DEPRESSION AND PSYCHOTIC
SYMPTOMS IN DEMENTIA
SUFFERERS

MD THESIS

DR. C.G. BALLARD
DEPRESSION AND PSYCHOTIC SYMPTOMS IN DEMENTIA SUFFERERS

Dr C.G. Ballard

MD THESIS

ABSTRACT

One hundred and twenty five patients with mild or moderate dementia according to the CAMDEX criteria, who were in contact with either a memory clinic or psychiatric services were assessed. Dementia was diagnosed according to the NINCDS ADRDA criteria, the Hachinski scale, DSMIIIR criteria, HAS AGECAT and the McKeith criteria for Senile Dementia of Lewy Body Type. Depression was diagnosed according to the DSMIIIR and RDC criteria and psychotic symptoms were assessed using the Burns Symptom Checklist. Cognitive impairment was evaluated using the CAMCOG schedule. Informants were interviewed at monthly intervals for one year concerning the symptoms of depression and psychotic symptoms experienced by the dementia sufferers. A repeat CAMCOG was undertaken one year after the initial assessment.

The one month prevalence rates of delusions, visual hallucinations and delusional misidentification were 48.4%, 35.5% and 29.0% respectively. Each had a distinct pattern of associations, an impression supported by a principal components analysis which generated four psychotic factors, the three categories already discussed and comfort phenomena. Only sixteen patients had any insight into their psychotic symptoms and 61% were distressed by them. The annual incidence rate of psychotic symptoms was 46.7% and 53% of patients experienced symptom resolution. The number of months during which psychotic symptoms were experienced was significantly associated with the magnitude of cognitive deterioration.

The one month prevalence rate of RDC major depression was 27.4%. An additional 27.4% of patients fulfilled the criteria for RDC minor depression. Having Alzheimer's disease was significantly inversely associated with both RDC major depression and DSMIIIR major depression. There were six patients with RDC depression in the context of vascular dementia, all of whom experienced depression for at least three months compared to only 33.3% of the patients with Alzheimer's disease. The annual incidence rate of RDC major depression was 10.6%. 
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>TABLE OF CONTENTS</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>OUTLINE</td>
<td>I-III</td>
</tr>
<tr>
<td>CHAPTER 1 Psychosis and Depression in Perspective</td>
<td>2</td>
</tr>
<tr>
<td>CHAPTER 2 Psychotic Symptoms in Patients with Dementia</td>
<td>6</td>
</tr>
<tr>
<td>Introduction</td>
<td>6</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>6</td>
</tr>
<tr>
<td>Associations</td>
<td>20</td>
</tr>
<tr>
<td>Complications of Psychotic Symptoms</td>
<td>27</td>
</tr>
<tr>
<td>Phenomenology of Psychotic Symptoms</td>
<td>29</td>
</tr>
<tr>
<td>Conclusion</td>
<td>32</td>
</tr>
<tr>
<td>CHAPTER 3 Depression in Dementia Sufferers</td>
<td>33</td>
</tr>
<tr>
<td>Introduction</td>
<td>33</td>
</tr>
<tr>
<td>Clinical Features</td>
<td>33</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>37</td>
</tr>
<tr>
<td>Associations</td>
<td>47</td>
</tr>
<tr>
<td>Excess Disability</td>
<td>54</td>
</tr>
<tr>
<td>Conclusion</td>
<td>55</td>
</tr>
<tr>
<td>Aims</td>
<td></td>
</tr>
<tr>
<td>CHAPTER 4 Aims of the Project</td>
<td>56</td>
</tr>
<tr>
<td>Method</td>
<td></td>
</tr>
<tr>
<td>CHAPTER 5 The Study</td>
<td>59</td>
</tr>
<tr>
<td>CHAPTER 6 The Selection of Instruments and Diagnostic Criteria</td>
<td>75</td>
</tr>
<tr>
<td>CHAPTER 7 Reliability</td>
<td>86</td>
</tr>
</tbody>
</table>
Results

CHAPTER 8 Demographic Data 88
CHAPTER 9 Prevalence and Phenomenology of Psychotic Symptoms 99
CHAPTER 10 The Use of Logistic Regression to Investigate the Associations of Psychotic Symptoms 110
CHAPTER 11 A Principal Component Analysis of Psychotic Symptoms 127
CHAPTER 12 Cognitive Deterioration In Patients with and without Psychotic Symptoms 131
CHAPTER 13 Psychotic Symptoms, Follow-up Data 134
CHAPTER 14 Prevalence, Associations and Symptoms of Depression 148
CHAPTER 15 A Principal Components Analysis of the Symptoms of Depression 169
CHAPTER 16 Depression, Follow-up Data 178

Discussion

CHAPTER 17 Methodological Issues 185
CHAPTER 18 Psychotic Symptoms 188
CHAPTER 19 Depression 200
CHAPTER 20 Psychotic Symptoms and Depression - Expanded Theoretical Models 209
Conclusions

REFERENCES

APPENDIX A  Burns' Symptom Checklist

APPENDIX B  Cornell Depression Scale

APPENDIX C  CAMCOG Subscales as Derived by Hooper & Bucks

APPENDIX D  Diagnostic Criteria for Dementia & Depression

APPENDIX E  Personal Contribution to the Project

ACKNOWLEDGEMENTS
OUTLINE

In this thesis, the current literature pertaining to both psychotic symptoms and depression arising in the context of dementia are reviewed in the introductory chapters, drawing on themes from the seminal studies. The method includes a detailed description of the study design, together with a section discussing the instruments used. The results are described in chapters considering demographic data, psychotic symptoms and depression. The chapters pertaining to psychotic phenomena include epidemiology, an evaluation of the associations of psychotic symptoms, a principal components analysis, an evaluation of cognitive decline and information about the incidence rates and resolution rates of these phenomena. The chapters focusing upon depression cover much the same areas, although no information is reported concerning the relationship between depression and cognitive decline. The discussion includes a section highlighting some of the methodological problems, as well as chapters drawing together the results pertaining to psychosis and depression. The discussion concludes with the presentation of theoretical models which attempt to explain the occurrence of psychotic symptoms and depression in dementia sufferers.
CHAPTER 1
INTRODUCTION - PSYCHOSIS AND DEPRESSION IN PERSPECTIVE.

Kraepelin (1909) and Bleuler (1916) assumed that an underlying arteriosclerotic psychosis, senile psychosis or alternative organic brain disorder was the cause of all psychiatric disorder in the elderly. Roth & Morrissey (1952) became aware that in their clinical practice the outcome and treatment response of patients with affective psychoses and those with senile or arteriosclerotic psychoses appeared to be different. Roth (1955) undertook a painstaking study to further test this hypothesis. Four hundred and sixty four sets of casenotes were examined and study diagnostic criteria were applied to classify patients as suffering from affective psychoses, paraphrenia, arteriosclerotic psychosis, senile psychosis or other organic brain disorders. In making these diagnostic judgements, mild symptoms of cognitive impairment were ignored if the presenting picture was that of an affective psychosis or paraphrenia. A substantially higher mortality rate was identified amongst patients with senile psychosis and arteriosclerotic psychosis, whilst a greater proportion of the patients with affective psychoses and paraphrenia achieved discharge from hospital. At four year follow up only 2.1% of patients with arteriosclerotic psychosis or senile psychoses had developed a persistent depression and only 2.4% of patients with affective psychosis developed dementia. One of the twenty-two patients with paraphrenia also developed cognitive impairment. The case for considering the disorders as discrete entities was hence supported by a considerable weight of evidence and the paper opened the door for further work studying these conditions as independent disorders.
A number of possible relationships do however exist between cognitive impairment and depression. Dementia "caused" by depression has been referred to as "pseudo dementia". The term has encompassed two categories of patient. Firstly, those who show reduced motivation to participate in cognitive assessment because of their mood disorder, who frequently give "I don't know" responses and often have subjective memory complaints which exceed the demonstratable deficits (Wells 1979). Secondly, patients who make sufficient efforts to participate in cognitive testing, but despite this show performance deficits (Folstein & McHugh 1978). Typically these cognitive deficits are to some extent reversible when the depression resolves, although a higher than expected proportion of these patients will develop true dementia (Alexopoulos & Abrams 1991).

Conditions such as Parkinson's disease, Huntington's disease, multiple sclerosis and a variety of toxic metabolic disturbances can lead to both mood disorder and cognitive impairment (Cummings 1989). Apathy, loss of interest, poor concentration, irritability, sleep disturbance, appetite disturbance and weight loss are all symptoms which can occur in both dementia and depression syndromes. At times it can be difficult to decide whether a symptom is related to a mood disturbance or not in the presence of dementia. It should not however prevent the recognition of depression if a full constellation of depressive symptoms are evident, although it could potentially lead to the false positive diagnosis of depression in some cases. One would expect the diagnosis of dementia to be a major life event which could predispose to a depressive illness, although in the absence of an association between retention of insight and depression (Verhey et al 1993, Ott & Fogel 1992) and the absence of a clearly elevated prevalence rate of depression in those with mild dementia, it is unlikely that this is a common occurrence. Depression
can also influence the symptoms of dementia. There is evidence to suggest that a concurrent depression detrimentally influences both performance on formal cognitive tests and activities of daily living (Greenwald et al 1989, Fitz & Teri 1994). It has been estimated that approximately 15% of people in the community over the age of sixty-five will suffer from depression (Copeland et al 1992) and that 5-10% (Cooper & Schwarz 1982) will suffer from dementia. One would hence expect approximately 1% of the population over the age of sixty-five to have both disorders concurrently by chance. A further area of overlap pertains to poor awareness of symptoms of depression even amongst patients with mild dementia (Ballard et al 1991a).

A similar pattern of distinction followed by the identification of areas of overlap has become evident for patients with delusional disorders in old age. Howard et al (1992), for example have suggested that certain patients with late paraphrenia, particularly those without first rank Schneiderian symptoms may have a degree of cerebral atrophy. It has also been noted that delusions and hallucinations may be the presenting symptoms of a dementia, sometimes preceding cognitive impairment (Haddad & Benbow 1992). In addition, patients with dementia commonly suffer from delusions and hallucinations (Wragg & Jeste 1989), although their type may differ somewhat from those seen in patients with late onset delusional disorder (Ballard et al 1995). Hence although it is important to distinguish late onset delusional disorders from dementia, areas of overlap do exist.

A further area of confusion pertains to the diagnostic terminology. The Churchill Medical Dictionary (1989) defines psychosis as "a class of mental disorders which usually
include organic mental disorder, schizophrenia, major affective disorders and certain paranoid states. In general psychoses are more severe or extensive than other forms of mental disorder". In this sense psychosis is an indication of the severity of the disorder. This was the way in which the term was used by Roth (1955). Affective disorders, senile dementia and arteriosclerotic dementia were all referred to as psychoses, but paradoxically paraphrenia was not. This usage of psychosis was also included in the ICD9 classification (World Health Organisation 1979). The evolution of the DSMIII (American Psychiatric Association 1980), although it did not fully achieve its aim of developing an atheoretical system of diagnosis, did facilitate a clearer definition of psychoses as "the presence of one or more of the following - hallucinations, delusions, grossly disorganised or catatonic behaviour and severe disorders of thinking such as incoherence, frequent derailment, loosening of associations or quality of thought". The opportunity is now available to improve our knowledge of phenomenology, as the symptoms in these areas of overlap can be studied independently of the primary diagnosis.

In a relatively short period of under forty years we have moved from the realisation that affective disorders, paraphrenia and dementia represent separate categories of illness, to identifying areas of overlap. These are important because of the potential for diagnostic confusion and the different treatment needs of patients with concurrent morbidity.
CHAPTER 2

INTRODUCTION - PSYCHOTIC SYMPTOMS IN PATIENTS WITH DEMENTIA

Psychosis has often been used as a euphemism to describe a broad range of behavioural disturbances in the elderly with dementia. Fortunately more rigorous definitions limiting the term psychosis to describe delusions and prominent hallucinations in clear consciousness have been used in the majority of recent studies. Several caveats have however been necessary, including the specification of a minimum duration which symptoms must last to qualify as psychotic symptoms in order to reduce the overlap with confabulation.

Psychotic symptoms in dementia sufferers cause a great deal of distress to carers (Rabins et al 1982), the patients themselves (Gilley et al 1991) and are associated with a number of behaviour difficulties (Cooper et al 1991, Deutsch et al 1991, Gilley et al 1991, Rockwell et al 1994). They reduce the likelihood of people continuing to live in their own homes (Steele et al 1990) and are probably associated with a greater speed of cognitive decline (Drevets & Rubin 1989, Rosen & Zubenko 1991, Förstl et al 1993). All of these factors make psychotic features in dementia sufferers an important area for study.

EPIDEMIOLOGY

Estimates of the prevalence of psychotic symptoms in patients with dementia vary greatly from 11.7% (Rothschild 1941) to 70.6% (Teeter et al 1976). For each study reported, unless stated the prevalence rate of psychotic symptoms given is the period prevalence up to the time of the first assessment.
Data pertaining to patients with pre-senile dementia were reported in twelve studies, none of which used standardised criteria (Coblentz et al 1973, Rosenstock 1970, Chen et al 1991, Nott & Fleminger 1975, Liston 1979, Sim & Sussman 1962, Sim et al 1966, Goodman 1953, Sjogren et al 1952, Eiden & Lechner 1950, Rubin et al 1993, Stern et al 1987). Prevalence rates between 18% (Sim & Sussman 1962, Sim et al 1966) and 41.2% (Rubin et al 1993) were reported. The lack of standardised instruments and operational criteria limits the amount of useful information which can be abstracted from these studies other than the existence of psychotic symptoms as a common problem.

Patients largely over the age of sixty-five were the focus of a further thirty-six studies. Five of these did not include standardised criteria either for the diagnosis of dementia or psychotic symptoms (Berrios & Brook 1985, Uriate et al 1992, Birkett 1972, Rothschild 1941, Teeter et al 1976) and five studies included standardised criteria for the diagnosis of dementia but not for psychotic symptoms. The reported prevalence rates of psychotic symptoms amongst these studies varied from 11.7% (Rothschild 1941) to 48.9% (Rabins et al 1982). Twenty-three studies included operationalised criteria both for the diagnosis of dementia and psychotic symptoms, although in some cases the criteria were not specifically stated (Rubin et al 1988, Drevets & Rubin 1989, Teri et al 1988). The DSMIIIIR criteria (American Psychiatric Association 1987) were used to decide the presence of delusions and hallucinations in the majority of studies, although many did not incorporate any form of structured questioning. Specifically designed instruments were only used in a handful of studies. Merriam et al (1988) and Patterson et al (1990) used the BEHAVE AD (Reisberg et al 1987), whilst Deutsch (1991) used an earlier version of the same schedule.
Clinical samples were the focus of twelve studies, reporting patients from a variety of settings, including out patients (Merriam et al 1988, Cummings et al 1987, Jeste et al 1992, Devanand et al 1992), day patients (Ballard et al 1991b), inpatients (Ballinger et al 1982) and all clinical referrals to a particular service or services (Burns et al 1990a, Cooper et al 1991, Binetti et al 1993, Rockwell 1994). They fall loosely into three groups, one estimating a prevalence rate of psychotic symptoms of approximately 30-35% (Cummings et al 1987, Cooper et al 1991, Burns et al 1990a, Sultzer et al 1993), one estimating a prevalence rate of 40-45% (Ballard et al 1991b, Jeste et al 1992, Binetti et al 1993) and a further group estimating a prevalence rate in excess of 60% (Ballinger et al 1982, Devanand et al 1992, Merriam et al 1988, Flynn et al 1991). Several studies (Flynn et al 1991, Sultzer et al 1993) contained relatively small numbers of patients, many of whom had been followed up since an earlier report. Devanand et al (1992) report a one month prevalence rate.

All four of the studies estimating a prevalence rate of 35% included patients diagnosed according to the NINCDS ADRDA criteria for probable Alzheimer's Disease (McKhann et al 1984), whilst three of the four studies reporting a prevalence rate in the 45% range included patients suffering from Alzheimer's Disease and patients suffering from vascular dementia. Three of the groups with a prevalence rate of 60% or over either used less restrictive diagnostic criteria or included patients with different dementias. As one of these groups reported a lower prevalence rate of psychotic symptoms in patients with vascular dementia (Ballard et al 1991b) and one only a slight excess (Cummings et al 1987), the incorporation of patients with vascular dementia per se is unlikely to explain the higher reported prevalence rate of psychotic symptoms. Three of the four studies
reporting a prevalence rate of 60% or more utilized a structured instrument for symptom ascertainment. Although some of the individual studies had their idiosyncrasies, such as a low mean age in Flynn et al's (1991) sample and a more severe degree of cognitive impairment in Binetti et al's (1993) study; the two main trends were a lower prevalence rate of psychotic symptoms in samples diagnosed according to the NINCDS ADRDA criteria and a higher prevalence rate in studies using purpose designed structured instruments.

The prevalence rate of psychotic symptoms amongst dementia patients in residential care is reported in three studies. Morriss et al (1990) report a period prevalence rate of 34.9% amongst eighty-four patients, Rovner et al (1986) report a prevalence rate of 32% in thirty-seven patients and Chandler & Chandler (1988) report a prevalence rate of 14.8% in twenty-seven patients. Each group investigated only a small sample and none used a structured instrument.

Most groups undertaking standardised studies have used research samples. In the majority of cases the origins of the samples are not at all clear which makes it difficult to generalise from the findings. Period prevalence rates vary from 15% (Lopez et al 1991) to 70% (Deutsch et al 1991). It is notable that a structured instrument was used in two of the studies with higher estimates of 50% (Patterson et al 1990) and 60-70% (Deutsch et al 1991) respectively. The research samples were younger, with a mean patient age under seventy and included patients with less severe cognitive impairment than those from clinical settings.
Skoog (1993) assessed a community sample of eighty-five and eighty-six year olds finding a total of one hundred and ninety-seven subjects with dementia, 20% of whom had either schizophreniform disorder or delusional disorder. Symptoms were rated using the Comprehensive Psychiatric Rating Scale. Unfortunately, the utilisation of an older age group and different diagnostic instruments makes comparison with other studies difficult. Nevertheless it is an important study as it is the only piece of work in which a representative community sample is described. A summary of the prevalence studies is given in Table 2.1.
<table>
<thead>
<tr>
<th>Study</th>
<th>AD dementia</th>
<th>AD prevalance of psychiatric symptoms - unstandardized</th>
<th>AD dementia</th>
<th>AD prevalance of psychiatric symptoms - standardizd</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>30.7%</td>
<td>367</td>
<td>30.7%</td>
<td>367</td>
</tr>
<tr>
<td></td>
<td>48.9%</td>
<td>55</td>
<td>48.9%</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>314</td>
<td>33.7%</td>
<td>314</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>217</td>
<td>33.7%</td>
<td>217</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>44</td>
<td>33.7%</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>60</td>
<td>33.7%</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>31</td>
<td>33.7%</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>146</td>
<td>33.7%</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>33.7%</td>
<td>198</td>
<td>33.7%</td>
<td>198</td>
</tr>
</tbody>
</table>

Possible to ascertain E = Estimation, uncertainties are presented in such a way that the exact prevalence rate is not.

**Key:**
- AD = Alzheimer's disease
- VD = Vascular dementia
- M = Mental health
- B = Blood
- CT = CT scan
- MRI = Magnetic resonance imaging
- NMDA = N-Methyl-D-aspartate
- NMDAR = N-Methyl-D-aspartate receptor
- ACC = Anterior cingulate cortex
- PFC = Prefrontal cortex
- SC = Subcortical
- FLAIR = Fluid-attenuated inversion recovery
- GM = Gray matter
- WM = White matter
- CSF = Cerebrospinal fluid
- PET = Positron emission tomography
- MRI = Magnetic resonance imaging
- EEG = Electroencephalogram
- TCD = Transcranial Doppler
- MRA = Magnetic resonance angiography
- MIP = Maximum intensity projection
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography
- FDG-PET = Fluorodeoxyglucose positron emission tomography
- DSA = Digital subtraction angiography
- CT = Computerized tomography
- MRI = Magnetic resonance imaging
- SPECT = Single photon emission computed tomography

Table 2.1a: Prevalence of Psychotic Symptoms - unstandardized students.
<table>
<thead>
<tr>
<th>Study</th>
<th>Prevalence of Psychotic Symptoms - Clinical Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Table 2.1: Prevalence of Psychotic Symptoms - Clinical Studies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Prevalence of Psychotic</th>
</tr>
</thead>
</table>

**Note:**
- The table provides data on the prevalence of psychotic symptoms among study participants, including specific clinical features and criteria.
Psychotic symptoms are divided into subgroups in fifteen studies, mainly delusions, hallucinations and delusional misidentification. The prevalence rates of the various phenomena are summarised in Table 2.2. With the exception of Burns et al (1990a), each has found a prevalence rate of delusions between 28.8% and 46% (Mendez et al 1990, Jeste et al 1992, Merriam et al 1988, Patterson et al 1990, Rosen & Zubenko 1991, Deutsch et al 1991, Ballard et al 1991b, Förstl et al 1993). Again, the four studies with the highest prevalence rates all used structured instruments (Patterson et al 1990, Deutsch et al 1991, Förstl et al 1993, Merriam et al 1988) and the NINCDS ADRDA criteria were used in three of the four studies with the lowest prevalence rates (Burns et al 1990a, Mendez et al 1990, Rosen & Zubenko 1991).

