness amongst carers, there was a relatively low rate of clinical depression (17% of women and 6% of men), particularly when compared to other studies where rates as high as 43% have been found among older female carers (Livingston et. al., 1996); although this rate was based upon a clinical assessment rather than a screening instrument. The rate found in this sample was, however, similar to that found by Ballard et al (1996) who found that 23% of older carers had major depression and 6% a minor depression (mean age of carers 64.8 years, 54% male). Carers were assessed monthly over a period of one year, and the authors were able to show that 50% of their sample experienced significant depression lasting a month or more during the period of follow-up; suggesting that symptoms fluctuate and that more in-depth or longer term assessment identifies higher rates of depression.

By comparison, rates of anxiety disorder were very high, particularly in women, 60% of whom rated as cases compared to only 12% of male caregivers. The rate of

anxiety disorder in men was similar to that found by Russo et al (1995) in a sample of older male and female caregivers (16%), but the younger female carers in this study have very high rates of anxiety.

These high rates of psychological distress and anxiety disorder suggest that there is considerable unrecognised and potentially treatable psychopathology among younger caregivers, particularly females.

Across the 4 sub-scales of the 2 burden measures used in this study a consistent relationship is seen between burden and GHQ caseness, and between burden and female gender. Moreover, there was no relationship between any of the burden measures and either disease severity or functional disability in the patients. These findings are entirely consistent with data from studies of carers of older people with dementia.

Our findings are also consistent with previous research in terms of the effect of marital quality; Stressed carers rated a lower marital quality. There were no differences in marital quality between male and female carers.

So, how does marital quality affect caregiving? Two main theories emerge from the literature: Firstly, those caregivers who have a good quality of marriage more willingly undertake the caring role, have less resentment, and gain more gratification from their role. Conversely, those with a poor marital quality may feel forced into the caregiving role, generating resentment, stress and burden (Morris et. al., 1988).

An alternative theory, based upon work by Brown & Harris (1978) with depressed women living in the community, views poor marital quality as a vulnerability factor for stress and depression, which in itself is a predictor of burden.

5.9.1 Limitations

It was unfortunate that only 56% of the carers identified by the study agreed to participate in the caregiving assessments. This potentially introduces bias into the sample, although it is not clear whether the decision to take part in the study was made by those who felt they were coping well, or those who were coping badly.

These data are cross-sectional which is limiting in terms of defining causal relationships and understanding the time related process of burden. The cohort does however, remain under follow-up and further work is in progress to examine longitudinal course and outcome.

The burden scales used are subjective and rely solely on the caregivers perception of burden. Although the scales have internal consistency it is impossible to externally validate them against other populations of non-caregivers, or caregivers for people with other illnesses. The lack of standardisation of burden measures also means that there are few similar studies to gain data from to compare with this sample.

The measures of well-being, distress and burden are all based upon self-reporting. It is possible that men and women experience emotion in different ways. Women may be more in-touch with their emotions and so rate more highly on these types of assessment. Men, by comparison, may be more inhibited, or less aware of emotion. These factors have been identified as limitations in other studies comparing male and female carers (Lutzky and Knight, 1994).

In terms of the assessment of marital quality, only the unaffected spouse was assessed. The Locke-Wallace scale is intended to be applied to both partners with a comparison of scores giving an indication of harmony or dis-harmony. We also asked the caregiver to rate their marital quality as it was before the onset of the dementia; this is likely to have introduced some bias with those caregivers who

were coping well 'idealising' their marriage, while the stressed caregivers take a more negative view.

We did not include any measure of coping style, which could potentially have been valuable. Previous research suggests that coping style is related to gender issues and caregiver burden. A logical next step in caregiver research will be to take poorly coping carers, identify their coping styles and vulnerabilities and attempt an intervention that modifies these factors towards those found in carers who are coping well.

5.9.2 Clinical Implications

- Psychological distress, anxiety and depression are as common among carers for younger people with dementia as for carers of older dementia sufferers.
- Female carers were very stressed, with particularly high levels of anxiety and burden.
- Male caregivers appeared to cope better, with lower levels of distress and low rates of depression, anxiety and burden.
- Psychological distress was associated with increased caregiver burden. Interventions that improve the psychological well-being of carers may reduce burden.
- The type of dementia, its severity, and the resulting functional disability is not related to burden.
- Non-cognitive symptoms predict higher rates of burden. Carers of patients with non-cognitive symptoms should be identified as priorities for support interventions.

6. The Direct Costs of Care for Younger People with Dementia

6.1 Introduction

The objective of the economic evaluation is to compare the direct cost-of-illness for this group with the costs estimated for patients with dementia in other studies. A secondary aim is to examine the effects of diagnosis and disease severity on cost-of-illness, and of cost-of-illness on caregiver burden.

Having established that this is a representative population of patients both in terms of the population of the catchment areas, and in terms of the prevalence of dementia when compared to other similar studies this is an appropriate population on which to base an economic analysis (Greenhalgh, 1997).

6.2 Costing of Care Interventions

The following table summarises the costings for each intervention used in the economic analysis of this study. Wherever possible costs have been obtained from sources used by other UK cost-of-illness studies in dementia. Costs have been adjusted to 1997 prices assuming inflation at an annual rate of 3% from their published date.

Intervention	Cost Adjusted to 1997 Prices Assuming Inflation at 3%	Original Source of Costing
Meals on Wheels	£4.56/meal	(Melzer, 1992)
Home Help	£6.28/hr	(Melzer, 1992)
Domicillary Care	£9.55/hr	(Kirk et. al., 1995)
Social Worker	£14.64/hr	(Melzer, 1992)
CPN	£16.34/hr	(Melzer, 1992)
GP Consultation	£18.04	(Melzer, 1992)
Day Care	£25.55/day	(Melzer, 1992)
Psychologist	£27.50/hr	Personal Communication (MSR)
Out Patient Appointment	£40.28	(Netten, 1994)
Admiral Nurse	£96.76 per contact	Dementia Relief Trust
Respite Care	£371.32 per week	(Kirk et. al., 1995)
Residential Care	£392.53 per week	(Kirk et. al., 1995)
Nursing Home Care	£615.32 per week	(Kirk et. al., 1995)
Long Stay Hospital Care	£668.37 per week	(Kirk et. al., 1995)
Acute Hospital (Medical or Psychiatric) Ward	£891.16 per week	(Kirk et. al., 1995)

Table 39 - Sources of Cost of Care Interventions

6.3 Population Studied

The population included in this health economic analysis consisted of the 86 patients and 40 carers included in the in-depth behavioural and caregiving assessments reported in Sections 4 and 5. Of the 86 patients 25 were in institutional care and 61 were resident in the community.

6.4 Costs of Community Care

The mean, maximum and total costs of the community resources being received by the study population are summarised in table 40.

Type of Care	Number in Receipt (%)	Mean Cost	95% CI	Maximum	Total
Domicillary Care	14 (23%)	£386	*(92-680)*	£9,072	£33,156
Day Care	11 (18%)	£249	*(101-397)*	£2,889	£21,383
Admiral Nurse	12 (20%)	£146	*(67-224)*	£1,045	£12,540
Respite Care	3 (5%)	£130	**unsuitable for analysis*	£5,950	£11,200
Social Work	30 (49%)	£56	*(39.5-72.5)*	£161	£4,819
Psychology	20 (33%)	£46	*(28-64)*	£198	£3,960
Outpatient care	50 (82%)	£41	*(33-44)*	£71	£3,538
GP Care	50 (82%)	£28	*(18-37)*	£85	£2,125
Meals on Wheels	2 (3%)	£24	**unsuitable for analysis*	£1,032	£2,064
Community Psychiatric Nurse	4 (7%)	£6	*(0.1-10)*	£111	£443
Total	*60 (98%)*			*£12,453*	*£95,228*

Table 40 - Annual Costs of Community Care Resources

The estimated mean cost per case of community, for the 61 patients resident in the community, is therefore £1,561 per annum.

6.5 Costs of Residential Care

Residential care costs were calculated for those patients not living at home. Costs include nursing home (8 patients), NHS hospital care (medical ward (2) and psychiatry ward (7)), local authority residential care (3) and hospital based long stay care (5). NHS hospital care included those patients who had been hospitalised for more than 4 weeks and was calculated from their length of admission and the averaged cost of a hospital bed. One patient in an acute ward (severe Alcohol Related Dementia) and four patients in the psychiatry wards had been inpatients for more than 12 months.

The total annual cost of institutional care for the 25 patients in the sample was £523,104, giving a mean cost per patient of £20,924 per year for those in institutional care.

6.6 Costs of Private Care

Six patients were receiving private care. These were services organised and paid for directly by the carer and not part of a package of care organised by social services as part of a needs based community care assessment. These costs were additional to any payments for private residential care that carers were making. In general they related to the employment of private home carers. Three of the six patients were of SEC I.

Carers were paying between £140 and £30,000 per year for private care. The services being purchased were for private home care and nursing care. Overall, the mean cost of private care was £655 per annum, although the very large range and skew in the data prevented confidence interval analysis. The total amount spent on private care was £58,320 per annum.

6.7 Total Cost-of-Illness

The total cost of all direct patient care was £676,652, or £618,332 if private care costs are excluded. This gives a mean per patient cost of £7,868 for all direct costs or £7,189 if private care costs are excluded.

The total cost of care for all 185 Young Onset Dementia patients from the two catchment areas can therefore be estimated to be £1,455,580, or £1,022,840 if only those patients who are still under the age of 65 years are included.

Extrapolating this further to the estimated 16,737 (13,975-19,879) patients under 65 years with dementia in the UK gives an estimated annual resource cost of £132 million (£110 million - £156 million).

6.8 Patient Associations With Cost of Care

The influence of major patient variables on cost of care was examined. Dementia severity showed a trend for increasing cost with increasing severity of disease, but the large variances of cost in each severity group, and small numbers of cases severely reduced the power to identify any significant trends (figure 31)

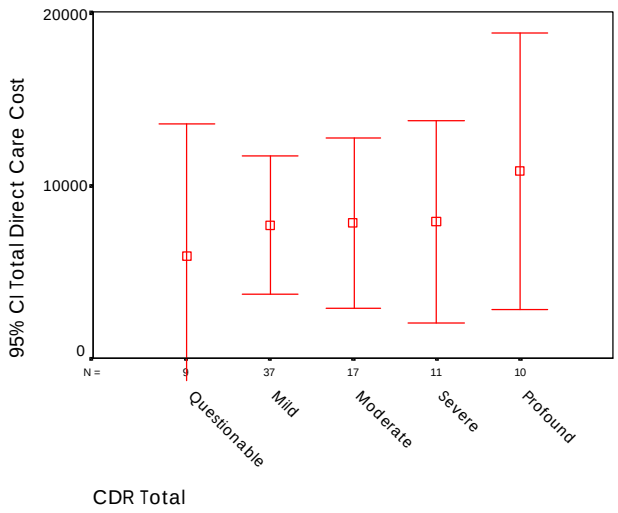


Figure 31 - Cost of Care by CDR Score

Similarly regarding the effect of diagnosis, although there was a trend for the ARD group to have a higher cost of care, the large variances of the costs involved reduced the power to determine any significant trends (figure 31)

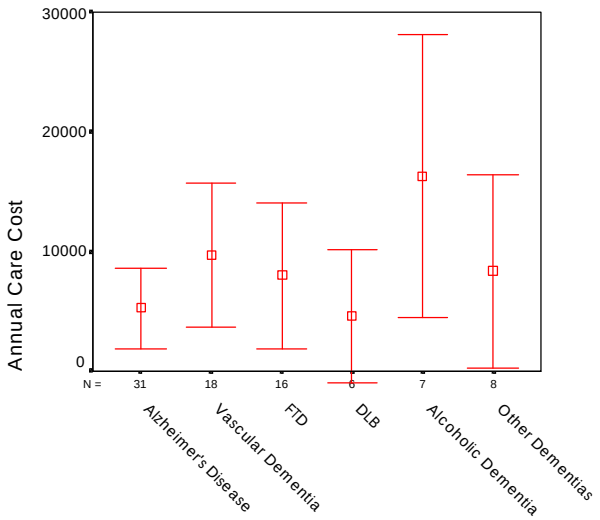


Figure 32 - Cost of Care by Diagnosis

There were no significant correlations of the major patient variables (BEHAVE-AD, Cornell, IDDD) and cost of care.

6.9 Caregiver Associations With Cost of Care

Exploring cost of care by caregiver GHQ caseness showed a non significant trend for the non-case caregivers to be receiving care of a higher cost (figure 33) .

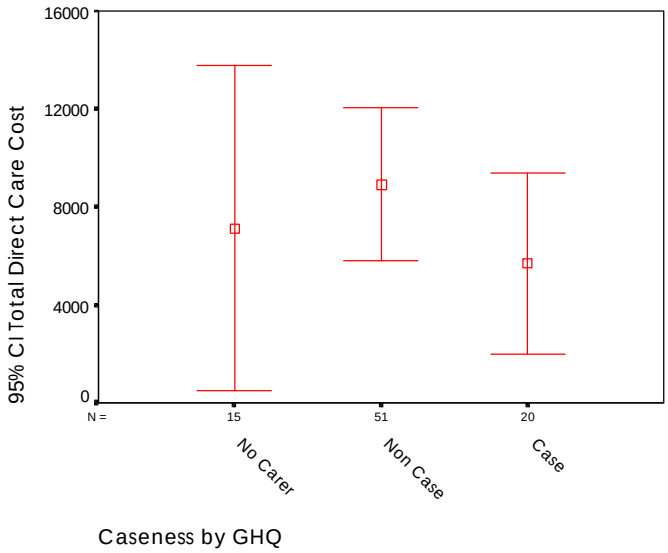
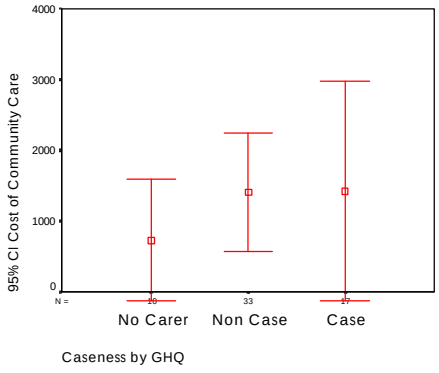


Figure 33 - Total Cost of Care by Carer GHQ Caseness

Comparing the costs by caregiver GHQ-caseness for patients in residential care, and those living in the community showed no difference between the two groups. However, amongst those patients without carers there was a trend for those living in the community to have lower costs than those with carers, while the trend was towards higher costs for those in institutional care. (Figure 34).

a



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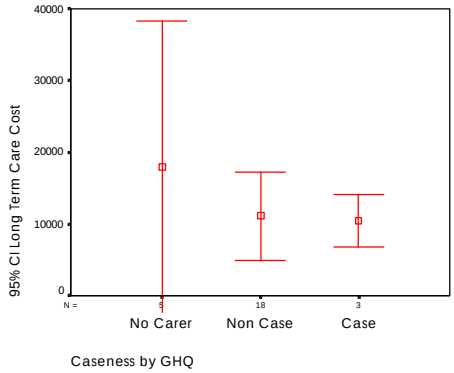

Figure 34 - Cost of Community (a) and Long Term (b) Care by Caregiver GHQ Caseness

There were no significant correlations between cost of care and the major caregiver variables (HAD, Burden1/2, SCB)