The prevalence rate of hallucinations is between 16.9% (Burns et al 1990a) and 34.3% (Rosen & Zubenko 1991). Seven groups found a prevalence rate between 25% and 34% (Merriam et al 1988, Mendez et al 1990, Gilley et al 1991, Rosen & Zubenko 1991, Rubin et al 1988a, Ballinger et al 1982, Förstl et al 1993), showing a high degree of consistency. Although the prevalence rate of visual hallucinations varied from 4.4% (Devanand et al 1992) to 21.9% (Rosen & Zubenko 1991), there was a good consensus with a prevalence rate of between 10% and 15% reported in the majority of studies (Patterson et al 1990, Gilley et al 1991, Jeste et al 1992, Rubin et al 1988, Burns et al 1990a).

The prevalence rate of auditory hallucinations varies from 1.1% (Devanand et al 1992) and 1.9% (Jeste et al 1992) to 15.6% (Rosen & Zubenko 1991) and 17% (Gilley et al 1991). Little consensus was evident and none of the differences in sample selection or
characteristics clearly explain the variability. Olfactory hallucinations are also reported in several studies, with prevalence rates varying from 0.5% (Deutsch et al 1991) to 12.5% (Rosen & Zubenko 1991). There is again very little consistency in these findings. The use of representative clinical samples assessed using structured instruments should help clarify the situation.

The prevalence rate of delusional misidentification syndromes was specifically reported in six studies. Gilley et al (1991), Merriam et al (1988) and Burns et al (1990a) all report prevalence rates of between 11% and 19.1%, whereas Deutsch et al (1991), Binetti et al (1993) and Förstl et al (1993) report prevalence rates of 30-35%. Studies within each of the two ranges include patients diagnosed according to more and less restrictive criteria, from a range of settings with some using structured instruments. Schedules based on the BEHAVE-AD include the category "believing that ones house is not ones own home", which is not described by other groups. In addition, there is a wide variation in the estimated prevalence rates of some of the individual phenomena such as the Capgras delusion and the phantom boarder syndrome, the delusional belief that there is a lodger in the house. Operational definitions for the individual symptoms were not used in the majority of studies. It is hence difficult to know how much of this variation is explained by the application of divergent diagnostic criteria.
Several studies measure incidence rates or give "point" prevalence rates as well as period prevalence rates allowing an estimate of incidence to be made. The annual incidence rate varies from 1% (Burns et al. 1990a), 1.6% (Jeste et al. 1992), and 2.4% (Flynn et al. 1991) to 4.2% (Cummings et al. 1987), 4.5% (Liston et al. 1979) and 5.3% (Chen et al. 1991). Of these studies only Jeste et al. (1992), Flynn et al. (1991), Cummings et al. (1987) and Burns et al. (1990a) used systematised diagnosis of psychotic symptoms and only Flynn et al. (1991) used a structured interview. The latter study was also the only one to use sequential interviews and is hence likely to be the most accurate, although the sample number was small. These studies are summarised in Table 2.3.
<table>
<thead>
<tr>
<th>Sample Population</th>
<th>From Clinic 1</th>
<th>From Clinic 2</th>
<th>Yes</th>
<th>No</th>
<th>Yes</th>
<th>No</th>
<th>1979</th>
<th>1982</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>90</td>
<td>45</td>
<td>74</td>
<td>74</td>
<td>5.34</td>
<td>4.37</td>
<td>4.49</td>
<td>2.48</td>
</tr>
<tr>
<td>45%</td>
<td>95</td>
<td>50</td>
<td>45</td>
<td>50</td>
<td>No</td>
<td>No</td>
<td>1979</td>
<td>1982</td>
</tr>
<tr>
<td>33%</td>
<td>69</td>
<td>77</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1.65</td>
<td>2.41</td>
</tr>
<tr>
<td>33%</td>
<td>70</td>
<td>107</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>1992</td>
<td>1994</td>
</tr>
</tbody>
</table>

**Table 2.1** Inclusion Rate of Psychotic Symptom
An annual resolution rate of 2.2% per year was reported by Rosen & Zubenko (1991) in a small study which did not use a structured instrument for the diagnosis of psychotic symptoms. The mean duration of psychotic symptoms was found to be 2.4 years by Cummings et al (1987) and 4.2 years by Jeste et al (1992). Both the incidence rate and the resolution rate of these symptoms appears to be low, although the limited number of longitudinal studies precludes any firm conclusions.

ASSOCIATIONS


The most striking feature is the lack of reported positive associations. A significant association between female gender and the presence of delusions has been reported in one study (Rockwell et al 1994), whereas another describes a significant excess of
delusions in males (Burns et al 1990a). The majority of groups have not found gender to be an important factor. Similarly education, race, duration of illness and age at onset have not been found to be associated with psychotic symptoms in the majority of studies, although a higher prevalence rate amongst black subjects has been reported (Deutsch et al 1991), as has an association between lower levels of education and delusions (Flynn et al 1991, Binetti et al 1993) and an association between psychosis and greater length of illness (Gilley et al 1991). Older age has been shown to be significantly associated with psychotic symptoms in several studies (Cooper et al 1991, Rockwell et al 1994), as has late onset (Förstl et al 1993, Rockwell et al 1994). Most of these factors are only significant in one or two out of eleven standardised studies, which would suggest that chance association is a likely explanation.

A more consistent but not entirely clear picture emerges for the degree of cognitive impairment. Hallucinations were found to be significantly associated with a higher level of impairment by Ballinger et al (1982), Flynn et al (1991), Gilley et al (1991) and Cooper et al (1991) but not Burns et al (1990a). Other work has reported an association between Mini Mental State Examination scores in the eleven to twenty range and psychotic symptoms in general (Jeste et al 1992). This finding is supported by a further study reporting an association with dementia of moderate severity (Ballard et al 1991b) and indirectly by a study reporting fewer psychotic symptoms amongst patients with mild dementia (Teri et al 1989). A further three groups found a greater impairment of cognitive function in patients with psychotic symptoms (Gilley et al 1991, Rockwell et al 1994, Devanand et al 1992), although each of these patient populations had a mean MMSE score in the eleven to twenty range. Two groups were unable to find an
association between delusions and the degree of cognitive impairment (Deutsch et al 1991, Burnt et al 1990a), whilst another found a higher prevalence rate of delusions in patients with less severe cognitive impairment (Binetti et al 1993). The mean MMSE score in the latter study was only 9.2, which could be interpreted as giving support to the categorical theory suggested by Ballard et al (1991b) and Jeste et al (1992), proposing that those with dementia of moderate severity have the highest prevalence rate of psychotic symptoms.

Several authors have suggested a greater speed of cognitive deterioration in patients with psychosis (Drevets & Rubin 1989, Förstl et al 1993). If correct, this is a confounding factor when studying a group of dementia patients with varying lengths of illness. On balance, there probably is an association between hallucinations and a greater degree of cognitive impairment and possibly a link between both psychotic symptoms in general and delusions and a moderate degree of cognitive impairment. Studies focusing on the associations of psychotic symptoms are summarised in Table 2.4.
<table>
<thead>
<tr>
<th>Year</th>
<th>Product</th>
<th>Code</th>
<th>Percent</th>
<th>T Test</th>
<th>F Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>100</td>
<td>10</td>
<td>79</td>
<td>4.0</td>
<td>0.01</td>
</tr>
<tr>
<td>1993</td>
<td>199</td>
<td>19</td>
<td>73</td>
<td>3.9</td>
<td>0.01</td>
</tr>
<tr>
<td>1994</td>
<td>199</td>
<td>19</td>
<td>72</td>
<td>3.8</td>
<td>0.01</td>
</tr>
<tr>
<td>1995</td>
<td>199</td>
<td>19</td>
<td>71</td>
<td>3.7</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 2.4: Association of Psychological Symptoms
va D)

va 3
w m

si
"8

> W

Vw

"0

H
> w

z

< 0
cr n
o

tn cr o
o

> e> en

H

» w

>

C gg
• wM
as 3 m

s M

tn »

H
M - IB

âS

m»

55

XQ ID

va 3
I—(0

m 3

ft ft

M Hm
0

a A
ff o
ft 3

a

V

m D- V
C V-

cr 8) p3
m yr

v->- o

MŒŒ
a
iD a a
M iD m
•o 3

en £

rt 0


Some specific aspects of cognitive impairment including memory impairment and conceptual impairment were associated with psychotic symptoms in Jeste’s et al (1992) study but not in Burns’ et al (1990a) report. This work is at an early stage but is an important area for further study.

An association between extra pyramidal symptoms and psychosis was proposed by Mayeux et al (1985ab) and supported by Gilley et al (1991), although Mayeux’s group (Chen et al 1991) later suggested that this was a confounding effect explained by the association of both phenomena with increased cognitive impairment. Other groups were not able to identify a significant association between the two symptom clusters (Jeste et al 1992, Rockwell et al 1994).

The link between type of dementia and psychotic symptoms has been explored in several studies. Cummings et al (1987) and Binetti et al (1993) found a similar proportion of patients with vascular dementia and Alzheimer’s Disease to have psychotic symptoms. Psychotic symptoms were identified in thirteen out of nineteen inpatients with Alzheimer’s Disease compared to seven out of fourteen with vascular dementia in Flynn’s et al (1991) study, a slight but non significant excess. A significantly greater prevalence rate of psychotic symptoms has been reported amongst patients with Alzheimer’s disease compared to those with vascular dementia in three studies, one in a day hospital sample (Ballard et al 1991b) and the other two in nursing home residents (Rovner et al 1986, Morriss et al 1990). Another group reported a difference of similar magnitude but in the opposite direction (Chandler & Chandler 1988). Each of these latter four studies included only a small number of patients with vascular dementia. The evidence from the
larger studies suggests a similar prevalence rate of psychotic symptoms in the two dementias. Work pertaining to psychotic symptoms in patients fulfilling neuropathological or clinical criteria for Senile Dementia of Lewy Body Type is still in its infancy. Forty eight percent of patients with neuropathologically diagnosed Lewy body dementia had visual hallucinations, 19% had auditory hallucinations and 57.1% had delusions in McKeith’s et al (1992) study. Ballard et al (1993a) reported a prevalence rate of visual hallucinations of 25% and a prevalence rate of delusions of 43.8% in patients fulfilling McKeith’s et al (1992) clinical criteria. These studies included only twenty-one and fourteen subjects with Senile Dementia of Lewy Body Type respectively and the findings must hence be considered provisional. Senile Dementia of Lewy Body Type is common, probably accounting for more than 10% of dementia cases (Burns et al 1990b, Byrne et al 1989, Clark et al 1986, Perry et al 1990) and probably should be considered as a discrete diagnostic entity, although its nosological status is not entirely clear and it has been considered as a variant of Alzheimer’s disease by some authors (Hansen et al 1990). It should be a priority to further our understanding of the symptomatology.

Sensory impairment has also been suggested as an association of psychotic symptoms in dementia sufferers. Cummings et al (1987) found two of the three patients with impaired visual acuity to have visual hallucinations, an interesting observation but the numbers were too small for meaningful statistical analysis. No significant association was found between deafness and CAMDEX Paranoid Disorder in a further study (Ballard et al 1991b). The association of sensory impairment with psychotic symptoms in patients without dementia (Kay & Roth 1961, Post 1966) would suggest that this is an important area for further research.
An association between systematised delusions and less severe atrophy on CT scan has been reported (Burns et al 1990a). It is debateable however whether these are a separate category of psychotic symptoms or an elaborate form of the same symptoms in patients with less severe cognitive impairment. Zubenko et al (1991) found an association between psychotic symptoms and a low level of 5-hydroxytryptamine in the prosubiculum and a high level of noradrenaline in the substantia nigra. There was also an association between psychotic symptoms and an increased number of senile plaques and neurofibrillary tangles in the prosubiculum and middle frontal cortex. This interesting study however only included twenty-seven patients and psychotic symptoms were not diagnosed in a standardised way. In addition, greater hippocampal cell loss may be linked to delusional misidentification and less severe hippocampal cell loss together with more severe cell loss in the dorsal raphe nucleus may be evident in patients with delusions and hallucinations (Förstl et al 1994). Again the number of subjects were small, thirteen patients with hallucinations, fourteen with delusional misidentification and nine with delusions were included. No clear pattern emerges, although it would appear that several different brain regions may be involved.

COMPLICATIONS OF PSYCHOTIC SYMPTOMS

discordance (Rockwell et al 1994). When both hallucinations and delusions are present, delusions have been found to explain the majority of the variance by Deutsch et al (1991) and hallucinations by Förstl et al (1993). There appears to be a link between many of the symptoms presenting difficulties to carers (Rabins et al 1982) and psychotic symptoms. In addition, psychotic symptoms result in distress for the patients themselves in 30% of cases (Gilley et al 1991). No other studies have examined patient distress and no data is available describing the factors leading to distress. It is not known whether dementia sufferers have any insight into their psychotic symptoms. Likewise the features associated with patients acting upon their psychotic symptoms have not been studied.

There is evidence to support a link between psychotic symptoms and admission to residential care in community dwelling dementia sufferers (Steele et al 1990). This needs to be investigated further to clarify whether it is the symptoms themselves or associated behaviours which are the important determinates. Despite the distress experienced by patients with psychotic symptoms, they are no more likely to suffer from concurrent depression (Zubenko et al 1991, Gilley et al 1991).

Drevets & Rubin (1989) were the first authors to suggest a greater speed of cognitive deterioration in patients with psychotic symptoms. In their sample of eighty-two patients from a University Memory Clinic, patients with psychotic symptoms and patients without initially scored similarly on a battery of cognitive tests. The patients with psychotic symptoms however performed significantly worse at fifteen month, thirty-six month and fifty month follow-up. This finding was supported by Rosen & Zubenko (1991) who found an average decline of 7.3 points in the Mini Mental State Examination over five
years in a group of patients with psychotic symptoms compared to 3.3 in patients without. Förstl et al (1993) also reported a significant association between the rate of cognitive decline, as assessed by the CAMCOG schedule (Roth et al 1986), over two years, in a research sample of fifty patients. Delusions and hallucinations but not delusional misidentification were significantly associated with greater decline, hallucinations explaining the greatest proportion of the variance. Burns et al (1990a) found a significantly greater decline in cognitive functioning, as measured by the CAMCOG schedule, over one year amongst patients with visual hallucinations but not in patients with other types of psychotic symptom. There is hence some evidence to support a greater speed of cognitive decline in patients with psychotic symptoms, although further work is needed to examine the pattern of deterioration in more detail.

PHENOMENOLOGY OF PSYCHOTIC SYMPTOMS

There are a number of studies which report the prevalence rate of individual symptoms (Jeste et al 1992, Lopez et al 1991, Merram et al 1988, Patterson et al 1990, Mendez et al 1990, Flynn et al 1991, Rubin et al 1988, Teri et al 1989, Devanand et al 1992, Deutsch et al 1991). It is difficult to compare studies, as structured instruments were not used in the majority. In order to estimate the relative frequency of individual symptoms, a Ranking Score was applied. Six points was assigned to the most commonly reported symptom in each study, five for the second, four for the third and so on down to one point for the sixth. Using this very approximate system, the most common symptoms in rank order were delusions of theft, delusions of suspicion, delusions of reference, delusions of strangers in the house, Capgras delusions, delusions that one's house is not one's own home, delusions of abandonment, grandiose delusions, depressive delusions
and delusions of infidelity. Other occasionally reported symptoms included other misidentification delusions, such as delusions that objects depicted in pictures or on television are real and delusions that mirror images represent other people; delusions of sexual abuse, somatic delusions and delusions of object transposition. Although not reported in the more standardised studies, other delusions including infestation (Renvoize et al 1987) and erotomania (Drevets & Rubin 1987, Huckle & Tanaghow 1991) have been reported in case studies. No studies report the existence of delusions of partition, the abnormal belief that one is being influenced by supernatural means which are believed to penetrate through normal barriers. The latter are common symptoms in elderly patients with functional psychoses (Howard et al 1992).

Most authors have classified hallucinations solely by their modality, although other characteristics such as their frequency, laterality, quality and the insight a sufferer has into the experience are obviously important. Only one study (Mendez et al 1990) has attempted to subclassify hallucinatory experiences, reporting categories such as hallucinations of deceased persons, unfamiliar persons, intruders, animals, familiar persons, inanimate objects, complex scenes and unformed images. These subdivisions were based on the authors' own impressions.

Clearly the psychotic symptoms of dementia cover a number of themes. Attempts to classify these symptoms have been rather limited. Burns et al (1990a) subdivided the symptoms into simple delusions, complex delusions, hallucinations and delusional misidentification. Some support was provided for the category of complex delusions which was associated with less cortical atrophy on CT scan. A similar schema was used
by Förstl et al (1993) except for the absence of the category "complex delusions". Förstl et al (1991) argued that the false percepts that strangers were in the house could best be seen as a misidentification syndrome based on a similar pattern of CT scan changes to patients with misidentification of television images. Patients with misidentification of mirror images however had a different pattern of changes and there were too few patients with Capgras syndrome for any meaningful comparisons to be made. The delusion that one's house is not one's own home shares an altered sense of perception and familiarity with the Capgras phenomenon. There continues to be some doubt about which phenomena should be regarded as part of the spectrum of delusional misidentification syndromes.

Flint (1991) discusses the phenomenological status of fantastic confabulation and delusions, arguing that absolute demarcation is not always possible. He further states, supported by the findings of Kopelman (1987) and Kapur & Coughlan (1980) that the degree of falseness of the belief and the content can be similar in delusions and fantastic confabulations, but that the same themes tend to be repeated with delusions. An alternative hypothesis would be that they are on a continuum, with some beliefs reiterated occasionally and others more frequently.

A further group of common hallucinations and delusions involve beliefs about the presence of familiar people, often parents, children or friends. This could be seen in some ways as a "comfort phenomenon" and could be hypothesized to represent a discrete group of symptoms giving a sense of security rather than fear or distress.
Several studies have attempted to subdivide psychotic symptoms into syndromes using statistical techniques. Ballinger et al (1982) found eight clusters of symptoms, three of which included either hallucinations or delusions, Berrios & Brook (1985) found two clusters which included psychotic symptoms and Gustafson (1975) identified fourteen clusters, two of which included psychotic phenomena. Each of these studies included a large number of symptoms in the analysis, only a small proportion of which were "psychotic". In most cases the symptoms were described as hallucinations or delusions. The symptom detail was hence insufficient to make a meaningful distinction between different psychotic syndromes. Nevertheless, cluster analysis techniques are an important first step in trying to identify meaningful clusters of symptoms which could represent separate sub-syndromes.

The Capgras syndrome is usually associated with a strong feeling of ambivalence towards the person who is the object of the misidentification (Berson 1983). Is this likely to be any different in subjects with dementia? Similarly it is not difficult to see how emotional factors could contribute to the development of other symptoms, such as delusions of jealousy and abandonment. The psychological aspects of psychotic symptoms have been rather neglected and merit further consideration.

CONCLUSION

In summary, psychotic symptoms occur in over 60% of dementia sufferers in contact with clinical services. They are persistent, causing distress to patients and their carers. Working towards a substantive classification, increasing our knowledge of how these symptoms affect sufferers and promoting our understanding of important psychological factors are priorities, if the situation is to be improved.
CHAPTER 3

INTRODUCTION - DEPRESSION IN DEMENTIA SUFFERERS

Depression occurring in the presence of dementia is an important disorder for a variety of reasons. It results in distress to the patients themselves (Burns 1991a) and may detrimentally influence cognitive function (Greenwald et al 1989), instrumental activities of daily living (Fitz and Teri 1994) and reduce life expectancy (Burns et al 1991b). In addition, depression in patients causes distress to carers (Rabins et al 1982, Greene et al 1982).