6.10 Discussion

Type of Service Received	This Study	Philp et al	Livingston et al
Day Care	14%	17.5%	25.6%
Home Help	17%	57%	43.6%
Meals on Wheels	2%	17.5%	35.9%
CPN	5%	12.3%	2.6%
Social Worker	35%	57%	-
Respite Care	3%	15.8%	-

Table 41 - Receipt of Community Services Compared to Other Studies

Unfortunately, cross-sectional prevalence studies of older patients with dementia have usually been based either upon community samples or institutional samples and it is difficult to identify the rate of institutional care use for an epidemiologically based sample of older people with dementia. Estimates of the number of people with dementia that require institutional care, can however, be inferred from other studies. Welch et al (1992) followed a population of 122 US community resident older people with AD over a period of up to 8 years and found that 75% required at least one period of institutional care. From their data they estimated that 40% of patients with AD require institutional care at any given time. Similarly from a UK study it has been estimated that 37% of people with dementia live in institutions (Morris, 1993). The requirement for residential care is also related to age, with 45% of residents being over 85 years, 40% between 75 and 84 years and only 15% between 65-74 years (Gray and Fenn, 1993). These figures suggest that the rate of institutional care requirement for this group of younger people with dementia is higher than would be expected for a 'younger' group of older people (i.e. those aged 65-74 years).

Taking all of this evidence together suggests that the estimated cost-of-illness derived from this study is an accurate reflection of the true cost-of-illness for this group of patients. These patients appear to make less use of community care services, but make use of institutional care facilities.

This study has not considered indirect costs, an area of cost-of-illness likely to be greater for younger people with dementia. The patients in this study are making less use of community care, and therefore, by inference, informal caregivers are likely to be filling this gap. Caregiver exhaustion and burden are the most frequently cited reasons for a patient having to enter residential care (Zarit et. al., 1980; Colerick and George, 1986; Gold et. al., 1995), yet there was no difference between community care costs for the 'stressed' and 'non-stressed' carers (figure 34a). However, when both community and institutional costs are taken into account, there was a slight trend for higher costs in the 'non-stressed' carer group, suggesting that this increased level of support may be reducing burden (figure 33). If stress and burden in caregivers were actively identified and supported by increased community resources, the need for institutional care might be reduced. As institutional care is almost 20 times more costly than community care this is likely to be cost effective.

In terms of the disease itself a slight, but non-significant trend for increasing cost with increasing severity of disease has been identified. This was a similar finding to other studies (Souetre et. al., 1995). As previously discussed the greatest predictor of cost is the need for institutional care. In our sample there were patients at all degrees of severity in institutional care, including one patient with alcohol related dementia at CDR=0.5. The presence of these very costly patients in all disease severity groups tends to hide any trend that might be present. However, even examining the costs for those resident in the community shows, that although some patients were receiving intensive input (table 40), with, for example, up to £9,000 being spent on domicilliary care, and £5,900 on respite care, these were very much outliers in the data set; in the majority of cases very little was being spent.

In summary, the cost-of-illness for dementia in younger people is at least as much as it is for older people, although with the many different methodologies it is not easy to compare figures between studies. The majority of the cost, as with older people, relates to institutional care. Disease severity has little overall effect on cost, although there is a suggestion that some types of dementia are more costly than others, with AD having a relatively lower cost. Alcohol related dementia, in particular, with its associated requirement for long term institutional care is the most costly form of dementia.

6.10.1 Limitations

This study considers only direct costs. In this group of younger people with dementia and their carers, indirect costs both in terms of informal care costs and morbidity and mortality costs are likely to be very high. Hay & Ernst (1987) estimated the net expected total cost, including morbidity and mortality costs, for individuals with AD in differing age groups (figure 35).

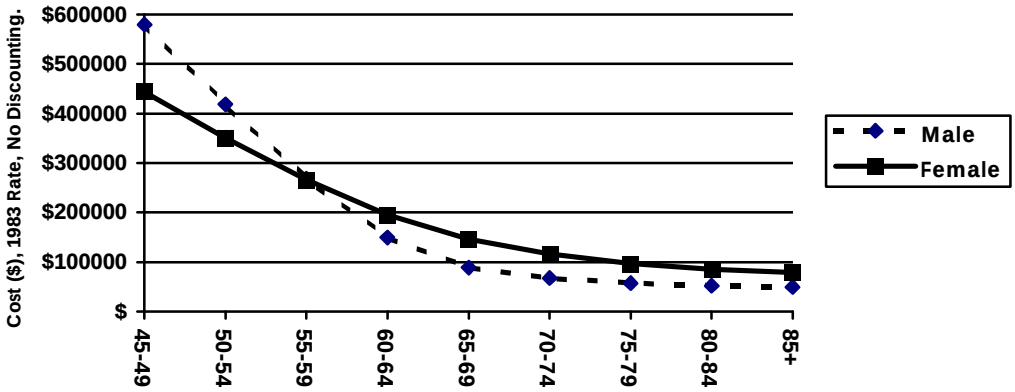

Figure 35 - Estimated Net Expected Total Costs for AD (After Hay & Ernst, 1987)

The morbidity and mortality costs are exceptionally high for younger people, resulting in net costs of up to 6 times those for older people.

The sample assessed for this study, although drawn from an epidemiological prevalence study is relatively small, with some cases incurring very high direct costs. Caution is required in extrapolating these figures, although the use of confidence intervals does provide an estimate of the range of potential costs in wider populations.

As already discussed, comparison of this study with other published studies is problematic due to the difficulties of comparing results derived by different methodologies. The figures presented are estimates only of the likely true cost.

7. Conclusions & Developments

7.1 Summary

I have identified a population of 185 people who developed a dementia before reaching their 65th birthday. This is the first study of it kind to cast a broad net for younger people with dementia in geographically defined catchment area. The prevalence results derived from this population are gratifying in that they appear to reflect accurately the results from a range of studies that have estimated prevalence for specific dementias such as AD, VaD and HD in this age group. Having confidence in the accuracy and completeness of the case finding means that the prevalence figures derived for FTD, DLB and ARD can also be considered to be relatively reliable. This is also the first research to report epidemiological data for the presenile forms of these diseases; what is particularly noticeable is the FTD is a relatively common form of young onset dementia, while DLB is relatively rare. This appears to be a reversal of the findings in the elderly where FTD is very rarely reported, even in neuropathological series, while DLB is thought to account for up to 20% of cases of dementia. Although these data on diagnosis need to be confirmed at autopsy, the results do suggest that there may be an intriguing age-related biological factor involved in these diseases, and that FTD may be a true young onset dementia.

The detailed prevalence figures will hopefully be used by planners in other areas to estimate the number, and differential diagnoses of patients who may use their services. Following the publication of the ADS strategy document on young onset dementia (Alzheimer's Disease Society, 1996), many health authorities and Trusts have begun to consider the needs of this group of patients in their area. In many cases that we have become aware of over the duration of this study, scarce resources were being used up performing short term, local attempts at case finding. Prevalence data from this study, potentially combined with data from other studies, can now be rapidly applied to census figures for a particular area or region to estimate, with some accuracy, the number of patients who might use a particular service. Resources can then be applied more effectively either to develop new services or to provide training or reconfiguration of existing services.

Diagnosis is a critical stage in the assessment of a younger person with dementia. Dementia at any stage is devastating, but when it affects someone under retirement age and with financial and family responsibilities it is particularly distressing. Prompt and thorough investigation is needed early in the course of the illness; the possibility of identifying a treatable cause for the symptoms must not be missed, and if anything is treatable, the earlier treatment is commenced the greater the possibility of recovery. This study only identified patients with degenerative dementia and it is not possible to know how many people presented with symptoms of dementia for which a treatable cause was identified. However, it is surprising that between 6% and 60% of patients, depending upon their diagnosis, never underwent neuroimaging as part of their diagnostic process. While neuroimaging itself will not necessarily diagnose a treatable cause for the symptoms of dementia, it does act as a marker of willingness to investigate further, particularly with more invasive or high-tech investigations. Other studies indicate that high rates of imaging are associated with being investigated by a neurologist, while psychiatrists tend to use neuroimaging less frequently. It was not within the objectives of this study to seek the reasons behind performing or not performing particular investigations, however, this would clearly make a suitable topic for further research. A lack of understanding of the role of neuroimaging and other investigation in dementia could be overcome with better training, while restrictions due to cost can be tackled with economic arguments. The Section of Old Age Psychiatry of the Royal College of Psychiatrists has issued

a Consensus Care Protocol on the assessment and investigation of elderly people with suspected cognitive impairment which specifies that people under the age of 70 should all undergo neuroimaging. As in other areas, this has not been happening in KC&W and Hillingdon.

Diagnosis is only the first stage in the management of the younger person with dementia. Having achieved a diagnosis, long term support and aftercare is needed. High levels of non-cognitive symptoms were identified in this population, and these were also associated with higher caregiver distress and burden. To support patients and carers with these types of problems, effective community care is needed which can provide an individual package of care. Sadly, at the time this study was carried out these types of services seemed to be used relatively less frequently than in equivalent groups of older people. Particularly striking was that only 7% of patients had a community psychiatric nurse (CPN) involved, although 20% of the cares were in contact with Admiral Nurses (CPN's specifically providing support to carers). Although this relatively low use of community care resources resulted in lower than expected costs, it appears that the burden was shifted to higher utilisation of institutional care. From this type of cross-sectional study it is not possible to draw associations of causality between these factors, however, there appears to be more that minimal evidence that these high levels of behavioural disturbance combined with low levels of community support, result in higher carer burden and earlier entry into residential care. Better co-ordination, communication and training of these community resources may well improve this situation; a process which is now in action and will be described further in the following section.

The mental health care needs of the group of carers identified by this study are substantial. More than half of the carers have such a degree of distress that they could be considered to have a formal psychiatric illness. The study did not identify whether carers had been recognised by formal services as being under stress, however, anecdotally, from having personally interviewed every carer, only a very small number mentioned that their own needs were being recognised. This type of support is particularly provided by the Admiral Nursing service within KC&W; unfortunately the number of carers with an allocated Admiral Nurse (12) was too small to allow a specific analysis of their effect on carer burden. As entry into institutional care is better predicted by carer factors than patient factors, interventions such as this offer an attractive model for providing better, more cost-effective care. The high levels of burden suggest that an assessment of the caregiver themselves should be an integral part of the overall assessment of the dementia patient. This assessment should probably begin once the diagnostic assessment for the patient is underway, but should be considered as an on-going process as the disease progresses and community aftercare takes over. Having identified those very stressed caregiver, additional support either from Admiral Nurses or CPN's, or through support groups or telephone services such as CANDID (Counselling and Diagnosis in Dementia) can be offered or suggested. Moreover, those carers who are clinically depressed warrant appropriate treatment in their own right. Indeed, these rights as a carer are enshrined in The Carers (Recognition and Services) Act (1995).

Finally, in terms of cost, dementia in younger people appears to be relatively more costly than dementia in older people. The methodology of economic evaluation of dementia care is, unfortunately, in its infancy and caution is needed in comparing results derived from different studies. The reasons, in terms of relative use of community and institutional care, for this difference have already been discussed above. Economic evaluation methodologies are set to develop rapidly, particularly as a result of the introduction of drug treatment for Alzheimer's disease (Kelly et. al., 1997). The enormous cost of institutional care for dementia patients is a substantial target for drug treatments, the ability to show a reduction in the requirement for institutional care, by even 6-12 months could result in significant cost savings. These types of studies are hampered by lack of standardisation of methodology, the very long duration of the studies required, and the limited availability of these new treatments. Hopefully this study will add

to the body of knowledge on the economics of dementia, in this case in younger people. The methodology used allowed rapid data collection and could quite effectively be applied in a longitudinal study to examine cost changes over time. Moreover, the data could have been collected in a telephone call to the carer; a particularly attractive option in a long term, large scale trial.

7.2 Service Developments

By way of a postscript to this report we are including brief descriptions of service developments that have occurred in the two study areas in the period up to the end of 1997. These developments have generally occurred independently of this project, and while project members have been involved in some, the main congratulations must go to the many people (most of whom are listed in Section 9) working in health, social services and the community who have driven these projects forwards. We do, however, hope and believe that this project has played a part in encouraging people working in this area to bring their ideas to fruition.

7.2.1 CANDID (Counselling And Diagnosis In Dementia)

The CANDID service (Harvey et. al., 1998) at The National Hospital for Neurology and Neurosurgery was launched in February 1995. The service is primarily a telephone help-line, though enquiries can also be made in person, by post and by electronic mail (e-mail). Clients are also seen in the CANDID office and on hospital wards for personal counselling.

A central aim of CANDID is that it should be more than a simple source of information, and that it should have the ability to influence and alter the care and management of younger patients with dementia. Moreover, it has a holistic approach liaising with professionals and family members, providing advice on the practical, social and legal issues of these diseases as well as the medical aspects.

The primary aims of the service are:

1. To provide a point of contact and information for patients and carers before, during and after the process of investigation and diagnosis of a dementia, both at The National Hospital and elsewhere.

2. To provide clinical management advice and guidance to the GP on patients who have either been seen in the clinic, or where the GP has referred the patient and provided clinical information which is recorded on the CANDID database.

In addition, its secondary aims are:

- To act as a source of expert knowledge and advice to doctors and other professionals caring for a younger person with dementia.

- To provide an education and liaison service in the field of young onset dementia, organising regular educational courses for healthcare professionals.

- To develop a communication network to co-ordinate the activity of other services providing care for this group of patients

- To provide information and support to the families of people with inherited dementias.

CANDID differs from other services by providing medical advice and intervention at a distance, which can be specific to the individual and be targeted at either the patient, carer, GP or other health care professional. Senior medical supervision of the service is integral to its aims, and information systems have been developed to ensure adequate record keeping, and to assist medical review of advice given.

From the beginning of the project the CANDID helpline has been available to patients and carers from the two catchment areas, and indeed CANDID now has a formal role within the co-ordinated care pathway introduced in KC&W (see below).

7.2.2 Kensington, Chelsea & Westminster

Within KC&W there have been a number of care and service developments for younger people with dementia. The first 18 months of this project was carried out in close collaboration with "The Care Must Be There" study (Quinn, 1996). A steering committee was formed which included representatives from the many health Trusts in the area, social services, the Dementia Relief Trust, myself and representative of voluntary services. Following the publication of the final report the steering committee became an action committee, chaired by a consultant in public health medicine. The aim of the action committee was to put the recommendations of the report into practice.

The committee focused on the need for accurate and early diagnosis, and of the locking of the patient and their carer into aftercare support following diagnosis. As a results of this work, a co-ordinated care pathway guideline for younger people with dementia was launched to General Practitioners in December 1997.

The guidelines require GP's and other doctors to ensure that all patients under the age of 65 years, presenting with suspected dementia, are referred for investigation by a neurologist, ideally at a specialist dementia clinic. Furthermore, each patient is required to be registered with the CANDID database, and each carer is given the option of being supported by an Admiral Nurse.

Within the two social services departments, and in every mental health Trust a lead officer for young onset dementia has been identified. CANDID and/or the Admiral Nurses remain in regular contact with the patient and carer; a minimum of a phone call every 6 months. Should a need arise for additional social service or health care input, a referral is then made through the appropriate lead officer. The system of lead officers ensures that the referral is taken seriously, routed to the most appropriate person and minimises the possibility of the patient/carer 'falling between two stools'.