Clinical Features

The symptoms of depression in dementia sufferers have been described widely (Lazarus et al 1987, Forsell et al 1993, Reding et al 1985, Sultzer et al 1993, Merriam et al 1988, Mackenzie et al 1989, Rubin & Kinscherf 1989, Ballard et al 1993b, Cummings 1988, Patterson et al 1990). There is a degree of consensus that dysphoria and loss of interest are the most common symptoms, although this might partly be due to the bias of the DSMIIIIR criteria which necessitate the presence of at least one of these symptoms to make a diagnosis of major depression. Psychomotor changes are also reported as common, occurring in between 50% and 60% of patients with depression (Patterson et al 1990, Ballard et al 1993b, Rubin & Kinscherf 1989). The reported frequency of other symptoms does however vary greatly. Appetite disturbance, for example, varies from 12% (Patterson et al 1990) to 70% (Merriam et al 1988) whilst other biological symptoms show similar variability. Psychological symptoms also differ greatly in their frequency. Guilt arose in only 6% of Merriam’s et al (1988) sample but occurred in 50% of Cummings’s (1988) patients. Pessimism, worthlessness and low self esteem show similar
differences in magnitude. The majority of symptoms reported as common amongst patients with functional depression occur frequently in patients with depression in the presence of a dementia. These include biological symptoms, psychomotor symptoms, negative cognitions, anxiety and suicidal thoughts, the latter occurring in up to 50% of subjects (Cummings 1988). Forsell et al (1993) suggest that guilt and suicidal ideation are more common in milder dementias. The overall findings do not however support this supposition as two of the groups studying more severely impaired patients (Cummings 1988, Ballard et al 1993b) reported high prevalence rates of guilt, suicidal thoughts and negative cognitions. There is also little support for Merriam’s et al (1988) suggestion that patients with dementia and depression have less intrapsychic symptoms and prominent mood reactivity. Greenwald et al (1989) compared the symptoms of ten dementia patients with concurrent depression to thirty-three depressed patients without dementia, finding boredom, initial insomnia, early morning wakening and delusions to be less frequent in those with both disorders. The small numbers are a severe limitation of the study.

Some groups have used statistical methods to examine whether the symptoms of depression can be divided into convenient clusters. Forsell et al (1993) undertook such an analysis on a sample of two-hundred and twenty-four patients. Two clusters emerged. One was characterised by a loss of interest, psycho-motor change, a loss of energy, poor thinking and impaired concentration. This cluster was associated with more severe dementia. The second cluster was characterised by dysphoria, reduced appetite, guilt and suicidal thoughts and was characteristic of patients with milder impairment. Although a very important finding, twenty-three of the patients in this study had questionable
dementia (Hughes et al 1982). Some of these patients are likely to have had depression in the absence of a progressive dementia which might have influenced the overall factor analysis. Greene et al (1982) looked at thirty-eight patients examining thirty-four depressive symptoms. Factors of apathy, activity disturbance and mood disturbance emerged. The analysis included all the patients, not just those who were depressed. In addition a large number of symptoms were entered into the analysis on a relatively small sample. Nevertheless, the apathy and mood disturbance categories are similar to the two clusters identified by Forsell et al (1993). Sultzer et al (1992) examined a more limited number of symptoms and identified one factor of anxiety and depression. Examining a broad range of symptoms which included some mood items Ballinger et al (1982) identified eight clusters, three of which had affective components. Factor four was histrionic depression, factor five paranoid affects and factor seven mood lability. Gustafson (1975) examined a wide range of symptoms in fifty patients with pre-senile dementia identifying fourteen factors, three of which had mood components. One described low mood and poor concentration, one psychomotor retardation and one hypochondriasis. Again two of the components emerging were psychomotor change and dysphoria offering support to Forsell’s et al (1993) findings. If separate clusters of depression exist this may help explain some of the apparent discrepancies in a number of areas including studies of actiology. None of these groups have examined the potential usefulness of the clusters identified.

The identification of "cases" of depression in dementia suffers is a difficult area. Either the DSMIII or DSMIIIR criteria have been used in most studies. These are not tailored to the diagnosis of depression in dementia patients. Community studies of depression in
the elderly using the DSMIIIR criteria report prevalence rates under 3% (Blazer et al 1987) compared to prevalence rates of 10-15% with alternative diagnostic systems such as the AGECAT (Copeland et al 1986). It appears that these criteria identify a highly selective group of patients with severe depression encompassing so called biological symptoms. It is unlikely that patients identified in this way are representative of patients with a significant number of depressive symptoms or that the majority of patients with these symptoms are identified. What alternatives exist? It is largely an arbitrary decision at what point depressive symptoms constitute a disorder. That decision should however be made directly from data concerning dementia patients, based upon a level of symptomatology which causes a significant level of distress and disability and which is likely to be persistent. As a first step to achieving this goal the use of less restrictive criteria, such as the Research Diagnostic Criteria for minor depression (Spitzer et al 1978) would allow the identification of a broader group of patients who suffer from some symptoms of depression. Distress, disability and the persistence of symptoms could then be studied.

Biological markers, in particular measures of REM sleep (Kupfer et al 1986) may offer some potential, particularly in the confirmation of more severe depression amongst patients with moderate to severe dementia. This technique has not however been studied specifically as a means of identifying depression in the context of dementia. Sophisticated ethological measures of depressed mood may also have potential. These techniques have proved valid in the measurement of depression amongst patients without cognitive impairments (Mackintosh et al 1986). The existence of activity disturbances as part of the dementia syndrome, the common occurrence of extrapyramidal symptoms in dementia
sufferers and the frequent use of neuroleptic drugs in this patient group may however present important obstacles.

Epidemiology
Although a number of early descriptive studies of dementia (Rothschild 1941, Clow 1940, Sim & Sussman 1962) describe depressive symptoms in patients with clear cut dementia, there was very little development of this work at the time and the main focus of attention became the differentiation of dementia from depressive pseudo-dementia (Mahendra 1985). A series of case reports and descriptive studies (Demuth & Rand 1980, Snow & Wells 1981, McCallister & Price 1982, Knesevich et al 1983) began to re-emphasize the presentation of both disorders concurrently.


The prevalence rate of depression varied from 0% (Burns et al 1990c) to 51.7% (Pozzi et al 1993). Förstl et al (1992) described fifty-two of Burns' et al (1990c) original sample of one hundred and seventy-eight patients who came to post-mortem, reporting a prevalence rate of major depression of 28%. The reason for this difference is not entirely clear. Prevalence rates between 15% (Mackenzie et al 1989) and 41% (Shuttleworth et al 1987) were reported in fourteen of the twenty studies. Prevalence rates of less than 10% were reported in three of the studies (Burns et al 1990c, Verhey et al 1993, Cummings et al 1987). It was unclear whether Verhey et al (1993) obtained information solely from patients, which may have led to under-reporting of symptoms. Burns et al (1990c) collected data from the GMS (Copeland et al 1976) and CAMDEX (Roth et al 1986) Schedules, both of which have relatively little detail regarding symptoms of depression in the informant sections. Prevalence rates between 10% and 19.9% were reported in a further four studies (Reding et al 1985, Mackenzie et al 1989, Greenwald et al 1989, Rovner et al 1989). Greenwald et al (1989) utilised a two stage design, identifying possible cases from a case note review. This may also have led to an underestimation. Prevalence rates of depression in the 20% to 29.9% range were identified in six studies (Förstl et al 1992, Cohen et al 1993, Reifler et al 1982, Burke et al 1992, Teri & Wagner 1991, Ballard et al 1993b) and a prevalence rate in excess of 30% was identified by a further seven groups (Pozzi et al 1993, Ott & Fogel 1992, Zweig et al 1988, Reifler et al 1986, Breen et al 1984, Shuttleworth et al 1987, Mulsant et al
1994). Only one of this latter group of studies had a sample size of more than fifty patients (Reifler et al 1986).

The frequency of depression was similar in the studies with more severely impaired patients (Burns et al 1990c, Rovner et al 1989, Mulsant et al 1994, Ballard et al 1993b, Cummings et al 1987), those with a male excess (Cummings et al 1987, Zweig et al 1988) and studies with a younger patient population (Rovner et al 1989, Shuttleworth et al 1987). There are few sample differences which could explain the diversity of results (Table 3.1). Nine of the thirteen studies with a sample size of more than fifty patients had prevalence rates between 14% (Burke et al 1989) and 29.3% (Teri & Wagner 1991). There is a trend for patients from memory clinics and in-patient sources to have higher rates of depression. There is also a tendency for samples diagnosed with criteria other than the DSMIIIIR criteria for major depression to have an increased prevalence rate.

Data based largely on research samples have been reported in ten studies. The prevalence rate of depression varied from 2% (Nyth & Gottfries 1990) to 85.7% (Merriam et al 1988). Prevalence rates exceeding 30% were identified in most reports (Zubenko & Moossy 1988, Zubenko et al 1990, Fitz and Teri 1994, Pearson et al 1989, Reifler et al 1989, Pearlson et al 1990, Alexopoulos et al 1988). Merriam et al (1988) found a much higher rate of depression than has been reported in any other study. Only the carers were interviewed which may have been a source of bias. The demographic characteristics of participants in these studies were similar to those of patients in the clinical samples, although higher prevalence rates of depression were reported. The patient origins are however rather uncertain, which makes it difficult to generalise.
<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Depression Prevalence</th>
<th>DSM III</th>
<th>Mean Age</th>
<th>Gender</th>
<th>Number of Patients</th>
<th>Severity Criteria</th>
<th>Mean MIDE</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11%</td>
<td>17.5</td>
<td></td>
<td></td>
<td></td>
<td>72%</td>
<td>1.73</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14%</td>
<td>18.5</td>
<td></td>
<td></td>
<td></td>
<td>72%</td>
<td>2.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.7%</td>
<td>18</td>
<td>61%</td>
<td></td>
<td></td>
<td>72%</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12.2%</td>
<td>18</td>
<td>61%</td>
<td></td>
<td></td>
<td>72%</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.4%</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td>72%</td>
<td>225</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0%</td>
<td>1.4</td>
<td>79%</td>
<td></td>
<td></td>
<td>72%</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 3.1 - The prevalence of depression among elderly dementia suffers in clinical settings
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with depression</th>
<th>Patients with depression mean MISE</th>
<th>Severity of depression</th>
<th>Patients with depression length of stay</th>
<th>Patients</th>
<th>Number of patients</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>32%</td>
<td>40%</td>
<td>20%</td>
<td>30%</td>
<td>1.5</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td>28%</td>
<td>35%</td>
<td>25%</td>
<td>35%</td>
<td>1.8</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Third</td>
<td>30%</td>
<td>38%</td>
<td>30%</td>
<td>38%</td>
<td>2.0</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Fourth</td>
<td>34%</td>
<td>42%</td>
<td>34%</td>
<td>42%</td>
<td>2.5</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

Note: The table provides a summary of studies with data on the prevalence and severity of depression, as well as the mean length of stay and the number of patients.
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td>37.9%</td>
<td>DSMIIIIR</td>
<td>109</td>
<td>\</td>
<td>\</td>
<td>80</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td>40.9%</td>
<td>DSMIII</td>
<td>\</td>
<td>59.5%</td>
<td>67.1</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td>29.3</td>
<td>DSMIIIIR</td>
<td>181</td>
<td>68.6%</td>
<td>74</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td>20.2%</td>
<td>DSMIII</td>
<td>115</td>
<td>\</td>
<td>\</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td>40.9%</td>
<td>DSMIII</td>
<td>183</td>
<td>74.5%</td>
<td>74</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

Study Participants Mean Age, Mean MISE Criteria Severity Prevalence Depression for Depression Criteria of MISE Center
Depression has also been studied amongst dementia sufferers in residential care. Morriss et al (1990) studied residents from six nursing homes, finding a 7.1% prevalence rate of major depression. Using a similar design Rovner et al (1986) found a prevalence rate of 10%. Teeter et al (1976) found 38.2% of nursing home residents with dementia to be depressed using clinical criteria. Chandler & Chandler (1988) did not find any cases of depression amongst twenty-seven dementia sufferers from six nursing homes. Abraham et al (1994) studied nine hundred and seventeen residents from residential homes with suspected depression. They reported mean Geriatric Depression Scale scores of 17.2 and mean Mini Mental State Examination scores of 18.7. The study unfortunately did not cite any prevalence figures per se.

The three groups using standardised criteria (Chandler & Chandler 1988, Morriss et al 1990, Rovner et al 1986) all reported prevalence rates of 10% or less, although two of these reports included less than fifty participants. The main difference demographically from clinical samples was the age of the residents which was generally over eighty. These results are rather surprising as studies of nursing home residents in general have shown high prevalence rates of depression (Clark 1992, Ames 1992). One would expect there to be no exception for those with cognitive impairment (Table 3.2).
<table>
<thead>
<tr>
<th>Presence of Depression</th>
<th>Criteria for Clinical Diagnosis</th>
<th>Mean Age</th>
<th>Number</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>DSMIII</td>
<td></td>
<td>50</td>
<td>1996; Kover et al.</td>
</tr>
<tr>
<td>38.2%</td>
<td>DSMIII</td>
<td>80% F</td>
<td>31</td>
<td>1976; Teeter et al.</td>
</tr>
<tr>
<td>7.4%</td>
<td>DSMIII</td>
<td></td>
<td>70</td>
<td>1990; Whorls et al.</td>
</tr>
<tr>
<td>0.9%</td>
<td>DSMIII</td>
<td></td>
<td>80.2</td>
<td>1988; Chandler et al.</td>
</tr>
</tbody>
</table>

The prevalence of depression among dementia sufferers in residential or nursing home care.

*Table 32*
Data concerning the prevalence rate of concurrent depression and dementia are reported in several community studies. Estimates of the frequency of depression in dementia sufferers vary from 5.1% (O'Connor 1990ab) to 38.1% (Cooper & Schwarz 1982). Prevalence rates of 5.1%, 12.4% and 20% respectively were reported in the three studies with the largest samples (O'Connor 1990ab, Forsell et al 1994, Skoog 1993). In each report the average age was over eighty and there was a female excess. Depression was diagnosed according to DSMIII or DSM-III-R criteria. The severity of dementia was not reported. The prevalence rate of depression is probably lower than is seen in clinical samples. The patients included in the community samples were older which might be one possible explanation. It is also possible that the severity of dementia may have been different, a hypothesis which cannot be tested in the absence of relevant data. A more likely explanation (Henderson 1990) would be the preferential referral to clinical services of people with cognitive deficits and concurrent depression.

The prevalence rate of depression in dementia sufferers is also considered in a number of unstandardised reports (Kral 1983, Lopez et al 1990, Lichtenberg et al 1992, Erkinjuntti 1987, Clow 1940, Hasegawa et al 1986). The prevalence rates identified in these reports varied from 8.8% (Lopez et al 1990) to 36.7% (Lichtenberg et al 1992), although the majority were in the 15% to 28% range (Kral 1983, Erkinjuntti 1987, Clow 1940, Hasegawa et al 1986). The findings are similar to those from studies using Standardised Criteria. In view of the absence of an operationalised diagnosis, further comparisons are difficult.
Prevalence rates of depression between 11% and 46% have been reported in patients with pre-senile dementia (Nott and Fleminger 1975, Liston 1979, Rosenstock 1970, Sim & Sussman 1962, Rubin et al 1993, Bucht & Adolfsson 1983). Most did not use standardised criteria and had small samples.

There is some consensus between the larger studies. The prevalence rate of depression amongst dementia sufferers in clinical settings is between 15% and 30%, tending towards the upper estimate amongst in-patients and those attending memory clinics. The rate in the community is lower, probably between 10% and 20%. Whilst these findings are based on a reasonable number of standardised studies, most have used restrictive diagnostic criteria necessitating further study of milder depressions. There are insufficient data of an acceptable quality to develop a consensus view concerning depression in patients with presenile dementia, although depression certainly occurs commonly in this patient group.

There are limited data available concerning the outcome of depression in dementia sufferers. Lopez et al (1990) followed up one-hundred and thirteen patients after one year, finding that patients who were suffering from concurrent depression at baseline had a mean Hamilton rating scale score of seventeen at follow-up. Although not reporting the number of depressed patients per se, this indicates persistent morbidity. Knesevich et al (1983), in an unstandardised study of thirty depressed patients, reported mean Hamilton Rating Scale scores of 5.5 at one year follow-up. The small numbers and the unstandardised nature of the sample limit the conclusions which can be drawn. O'Connor et al (1990a,b) found eight out of one-hundred and fifty patients to have major depression in a community study. At one year follow-up four of these eight patients had
died, although none of the four survivors were still depressed. Snowden & Lane (1994) followed up a research sample of thirteen patients with concurrent depression and dementia at four years. Eleven of the patients were traced, eight of whom had died. Two of the three survivors were still depressed. The small number of survivors makes it difficult to draw too many conclusions about the outcome of depression. A more striking finding is the high mortality rate. This impression is supported by Zweig et al (1988) and Burns et al (1991b) who both found reduced survival rates in patients with concurrent depression and dementia. No studies were found which included any information pertaining to the incidence rate of depression amongst patients with dementia.

**Associations**


Although an appealing theory there is little evidence to support any relationship between the retention of insight into the dementing process and depression. Neither Verhey et
al (1993) nor Ott & Fogel (1992), both of which used a well designed structured instrument for the ascertainment of insight, were able to demonstrate any link with depression. Ballard et al (1993b) in a smaller sample, demonstrated a trend towards an association between retention of insight and depression. This was possibly explained by the high prevalence rate of depression in patients with CAMDEX minimal dementia, who may represent a mixed diagnostic group.

Opinion is divided regarding the relationship between depression and the severity of cognitive impairment. Data relevant to the issue are presented in twelve standardised studies with more than fifty participants. A significant association between depression and less severe cognitive impairment was reported in four studies (Cooper et al 1990, Reifler et al 1982, Teri & Wagner 1991, Reifler et al 1989), whilst no association was apparent in a further five (Reding et al 1985, Verhey et al 1993, Fitz and Teri 1994, Fischer et al 1990, Swearer et al 1988). Burns et al (1990c) indirectly supported a link between less severe cognitive impairment and depressive symptoms by demonstrating significantly less ventricular enlargement amongst these patients. Burns et al (1990c) also reported significantly less severe cognitive impairment amongst patients who identified themselves as depressed but not amongst patients thought to be depressed by an interviewer. A contrary finding suggesting a relationship between depression and more severe cognitive impairment was reported by two groups (Rovner et al 1989, Greenwald et al 1989), although this difference disappeared when the depression was treated in the latter study. Fitz and Teri (1994) reported an association between less severe cognitive impairment in patients with depression in the context of mild dementia but more severe cognitive impairment in depressed patients with dementia of moderate severity. The
patients included in Rovner's et al (1989) study, where dementia was associated with more severe cognitive impairment, had a mean Mini Mental State Examination score of eleven, compared to a mean of approximately eighteen in most of the other reports. The pattern of associations is hence consistent with Fitz and Teri's (1994) suggestion. Although this hypothesis merits further examination the influence of confounding factors such as the under diagnosis of depression in more severely impaired patients and the influence of depression on motivation to undertake cognitive assessments cannot be dismissed. The results of more detailed cognitive assessments have been reported in two studies, neither demonstrating any links between impairment of specific cognitive functions and depression (Burns et al 1990c, Fitz and Teri 1994).

The majority of groups used DSM III or DSMIIIIR criteria to report samples with a female excess and a mean age between seventy and eighty. There is little demographic variation which could account for any of the disparities.

Pearson et al (1989) and Teri & Wag:er (1991) both found an inverse association between the level of education and the likelihood of suffering from a concurrent depression. Rubin et al (1991) and Forse l et al (1994) were unable to demonstrate any link. This finding is of interest and requires further study. The possibility must be considered that the effect may be explained by confounding factors such as a link between higher levels of education and better levels of financial provision.

A history of psychiatric illness has also been explored as an association of depression by several authors. O'Connor et al (1990a,b) found a significant association between a
personal history of depression and the occurrence of depression in the context of dementia. The study however only included eight patients with both disorders concurrently. The findings were supported in Rovner's et al (1989) study. There is also evidence from one study (Pearson et al 1990) that patients with a family history of depression are more at risk of suffering from depression in the presence of dementia. There is a possibility that similar genetic factors may control depression in dementia and "functional" depression, which requires clarification. Many areas of potential importance have received little attention. Cohen et al (1993) found an association between depression and living alone. Other potential stresses or life events have received no attention whatsoever. Förstl et al (1992) reported seven out of fourteen patients with depression to have either visual or auditory impairment. Figures for the non depressed population are not given which makes comparison difficult. Sensory impairment, pain and life events all merit further study.

The prevalence rate of depression in vascular dementia compared to Alzheimer's disease has also been investigated. Greenwald et al (1989) and Cummings et al (1987) both found a higher prevalence rate of depression amongst patients with vascular dementia. Greenwald et al (1989) described a large sample, although Cummings et al's (1987) study included only forty-five patients, fifteen of whom had multi-infarct dementia. The latter study was also biased in that patients with vascular dementia had a less severe degree of cognitive impairment and there was a rather uncharacteristically low rate of depression amongst the patients with Alzheimer's disease. Rovner et al (1986) found 44.4% of nine patients with multi-infarct dementia to have depression, compared to only 17.9% of twenty-eight patients with Alzheimer's disease. This tended towards statistical
Sultzer et al (1993) found patients with vascular dementia to have significantly higher scores on the Hamilton Rating Scale For Depression. Several other groups (Ballard et al 1993b, Verhey et al 1993) found a similar prevalence rate of depression in patients with vascular dementia and those with Alzheimer's disease and Bucht & Adolfsson (1983) did not find any significant difference between the mean depression rating scales scores of patients with the two dementias. A significantly higher prevalence rate of depression was reported amongst patients with Alzheimer's disease in one study (Reding et al 1985). Although the picture is not entirely clear, the evidence does favour the conclusion that there is a higher prevalence rate of depression amongst patients with vascular dementia. The prevalence rates of depression amongst subjects with vascular dementia vary from 6.25% (Reding et al 1985) to 44.4% (Rovner et al 1986), with only Rovner's et al (1986) group reporting a prevalence rate in excess of 30%. The reported prevalence rates for depression in the context of vascular dementia are similar to the overall prevalence rates of depression amongst dementia sufferers in contact with clinical services. Studies comparing the two dementias report an unusually low prevalence rate of depression in subjects with Alzheimer's disease, although there is no identifiable reason why this should be so. Most of the studies had an adequate overall sample size but none included more than sixteen patients with vascular dementia.

Cummings (1988) suggests that patients with vascular dementia are more vulnerable to the development of depressive illness, citing evidence from unstandardised studies (Clow 1940, Erkunjunnti 1987). The paper explores several possible explanations including the possibility of an association with greater physical disability. Babikan and Roper (1987) postulated that certain sub-categories of patients, such as those with Binswanger's
disease, may be particularly at risk of developing depression (Babikan and Roper 1987).

Coffey et al (1990) found a preponderance of white matter hyperintensities amongst a series of patients with severe depression. It is possible that sub-cortical vascular lesions may be important in the genesis of depression, even in the absence of Binswanger's disease. Patients with vascular dementia involving the left frontal lobe may represent another group of patients who are more vulnerable to affective disorder based on Starkstein's et al (1987) study of stroke patients. A further model could be suggested by drawing a parallel with the work pertaining to depression amongst patients with Alzheimer's disease, where a link with degeneration of the ascending monoamine tracts is thought to be important (Zweig et al 1988). One might expect vascular damage to the ascending monoamine pathways to lead to the same result.

Fewer studies have considered depression in patients with neuropathologically or clinically diagnosed Senile Dementia of Lewy Body Type. McKeith et al (1992) found eight out of twenty-one patients (38%) with Senile Dementia of Lewy Body Type diagnosed neuropathologically to suffer from substantial depressive symptoms, of whom three (14.3%) suffered from DSMIIIIR major depression. Fifteen per cent of patients with Alzheimer's disease had depressive symptoms, which was significantly less than the corresponding percentage for patients with Senile Dementia of Lewy Body Type, although the two groups were not compared for the prevalence of major depression. Ballard et al (1993a) described sixteen patients with idiopathic clouding of consciousness, fourteen of whom fulfilled the McKeith criteria (McKeith et al 1992) for Senile Dementia of Lewy Body Type. Seven of these sixteen patients had depression according to the CAMDEX criteria compared to seven out of forty-four patients with Alzheimer's
Data from post-mortem studies have considerably advanced our understanding of organic factors which may contribute to depression in Alzheimer's disease. Zubenko & Moossy (1988), Zweig et al (1988) and Förstl et al (1992) all found significantly lower neuronal counts in the locus coeruleus amongst patients with depression in thirty-seven, twenty-five and fifty-two patients respectively. Zubenko & Moossy (1988) also reported greater cell loss in the substantia nigra although this was not found in the other studies. Zweig et al (1988) reported more cell loss in the Raphe nucleus amongst depressed patients and a trend in the same direction was found by Förstl et al (1992). In Zubenko & Moossy's (1988) study the neuropathological changes were able to differentiate depressed from non-depressed patients with 90% sensitivity and 95% specificity. In a further study of the same sample, Zubenko et al (1990) reported an association between a decrease of noradrenaline in the hippocampus and neo-cortex and the presence of depression. The difference between depressed and non-depressed patients was in the order of ten to twenty fold. A trend was also found for a reduction in five hydroxytryptamine in these brain areas, although the magnitude of difference was much less striking. Convincing evidence is provided that lesion location is important in the development of depression amongst patients with Alzheimer's disease, which makes it surprising that neuropsychological studies have not demonstrated any differences in the pattern of cognitive impairments. It may also help in devising some testable hypotheses regarding treatment. If, for example, patients have a relatively selective neuronal loss affecting their ascending nor-adrenaline tracts; one might expect pharmaceutical agents which act on
nor-adrenaline to be more effective. In addition if the problem is mainly one of decreased input from the locus coeruleus a prompt response to anti-depressants over a few days would be expected.

Excess Disability

Greenwald et al (1989) in a sample of one hundred and sixty-one dementia sufferers, found depressed patients to have a more severe degree of cognitive impairment. The difference between depressed and non depressed patients disappeared with treatment of the depression, although the depressed patients continued to score within the dementia range. Fitz and Teri (1994), in a sample of ninety-one patients, demonstrated that depression significantly worsened performance on instrumental activities of daily living. Thirteen percent of the variance was accounted for. Communication skills were also effected, explaining 21% of the variance. A variety of behaviour problems, including depression, are perceived as stressful or cause distress to carers (Gilhooly 1984, Rabins et al 1982, Greene et al 1982). There is limited evidence however to suggest that they are actually associated with depression in carers per se (Morris et al 1988).

Depression may also influence the length of in-patient stay. Greenwald et al (1989) found the length of hospital stay to be seventy-seven days in patients with dementia and depression compared to forty-four days in patients with dementia alone. Patients with concurrent depression and dementia are also more likely to be admitted to residential care (Steele et al 1990) and have increased mortality rates (Zweig et al 1988, Burns et al 1991b).
A handful of studies have examined the possibility that depression is associated with a different rate of progression of cognitive impairment. Rosen and Zubenko (1991) were unable to undertake any statistical analysis because of small numbers. None of the other groups (Burns et al 1990c, Reding et al 1985, and Reifler et al 1982) were able to identify any significant differences.

Conclusion

Work in this area has achieved a reasonable consensus from well designed studies reporting the prevalence rate of major depression amongst dementia sufferers in clinical and community settings. There is however a complete absence of data pertaining to milder depressions and very little is known about the course of depression in dementia sufferers, an important prerequisite to making informed treatment decisions. In addition many of the potentially important aetiological factors have not been investigated. Life events, the quality of social support and the quality of the living environment are all important areas which have been little researched. It is clear that concurrent depression bestows considerable excess disability on dementia sufferers.
CHAPTER 4

AIMS OF THE PROJECT

The general aim of the study was to investigate in detail the nature of psychotic symptoms and depression in dementia sufferers.

Psychotic symptoms

1. To describe in detail the prevalence rate, incidence rate and resolution rate of psychotic symptoms in general and the symptom groups: delusions, visual hallucinations and delusional misidentification. In addition to describe the individual psychotic symptoms experienced by dementia sufferers.

2. To compare the type of symptoms, prevalence rate and course of psychotic symptoms in patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type.

3. To investigate the association of psychotic symptoms in general and the symptom groups: delusions, visual hallucinations and delusional misidentification with deafness, visual impairment, physical health problems, gender, age, confabulation, education, duration of dementia, age at time of onset of dementia, past history of psychiatric disorder, bereavement, life events, living alone and the type of dementia using a logistic regression model.

4. To examine associations between the overall severity of cognitive impairment (measured using the CAMCOG schedule and each of the CAMCOG subscales) and psychotic symptoms in general, visual hallucinations, delusions and delusional misidentification using a logistic regression model.
5. To use a Principal Component Analysis to examine whether different psychotic syndromes of dementia can be identified.

6. To compare the rate of cognitive decline in patients with and without psychotic symptoms in general and to compare the rate of cognitive decline in patients with visual hallucinations, delusions, and delusional misidentification to those without the respective category of psychotic symptoms.

7. To describe the amount of emotional distress experienced by patients with psychotic symptoms and their insight into the presence of these symptoms.

**Depression**

1. To ascertain the prevalence rates of major and minor depressive disorder and to describe in detail the depressive symptoms experienced by dementia sufferers.

2. To describe the prevalence rate of depressive disorders and the type of depressive symptoms in patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type.

3. To examine retention of insight, gender, age at time of onset of the dementia, physical health problems, bereavement, life events, deafness, severe visual impairment, number of years of education, a past history of psychiatric disorder, living alone and the type of dementia as associations of both major and minor depression in a logistic regression model.

4. To examine the associations between the overall severity of cognitive impairment (as measured by the CAMCOG and each of the CAMCOG subscores) and the presence of major and minor depression respectively, using a logistic regression model.
5. To use a Principal Component Analysis to examine whether distinct depressive syndromes of dementia can be identified.

6. To examine the incidence rate and resolution rate of major and minor depression.
CHAPTER 5

METHOD - THE STUDY

A list of consecutive referrals to four old age psychiatry services in the West Midlands (three at the Queen Elizabeth Psychiatric Hospital in Birmingham and one at the Walsgrave Hospital in Coventry) and a Memory Clinic in Bristol was obtained. The casenotes of all patients of sixty-five years of age or over were reviewed. Patients who approximately fulfilled the CAMDEX criteria for mild or moderate dementia (Roth et al. 1986) and had an informant in contact at least once a week were selected. This allowed patients who clearly did not have dementia and those who were too severely impaired to be interviewed to be excluded. All those who fulfilled the entry criteria were contacted, together with their carer and asked if they would like to participate in the study. This procedure continued from April 1993 until the target number of participants had been achieved in December 1993. A comprehensive assessment was completed which included a Geriatric Mental State Schedule (Copeland et al. 1976) and a History and Aetiology Schedule (Dewey et al. 1992) regarding the patient. Psychotic symptoms were rated using the Burns' Symptom Checklist (Ballard et al. 1995). The scale includes items pertaining to emotional distress and the degree of insight into the psychotic symptoms as well as a detailed description of individual symptoms. The scale is described in more detail in the instrument section of the method and is shown in Appendix A.

Delusional beliefs had to be false, firmly held and impervious of evidence to the contrary (Burns et al. 1990a), not to be explicable entirely by cognitive failure and to have been experienced at least twice, on occasions more than one week apart. Hallucinations were considered to be present if described by the patient or if clearly described to the
informant by the patient. Delusional misidentification encompassed the symptoms: delusional misidentification of mirror images, television images, people, objects, one's house and the phantom boarder syndrome. Symptoms also had to fulfil the criteria for a delusion. Delusional misidentification of television images focuses upon the belief that people in the television set are real and exist in the environment of the patient. Patients often express secondary delusional beliefs where perceived ill-intent is attributed to the images. The delusional misidentification of mirror images describes the belief that the reflection seen in a mirror is a different person from the individual whose reflection it is, and that the person exists in a tangible sense. Patients often harbour related beliefs pertaining to a world behind the mirror or believe that the mirror represents a door to a different room. Again perceived ill-intent is often attributed to the image. To be considered as a delusional misidentification the belief that one's house was not one's home had to be more than failure to recognise one's own house, delusional explanations had to be given. Examples of such beliefs include "I went for a walk and when I came back someone had changed the house" or "when I came back from the day centre I had moved into a neighbour's house". People may comment upon the similarity of the house to their own, but identify minor differences. The delusional misidentification of people and objects have the same characteristics as the Capgras syndrome in younger adults. In view of the controversial nature of the inclusion of the phantom boarder syndrome as part of the delusional misidentification category, all analyses were undertaken with and without this symptom as part of the category. For each type of psychotic symptom the one month prevalence rate is reported and the symptoms had to occur on occasions at least one week apart. Each of the four raters participated in a one week training course, emphasising the importance of including all symptoms which were possibly psychotic in
nature and describing each of these in detail. All the schedules were then reviewed by one of the raters (CB) who decided whether they fulfilled the study definition for one of the categories of psychotic symptoms.

Symptoms of depression were rated on the Cornell Depression Scale (Alexopoulos et al 1988). This is a nineteen item schedule covering a range of symptoms of depression on a zero to two scale. The scale is shown in Appendix B. The rating instructions were slightly modified so that symptoms were included if they were present for two weeks during the previous month. Both the patient and carer were interviewed regarding the patient's symptoms of depression. If any discrepancy existed the rater used their own judgement as to the correct rating. A diagnosis was then made from this symptom checklist according to the DSMIIIIR (American Psychiatric Association 1987) and Research Diagnostic Criteria (Spitzer et al 1978). The specifications in the DSMIIIIR criteria, that patients with depression caused by an organic disorder should be excluded, was waived. The HAS schedule includes an item confirming the presence of depression for at least two weeks during the previous month and a further item pertaining to the social disability attributable to the depressed mood. The four raters who completed these schedules all participated in a one week training course, during which the standardised rules for rating each of the symptoms included in the Cornell Depression Scale were emphasised. Although the items of the Cornell Depression Scale were rated by four separate raters, the diagnostic criteria were all applied by one of the raters (CB).

Cognitive function was assessed using the CAMCOG schedule (Roth et al 1986). A total CAMCOG score was reported, as were subscores for orientation, language
comprehension, language expression, praxis, recent memory, visual memory, remote memory, attention and calculation, perception, abstract thinking and verbal fluency. These were derived as described by Hooper and Bucks (1993) and is shown in Appendix C. A physical examination and a full blood screen were undertaken and the Secondary Dementia Schedule, a sister instrument of the GMS/HAS AGECAT package and the physical examination section of the CAMDEX were completed. This allowed identification of deafness, severe visual impairment and Parkinsonian symptoms.

The information documented as part of the GMS/HAS interview allowed a diagnosis of dementia to be made according to the NINCDS ADRDA criteria (McKhann et al 1984) DSMIIIIR criteria (American Psychiatric Association 1987), the Hachinski Scale (Hachinski et al 1975), the McKeith criteria for Senile Dementia of Lewy Body Type (McKeith et al 1992) and the HAS AGECAT criteria (Dewey et al 1992). The McKeith criteria were first applied, any patients not fulfilling the criteria for Senile Dementia of Lewy Body Type were then entered into the next stage of the process. The NINCDS ADRDA criteria were then applied. If patients fulfilled the criteria for probable or possible Alzheimer's disease they were diagnosed as such. Those that did not fulfil these criteria were then entered into the next stage. Those who had Hachinski scores (Hachinski et al 1975) of seven or more and fulfilled either the DSMIIIIR criteria or the HAS AGECAT criteria for vascular dementia were diagnosed as having the latter condition. Any patient not fulfilling any of these criteria but fulfilling the DSMIIIIR criteria for dementia were considered to have dementia of unknown cause. The diagnostic system is schematised in Figure 5.1.
Figure 5.1  DIAGNOSTIC PROCEDURE

1. Apply DSM III R Criteria for dementia.
   - Patient fulfils criteria.
   - Patient does not fulfil criteria.
     - Excluded from the study.

2. Apply McKeith Criteria.
   - Patient does not fulfil criteria.
   - Patient fulfils criteria.
     - DIAGNOSIS: Senile Dementia of Lewy Body type.

3. Apply NINCDS ADRDA Criteria.
   - Patient does not fulfil criteria.
   - Patient fulfils criteria.
     - DIAGNOSIS: Probable Alzheimer's Disease.
     - DIAGNOSIS: Possible Alzheimer's Disease.

4. Apply Hachinski Scale.
   - Score $\geq 7$
   - Score $< 7$
     - DIAGNOSIS: Dementia unspecified.

5. Apply HAS AGECAT & DSM III R Criteria for Vascular Dementia.
   - Patient fulfils one or both criteria.
     - DIAGNOSIS: Vascular Dementia.
   - Patient does not fulfil either criteria.
     - DIAGNOSIS: Dementia unspecified.
Byrne's et al (1991) criteria for Senile Dementia of Lewy Body type were also applied to the sample. The assessments were completed by the same four raters, but again the diagnostic criteria were all applied by one of the raters (CB). This was undertaken independently of the other diagnostic schema, to allow the concurrent validity with the McKeith et al (1992) criteria to be calculated. All of the diagnostic criteria are shown in Appendix D.

Two of the raters were trained in the use of the GMS/HAS package at a formal training course in the university of Liverpool. With the approval and guidance of Liverpool university a one week training course incorporating formal tuition and the rating of video material was undertaken to train the other two raters. The study design specified that one of the raters (CB) would undertake thirty-five interviews and that each of the other participants would complete thirty. One of the interviewers completed only seven interviews before dropping out of the study. The additional twenty-three interviews were completed by CB. The three interviewers completing their quota each videotaped two interviews, which were rated independently by each of the three major participants to allow an assessment of inter-rater reliability. As the interviewer who completed only seven interviews did not videotape any of the assessments, no formal evaluation of inter-rater reliability was possible. The diagnostic balance of this small group of patients were similar to the remainder of the sample (five Alzheimer's disease, two vascular dementia), and the informal assessment of this rater during the training course was adequate. As the diagnostic criteria were all applied by CB and there were no reasons to suspect that the individual items were not being rated appropriately according to the GMS/HAS handbook, it was felt to be acceptable to include these data in the overall sample.
The Geriatric Mental State Schedule includes an item pertaining to the tendency to confabulate implausibly whilst the History and Aetiology Schedule gives detailed information regarding a wide range of demographic factors. These include the patient’s age, gender, the length of the dementia, the age at the time of onset of the dementia and the number of years of education. It also gives information regarding severe or painful physical health problems, any past history of psychiatric disorder, bereavements within the previous six months, life events within a six month period and whether the dementia sufferer lived alone. Each of these items were rated according to the criteria specified in the GMS/HAS handbook.

The HAS schedule describes four categories of deafness. To be considered as deaf for the current study, a patient had to be "totally deaf", "almost totally deaf" or need conversation to be shouted with most questions repeated at least several times. Section D of the CAMDEX defines visual defects as occurring if patients are unable to see the material in the CAMCOG schedule, or can only see the material with difficulty. The study definition of severe visual impairment included patients in these categories together with patients who were registered blind or partially sighted or had been informed by a doctor that they could be.

Each of the informants was contacted at monthly intervals after the initial assessment for one year. The interviews took place by telephone on months two, four, five, seven, eight, ten and eleven and in person on months one, three, six and nine for the patients in Birmingham and Coventry. All the month one to eleven interviews were completed by
telephone for the Bristol participants. At this time the carers section of the Burns' Psychotic Symptom Checklist was completed together with the informant section of the Cornell Depression Scale. The diagnosis of depression and the identification of psychotic symptoms were undertaken in the same way as described for the initial interviews. Each follow up interview had to be completed within two weeks of the due date to be considered valid. For the whole year of interviews to be considered valid, at least nine of the monthly interviews had to be completed, with no gaps of more than two months between interviews. If one month gaps existed, the diagnosis of depression was considered to be identical to the previous interview. The schedules completed in the various interviews are highlighted in Figure 5.2.

One year after the initial interview, carers and patients were again interviewed at their own homes to complete the patient and informants sections of the Burns' Psychotic Symptoms Checklist and the Cornell Depression Scale regarding the psychiatric morbidity of the patient. During this assessment the cognitive status of the patient was re-evaluated using the CAMCOG schedule. The sub-scores were derived in the same manner as described for the initial assessments. The aim was to complete the one year interviews within two weeks of the due date, although they were considered to be valid if completed within four weeks of the specified day. The follow-up interviews were undertaken by five interviewers, CB who had also undertaken initial assessments and four interviewers who had not been involved in the baseline assessments. Each of the interviewers participated in the same training course as those involved in the baseline part of the study.
### Figure 5.2

**Timing and Details of the Interviews**

<table>
<thead>
<tr>
<th>Interview</th>
<th>Schedules completed</th>
</tr>
</thead>
</table>
| Baseline interview | GMS/HAS/Secondary dementia Schedule  
                  | CAMCOG  
                  | Burns Symptom Checklist  
                  | Cornell Depression Scale  
                  | Carers Stress Scale       |
| Follow up interviews month 1 - month 11 | Burns Symptom Checklist  
                                          | Cornell Depression Scale       |
| Follow up interviews Month 12 | Burns Symptom Checklist  
                              | Cornell Depression Scale  
                              | CAMCOG                     |
Statistical Analysis

Statistical evaluations were undertaken using the SPSS Windows package (SPSS 1988).

Demographic Characteristics

The gender balance and the number of people living alone were compared between the three service settings using odds ratios with 95% confidence intervals. Age and the CAMCOG scores were compared between the different services using the Mann-Whitney U test. The diagnoses of dementia were compared using the Chi² test.

Symptom Characteristics

Associations between insight and distress respectively and the number and frequency of psychotic symptoms were examined using the Kruskal-Wallis test. Associations between the type of psychotic symptoms and distress and insight were investigated using Spearman's rank correlation. The relationship between delusions, visual hallucinations and delusional misidentification respectively and insight and distress were calculated using Pearson's R. The number of patients with and without delusions, visual hallucinations and delusional misidentification were compared between the diagnostic categories of Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type using odds ratios with 95% confidence intervals. The number and frequency of psychotic symptoms were compared between the different dementias using the Mann-Whitney U test. The link between the type of dementia and the type of psychotic symptoms was examined using Spearman's rank correlation. The symptom profiles of RDC major and minor depression were also compared using this method, as were the symptom profiles of depressive symptoms in patients with the three different dementias. The number of patients with and without RDC major depression were compared between the memory clinic and the psychiatric services using the Chi² test. Odds ratios
with 95% confidence intervals were used to compare the number of patients with and without RDC major depression between patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type respectively.