In many ways this model is one of ideal care for this group of patients. No new services or personnel have been required, and the co-ordination process attempts to make the best use of the available services in as flexible a way as possible. The pre-emptive regular contact with carers can rapidly identify problems and institute support.

In addition to the care pathway, a specialist day centre (Richard Castillo Centre) now has two days per week set aside specifically for younger people with dementia. Staff at the centre have also been receiving special training in young onset dementia.

Westminster Social Services are currently re-building a long term care facility in the borough which will have 6-8 beds set aside in a separate area for younger people with dementia.

7.2.3 Hillingdon

In Hillingdon a psychologist has been appointed as co-ordinator for younger people with dementia, with specific sessions set aside for this role. This has formalised the existing arrangement where the majority of younger people with dementia had been referred through a single person.

A training course for the carers of younger people with dementia has been developed, although initial interest from caregiver was relatively low.

The ADS has developed two specific projects. A support group for carers of younger people with dementia now meets regularly. In addition, the ADS has refurbished and opened a day centre (The Templeton Centre) for people with dementia, which has several days each week set aside specifically for younger patients.

Finally, this project has provided me with valuable research and clinical training experience, interesting and unique data, and has played a part in improving the care and services for this group of very needy patients and carers.

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8. Appendices

Appendix 1 - Diagnostic Criteria

A1.1 DSM-IV Criteria for Dementia

I. Development of multiple cognitive deficits that include memory impairment and at least one of:

   A. Aphasia

   B. Apraxia

   C. Agnosia

   D. Disturbance of Executive Function

II. The cognitive deficits must be sufficiently severe to cause impairment in occupational or social functioning and must represent a decline from a previously higher level of functioning.

III. A diagnosis of dementia should not be made if the cognitive deficits occur exclusively during the course of a delirium.

IV. Dementia may be etiologically related to a general medical condition, to the persisting effects of substance use (including toxin exposure), or to a combination of these factors.

A1.2 NINCDS/ADRDA Criteria for Alzheimer's Disease

I. Probable Alzheimer's Disease

- A. Presence of dementia
- B. Deficits in at least two areas of cognition
- C. Progressive Deterioration
- D. No clouding of consciousness
- E. Age 40-90
- F. Absence of systemic disorders

II. Diagnosis supported by:

- A. Progressive deterioration of individual cognitive function
- B. Impaired activities of daily living
- C. Family history of dementia
- D. Normal lumbar puncture, EEG, and evidence of atrophy on CT

III. Features consistent with the diagnosis:

- A. Plateaux in the course of the disease
- B. Associated psychiatric symptoms
- C. Neurological signs
- D. Seizures
- E. Normal CT scan

IV. Diagnosis of Alzheimer's disease is unlikely if:

- A. Sudden onset
- B. Focal neurological signs
- C. Seizures or gait disturbance early in the disease

V. Possible Alzheimer's disease:

- A. In the presence of atypical features
- B. In the presence of systemic disease (not considered to be the cause of dementia)
- C. In the presence of a single progressive cognitive deficit

VI. Definite Alzheimer's disease

- A. Clinical criteria for probable Alzheimer's disease and
- B. Histopathological evidence of the disorder

A1.3 NINDS-AIREN criteria for Vascular Dementia

I. For Probable VaD

A. Dementia defined by deficits in multiple domains of cognitive function, confirmed clinically and neuropsychologically, and interfering with everyday life.

B. Cerebrovascular disease confirmed by focal neurological signs and evidence of vascular disease on CT or MRI.

C. A temporal relationship between IA and IB.

II. Features consistent with a probable diagnosis include:

A. Early gait disturbance

B. Unsteadiness or falls

C. Urinary symptoms

D. Pseudobulbar palsy

E. Personality and mood changes

III. Features that make the diagnosis unlikely include:

A. Early memory deficit and progressive worsening of specific cognitive deficits without evidence of focal brain lesions on neuroimaging.

B. Absence of focal neurological signs.

C. The absence of vascular lesions on CT or MRI.

IV. Clinical features of possible vascular dementia include:

A. Features of section IA, with focal neurological signs, but where neuroimaging has not been performed to confirm the presence of vascular lesions.

B. The absence of a temporal relationship between IA and IB.

C. The presence of a subtle and variable course in the disease.

V. Criteria for definite VaD are:

A. Clinical criteria for probable VaD.

B. Histopathological evidence from biopsy or autopsy.

C. Absence of neuropathological features of AD.

D. Absence of other clinical or pathological cause for the disease.

A1.4 Consensus Criteria for Diagnosis of Probable Dementia with Lewy Bodies

I. Progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent memory impairment may not occur in the early stages but is evident with progression of the disease. Deficits on tests of attention and of frontal subcortical skills and visuospatial ability may be especially prominent.

II. Two of the following core features are essential for a diagnosis of probable DLB:

- A. fluctuating cognition with pronounced variations in attention and alertness
- B. visual hallucinations which are typically well formed and detailed
- C. motor features of parkinsonism.

III. Features supportive of the diagnosis include:

- A. repeated falls
- B. syncope
- C. transient disturbances of consciousness
- D. neuroleptic sensitivity
- E. systematised delusions
- F. hallucinations in other modalities

IV. A diagnosis of DLB is less likely in the presence of:

- A. stroke disease, evident as local neurological signs or on brain imaging
- B. evidence on physical examination and investigation of any physical illness, or other brain disorder, sufficient to account for the clinical picture.

A1.5 Manchester/Lund Criteria for Frontotemporal Dementia

I. Core Diagnostic Features

A. Behavioural Disorder

1. Insidious onset and slow progression
2. Early loss of personal awareness (neglect of personal hygiene and grooming)
3. Early loss of social awareness (lack of social tact, misdemeanours such as shoplifting)
4. Early signs of disinhibition (such as unrestrained sexuality, violent behaviour, inappropriate jocularity, restless pacing)
5. Mental rigidity and inflexibility
6. Hyperorality (oral/dietary changes, overeating, food fads, excessive smoking and alcohol consumption, oral exploration of objects)
7. Stereotyped and perseverative behaviour (wandering, mannerisms such as clapping, singing, dancing, ritualistic preoccupation such as hoarding, toileting and dressing)
8. Utilisation behaviour (unrestrained exploration of objects in the environment)
9. Distractibility, impulsivity and impersistence
10. Early loss of insight into the fact that the altered condition is due to a pathological change of own mental state.

B. Affective Symptoms

1. Depression, anxiety, excessive sentimentality, suicidal and fixed ideation, delusions
2. Hypochondriasis, bizarre somatic preoccupation
3. Emotional unconcern (emotional indifference and remoteness, lack of empathy and sympathy, apathy)
4. Amimia

C. Speech Disorder

1. Progressive reduction of speech (aspontaneity and economy of utterance)
2. Stereotypy of speech (repetition of limited repertoire of words, phrases, or themes)
3. Echolalia and perseveration
4. Late mutism

D. Spatial orientation and praxis preserved

E. Physical Signs

1. Early primitive reflexes
2. Early incontinence
3. Late akinesia, rigidity, tremor
4. Low and labile blood pressure

F. Investigations

1. Normal EEG despite clinically evident dementia
2. Brain imaging (structural or functional, or both): predominant frontal or anterior temporal abnormality, or both.
3. Neuropsychology: profound failure on "frontal lobe" tests in the absence of severe amnesia, aphasia, or perceptual spatial disorder