**Associations**

The variables: deafness, severe visual impairment, the type of dementia, physical health problems, gender, age, tendency to confabulate, number of years of education, duration of the dementia in months, the age of onset of the dementia, a past history of psychiatric disorder, bereavement within the last six months, experiencing a life event within the last six months and living alone were entered as the independent variables into a logistic regression analysis using a stepwise technique. The mixture of categorical and continuous variables necessitated a logistic technique. These analyses were undertaken with psychotic symptoms in general, delusions, visual hallucinations and delusional misidentification respectively as the dependant variables. Descriptive data is given for each of the studied variables. The same statistical analysis and the same variables were used to evaluate each category of psychotic symptoms in patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type if there were at least fifteen patients with and without the symptom in question. If the numbers were between five and fifteen, the comparisons were made using odds ratios with 95% confidence intervals, Fisher's exact test or the Mann-Whitney U test depending on the nature of the individual variables. Groups including less than five people were considered too small for statistical analysis.

The same statistical techniques were also utilised to evaluate insight, gender, age at the onset of the dementia, physical health problems, bereavement, life events, deafness,
severe visual impairment, years of education, a past history of psychiatric disorder, living alone and the type of dementia as associations of DSMIIIIR major depression, RDC major and RDC minor depression respectively, in the overall sample and in patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type separately. Descriptive information is given for each of the studied variables. The same study criteria were applied regarding group sizes. The same analyses were again used to look at associations between depression and psychotic symptoms respectively and the pattern of sub-scale scores on the CAMCOG schedule. A linear regression would not have been appropriate given the skewed distribution of CAMCOG scores. The evaluations were again undertaken examine the associations for the whole sample, patients with Alzheimer's disease, patients with vascular dementia and those with Senile Dementia of Lewy Body Type. Descriptive information is provided regarding the studied variables. The same rules were applied regarding group sizes, although if group sizes were between five and fifteen, the total CAMCOG scores were compared using the Mann-Whitney U test but no comparisons of the sub-scores were undertaken. The number of patients scoring within the twenty-one to forty range were compared between those with and those without psychotic symptoms using the Chi² test. In view of the potential overlap between age, age of onset, visual impairment and deafness, the correlation between these variables was assessed using Pearson’s R.

Symptom Groups

Potential sub-groupings of psychotic symptoms and depression were derived using the principal components analysis programme of the SPSS package. Only psychotic symptoms which occurred in at least five patients were included in the analysis, but individual patients only needed to experience one or more of these symptoms. Two, three, four and
five factor solutions were studied. For depression, one, two, three and four factor solutions were examined. The analysis was conducted looking at the whole sample and separately focusing upon patients with RDC major or minor depression. In order for a symptom to be recognised as part of a depression or psychosis factor it was decided that it should have a correlation of at least +0.6 with that factor and no correlations of greater than +0.6 with any of the other factors (Forsell et al 1993). The final solution of both the analyses used a varimax rotation. The most satisfactory factor solution for psychotic symptoms was chosen and patients allocated to the most appropriate factor, which was termed a symptom group. To belong to a specific symptom group a patient had to experience only symptoms from that group, experience more symptoms from that group or experience an equal number of symptoms from two groups, but to have one group of symptoms more frequently. The symptom characteristics insight and emotional distress were compared between the different groups using Pearson's R.

The same criteria were used to assign symptoms to each "depression factor". Patients were then allocated to a depression symptom group based on the symptoms associated with each of the factors. To be considered as part of a symptom group, patients had to experience at least two symptoms from the group of symptoms associated with the corresponding factor and to either have more symptoms from that symptom group than any other or to have an equal number of symptoms from two different symptom groups, but to have one group of symptoms more severely. The depression symptom groups were evaluated using the same statistical techniques and the same variables used to look at major and minor depression, using the same study criteria for group sizes.
Follow-Up Data

The differences in total CAMCOG scores between the initial assessment and the one-year assessment were compared between patients with and without psychotic symptoms overall, visual hallucinations, delusions and delusional misidentification using the Mann-Whitney U test. These comparisons were also undertaken separately for patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body Type. Comparisons were only undertaken when there were at least five patients with and five patients without the category of symptom being studied. Pearson's correlation coefficients were calculated to assess the correlation between the number of months during which psychotic symptoms (or the relevant sub-category - delusions, visual hallucinations and delusional misidentification) were experienced and the deterioration on the CAMCOG score.

A range of descriptive data is reported including the baseline distribution of Cornell Depression Scale scores and the prevalence rates and incidence rates of major depression, minor depression and psychotic symptoms. The latter is considered in the categories of delusions, visual hallucinations, delusional misidentification (with and without phantom boarder delusions), comfort phenomenon and individual symptoms. The prevalence rates reported for depression and psychotic symptoms are one month prevalence rates at the time of the initial assessment. Annual incidence rates are reported for both phenomena. The annual resolution rates of major and minor depression and each category of psychotic symptom are described. If a patient with depression or psychotic symptoms did not fulfil the study criteria for the respective disorder for three consecutive months, they were considered to have recovered. For each
category of depression and psychotic symptoms the proportion of recovered patients who subsequently relapsed is reported.

Figures are used to illustrate the number of months during which each category of psychotic symptom was experienced. Patients with unresolved psychotic symptoms, in each of the categories of symptom, were compared to those who had experienced the symptoms for at least one month but no more than three months. The variables analyzed were deafness, severe visual impairment, a duration of psychotic symptoms of three months or more at the baseline interview, a frequency of psychotic symptoms of at least daily at the baseline interview, three or more different psychotic symptoms at the baseline interview, age at the time of onset of the dementia and the baseline CAMCOG score. Fisher's exact test or the Mann-Whitney U test were used to make the comparisons depending on the individual variables.

The number of months of depression experienced by patients in each diagnostic group is described. The correlations between the number of months of RDC major or minor depression experienced and each of the variables considered as potential associations of depression (with the exception of life events, excluded because of small numbers) is reported using Pearson's R. The likelihood of patients with RDC major depression at baseline experiencing three months or more of depression were compared between patients with Alzheimer's disease, vascular dementia and Senile Dementia of Lewy Body type using Fisher's exact test.
Concurrent Validity And Inter-Rater Reliability

The correlation between the DSMIIIIR and RDC criteria for major depression and the correlation between the McKeith criteria and the Byrne criteria for Senile Dementia of Lewy Body Type are reported using the Kappa Statistic. The diagnostic agreement between the GMSHAS videotaped interviews is described for the HAS-AGECAT diagnoses. CB applied the study criteria to each of these schedules and the diagnostic agreement is described.

The concurrent validity between the recommended cut-off score of ten on the Cornell Depression Scale and an RDC diagnosis of major depression was calculated using the Kappa statistic. The same method was used to compare the agreement between the baseline and month one interviews and the month one and month two interviews for the RDC diagnoses of depression (no depression, minor depression, major depression) and for the presence of psychotic symptoms overall, delusions, visual hallucinations and delusional misidentification (inclusive and exclusive of the phantom border syndrome).
(a) Psychotic Symptoms: The BEHAV AD (Reisberg et al 1987) is a standardised scale for the assessment of psychotic symptoms in dementia sufferers which rates six specific delusional items including stealing, believing that one's house is not one's own home, believing one's spouse to be an impostor, delusions of abandonment, delusions of infidelity and suspiciousness/paranoia as well as a seventh category for "other delusions". Many of the common delusional beliefs in subjects with dementia are omitted. In addition for certain items, particularly the belief that one's house is not one's home, the difference between a delusional belief and difficulties with recognition are not clearly made. Devanand et al (1992) reported a further scale, the CUSPAD, which contains three delusional items, four items reporting delusional misidentification and five items reporting hallucinations. This scale covers a broader range of psychotic symptoms common in Alzheimer's Disease, although still omits some important symptoms. It has good back to back inter-rater reliability and represents an important advance. Förstl et al (1993) have also used a standardised schedule, although it has not yet been formally described. The CUSPAD is undoubtedly the best instrument in current use, although it does omit some important symptoms and no information is gathered pertaining to the characteristics of symptoms, such as whether they cause distress to the patient or whether the patient has any insight into the abnormal nature of a particular symptoms. As one of the main aims of the current study is to describe in detail these symptom characteristics, it was necessary to devise a more detailed scale incorporating these features.
The Burns' Symptom checklist is a specially devised instrument to examine the prevalence rate of psychotic symptoms together with the degree of insight and distress. It comprises of sixteen questions pertaining to psychotic symptoms with several specific prompts allowing the questions to cover a broad spectrum of different symptoms in the categories of delusions, hallucinations and delusional misidentification. The same questions were asked to both patients and informants. In the presence of psychotic symptoms, unpleasant emotion was rated on a three point scale from zero representing no distress, to two representing marked distress. Insight was measured on a four point scale with zero representing no insight and patients acting on their symptoms, one representing no insight but patients not acting on their symptoms, two representing partial insight and three representing complete insight. The frequency of symptoms was described on a five point scale where one represented a frequency of between once and three times a month, two represented a frequency of weekly, three a frequency of twice to six times a week, four daily and five twice or more a day. The instrument was entitled "The Burns' Symptom Checklist" as many of the symptoms came from Burns' et al (1990a) description. The questions included in the schedule are shown in Appendix A.

al 1990), the Zung Depression Scale (Gottlieb et al 1988, Knesevich et al 1983), the Montgomery Asperg Depression Rating Scale (Nyth & Gottfries 1990) and the Cornell Depression Scale (Patterson et al 1990). Few validation studies have however been undertaken. Lichtenberg et al (1992) studied thirty in-patients looking at the ability of the Hamilton Rating Scale for depression (using a cut-off of seventeen) and the Geriatric Depression Scale (using a cut-off of ten) to identify cases of DSMIIIIR depression. The Hamilton Rating Scale was only able to identify one out of seventeen cases, whereas the Geriatric Depression Scale identified nine out of eleven with only one false positive. Lazarus et al (1987), in a research sample of forty-four patients, found the Hamilton Rating Scale to have an inter-rater reliability of 0.68. Although performing well in Lichtenberg et al's (1992) study the Geriatric Depression Scale has not performed as well in other samples. Burke et al (1989) did not find any cut-offs on the Geriatric Depression Scale which had better than 65% sensitivity or specificity amongst seventy patients with dementia. Kafonek et al (1989) only found the Geriatric Depression Scale to have a sensitivity of 47% and this was reduced to 25% in those with Mini Mental State Examination scores under twenty-three. The specificity was 75%. Other depression scales examined include the Sandoz Scale which was found to have an inter-rater reliability of 0.92 by Lazarus et al (1987).

Sunderland et al (1988) studied a research sample of twenty-one patients, all of whom had major depression. A specially devised scale, the Dementia Mood Assessment Scale was used and found to have an inter-rater reliability of 0.74 and a modest correlation of 0.47 with the Hamilton Rating Scale For Depression. The seventeen mood items were derived largely from the Hamilton Rating Scale for Depression and were scored on a six
point scale based on the patients' responses and the clinicians' observations. All of the patients had depression, precluding an analysis of sensitivity and specificity. The scale needs further validation. Alexopoulos et al (1988) utilised a nineteen item specifically designed schedule entitled the Cornell Depression Scale. In a sample of eighty-three research subjects with dementia this was found to have an inter-rater reliability of 0.63. The internal consistency of the items measured with the Alpha co-efficient was 0.79 and there was a significant positive correlation between the Cornell scores and the rank order of RDC diagnoses (major depression, minor depression, no depression). There was also a significant difference between the scores of patients who qualified for a diagnosis of RDC depression and those who did not. Sensitivity and specificity figures were however not given. Although these results are encouraging, further validation is required. The nineteen items cover a spectrum of symptoms in the categories mood related signs, behavioural disturbance, physical signs, cyclical functions and ideational disturbance.

The majority of studies have specified that both patient and carer information as well as observational data were used in order to complete the depression rating scales. Most scales designed for other groups of patients have however not been validated using this type of methodology. Further doubts must be cast upon this method of assessment in view of the limited description of rules for making a consensus judgement about each symptom. Several studies (Burns et al 1990c, Teri & Wagner 1991, Ott & Fogel 1992) have commented upon the differences in patient, carer and clinician perception of depression. The Cornell Depression Scale (Alexopoulos et al 1988) does have the advantage of more operationalised rules. The symptoms are reported separately by the patients and the carers and where any discrepancy exists the clinician uses their own
judgement as to which is more accurate. Ballard et al (1991a) found that although there
was poor agreement between patients and carers concerning the presence of depressive
symptoms, when patients did report symptoms as present, they were likely to be correct.
Hopefully more work concerning the factors which influence the accuracy of patients and
carers reports will help refine a set of rules which can be used for making these
decisions.

The diagnosis of depression is also a difficult area. The vast majority of studies have used
either DSMIII or DSMIIIR criteria. A smaller number of studies have used either the
Research Diagnostic Criteria or cut-off scores on rating scales. Although there is no
major discrepancy between the small number of studies using other criteria and those
using the DSMIII or DSMIIIR in the reported prevalence rate of depression, there is
a need for work which comprehensively compares different diagnostic criteria. The
Cornell Depression Scale is the best instrument currently available for the assessment of
depression in dementia sufferers. Sufficient information is recorded to allow DSMIIIR
and RDC criteria to be applied, which has the advantage of allowing comparison with
other studies, as well as facilitating the characterisation of a group of patients with milder
depressive disorders.

c) Cognitive Assessment: Probably the most widely used instrument for cognitive
assessment amongst patients with dementia is the Mini Mental State Examination
(Folstein et al 1975). This scale is however very brief and does not include sufficient
detail to be able to accurately assess important aspects of global cognitive functioning;
for example, abstract thinking and verbal fluency are not assessed. The Cambridge
Mental Disorders in the elderly (CAMDEX) schedule (Roth et al. 1986) includes a section entitled the CAMCOG. In the original validation study, the CAMCOG was well tolerated by subjects with dementia and attained excellent inter-rater reliability scores with phi coefficients of 0.90. The scale includes items from a number of schedules including the Clinical Dementia Rating Scale (Hughes et al. 1982), the Global Deterioration Scale (Reisberg et al. 1982) and the Mini Mental State Examination (Folstein et al. 1975). It is scored out of a total of one hundred and six points. In Roth's et al. (1986) validation study the optimal cut-off was between seventy-nine and eighty. This achieved a sensitivity of 92% and a specificity of 96% with a diagnosis of dementia.

A further study with the CAMCOG (Blessed et al. 1991) in a series of more than two hundred patients showed a similarly good sensitivity and specificity of 97% and 91% respectively. The optimal cut-off in this study was however sixty-nine to seventy, using the AGECAT (Copeland et al. 1976) to identify organic disorder. The study also examined the optimal sensitivity and specificity figures for a number of shorter cognitive assessment instruments, none of which approached the performance of the CAMCOG. The Mini Mental State Examination had a 100% sensitivity using a cut-off of twenty-three to twenty-four, but with this cut-off achieved a specificity of only 77%. The CAMCOG schedule hence performs better than the shorter rating scales and achieves excellent sensitivity and specificity figures. The two main validation studies have however identified discrepant cut-off points, which produces a dilemma. For the purposes of the current study, where one of the objectives of the CAMCOG was to provide confirmation of impaired performance on a standardised test of cognitive function to fulfil part of the NINCDS-ADRDA criteria for probable Alzheimer's disease (McKhann et al. 1984), the cut-off of seventy-nine to eighty was chosen. As the study criteria also specified that the
DSMIIIR (American Psychiatric Association 1987) criteria for dementia had to be fulfilled, the number of false positive cases should be few.

A further issue pertains to the use of CAMCOG subscales. One of the aims of the present study was to examine associations of psychotic symptoms with different patterns of cognitive deficit, it was therefore particularly important to break down the cognitive functions into meaningful groups. Studies which have used the CAMCOG in this way have varied in their choice of subscale items. O'Connor et al (1989) looked at the subscales orientation and memory, whereas Burns et al (1990c) used the items: memory, language and praxis. The constituents of the scales varied between the two studies with Burns et al (1990c) scoring memory out of twenty-seven and O'Connor et al (1989) out of thirty-three. Blessed et al (1991) used a large number of subscales including orientation, memory, language, praxis, perception and abstraction. Whilst some of the scales such as perception (which measures agnosia), abstraction and praxis measure separate cognitive functions, other items such as language do not. This latter item encompasses expressive and receptive language functions as well as verbal fluency. Clearly each of these has a separate regional affiliation and it makes little sense to group them together as one entity. In order to address some of these difficulties Hooper & Bucks (1993) have reformulated the CAMCOG into the subscales orientation, language comprehension, language expression, praxis, recent memory, visual memory, remote memory, attention and calculation, perception, abstract thinking and verbal fluency. The authors have configured a graph of maximum scores and scores which would cause concern on each of the sub-sections based upon their own clinical data. The scales have not however been formally validated. Whilst this would have been preferable, the
traditional CAMCOG subscales clearly do not measure independent cognitive functions. It was therefore decided to use the Hooper & Bucks (1993) configuration of subscales in the current study. The items included in each of these subscales are shown in Appendix C.

d) Information Collection: The two most widely used instruments for the standardised collection of information regarding elderly patients with cognitive impairment have been the CAMDEX (Roth et al 1986) and the Geriatric Mental State Schedule (Copeland et al 1976). The CAMDEX has been correctly criticised for a paucity of information regarding the non cognitive symptoms of dementia (Burns et al 1990c), although as discussed earlier the cognitive assessment included within the schedule has achieved excellent sensitivity and specificity in validation studies. The Geriatric Mental State Schedule is linked to a diagnostic system, the AGECAT (Copeland et al 1986, Dewey & Copeland 1986). This package is however only able to make diagnosis of organic disorder for patients with cognitive impairment. It does not distinguish between dementia and delirium or between any of the subtypes of dementia. More recently, the History And Aetiology Schedule has been added to the package. This schedule is completed by an interview with an informant and collects detailed information regarding the history and aetiology of the illness. Sections pertaining to living conditions, history of the present illness, past similar illnesses, symptoms of the onset of the present illness compared to the present state, past psychiatric and neurological history, general medical and surgical history, family history of psychiatric illness, life events, specific organic symptoms and their history, past educational and occupational history, medication, physical health, alcohol consumption and confidence in the data are included. The information collected
from the Geriatric Mental State Schedule and the History and Aetiology Schedule together with information from a further scale called the Secondary Dementia Schedule (which includes a physical examination and details of a full blood screen), can be used to obtain diagnoses from a new computer algorithm, the HAS AGECAT. Data from the HAS AGECAT diagnostic package has only been reported in one provisional study (Dewey et al 1992). Good agreement with expert clinical diagnoses was achieved, with Kappa values of 0.76, however this has to be considered as a provisional validation study. In particular there were only a small number of cases with vascular dementia included in the study, hence little information was available regarding the ability of the package to distinguish between patients with Alzheimer's disease and vascular dementia. The History and Aetiology Schedule does however include each of the items from the Hachinski Scale (Hachinski et al 1975) and sufficient information for each of the major sets of diagnostic criteria to be applied.

The NINCDS ADRDA criteria for probable Alzheimer's disease (McKhann et al 1984) have been validated in a series of post-mortem studies, achieving a positive predictive value of more than 80% in most studies (Martin et al 1987, Morris et al 1987, Tierney et al 1988, Boller et al 1989, Jellinger et al 1989, Burns et al 1990b, Kukull et al 1990). The criteria for possible Alzheimer's disease (McKhann et al 1984) have also been validated against post-mortem diagnosis achieving a positive predictive value of 77% (Burns et al 1990b). There is no doubt that the NINCDS ADRDA criteria are the best clinical criteria currently available for the diagnosis of Alzheimer's disease. There are far fewer validation studies available concerning the diagnosis of vascular dementia (Chui et al 1992). Although much criticised, the Hachinski Scale (Hachinski et al 1975) has
been the most widely used diagnostic instrument for this purpose. Many of the items focus upon cerebral infarcts, consequently vascular dementia arising from other vascular causes such as hypoxia may be missed (Chui et al 1989). Good discrimination between Alzheimer's disease and vascular dementia has however been achieved, with a sensitivity and specificity of between 70% and 80% (Rosen et al 1980, Loeb & Gandolfo 1983, Small 1985). The criteria are less successful in distinguishing cases of vascular dementia from mixed cases of vascular dementia and Alzheimer's disease where sensitivities and specificities in the region of 15% to 20% have been reported (Katzman et al 1988). Patients with mixed dementia are likely to be diagnosed as having vascular dementia. Furthermore, patients with "mixed dementia" account for up to 20% of post-mortem cases with vascular dementia (Chui et al 1992). Although the Hachinski Scale clearly has its limitations, it is the best validated scale for the diagnosis of vascular dementia and has been used widely. It does however have to be accepted that the category identified will include both patients with pure vascular dementia and those with mixed vascular dementia and Alzheimer's disease. In the current study an additional specification was made that patients should fulfil either the DSMIIIIR or the HAS/AGECAT criteria for vascular dementia. This should increase the specificity of the diagnosis.