II. Supportive Diagnostic Features

A. Onset before 65 years

B. Positive family history of similar disorder in a first degree relative

C. Bulbar palsy, muscular weakness and wasting, fasciculation.

III. Diagnostic Exclusion Features

A. Abrupt onset with ictal events

B. Head trauma related to onset

C. Early severe amnesia

D. Early spatial disorientation, lost in surroundings, defective localisation of objects

E. Early severe apraxia

F. Logoclonic speech with rapid loss of train of thought

G. Myoclonus

H. Cortical bulbar and spinal deficits

I. Cerebellar ataxia

J. Choreoathetosis

K. Early, severe, pathological EEG

L. Brain imaging: predominant post-central structural or functional deficit. Multifocal cerebral lesions on CT or MRI

M. Laboratory tests indicating brain involvement or inflammatory disorder (such as multiple sclerosis, syphilis, AIDS and herpes simplex encephalitis)

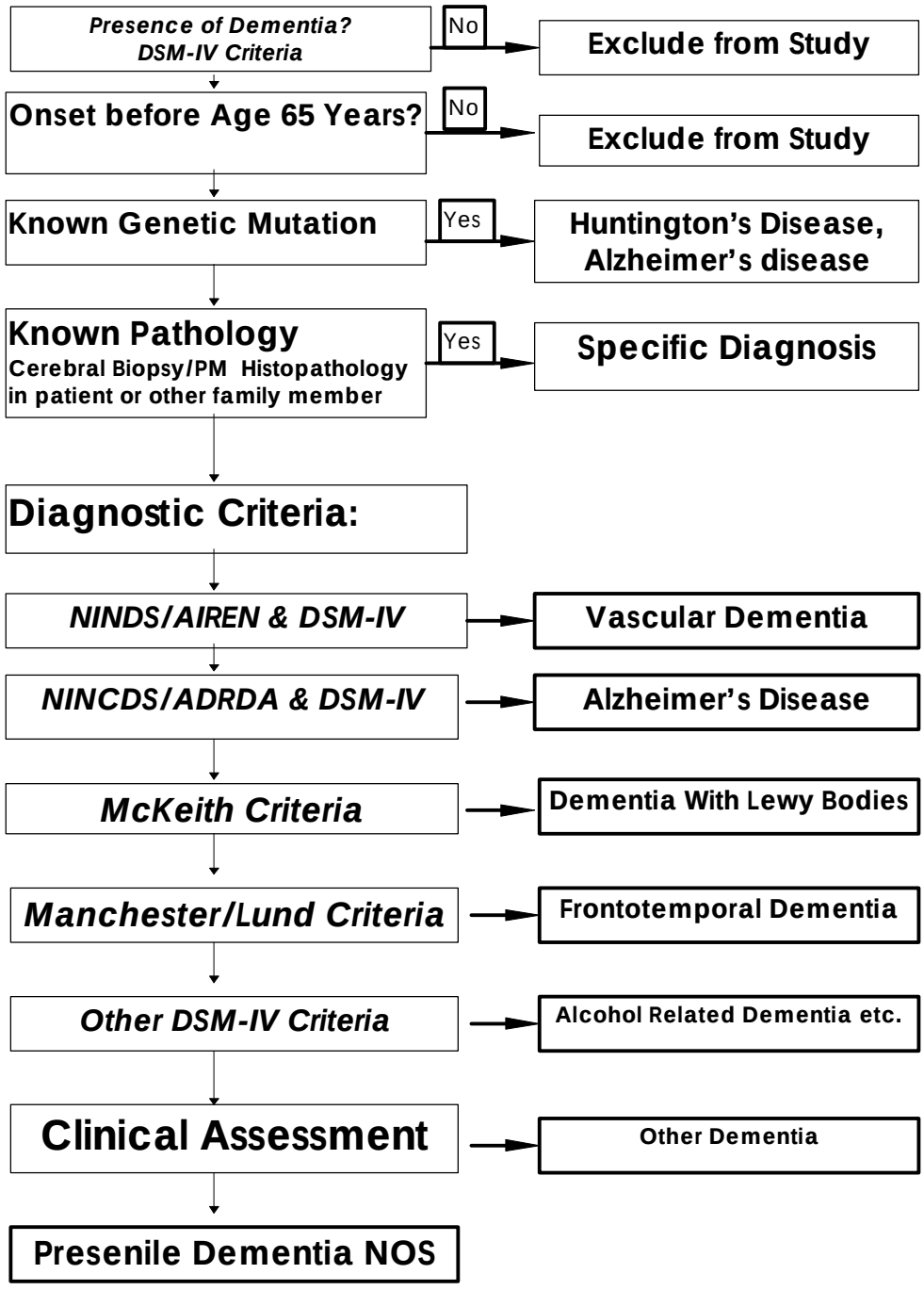
IV. Relative Diagnostic Exclusions Features

A. Typical history of chronic alcoholism

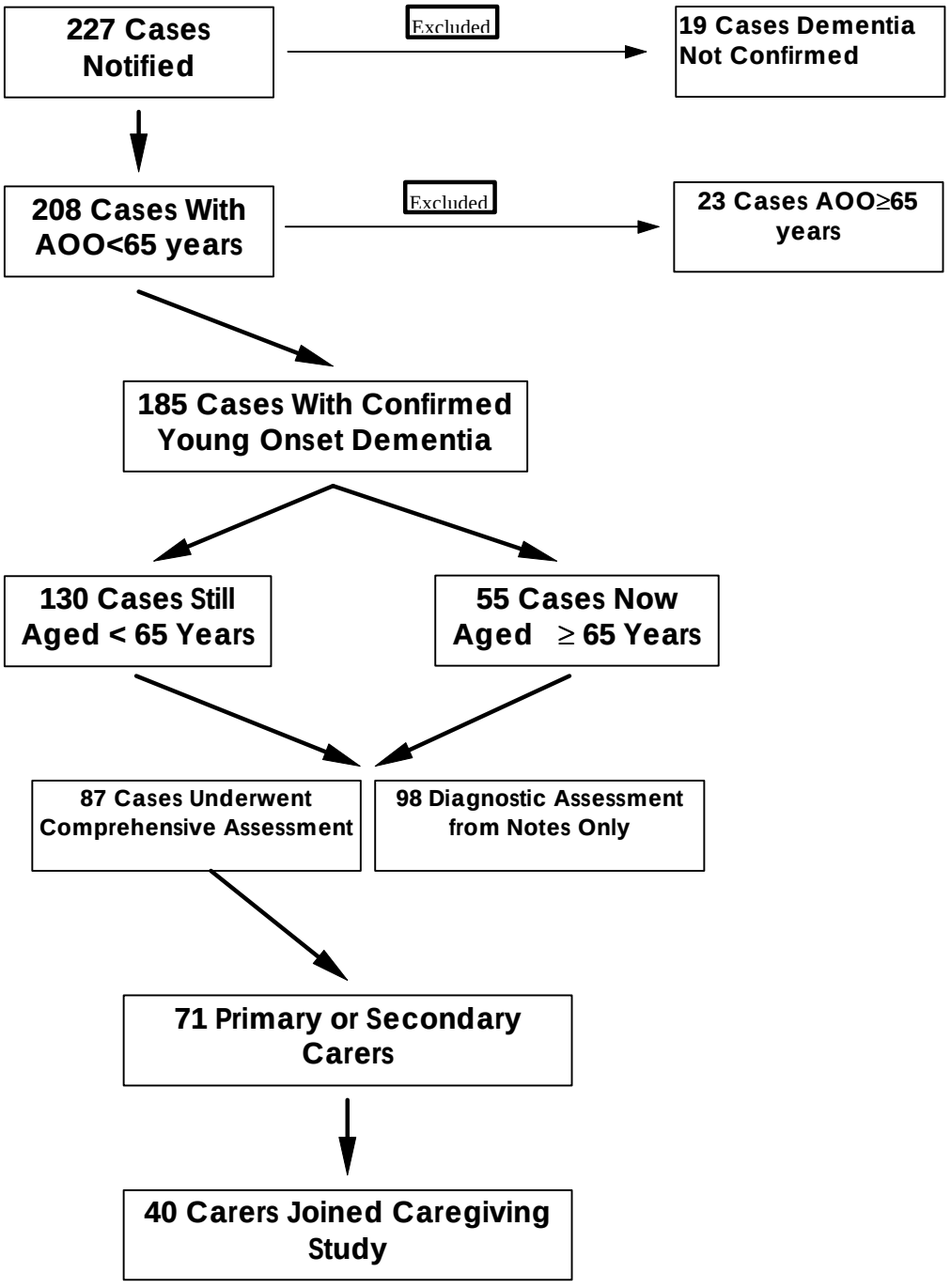
B. Sustained hypertension

C. History of vascular disease (such as angina, claudication)

Appendix 2 - Diagnostic Algorithm



Appendix 3 - Patient & Caregiver Population Flowchart



Appendix 4 - Hospital Information Systems Search Strategy

Diagnostic Rubric - ICD9 (include any sub-codes)