There are no prospectively validated criteria for the diagnosis of Senile Dementia of Lewy Body Type. McKeith et al (1992) reported a retrospective positive predictive value of 80% for the criteria derived from that study. Byrne et al (1991) have also suggested criteria for the diagnosis of probable or possible Dementia of Lewy Body Type. These criteria focus upon dementia associated with Parkinson's disease and similarly to the McKeith et al (1992) criteria have not been prospectively validated. The current study
utilises the McKeith et al (1992) criteria but reports the concurrent validity with Byrne’s et al (1991) criteria. Although the use of criteria which have not been prospectively validated is not ideal, Senile Dementia of Lewy Body Type probably accounts for more than 10% of dementia cases in contact with clinical services (Ballard et al 1993a, Shergill et al 1994) and is a major source of mis-diagnosis when applying the NINCDS ADRDA criteria (Burns et al 1990b). In the current study Senile Dementia of Lewy Body Type is referred to as a discrete diagnostic entity. This is a controversial issue given the occurrence of Alzheimer’s disease pathology in the majority of cases (Hansen et al 1990), although it appears warranted given the distinct symptom profile (McKeith et al 1992).

Deciding the best method for applying the diagnostic criteria also creates a dilemma. None of the major diagnostic systems include the category Senile Dementia of Lewy Body Type. In order to apply the criteria for Senile Dementia of Lewy Body Type, Alzheimer’s disease and vascular dementia it is therefore necessary to decide an order of application. As patients with Senile Dementia of Lewy Body type have frequently been included in studies applying the NINCDS ADRDA criteria of Alzheimer’s disease, it was felt that it would be appropriate to first apply the McKeith et al (1992) criteria to reduce diagnostic confusion. In addition, many of the cases of Senile Dementia of Lewy Body Type would have met the NINCDS ADRDA criteria for possible Alzheimer’s disease and could not have been studied as a separate group in a hierarchical model unless applied first. The NINCDS ADRDA criteria (McKhann et al 1984) were applied second, followed by the criteria for vascular dementia. A residual category was created for patients who fulfilled the DSMIIIIR (American Psychiatric Association 1987) criteria for dementia but did not fulfil any of the other criteria specified.
CHAPTER 7

METHOD - RELIABILITY

Three of the interviewers, who between them completed one hundred and seventeen of the diagnostic assessments, each video recorded two of their GMS/HAS interviews. According to the HAS AGECAT diagnostic programme each of the patients were assigned to the category of vascular dementia from the interviews of all three raters, achieving perfect inter-rater reliability. When CB applied the study diagnostic system to the interviews, two of the interviews resulted in diagnoses of Alzheimer's disease for patients A and C and diagnoses of vascular dementia for the other four patients. These were identical to the diagnoses assigned to the patients during the study. The third rater's interviews led to the same diagnoses as the interviews of the other two raters for patients B, C, D, E and F but resulted in a diagnosis of vascular dementia for patient A.

Twelve patients fulfilled the McKeith et al (1992) criteria for Senile Dementia of Lewy Body Type. Six of these patients fulfilled Byrne's et al (1991) criteria for Probable Lewy Body Dementia, whilst a further four were diagnosed as having Possible Lewy Body Dementia according to these criteria. Two patients did not fulfil the criteria for either category. A further six patients who did not fulfil the McKeith et al (1992) criteria were diagnosed as having Possible Lewy Body Dementia according to the Byrne et al (1991) criteria. The Kappa value for the correlation between Possible or Probable Lewy Body Dementia and Senile Dementia of Lewy Body Type was 0.68. The concurrent validity between the two sets of criteria was adequate. Although this is reassuring, neither set of criteria has been prospectively validated and the relationship between the type of patients identified by the different criteria is not entirely clear.
There was good concurrent validity between the Cornell Depression Scale, using the recommended cut-off score of ten or more, and the RDC criteria for major depression. Twenty seven of the thirty-three patients scoring above the cut-off were diagnosed as having RDC major depression (specificity 81.8%), whilst only four of the thirty-one patients diagnosed as having RDC major depression had a score below the cut-off (sensitivity 87.1%).

The Kappa value for the correlation between the presence of psychotic symptoms during the baseline interview and during the month one interview was +0.81 and the Kappa value for the agreement between the presence of psychotic symptoms during the month one and the month two interviews was +0.75. The Kappa values for the agreement between the individual categories of psychotic symptoms were also within acceptable limits (delusional misidentification at baseline versus month one, Kappa = +0.66; delusional misidentification month one versus month two, Kappa = +0.82; visual hallucinations at baseline versus month one, Kappa = +0.58; visual hallucinations month one versus month two, Kappa = +0.83; delusions at baseline versus month one, Kappa = +0.76; delusions at month one versus month two, Kappa = +0.75).

The Kappa values for the agreement between the diagnosis of depression at the baseline interview compared to month one, and month one compared to month two interviews were satisfactory. The Kappa values for agreement between the baseline and month one interviews and between month one and month two interviews were similar (RDC depression, baseline interview versus month one, Kappa = +0.51; RDC depression, month one versus month two, Kappa = +0.54).
CHAPTER 8
RESULTS - DEMOGRAPHIC DATA

Ninety point four percent of patients approached agreed to participate in the study. Of the one hundred and twenty-five participants, one hundred and twenty-four fulfilled the DSM III-R criteria for dementia. The youngest patient was sixty-six and the oldest ninety-one. The mean age was 79.94 with a standard deviation of 5.87. Eighty one (65.3%) of the patients were female and 33 (26.6%) were male. The average age of female patients was 80.60 (standard deviation 5.92) and the average age of male patients was 78.12 (standard deviation 5.53). The age distribution in five year age bands for the whole sample is shown in Figure 8.1.

Eighty three (66.9%) were in contact with outpatient services, thirty-nine (31.5%) were in contact with day patient facilities and two (1.6%) were undergoing an assessment in an inpatient facility. This is displayed diagrammatically in Figure 8.2.

Sixty two of the patients were living at home accompanied by a family member or friend. Forty seven were living with a marital partner, ten with a daughter, one with a son, one with a sibling and three with a friend. A further forty-seven patients were living alone supported by a family member or friend, whilst nine were living alone supported by professional carers. Six of the patients were living in residential or nursing home facilities. The living arrangements are illustrated in Figure 8.3.
Fifty five (44.4%) of the patients received a diagnosis of probable Alzheimer's disease, thirty-three (26.6%) received a diagnosis of possible Alzheimer's disease, twenty (16.1%) had a diagnosis of vascular dementia and twelve (9.7%) received a diagnosis of Senile Dementia of Lewy Body Type. Four patients fulfilled the DSM IIIR criteria for dementia but did not fulfill the study criteria for any of the aforementioned categories. These were diagnosed as having dementia unspecified. The diagnostic breakdown is displayed in Figure 8.4.

The median length of illness was between twenty-four and thirty-six months. Twelve patients had a duration of dementia less than a year whilst ten patients had been suffering from dementia for more than six years. The distribution is shown in more detail in Figure 8.5.
Figure 8.1

Age Distribution

Number of Patients

AGE (years)

65-69
70-74
75-79
80-85
86-89
90-94

Number of Patients

0
10
20
30
40
50

4
22
28
45
16
9
Contact with Services  
(n = 124)

- In-patients: 1.6%
- Day Patients: 31.5%
- Out-patients: 66.9%
Figure 8.3

Living Arrangements (n = 124)

- 37.9%
- 8.9%
- 7.3%
- 4.8%
- 2.4%
- 0.8%
- 0.4%

Legend:
- With marital partner
- With son or daughter
- Living with friend
- Residential or Nursing Home care
- Living with sibling
- Alone, with professional support
- Alone, with family support

Total: 100%
Figure 8.4

Diagnoses (n = 124)

- 44.4% Possible Alzheimer's disease
- 26.6% Vascular Dementia
- 16.1% Senile Dementia of Lewy Body type
- 9.7% Dementia unspecified
- 3.2% Other
Length of Illness

Figure 8.5
Seventy-nine of the patients were in contact with old age psychiatry services at the Queen Elizabeth Psychiatric Hospital in Birmingham, twenty were in contact with old age psychiatry services in Coventry and twenty-five were in contact with a memory clinic in Bristol. The gender mix of the patients in the three service settings was similar (memory clinic vs Birmingham: odds ratio 1.30, 95% confidence intervals 0.46, 3.67; memory clinic vs Coventry: odds ratio 0.75, 95% confidence intervals 0.18, 3.10; Birmingham vs Coventry: odds ratio 0.61, 95% confidence intervals 0.18, 2.01).

There were no significant differences in the likelihood of dementia sufferers living alone in the different service settings (memory clinic vs Birmingham: odds ratio 0.51, 95% confidence intervals 0.19, 1.40; memory clinic vs Coventry: odds ratio 0.48, 95% confidence intervals 0.14, 1.65; Birmingham vs Coventry: odds ratio 0.92, 95% confidence intervals 0.34, 2.48), although only 28% of the patients in contact with the memory clinic were living alone, compared to approximately 45% of patients in contact with both of the psychiatric services.

The age distribution of patients in the three settings was also similar (memory clinic vs Birmingham: Mann-Whitney U test, $u = 356, z = -1.00, p = 0.32$; memory clinic vs Coventry: Mann-Whitney U test, $u = 216, z = -0.78, p = 0.44$; Birmingham vs Coventry: Mann-Whitney U test, $u = 762.5, z = -0.24, p = 0.81$) but the patients in contact with the memory clinic (Mann-Whitney U test, $u = 147, z = -2.35, p = 0.02$) and those in contact with psychiatric services in Birmingham (Mann-Whitney U test, $u = 382.5, z = -3.55, p = 0.0004$) had significantly higher CAMCOG scores than patients in contact with
the Coventry service. There was no significant difference between the CAMCOG scores of patients in contact with the Birmingham and Bristol services (Mann-Whitney U test, $u = 803, z = -1.40, p = 0.16$) and there were no significant differences in the pattern of diagnoses in the three services ($\chi^2 3.42, 10$df, ns), although there were a lower proportion of patients with Alzheimer's disease in contact with the memory clinic. Details are given in Table 8.1.
<table>
<thead>
<tr>
<th>(%)</th>
<th>(%)</th>
<th>(%)</th>
<th>0 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 (10%)</td>
<td>1</td>
<td>4 (16%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>12 (15.2%)</td>
<td>6 (24%)</td>
<td>15 (60%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>27 (32.2%)</td>
<td>45 (57.8%)</td>
<td>90 (60%)</td>
<td>60 (40%)</td>
</tr>
</tbody>
</table>

**Type of Dementia**

- Vascular Dementia
- Alzheimer's Disease
- Lewy Body Dystonia
- Severe Dementia of Uncertain Type

**Mean CAMCOG Scores**

<table>
<thead>
<tr>
<th>29.9 (SD 11.9)</th>
<th>41.96 (SD 18.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.1 (SD 17.7)</td>
<td>41.96 (SD 18.2)</td>
</tr>
</tbody>
</table>

**Moments of Care**

- Arrangements
- Living
- Balance
- Medication

**Demographic Features of Patients in Contact With the Different Services**

**Table 8.1**
Eighty nine of the one hundred and twenty-four participants with dementia completed the one year follow-up period, whilst thirty-five did not. Twenty one of the patients died, four moved to different areas of the country and five dropped out of the study or withdrew consent. There were too many months of missing follow-up data for a further five patients to be included.

Of those who did complete the follow-up section of the study, eighteen patients had one missing month of follow-up and twenty patients had two months missing. The follow-up data for two patients were adequate to fulfil the study criteria concerning depression, but there were too many missing months of follow-up pertaining to psychosis. Fifty five (61.8%) of the eighty-nine patients completing the follow-up period were in contact with psychiatric services in Birmingham, fourteen (15.7%) were in contact with psychiatric services in Coventry and twenty (22.5%) were in contact with the Memory Clinic in Bristol. Sixty six (74.2%) of the patients were female and twenty-three (25.8%) male. Their mean age at the start of the study was 79.65 years. The mean baseline CAMCOG score for this group of patients was 46.16 with a standard deviation of 19.23. Sixty-three (70.8%) of the patients had Alzheimer's disease, fifteen (16.9%) had vascular dementia, nine (10.1%) had Senile Dementia of Lewy Body Type and two (2.2%) had dementia unspecified. The demographic characteristics of the patients completing the follow-up period were hence similar to those of the overall sample.
CHAPTER 9

RESULTS - PREVALENCE AND PHENOMENOLOGY OF PSYCHOTIC SYMPTOMS

Eighty-three of the one hundred and twenty-four patients (66.9%) had at least one psychotic symptom. This included sixteen of the twenty-five patients (64.0%) from the memory clinic, fifty-four of the seventy-nine patients from the old age psychiatry services in Birmingham (60.7%) and thirteen of the twenty patients in contact with old age psychiatry services in Coventry (65%). A more detailed breakdown of the psychotic symptoms experienced by patients in the three settings is given in Table 9.1. Forty four (35.5%) of the patients had at least one type of visual hallucination and sixty (48.4%) had at least one different type of delusional belief. The constituents of delusional misidentification have varied from study to study. If the category is considered to constitute mirror image misidentifications, t.v. and photograph misidentifications, Capgras syndrome, Fregoli syndrome, delusional misidentification of one's house and delusional misidentification of objects, eighteen patients (14.5%) had at least one of these symptoms. When the phantom boarder delusion was also included the number of patients rose to thirty-six (29.0%).

The most common symptoms were delusions of reference, delusions of theft, the phantom boarder syndrome, visual hallucinations of strangers and delusions of persecution which all occurred in approximately 20% of subjects. One patient exhibited a Fregoli delusion and one exhibited a delusion of partition (i.e., the belief that one is being influenced by supernatural means through boundaries such as walls or windows), neither of which has been previously described in dementia subjects. The full list of symptoms experienced together with their frequency are described in Figure 9.1.
Overall twenty-six subjects had one different psychotic symptom and twenty-five had two symptoms, whilst thirty-two had more than two. This is shown graphically in Figure 9.2 and demonstrates a descending linear distribution. The frequency of psychotic symptoms experienced by each individual is shown graphically in Figure 9.3. This approximated a normal distribution with a significant minority of subjects having symptoms either less than four times a month or multiple times each day and the majority experiencing symptoms between weekly and daily. There was a significant positive correlation between the number and frequency of symptoms (Spearman's $r = +0.60$, $p < 0.0001$).
<table>
<thead>
<tr>
<th></th>
<th>8 (40%)</th>
<th>8 (72%)</th>
<th>7 (28%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Hallucinations</td>
<td>1 (69.2%)</td>
<td>12 (48.8%)</td>
<td>16 (64.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delusional</td>
<td>6 (76.0%)</td>
<td>31 (79.2%)</td>
<td>43 (87.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delusional</td>
<td>8 (42.5%)</td>
<td>3 (15.8%)</td>
<td>4 (20.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>13 (65.0%)</td>
<td>54 (68.4%)</td>
<td>74 (79.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Psychiatric Symptoms in the Different Service Settings

**Table 9.1**
Symptoms occurring in patient - delusion of partition, delusion of speech, delusion of reference, auditory hallucination, delusion of sexual intercourse, visual hallucination of a relative, Fregoli syndrome, mania, delusion of being a clone, delusion of being an invisible person. 

Figure 9.1: % Prevalence for whole sample displayed
Frequency of Symptoms

- Greater than 2 per day
- Daily
- 2-6 per week
- Weekly
- 1-3 per month
- 0

Number of People

- 0
- 5
- 10
- 15
- 20
- 25
- 30

Frequency of Symptoms

Figure 9.3
Twenty-four patients had no insight into their psychotic symptoms and acted upon them, forty-three had no insight but did not act upon their symptoms, fifteen had partial insight and only one patient had full insight into their symptoms. There was a significant positive correlation between the symptom profiles of those with differing degrees of insight (0 versus 1 Spearman's $R = +0.65$ $p < 0.001$, 0 versus 2 Spearman's $R = +0.63$ $p < 0.001$, 1 versus 2 Spearman's $R = +0.82$ $p < 0.0001$). Using the Kruskal Wallis test there was however a significant association between increasing numbers of symptoms and less insight ($\chi^2 11.6$ $p < 0.01$) and between a greater frequency of symptoms and less insight ($\chi^2 12.28$ $p < 0.01$).

Thirty-two subjects were not at all distressed by their symptoms, thirty-seven were mildly distressed and fourteen were severely distressed. There was a significant association between a greater number of symptoms and increased distress (Kruskal Wallis test $\chi^2 18.0$ $p < 0.01$) and between increasing frequency of symptoms and a greater degree of distress (Kruskal Wallis test, $\chi^2 25.23$ $p < 0.01$). The symptom profile of patients with different degrees of distress were similar (Spearman's correlation co-efficients 0 versus 1 $R = +0.57$ $p < 0.001$, 0 versus 2 $R = +0.065$ $p < 0.001$, 1 versus 2 $R = +0.076$ $p < 0.0001$). Looking however at the twenty-six patients with just one symptom it is notable that although most symptoms were associated with a similar degree of distress, none of the three patients whose only symptom was a visual hallucination of a relative experienced any unpleasant emotion. There were no significant positive or inverse associations between delusions, visual hallucinations or delusional misidentification and the level of unpleasant emotion (delusions $R = +0.17$, $p = 0.13$, visual hallucinations $R = +0.07$, $p = 0.43$, delusional misidentification $R = +0.11$, $p = 0.32$). Visual
hallucinations were significantly inversely associated with insight (R = -0.29, p = 0.008). Delusions were significantly associated with a greater number of psychotic symptoms (R = +0.28, p = 0.01) but not an increased frequency (R = +0.05, p = 0.63). Visual hallucinations and delusional misidentification were both significantly associated with a greater frequency and a greater number of psychotic symptoms (visual hallucinations, frequency of symptoms R = +0.27, p = 0.02; number of symptoms R = +0.39, p < 0.001; delusional misidentification, frequency of symptoms R = +0.35, p = 0.001; number of symptoms R = +0.40, p < 0.001).

Thirty six (65.5%) patients with probable Alzheimer's disease, twenty-two (66.7%) patients with possible Alzheimer's disease, eleven (91.7%) patients with Senile Dementia of Lewy Body Type and fourteen (70%) patients with vascular dementia experienced at least one psychotic symptom. There was a significant positive correlation between the symptom profile of patients with possible and probable Alzheimer's disease (Spearman's R = +0.62 p < 0.001). Therefore all comparisons consider Alzheimer's disease as one diagnostic group.

Patients with Senile Dementia of Lewy Body Type showed a trend to having a greater prevalence of psychotic symptoms overall than either patients with Alzheimer's disease (Odds ratio 5.69, 95% confidence intervals 0.70, 46.53) or vascular dementia (odds ratio 4.71, 95% confidence intervals 0.49, 45.15). There was however a similar prevalence of psychotic symptoms in patients with Alzheimer's disease and vascular dementia (odds ratio 1.21 95% confidence intervals 0.42, 3.46).
Patients with Senile Dementia of Lewy Body Type were significantly more likely to experience visual hallucinations (odds ratio 33, 95% confidence intervals 4.06, 270.4) and symptoms of delusional misidentification (odds ratio 3.73, 95% confidence intervals 1.09, 12.81) than patients with Alzheimer's disease, and showed a trend towards being more likely to experience delusions (odds ratio 3.6, 95% confidence intervals 0.84, 13.07). They were not however significantly more likely to experience visual hallucinations (odds ratio 3.33, 95% confidence intervals 0.57, 19.50), delusional misidentification (odds ratio 2.33, 95% confidence intervals 0.53, 10.28) or delusions (odds ratio 2.45, 95% confidence intervals 0.51, 11.82) than patients with vascular dementia.

Patients with vascular dementia were significantly more likely to experience visual hallucinations than patients with Alzheimer's disease (odds ratio 4.16, 95% confidence intervals 1.51, 11.59), although the likelihood of having symptoms of delusional misidentification (odds ratio 0.95, 95% confidence intervals 0.36, 3.06) or delusions (odds ratio 1.47, 95% confidence intervals 0.59, 3.86) were similar in the two dementias. The prevalence rates of the psychotic symptoms in the different dementias are shown in Table 9.2.