290.0	Senile Dementia
290.1	Presenile Dementia
290.2	Senile Dementia depressed or paranoid
290.3	Senile Dementia acute confusional
290.4	Vascular Dementia
290.8	Other organic psychotic condition
290.9	Unspecified organic psychotic condition
291.2	Other alcoholic dementia
294.1	Dementia in conditions elsewhere classified
331.0	Alzheimer's disease
331.1	Pick's disease
331.2	Senile degeneration of the brain
331.3	Communicating hydrocephalus
331.4	Obstructive hydrocephalus
331.5	Jacob Creutzfeldt disease
331.7	Cerebral degeneration in other disease
331.8	Other cerebral degeneration
331.9	Unspecified cerebral degeneration

Diagnostic Rubric - ICD10 (- Include all sub-codes)**

F00.**	Dementia in Alzheimer's disease
F01.**	Vascular dementia

F02.**	Dementia in other disease classified elsewhere
F03.**	Unspecified Dementia
F04.**	Organic Amnestic syndrome
F05.**	Delirium
F06.**	Other mental disorders due to brain damage and dysfunction
F07.**	Personality and behavioural disorders due to brain disease, damage and dysfunction
F09.**	Unspecified organic or symptomatic mental disorder

Age Cut Off: INCLUDE any patient born *after* 1/4/1920

Post Codes

Kensington, Chelsea & Westminster: W1, W2, W8, W9, W10, SW1, SW3, SW5, SW7, SW10, NW8, WC2.

Hillingdon: TW6, UB3, UB4, UB8, UB9, UB10, UB11, HA4, HA6

Data Requested

Patient Name

Patient Address & Post Code

Next of Kin Name - if available

Next of Kin Address

GP Name

GP Address & Post Code

GP Phone Number

Diagnosis Code(s)

Consultant

Hospital Number

Appendix 5 - Summary Of Independently Published Reports On Young Onset Dementia

Compiled by Richard Mepham & Richard Harvey

A5.1 Services for Younger People with Dementia: A report by the Alzheimer's Disease Society.

Date of Publication: 1995.

This report details available services, and how they apply to this client group. It was compiled by analysis of questionnaires completed by Alzheimer's Disease Society branches from England, Wales and Northern Ireland and launched at the Alzheimer's Disease Society conference in Brighton in 1994.

The report noted the differing circumstances and experiences of young onset sufferers and their carers. Main findings were:

- There are currently 17,000 sufferers in the UK
- Present services are amied at older onset patients
- Service access is dependent on gelography rather than need
- Local health authorities have yet establish what level of need exists in their area
- There is a lack of consultants with specific responsibility for YOD
- There is a shortage of genetic counselling for families
- Specialised day, respite, residential and home help care services for YOD are very limited

Recommendations were for a comprehensive evaluation of need and prevalence by all local health authorities, appointment of consultants with specific responsibility and an acknowledgement of the rights of young onset dementia sufferers and their families.

A5.2 Early Onset Dementia Services: A Case of Need. Wilson,K. & Grocott,F.

Undertaken in Liverpool this study assessed the number of sufferers in the area and monitored their progression through the health care system. Monitoring occurred on an event triggered basis focusing on 59 sufferers over a 12 month period.

The main conclusion of this work were that patients are not receiving the few services that do exist because of a lack of a co-ordinated referral pathway. Some patients receive no services, or ones that are inappropriate to their need. Many patients are diagnosed yet given no on-going support or follow-up arrangements. Memory clinics may address some of these issues, although specialist inpatient facilities would improve the situation still further.

A5.3 Hour to Hour, Day to Day - A Survey of the Service Experiences of Carers of People with Pre-Senile Dementia in the London Borough of Sutton. Furst,M, & Sperlinger,D.

Date of Publication: 1992.

This study projected the prevalence of young onset dementia in the London borough of Sutton. It builds up a picture of carer's experiences and their opinions on what services should be provided. It was intended that this should contribute to the development of targeted services in the area. Fifiteen, current and previous carers of pre-senile dementia patients were interviewed. Interviews were semi-structured and captured experiences from onset of symptoms to the present day.

The following conclusions emerged: elderly mental health teams (EMHT) were very helpful as were EMH CPN's, but delay in diagnosis (and subsequent referral to the EMHT), lack of support and information at diagnosis, absence of specialist day care, and little support for carer on long term care issues were all significant areas of unmet need. The report recommended improvements including day care provision, GP training, improved service information and particularly, carer support at the time of diagnosis and hospital admissions.

A5.4 Day care for Younger People with dementia. Foster,K. & Kohls,M.

Date of Publication: 1992

This report concerns the establishment, function and operation of a Scottish day care centre committed to the care of people suffering from young onset dementia. Research was based on a literature review and an assessement of the need this service fulfils. It also includes a case study on a day in the life of the specialist day care centre.

The service is based on the model of supporting the carer before some form crisis occurs, hopefully overting the need for later intervention (such as institutionalisation). Being a collective action group, the staff recognised that young onset dementia sufferers need age appropriate activities and that young onset dementia presents problems because of the stage of life at which the disease occurs. Good practice in this area maintains the carers and patients dignity but is difficult to maintain with limited resources.

Recommedndation included that services should be flexible, age appropriate, small scale and carer orientated. Such measures in the day centre setting fulfill practical (advice, support, transport and adaptations), social (support groups and counselling) and educational (information and resource databases) needs, and as such, fill a shortfall in community services.

A5.5 "A Home from Home" - An Investigation into the Needs of Younger People with Dementia. Alzheimer's Support West Wiltshire.

Date of Publication: 1993

This study centred on levels of incidence and needs of need in West Wiltshire. Recommendations were arrived at by a postal survey of GP's and interviews with carers.

Carers and GP's responses were similar on many points, including that there should be a local specialist service for diagnosis and support, integrated day, respite and residential care operating throughout the day and at weekends. Training and support for carers (via telephone support and group work) should also be forthcoming. GP's identified psychometric testing as a scare resource in their investigations, and the need for transport for patients and carers.

A5.6 Early Onset Dementia in the Maidstone area: Identifying needs of sufferers and carers. Lloyd,M.A.

Date of Publication: 1993

This report presented prevalence figures and qualitative data from carers in the Maidstone area. Qualitative data were derived from carer questionnaires and interviews, while prevalence was estimated and compared with similar studies. Estimates, based on previous research suggested that 34 young onset dementia sufferers would expected, the actual figure identified was 58.

The conclusions noted the adverse effects of length of time to diagnosis, employment consequences and the financial problems experienced by families. Development recommendations were made in the areas of carer and family support and counselling, advice and information, respite, day and residential care and providing an admiral nurse service. Finally the report recommended that there should be definite lines of responsibility within health and social servivesfor this client group.

A5.7 Young Alzheimer's Disease Sufferers and their Carers: People Living with Dementia or a Distinct Client Group with Very Special Needs. Tindall,L. (Dissertation)

Date of Publication: 1993.