There was a high degree of correlation between the symptom profile of psychotic symptoms in the three different dementias (Alzheimer's disease versus vascular dementia Spearman's R = +0.66 p < 0.001, Alzheimer's disease vs Senile Dementia of Lewy Body Type R = +0.081 p < 0.001, Senile Dementia of Lewy Body Type vs vascular dementia R = +0.72 p < 0.001). Comparing the different types of visual hallucinations between the different dementias, a high degree of correlation emerged (Senile Dementia of Lewy
Body Type vs Alzheimer's disease $R = +0.96$, Senile Dementia of Lewy Body Type vs vascular dementia $R = +0.96$, Alzheimer's disease vs vascular dementia $R = +0.95$). Significance figures are not given for the correlations as there was only five different types of visual hallucinations to rank.

Patients with Senile Dementia of Lewy Body Type did have significantly more different types of psychotic symptom than patients with Alzheimer's disease (Mann-Whitney U test $z = 3.23 \ p < 0.001$) or vascular dementia (Mann-Whitney U test $z = 2.73 \ p < 0.005$).

Patients with Senile Dementia of Lewy Body Type had a mean of 4.27 symptoms, whereas patients with vascular dementia had a mean of 2.7 symptoms and patients with Alzheimer's disease had a mean of 2.67 symptoms.

Patients with Senile Dementia of Lewy Body Type also experienced psychotic symptoms significantly more frequently than patients with Alzheimer's disease (Mann-Whitney U test $z = 1.73, p = 0.039$) but not significantly more frequently than patients with vascular dementia (Mann-Whitney U test $z = 0.72, p = 0.22$). Patients with Alzheimer's disease and vascular dementia experienced a similar number of different psychotic symptoms (Mann-Whitney U test $z = 0.34 \ p = 0.37$) at a similar frequency (Mann-Whitney U test $z = 0.62 \ p = 0.27$). Overall 54.5% of patients with Senile Dementia of Lewy Body Type had four or more different psychotic symptoms compared to 17.2% of patients with Alzheimer's disease and 7.1% of patients with vascular dementia.
<table>
<thead>
<tr>
<th></th>
<th>Hallucinations</th>
<th>Visual Delusions</th>
<th>Auditory Delusions</th>
<th>Delusions</th>
<th></th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewy Body Disease</td>
<td>6 (9.0%)</td>
<td>11 (16.7%)</td>
<td>9 (13.6%)</td>
<td>0 (0.0%)</td>
<td>1</td>
<td>6 (8.3%)</td>
</tr>
<tr>
<td>Senile Dementia</td>
<td>12 (18.6%)</td>
<td>21 (32.3%)</td>
<td>14 (21.0%)</td>
<td>1 (0.0%)</td>
<td></td>
<td>14 (21.0%)</td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td>22 (34.8%)</td>
<td>41 (62.6%)</td>
<td>58 (89.9%)</td>
<td>30 (43.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

One Month Prevalence Rate of Psychotic Symptoms in Patients with Different Dementias

TABLE 9.2
CHAPTER 10

RESULTS - THE USE OF LOGISTIC REGRESSION TO INVESTIGATE THE ASSOCIATIONS OF PSYCHOTIC SYMPTOMS

Associations are reported for psychotic symptoms in general, delusions, visual hallucinations and delusional misidentification respectively, in the overall sample. In addition, separate analyses were undertaken for patients with Alzheimer's disease and patients with vascular dementia. There were too few patients with Senile Dementia of Lewy Body Type who did not have psychotic symptoms to permit statistical analysis.

From the analysis of the overall sample, deafness (Wald = 7.57, p = 0.01), visual impairment (Wald = 5.24, p = 0.02) and suffering from vascular dementia (Wald = 5.03, p = 0.03) or Senile Dementia of Lewy Body Type (Wald = 11.08, p = 0.0009) were significantly associated with psychotic symptoms in general. No other factors showed a significant association. Deafness (Wald = 3.91, p = 0.04), experiencing life events (Wald = 7.50, p = 0.01), being older (Wald = 6.96, p = 0.01) and the presence of Senile Dementia of Lewy Body Type were significantly associated with the presence of delusions (Wald = 7.91, p = 0.005).

Patients with visual hallucinations were significantly more likely to have severe visual impairment (Wald = 11.01, p = 0.009) and later age of onset (Wald = 3.81, p = 0.04). The association with visual impairment was stronger than that seen for psychotic symptoms in general. In addition there was a significant association between the type of dementia and the presence of visual hallucinations (Wald = 14.54, p = 0.002). Breaking
down this latter pattern in more detail there was an inverse association between probable or possible Alzheimer's disease (Wald = 7.54, p = 0.006, R = -0.19) and a positive association between the presence of visual hallucinations and Senile Dementia of Lewy Body Type (Wald = 8.15, p = 0.004).

No factors were significantly associated with delusional misidentification although a trend was seen for an association with physical health problems (Wald = 3.90, p = 0.05) amongst patients with delusional misidentification defined as including the phantom boarder syndrome. Neither were there any significant associations in a re-analysis of misidentification syndromes omitting patients with just the phantom boarder symptom, although in this group of patients there was a trend towards an association with less years of education (Wald 3.78, p = 0.05). There was a high positive correlation between age and the age of onset of the dementia (R = +0.91) and weak positive correlations between age and visual impairment (R = +0.20) and age and deafness (R = +0.20) respectively. A more detailed description of the variables is given in Table 10.1 and a breakdown of the logistic regression is shown in Table 10.2.
The association of psychosocial symptoms in all patients with dementia - Descriptive data

**TABLE 1A**
<table>
<thead>
<tr>
<th>Type of Domain</th>
<th>A (with Phonion border)</th>
<th>B (without Phonion border)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.50 0.47 0.07</td>
<td>1.27 0.40 0.04</td>
</tr>
<tr>
<td>Gender</td>
<td>0.00 0.00 0.00</td>
<td>0.00 0.00 0.00</td>
</tr>
<tr>
<td>Physical Health</td>
<td>0.04 0.03 0.03</td>
<td>0.04 0.03 0.03</td>
</tr>
<tr>
<td>Education</td>
<td>0.03 0.02 0.01</td>
<td>0.03 0.02 0.01</td>
</tr>
<tr>
<td>Duration of dementia</td>
<td>0.00 0.00 0.00</td>
<td>0.00 0.00 0.00</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>0.01 0.00 0.00</td>
<td>0.01 0.00 0.00</td>
</tr>
<tr>
<td>Psychological symptoms</td>
<td>0.00 0.00 0.00</td>
<td>0.00 0.00 0.00</td>
</tr>
<tr>
<td>Visual Impairment</td>
<td>0.00 0.00 0.00</td>
<td>0.00 0.00 0.00</td>
</tr>
<tr>
<td>Physical health</td>
<td>0.01 0.00 0.00</td>
<td>0.01 0.00 0.00</td>
</tr>
<tr>
<td>Visual health</td>
<td>0.01 0.00 0.00</td>
<td>0.01 0.00 0.00</td>
</tr>
</tbody>
</table>

The associations of psychological symptoms in dementia sufferers, a logistic regression analysis.
A separate logistic regression analysis was undertaken, using the same variables, focusing on psychoses, delusions and delusional misidentification (with phantom boarder delusions) amongst patients with Alzheimer's disease. The results were very similar to the analysis for the overall sample and no new variables emerged as important. Deafness was again significantly associated with psychotic symptoms overall (Wald 8.36, p = 0.004). In addition deafness (Wald 5.24, p = 0.02), age of onset (Wald 6.78, p = 0.01) and life events (Wald 8.03, p = 0.005) were significantly associated with delusions and visual impairment was significantly associated with visual hallucinations (Wald 8.90, p = 0.003). Descriptive data is shown in Table 10.3 and the logistic regression analysis is shown in Table 10.4. Delusional misidentification excluding phantom boarder delusions was not subject to a logistic regression analysis as there were only thirteen patients in this category, but again no significant associations were identified (deafness odds ratio 0.94, 95% confidence intervals 0.26, 3.35; severe visual impairment odds ratio 2.72, 95% confidence intervals 0.77, 9.58; physical health problems odds ratio 0.95, 95% confidence intervals 0.23, 3.94; male gender odds ratio 2.98, 95% confidence intervals 0.82, 10.80; a past history of psychiatric disorder odds ratio 0.96, 95% confidence intervals 0.11, 8.76; bereavement odds ratio 1.75, 95% confidence intervals 0.41, 7.46; life events odds ratio 1.17, 95% confidence intervals 0.12, 10.91; living alone odds ratio 0.71, 95% confidence intervals 0.18, 2.31; confabulation odds ratio 6.64, 95% confidence intervals 0.90, 48.91; education for 10 years or more odds ratio 1.73, 95% confidence intervals 0.42, 7.10, age at onset of the dementia Mann-Whitney U test, u = 474.5 z = -0.15 p = 0.88; age Mann-Whitney U test u = 275 z = -0.84 p = 0.40; duration of dementia Mann-Whitney U test u = 644.0 z = 0.78 p = 0.44).
Females with Vascular Dementia were significantly more likely to experience psychotic symptoms than males (Fisher's exact test $p = 0.02$) and patients with vascular dementia who experienced psychotic symptoms were significantly older than those who did not (Mann-Whitney U test $u = 14 z = 2.06 p = 0.04$). The same association with age was seen for patients with delusions (Mann-Whitney U test $u = 17.5 z = 2.47 p = 0.01$). There were no other significant associations for any of the studied variables (psychotic symptoms overall, deafness Fisher's exact test $p = 0.28$, severe visual impairment Fisher's exact test $p = 0.32$, physical health problems Fisher's exact test $p = 0.12$, confabulation Fisher's exact test $p = 0.75$, education for ten or more years Fisher's exact test $p = 0.25$, past history of psychiatric disorder Fisher's exact test $p = 0.29$, bereavement Fisher's exact test $p = 0.44$, life events Fisher's exact test $p = 1.00$, Living alone Fisher's exact test $p = 0.38$, age of onset Mann-Whitney U test $u = 17 z = 1.80, p = 0.07$, duration of dementia Mann-Whitney U test $u = 28.5 z = -0.80 p = 0.42$; delusions, deafness Fisher's exact test $p = 0.25$, severe visual impairment Fisher's exact test $p = 0.33$, physical health problems Fisher's exact test $p = 0.24$, confabulation Fisher's exact test $p = 0.50$, education for ten years or more Fisher's exact test $p = 0.50$, a past history of psychiatric disorder Fisher's exact test $p = 0.35$, bereavement Fisher's exact test $p = 0.35$, life events Fisher's exact test $p = 1.00$, living alone Fisher's exact test $p = 0.35$, age of onset Mann-Whitney U test $u = 28 z = 1.67 p = 0.10$, duration of dementia Mann-Whitney U test $u = 39 z = 0.85, p = 0.40$; visual hallucinations, deafness Fisher's exact test $p = 0.07$, severe visual impairment Fishers exact test $p = 0.21$, physical health problems Fisher's exact test $p = 0.18$, gender Fisher's exact test $p = 0.15$, confabulation Fisher's exact test $p = 0.55$, education for ten years or more Fisher's exact test $p = 0.44$, past history of psychiatric disorder Fisher's exact test $p = 0.30$, bereavement Fisher's
exact test \( p = 0.38 \), life events Fisher's exact test \( p = 1.00 \), living alone Fisher's exact test \( p = 0.39 \), age Mann-Whitney U test \( u = 29.5 \ z = 1.53 \ p = 0.13 \), age of onset Mann-Whitney U test \( u = 29.5 \ z = 1.53 \ p = 0.13 \), duration of dementia Mann-Whitney U test \( u = 36.5 \ z = -1.01 \ p = 0.31 \); delusional misidentification including the phantom border syndrome, deafness Fisher's exact test \( p = 0.28 \), severe visual impairment Fisher's exact test \( p = 0.39 \), physical health problems Fisher's exact test \( p = 0.39 \), gender Fisher's exact test \( p = 0.14 \), confabulation Fisher's exact test \( p = 0.75 \), education for ten years or more Fisher's exact test \( p = 0.75 \), a past history of psychiatric disorder Fisher's exact test \( p = 0.44 \), bereavement Fisher's exact test \( p = 0.29 \), life events Fisher's exact test \( p = 1.00 \), living alone Fisher's exact test \( p = 0.39 \), age Mann-Whitney U test \( u = 18.5 \ z = 1.67 \ p = 0.10 \), age of onset Mann-Whitney U test \( u = 27 \ z = 0.92 \ p = 0.36 \), duration of dementia Mann-Whitney U test \( u = 36.5 \ z = -0.09 \ p = 0.93 \). Descriptive data pertaining to these variables are shown in Table 10.5.
<table>
<thead>
<tr>
<th>(p&lt;0.05)</th>
<th>(p&lt;0.01)</th>
<th>(p&lt;0.001)</th>
<th>(p&lt;0.0001)</th>
<th>(p&lt;0.00001)</th>
<th>(p&lt;0.000001)</th>
<th>(p&lt;0.0000001)</th>
<th>(p&lt;0.0000000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>0.01</td>
<td>0.001</td>
<td>0.0001</td>
<td>0.00001</td>
<td>0.000001</td>
<td>0.0000001</td>
<td>0.0000000</td>
</tr>
</tbody>
</table>

The association of Page 40s symptoms in patients with Alzheimer's disease - Descriptive Data.
<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>360</td>
<td>100</td>
<td>260</td>
<td>100</td>
<td>500</td>
<td>05</td>
<td>170</td>
</tr>
<tr>
<td>160</td>
<td>100</td>
<td>260</td>
<td>95</td>
<td>170</td>
<td>05</td>
<td>170</td>
</tr>
<tr>
<td>170</td>
<td>120</td>
<td>96</td>
<td>96</td>
<td>170</td>
<td>10</td>
<td>110</td>
</tr>
<tr>
<td>160</td>
<td>090</td>
<td>88</td>
<td>80</td>
<td>170</td>
<td>10</td>
<td>110</td>
</tr>
<tr>
<td>150</td>
<td>170</td>
<td>170</td>
<td>170</td>
<td>100</td>
<td>120</td>
<td>060</td>
</tr>
<tr>
<td>080</td>
<td>200</td>
<td>170</td>
<td>100</td>
<td>120</td>
<td>060</td>
<td>120</td>
</tr>
<tr>
<td>070</td>
<td>070</td>
<td>170</td>
<td>100</td>
<td>060</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>060</td>
<td>050</td>
<td>070</td>
<td>070</td>
<td>060</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>050</td>
<td>060</td>
<td>050</td>
<td>070</td>
<td>060</td>
<td>120</td>
<td>120</td>
</tr>
</tbody>
</table>

The Association of Tracheal Arteries in relation with the Larynx, Trachea, and Esophagus.

TABLE 163
<table>
<thead>
<tr>
<th>Disease</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Cancer</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
| Table 1.2 | Association of Risk Factors with Weight Trajectory

- Risk Factors
The total CAMCOG scores were significantly lower amongst patients with psychosis (wald 5.86, p = 0.02) in the overall sample. Expressive language function (wald 4.33, p = 0.04) and perception (wald 5.16, p = 0.02) were also significantly more impaired amongst patients experiencing psychotic symptoms. Patients with delusions had significantly greater impairment of recent memory (wald 5.47, p = 0.02) and patients who experienced delusional misidentification (including patients with the phantom boarder syndrome) showed a trend towards more impaired receptive language function (wald 3.37, p = 0.07). A re-analysis looking at patients with delusional misidentification in the absence of the phantom boarder delusion showed a weaker trend towards an association with impaired receptive language function (wald 2.59, p = 0.11), but a stronger trend towards greater impairment of perception (wald 3.66, p = 0.06). Patients with visual hallucinations did not differ significantly from those without. Descriptive data are given in Table 10.6 and the results of the logistic regression analysis are shown in Table 10.7.

Looking at the total CAMCOG scores of those with and without psychosis it can be seen that there is a marked clustering of patients with psychotic symptoms scoring between twenty-one and forty on the total CAMCOG schedule, with 37.5% of patients scoring within this range compared to only 10.3% of patients without psychosis. Patients with psychosis were significantly more likely to score within the twenty-one to forty range on the CAMCOG schedule (chi sq 43.75, p < 0.0001).

A further logistic regression analysis, using the same variables, was undertaken to examine the associations of psychotic symptoms, delusions, delusional misidentification
(with phantom border delusions) and visual hallucinations in patients with Alzheimer’s disease. No significant findings emerged. Delusional misidentification without phantom border delusions was not subject to a logistic regression because of the small number of patients in this category. Patients with this symptom did not however differ significantly from the patients without psychotic symptoms in their total CAMCOG score (Mann-Whitney U test $u = 433 \ z = 0.64 \ p = 0.52$). The mean scores and their standard deviation for the total CAMCOG and each of the sub-scale scores are shown in Table 10.8 and the logistic regression analysis is shown in Table 10.9. Similarly there were too few patients with vascular dementia to undertake a logistic regression analysis. Comparison of the total CAMCOG scores did not reveal any significant associations (psychotic symptoms overall Mann-Whitney U test $u = 18 \ z = -1.70 \ p = 0.09$; delusions Mann-Whitney U test $u = 43.5 \ z = -0.49 \ p = 0.62$; visual hallucinations Mann-Whitney U test $u = 26.0 \ z = -1.79 \ p = 0.07$; delusional misidentification including the phantom border syndrome Mann-Whitney U test $u = 31.5 \ z = -0.52 \ p = 0.60$), although there were trends for both patients with psychotic symptoms overall and patients with visual hallucinations to have lower CAMCOG scores. The mean total CAMCOG scores for patients with and without each category of psychotic symptom is shown in Table 10.10.
<table>
<thead>
<tr>
<th></th>
<th>80</th>
<th>90</th>
<th>100</th>
<th>110</th>
<th>120</th>
<th>130</th>
<th>140</th>
<th>150</th>
<th>160</th>
<th>170</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
<td>3</td>
<td>3.5</td>
<td>4</td>
<td>4.5</td>
<td>5</td>
<td>5.5</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
<td>3</td>
<td>3.5</td>
<td>4</td>
<td>4.5</td>
<td>5</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>1</td>
<td>1.5</td>
<td>2</td>
<td>2.5</td>
<td>3</td>
<td>3.5</td>
<td>4</td>
<td>4.5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 12**

**CANCER CAUSE-SELECT** for animals with and without radon exposure - all strains.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Animals with Radon Exposure</th>
<th>Animals without Radon Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: The table data is not fully transcribed.*

<table>
<thead>
<tr>
<th>Subtest</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Memory</td>
<td></td>
</tr>
<tr>
<td>Visual Memory</td>
<td></td>
</tr>
<tr>
<td>Visual Memory</td>
<td></td>
</tr>
<tr>
<td>Recent Memory</td>
<td></td>
</tr>
<tr>
<td>Recent Memory</td>
<td></td>
</tr>
<tr>
<td>Remote Memory</td>
<td></td>
</tr>
<tr>
<td>Remote Memory</td>
<td></td>
</tr>
<tr>
<td>Attention &amp; Calculation</td>
<td></td>
</tr>
<tr>
<td>Attention &amp; Calculation</td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td></td>
</tr>
<tr>
<td>Abstract thinking</td>
<td></td>
</tr>
<tr>
<td>Abstract thinking</td>
<td></td>
</tr>
<tr>
<td>Language Expression</td>
<td></td>
</tr>
<tr>
<td>Language Expression</td>
<td></td>
</tr>
<tr>
<td>Language Comprehension</td>
<td></td>
</tr>
<tr>
<td>Language Comprehension</td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
</tr>
<tr>
<td>Total CAMCOC</td>
<td></td>
</tr>
</tbody>
</table>