This dissertation examined the differing challenges posed by young AD sufferers in comparison with older AD sufferers. Methodologically the research was based on a literature review. The author noted that young onset AD was an under researched area at the time of writing.

Four main differences emerged between senile and pre-senile Alzheimer's Disease: faster deterioration to a severe state, shorter life expectancy, symptoms presenting in a different order and the fact that younger onset often suggests that the disease is not of the Alzheimer's type. Recommendations were that young onset sufferers should be recognised as distinct from senile dementia sufferers because of the difference in the course, prognosis, family dynamics and health concerns for this group. The impact of YOD is compounded by the shock of its unexpected outcome, rarity and the lack of specialist services. A step toward alleviating some of these problems would be the appointment of a development worker with responsibility for education, advice, resources and keeping a register of sufferers and carers.

A5.8 Dependency and Community Care in Pre senile Alzheimer's Disease. Newens,A.J., Forster,D.P. and Kay,D.W.K.

Date of Publication: 1993.

This work from Newcastle assessed the complex relationship between dependency, use of support services and residence from the time of a diagnosis of pre senile dementia of Alzheimer's type being given. Interviews, case histories, patient and carer assessments were used. Measurements included independence ratings on six aspects of daily living.

The results suggested that age appropriate day and respite care were essential, and that family education, counselling and stress management were extremely beneficial. The report also put forward the recommendation that CPN's should be allocated to young onset families to improve communication between the family and helath/social services. The study found incontinence to be the strongest predictor of institutionalisation and suggest that the involvement of incontinence nurses might delay institutionalisation.

A5.9 A Guide to Early Onset Dementia. Cox,S. & McLennan,J.

Date of Publication: 1994.

This paper is based on a comprehensive literature review of reports and papers published up to 1994. Many of the points made in the text are illustrated using a single case history. The main conclusions of the review are that:

appropriate health care services should be streamlined to ensure early diagnosis and improved access for patients and carers. To aid the flow of information locally a central register should be compiled with details of all local sufferers and families and a telephone information/support line should be established. Another important point to emerge from this report is that support should be provided to patients and carers during the latter stages of the disease, particularly in the form of day and respite care.

A5.12 Working Party Report on Services to Younger People with Dementia and their carers. South Glamorgan Health Authority

Date of Publication: 1995.

The report was derived from a series of working parties (comprising carers and members of the EMI service in South Glamorgan), meetings, case histories and carer interviews.

Recommendations were that meeting need in this area could be achieved by providing support for the patient and family (particularly children) at pre- and post- diagnosis stages with genetic, sexual, bereavement and financial counselling services being the focus. Other more practical measures would include a specialist consultant services and clinics, age appropriate day and respite care, terminal care, support groups and ongoing needs assessment with carer input. All the above services should be integrated and co-ordinated to ensure that complete and appropriate care is on offer.

A5.13 The Needs of Younger People with Dementia and their Carers in Rotherham. Smith,M., Cook,S. and Miller,J.

Date of Publication: 1995

This study assessed need in younger people suffering from dementia in the Rotherham area. Over a six month period, the methodology included a prevalence survey , interviews and focus groups. Fifty five young onset dementia sufferers were identified in the area via medical records, GPs, social and health service personnel, independent organisations and publicity.

Findings highlighted a need for the health authority to recognise YOD as a distinct client group, hold a register of young onset sufferers, provide special training for health and social services staff, meet needs in the locality (not in nationalised centres outside the area), provide age appropriate assessment and care planning involving carers, provide support and to improve the information available to families and carers. The report recommended that these features should be built into annual purchasing plans to ensure proper service provision and recognition of this client group.

A5.14 Purchasing Strategy for Services for Younger People with Dementia. Sheffield Health Authority.

Date of Publication: 1995.

Sheffield Health Authority assessed prevalence of YOD and examined the issues of how best to utilise budget funds available to this client group. Methodology comprised evaluation of a local day centre project and service evaluations gathered from professionals, carers and sufferers.

It was estimated that 51 people were suffering from dementia with onset below the age of 65 in the Sheffield area. The following recommendations arouse from service evaluations: early investigation and support are essential, comprehensive care planning, (age) appropriate day care (along the lines of the centre evaluated

earlier in this report), respite care, intensive home care, specialist residential care, palliative care, support groups for carers and awareness training for all concerned.

A5.15 Report from the Harrow Mental Health JSPT Working Group on Early Onset Dementia. Patmore,C.

Date of Publication: 1996.

This report presented the London Borough of Harrow's estimated prevalence of early onset dementia and the details of current and optimal service provision. Results came from survey data and working party discourse. The report pointed out a couple of current service failings to Harrow's 25 - 40 early onset dementia sufferers. Harrow lacks a specialist memory disorders clinic and a consultant for diagnostic referrals and that moreover that there is no clear pathway to effective care.

It was recommended that one medical specialist have responsibility, fewer care managers are involved in the area, and that agencies run a more integrated system of services. This co-ordination could lead to the formation of a team to oversee issues facing sufferers and their families from first presentation to death.

A5.16 Younger People with Dementia: the impact on the children. Robertson,S.

Date of Publication: 1996.

This work examined the lack of YOD services and support for children in the affected family. The project consisted of a literature review supplemented with interview data from children of affected parents.

Intervies revealed that children felt sadness at the loss of a relationship with the ill parent, being closer to the caregiving parent and experiencing a feeling of taking each day as it comes. In terms of need, the children felt there to be practical (age appropriate day and respite care, befriending etc.) needs that were not well met, that carers needed more support and counselling (especially at the time of diagnosis), not enough information (such as genetic counselling) was forthcoming and that families should be put in contact with others in a similar position. There was also felt to be a need for specialist advice for children on how to cope with a parents challenging behaviours.

A5.17 The Care Must Be There: Improving Services for People with Young Onset Dementia and their Families. Christine Quinn

Date of Publication: 1996.

This qualitative project conducted in Kensington, Chelsea and Westminster focused on service experiences, areas where need and service do not meet and suggested strategies for improvement.

Respondents were contacted through social workers, care managers, admiral nurses and the Dementia Research Group. Those contacted formed an interview group providing in-depth, semi-structured qualitative data, and ratings of the services that they had come into contact with. Service providers, social workers, care managers and CPN's were also interviewed.

Problems with diagnosis, the accessibility and appropriateness of services, information and co-ordination emerged as serious problems for young onset dementia sufferers. Recommendations intended to improve care focused on diagnosis and service provision. An early, sensitively given diagnosis, the

availability of counselling to the patient and family, social services needs assessments, access to information on all aspects of the disease and consideration of the effects on children were all identified as stress relieving measures. Hospital admissions, where necessary, should be in to age appropriate settings. All services to YOD sufferers should promote dignity: staff should be well trained, there should be continuity in home care and befriending services, activities should be age appropriate and reliable, and where personal care is performed it should be given in the same manner as the primary carer would have done.

A5.18 "A Forgotten Age" - A Report on the Circumstances and Service Needs of Younger People with dementia and their carers. Penfold,M.

Date of Publication: 1998.

This report provides a comprehensive assessment of needs of YOD sufferers and their carers. Based on data collated in outer London and the home counties, this study employed a survey of carers and relatives.

Results revealed a complex interaction of variables compounding the problems already inherent for carers, relatives and sufferers. Sustaining home care and the role of the carer should be the primary objective, however, carers felt there was a shortfall in information and advice, assistance in home care and a lack of day centres. A comment not seen in other similar surveys was that not enough attention is paid to the financial needs of carers, particularly in respect to the changing employment situation of both carer and sufferer.

Existing services are failing YOD sufferers. Extending respite and home care, redesigning some existing residential services and encouraging more providers are all suggested strategies. Current resources could achieve far greater than they presently do by reallocating funds and making specific provision for YOD, improving training and information resources, and setting quality standards (e.g. through a charter mark) for this disadvantaged group.

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