**CAMCOC Sub-Scores in Patients with Psychotic Symptoms: A Logistic Regression Analysis - All Domains**

**TABLE 10.7**
<table>
<thead>
<tr>
<th></th>
<th>No Psychotic Symptoms (n = 27)</th>
<th>Psychotic Symptoms overall (n = 55)</th>
<th>Delusions (n = 39)</th>
<th>Visual Hallucinations (n = 21)</th>
<th>Delusional Misidentification (a) (n = 22)</th>
<th>Delusional Misidentification (b) (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
<td>mean</td>
<td>SD</td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>Total CAMCOG score</td>
<td>42.37</td>
<td>21.16</td>
<td>42.84</td>
<td>16.23</td>
<td>42.66</td>
<td>17.30</td>
</tr>
<tr>
<td>Orientation</td>
<td>4.70</td>
<td>3.00</td>
<td>4.33</td>
<td>2.18</td>
<td>4.31</td>
<td>2.10</td>
</tr>
<tr>
<td>Comprehension</td>
<td>6.30</td>
<td>2.09</td>
<td>5.95</td>
<td>2.00</td>
<td>6.08</td>
<td>2.07</td>
</tr>
<tr>
<td>Expression</td>
<td>7.78</td>
<td>5.61</td>
<td>7.84</td>
<td>2.91</td>
<td>7.81</td>
<td>3.16</td>
</tr>
<tr>
<td>Praxis</td>
<td>7.07</td>
<td>2.91</td>
<td>6.31</td>
<td>2.75</td>
<td>6.49</td>
<td>2.86</td>
</tr>
<tr>
<td>Recent Memory</td>
<td>1.26</td>
<td>1.87</td>
<td>1.25</td>
<td>1.65</td>
<td>1.38</td>
<td>1.79</td>
</tr>
<tr>
<td>Visual Memory</td>
<td>2.67</td>
<td>1.57</td>
<td>2.67</td>
<td>1.58</td>
<td>2.64</td>
<td>1.65</td>
</tr>
<tr>
<td>Remote Memory</td>
<td>2.81</td>
<td>1.54</td>
<td>2.93</td>
<td>2.09</td>
<td>2.67</td>
<td>2.03</td>
</tr>
<tr>
<td>Attention &amp; Calculation</td>
<td>1.56</td>
<td>1.37</td>
<td>1.85</td>
<td>1.90</td>
<td>1.95</td>
<td>1.18</td>
</tr>
<tr>
<td>Perception</td>
<td>4.56</td>
<td>2.58</td>
<td>5.00</td>
<td>2.14</td>
<td>5.08</td>
<td>2.32</td>
</tr>
<tr>
<td>Abstract Thinking</td>
<td>2.26</td>
<td>2.61</td>
<td>1.44</td>
<td>1.83</td>
<td>1.41</td>
<td>1.90</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>1.59</td>
<td>0.80</td>
<td>1.64</td>
<td>0.82</td>
<td>1.56</td>
<td>2.85</td>
</tr>
</tbody>
</table>

\(a\): with Phantom border delusions

\(b\): with Phantom border delusions

124
<table>
<thead>
<tr>
<th></th>
<th>0.00</th>
<th>0.57</th>
<th>0.10</th>
<th>0.00</th>
<th>0.34</th>
<th>0.08</th>
<th>0.03</th>
<th>0.85</th>
<th>0.01</th>
<th>0.02</th>
<th>0.02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Health</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Function</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Emotional Function</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Social Function</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Cognitive Function</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Function (with Emotional Function)</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Emotional Function (with Physical Function)</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Total QOL Score</td>
<td>0.00</td>
<td>0.57</td>
<td>0.10</td>
<td>0.00</td>
<td>0.34</td>
<td>0.08</td>
<td>0.03</td>
<td>0.85</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
</tr>
</tbody>
</table>

A higher score indicates a higher quality of life. A lower score indicates a lower quality of life.
### TABLE 10.10

Psychotic Symptoms - Mean Total CAMCOG Scores in Patients with Vascular Dementia

Mean CAMCOG score

<table>
<thead>
<tr>
<th>Symptoms Present</th>
<th>Symptoms Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotic Symptoms Overall (n = 15)</td>
<td>39.47</td>
</tr>
<tr>
<td>Delusions (n = 10)</td>
<td>41.40</td>
</tr>
<tr>
<td>Visual Hallucinations (n = 11)</td>
<td>36.55</td>
</tr>
<tr>
<td>Delusional Misidentification (n = 5)</td>
<td>36.80</td>
</tr>
</tbody>
</table>

(with the Phantom Boarder Syndrome)
CHAPTER 11

RESULTS - A PRINCIPAL COMPONENT ANALYSIS OF PSYCHOTIC SYMPTOMS

The grouping of symptoms was investigated amongst all patients with one or more psychotic symptom using a principal components analysis. Thirteen symptoms occurred in five or more subjects. Only the four factor solution approached the criteria specified for a satisfactory solution. The Kaiser Meyer Olkin measure of sampling adequacy was 0.57 and the Bartlett test of sphericity was 333.77. The Eigenvalues of factors one to four were 2.98, 1.64, 1.39 and 1.27 respectively accounting for 22.9%, 12.6%, 10.7% and 9.8% of the variance. Phantom boarder delusions, visual hallucinations of animals and insects and visual hallucinations of strangers correlated with Factor one. Delusions of abandonment, persecutory delusions and delusions of reference correlated with Factor two. Auditory hallucinations of strangers, delusional misidentification of television images and delusional misidentification of mirror images correlated with Factor three and visual hallucinations of relatives and delusions of relatives in the house correlated with Factor four. As can be seen from Table 11.1 the vast majority of correlations with each of the factors exceeded 0.65, and only one of the associations was lower than 0.6.

Twenty-six patients were assigned to symptom group one (visual hallucinations), twenty-seven were assigned to symptom group two (delusions), seven patients were assigned to symptom group three (delusional misidentification) and five were assigned to symptom group four (comfort phenomenon). The other patients with psychotic symptoms could not be clearly assigned according to the study criteria. Visual hallucinations showed a
strong trend towards an inverse association with the retention of insight, delusions were significantly associated with emotional distress and comfort phenomenon were significantly inversely associated with emotional distress. More details are shown in table 11.2.
The Pearson did not report correlations between 0.1 and 0.01.

<table>
<thead>
<tr>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
<th>Factor 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84745</td>
<td>0.71604</td>
<td>0.72360</td>
<td>0.73851</td>
</tr>
<tr>
<td>0.9639</td>
<td>0.69084</td>
<td>0.13217</td>
<td>0.4654</td>
</tr>
<tr>
<td>0.73762</td>
<td>0.9667</td>
<td>0.1033</td>
<td>0.2739</td>
</tr>
<tr>
<td>0.1014</td>
<td>0.38744</td>
<td>0.1117</td>
<td>0.4003</td>
</tr>
<tr>
<td>0.1056</td>
<td>0.0956</td>
<td>0.2277</td>
<td>0.4875</td>
</tr>
</tbody>
</table>

**Table 1.1**

Correlations of Psychotic Symptoms with the Factors Identified From Principal Components Analysis.
### TABLE 11.2

Characteristics Associated With Psychotic Symptoms

<table>
<thead>
<tr>
<th>Symptom Group</th>
<th>Insight R</th>
<th>Insight P</th>
<th>Distress R</th>
<th>Distress P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Hallucinations (Factor 1)</td>
<td>-0.24</td>
<td>0.05</td>
<td>-0.13</td>
<td>0.29</td>
</tr>
<tr>
<td>Delusions (Factor 2)</td>
<td>0.24</td>
<td>0.06</td>
<td>0.27</td>
<td>0.03*</td>
</tr>
<tr>
<td>Delusional Misidentification (Factor 3)</td>
<td>-0.05</td>
<td>0.68</td>
<td>0.07</td>
<td>0.56</td>
</tr>
<tr>
<td>Comfort Phenomena (Factor 4)</td>
<td>0.01</td>
<td>0.90</td>
<td>-0.29</td>
<td>0.02*</td>
</tr>
</tbody>
</table>
CAMCOG schedules were completed for seventy-six of the eighty-seven patients followed up for one year, for whom adequate information was available regarding symptoms of psychosis. The mean deterioration of total CAMCOG scores in patients who had psychotic symptoms at the initial assessment was 13.96 with a standard deviation of 13.65, compared to a deterioration of 14.88 with a standard deviation of 14.50 amongst patients who did not have psychotic symptoms at the baseline interview. This was a non significant difference (Mann-Whitney U test $u = 627.5 \; z = 0.25 \; p = 0.80$). Similarly there were no significant differences in the magnitude of deterioration comparing patients who had delusions to those who did not at the baseline interview (Mann-Whitney U test $u = 696.5 \; z = 0.22 \; p = 0.82$), those who had delusional misidentification at the baseline interview compared to those who did not (Mann-Whitney U test $u = 538.5 \; z = 0.45 \; p = 0.65$) or between those who had visual hallucinations compared to those who did not at the baseline assessment (Mann-Whitney U test $u = 653.5 \; z = 0.20 \; p = 0.84$). The magnitude of cognitive deterioration was also compared between patients with unresolved psychosis and those who did not experience psychotic symptoms at any stage of the study. Again no significant differences were evident (Mann-Whitney U test $u = 125.0 \; z = 1.24 \; p = 0.22$).

There was however a significant positive correlation between the number of months during which patients experienced psychotic symptoms and the deterioration in CAMCOG scores ($\text{Pearson's } R = +0.26 \; p = 0.03$). Significant correlations were also
seen for the number of months of delusional misidentification (Pearson’s R = +0.30 p = 0.01) and the number of months of visual hallucinations (Pearson’s R = +.29 p = 0.01). A trend in the same direction was seen for the number of months during which patients experienced delusions (Pearson’s R = +0.21 p = 0.07).

The Mann-Whitney U test was also used to compare the deterioration in patients with and without each class of psychotic symptom at baseline, in the fifty-three patients completing a CAMCOG schedule at the one year follow-up interview, with a diagnosis of Alzheimer’s disease. Again none of the comparisons reached statistical significance (psychotic symptoms overall u = 264.5 z = 1.3 p = 0.19, delusional misidentification u = 201.5 z = 1.45 p = 0.15, delusions u = 339.5 z = 0.15 p = 0.88, visual hallucinations u = 167 z = 1.68 p = 0.09).

Table 12.1 shows the pattern of deterioration amongst the thirty-two patients with Alzheimer’s disease, the twelve patients with vascular dementia and the six patients with Senile Dementia of Lewy Body type with at least one psychotic symptom at baseline, who were followed up for one year and completed a repeat CAMCOG schedule. Whilst the majority of patients with Alzheimer’s disease and most patients with vascular dementia had a deterioration of thirty points or less on the CAMCOG schedule over the year, three of the six patients with Senile Dementia of Lewy Body type had a deterioration of more than thirty points.
TABLE 12.1

Deterioration in Total CAMCOG Scores Amongst Patients with Alzheimer's Disease, Vascular Dementia and Senile Dementia of Lewy Body type.

<table>
<thead>
<tr>
<th>Deterioration</th>
<th>0 - 9</th>
<th>10 - 19</th>
<th>20 - 29</th>
<th>30 - 39</th>
<th>$\geq$ 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease (n=32)</td>
<td>15 (46.9%)</td>
<td>10 (31.3%)</td>
<td>4 (12.5%)</td>
<td>3 (9.4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Vascular Dementia (n = 12)</td>
<td>6 (50%)</td>
<td>1 (8.3%)</td>
<td>4 (33.3%)</td>
<td>0 (3%)</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Senile Dementia of Lewy Body type (n = 6)</td>
<td>1 (16.7%)</td>
<td>1 (16.7%)</td>
<td>1 (16.7%)</td>
<td>1 (16.75)</td>
<td>2 (33.3%)</td>
</tr>
</tbody>
</table>
CHAPTER 13
RESULTS - PSYCHOTIC SYMPTOMS, FOLLOW-UP DATA

Thirty patients who did not have any psychotic symptoms at the time of the baseline interview were followed up for one year. Fourteen (46.7%) of these patients developed at least one psychotic symptom during the follow-up period. Three (21.4%) patients experienced only delusions, two (14.3%) experienced only delusional misidentification, one (7.1%) experienced only visual hallucinations and one (7.1%) experienced only comfort phenomenon. The other patients experienced a combination of symptom types. Three (21.4%) experienced a combination of delusions and visual hallucinations, two (14.3%) experienced both delusions and delusional misidentification, one (7.1%) patient experienced visual hallucinations and comfort phenomena, whilst one (7.1%) patient experienced visual hallucinations, delusions and delusional misidentification.

Focusing upon the individual symptoms, four developed delusions of reference, four delusions of persecution, three delusions of theft, three phantom boarder delusions, three visual hallucinations of animals, two delusions of relatives in the house and two developed visual hallucinations of strangers. A number of other symptoms were experienced by individual patients. This is shown in more detail in Figure 13.1.
auditory hallucinations of relatives & object from hallucinations arose in 1 patient.

Delusional misidentifications of TV, visual hallucinations of children, capsular delusion.

<table>
<thead>
<tr>
<th>NUMBER OF PATIENTS</th>
<th>SYMPTOM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visual hallucinations of strangers</td>
</tr>
<tr>
<td></td>
<td>Delusions of relatives in the house</td>
</tr>
<tr>
<td></td>
<td>Visual hallucinations of animals</td>
</tr>
<tr>
<td></td>
<td>Phantom border delusions</td>
</tr>
<tr>
<td></td>
<td>Delusions of guilt</td>
</tr>
<tr>
<td></td>
<td>Delusions of persecution</td>
</tr>
<tr>
<td></td>
<td>Delusions of reference</td>
</tr>
</tbody>
</table>

amongst patients without psychotic symptom at the baseline assessment.
Eleven (45.8%) of the twenty-four patients with Alzheimer's disease developed at least one psychotic symptom, as did one (33.3%) of the three patients with vascular dementia. Only one patient with Senile Dementia of Lewy Body Type followed up for a year did not have psychotic symptoms at baseline. This patient did not develop any psychotic symptoms (two patients with unspecified dementia also developed psychotic symptoms).

Fourteen (30.4%) of the forty-six patients who did not have delusions at the baseline interview experienced at least one month of these symptoms during the one year of follow-up, this included one (50%) of the two patients with Senile Dementia of Lewy Body type, two (25%) of the eight patients with vascular dementia and ten (29.4%) of the thirty-four patients with Alzheimer's disease.

Fifty six patients followed up for one year did not have visual hallucinations at the time of the baseline assessment. Nine (16.1%) of these patients developed visual hallucinations during the follow-up year. Eight (16.7%) of the forty-five patients with Alzheimer's disease developed visual hallucinations but none of the five patients with vascular dementia or the two patients with Senile Dementia of Lewy Body Type who did not have these symptoms initially, developed them during the follow-up period.

Sixty-one patients completing the follow-up period did not have delusional misidentification at the initial assessment. Fourteen (23.0%) of these patients developed these symptoms during the year. This included eight (17.8%) of the forty-five patients with Alzheimer's disease, four (33.3%) of the twelve patients with vascular dementia and two (50%) of the four patients with Senile Dementia of Lewy Body Type. Excluding
patients with the phantom border syndrome from this category, seventy-four patients did not have delusional misidentification at the baseline interview of whom nine (12.2%) developed these symptoms during the follow-up period. This included three (5.7%) of the fifty-three patients with Alzheimer’s disease, four (26.7%) of the fifteen patients with vascular dementia and two (33.3%) of the six patients with Senile Dementia of Lewy Body Type. Ten (12.5%) patients developed comfort phenomenon over the follow-up year.

The number of patients with vascular dementia and Senile Dementia of Lewy Body Type were too small to permit meaningful statistical analysis for some of the comparisons. It was apparent however, that the incidence rates of delusions in patients with Alzheimer’s disease and patients with vascular dementia were similar (odds ratio 1.25, 95% confidence intervals 0.21, 7.24) and that patients with vascular dementia were significantly more likely to develop delusional misidentification (excluding the phantom border syndrome) than patients with Alzheimer’s disease (odds ratio 6.06, 95% confidence intervals 1.18, 30.88), as were patients with Senile Dementia of Lewy Body Type (odds ratio 8.33, 95% confidence intervals 1.05, 64.07).

Fifty-six patients who had at least one psychotic symptom at the initial interview were followed up for one year. Thirty-three (58.9%) of these patients developed new individual symptoms during the follow-up period. The most common new symptoms were delusions of reference, delusions of persecution, the phantom border syndrome, visual hallucinations of relatives and visual hallucinations of strangers. The full breakdown of these new symptoms is shown in Figure 13.2.
Figure 13.2

Delusions of partition, delusional jealousy & Fregoli delusions each arise in 1 patient.

Number of Patients

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grandiose delusions</td>
</tr>
<tr>
<td>Visual hallucinations of religious</td>
</tr>
<tr>
<td>Simple auditory hallucinations</td>
</tr>
<tr>
<td>Delusions of grandamoment</td>
</tr>
<tr>
<td>Visual hallucinations of relatives</td>
</tr>
<tr>
<td>Delusional misidentification of mirror image</td>
</tr>
<tr>
<td>Delusions of Heil</td>
</tr>
<tr>
<td>Capgras delusions</td>
</tr>
<tr>
<td>Auditory hallucinations of relatives</td>
</tr>
<tr>
<td>Delusional misidentification of House</td>
</tr>
<tr>
<td>Delusional misidentification of L.V.</td>
</tr>
<tr>
<td>Auditory hallucinations of strangers</td>
</tr>
<tr>
<td>Visual hallucinations of relatives</td>
</tr>
<tr>
<td>Delusions of relatives in the House</td>
</tr>
<tr>
<td>Phantasmic border delusions</td>
</tr>
<tr>
<td>Delusions of reference</td>
</tr>
</tbody>
</table>

Amongst patients who had at least 1 psychotic symptom at the baseline assessment, new symptoms of psychoses.
Resolution of psychotic symptoms occurred in thirty (52.6%) of the fifty-seven patients with psychosis followed up for a year. This included twenty-four (63.2%) of the thirty-eight patients with Alzheimer’s disease, four (33.3%) of the twelve patients with vascular dementia and two (28.6%) of the seven patients with Senile Dementia of Lewy Body Type. Eight (27.6%) of these patients however experienced a further psychotic episode.

Resolution of symptoms occurred in thirty (73.1%) of the forty-one patients with delusions, of whom five (16.7%) experienced a relapse. Visual hallucinations resolved in nineteen (61.3%) of the thirty-one patients experiencing these symptoms, only one (5.3%) of whom relapsed. Delusional misidentification resolved in fifteen (65.2%) of the twenty-six patients with these symptoms, two (13.3%) of whom relapsed. When excluding patients with the phantom border syndrome from this category, seven (53.8%) of the thirteen patients experienced symptom resolution. None of these patients relapsed. Seven of the patients with comfort phenomenon at the baseline interview were followed up for one year, three (42.9%) of whom experienced resolution of their symptoms. None of these patients experienced further comfort phenomenon.

Comparison of the resolution of certain sub-categories of psychotic symptom between patients with different types of dementia was precluded by small numbers of patients with vascular dementia and Senile Dementia of Lewy Body type. There were no significant differences between any of the dementias in the resolution rate of psychotic symptoms overall (vascular dementia versus Alzheimer’s disease odds ratio 3.43, 95% confidence interval 0.87, 13.46; Senile Dementia of Lewy Body type versus Alzheimer’s disease odds ratio 4.29, 95% confidence intervals 0.73, 25.53; Senile Dementia of Lewy
Body type versus vascular dementia Fisher's exact test $p = 0.38$). Similarly there were no significant differences in the number of patients with delusions whose symptoms resolved between the different dementias (Alzheimer's disease versus vascular dementia Fisher's exact test $p = 0.13$, Alzheimer's disease versus Senile Dementia of Lewy Body Type Fisher's exact test $p = 0.22$, vascular dementia versus Senile Dementia of Lewy Body Type Fisher's exact test $p = 0.07$). Eleven out of fifteen patients with Alzheimer's disease experienced resolution of their visual hallucinations compared to only one out of six patients with Senile Dementia of Lewy Body type, this was a significant difference (Fisher's exact test $p = 0.03$). A trend in the same direction was seen for patients with Senile Dementia of Lewy Body Type compared to those with vascular dementia, 70% of whom experienced resolution of their visual hallucinations (Fisher's exact test $p = 0.06$). There was no significant difference in the number of patients whose visual hallucinations resolved comparing vascular dementia and Alzheimer's disease (Fisher's exact test $p = 0.34$). Only three patients with vascular dementia experienced delusional misidentification at the baseline interview were followed up for the whole year. There was no significant difference between the likelihood of symptoms of delusional misidentification resolving in patients with Alzheimer's disease compared to those with Senile Dementia of Lewy Body Type (Fisher's exact test $p = 0.35$).

Tables 13.1 to 13.4 show the number of months of psychotic symptoms, delusions, visual hallucinations and delusional misidentifications (including the phantom boarder syndrome) respectively, experienced by patients who had these symptoms at the baseline interview. The figures are given separately for patients with different types of dementia. As can be seen, the distribution of the number of months of symptoms for each of the
categories of psychotic symptoms follows a bimodal distribution with a cluster of patients experiencing relatively brief symptoms and a further cluster experiencing highly persistent disorders. The only visible exceptions to this pattern were the rarity of persistent delusions amongst patients with vascular dementia and the paucity of brief episodes of the combined category of psychotic symptoms amongst patients with Senile Dementia of Lewy Body Type.
<table>
<thead>
<tr>
<th>No. of months of symptoms during the 12 mth follow-up</th>
<th>Alzheimer’s Disease</th>
<th>Vascular Dementia</th>
<th>Senile Dementia of Lewy Body type</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>
**TABLE 13.2**

No. of months of delusions amongst patients who had at least one delusional symptom at Baseline.

<table>
<thead>
<tr>
<th>No. of months of delusions during the 12 mth follow-up</th>
<th>Alzheimer's Disease</th>
<th>Vascular Dementia</th>
<th>Senile Dementia of Lewy Body type</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>7</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>No. of months of delusional misidentification during the 12 mth follow-up</td>
<td>No. of months of Visual Hallucinations in patients who had at least one visual hallucination at Baseline.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIAGNOSIS</td>
<td>ADNOSIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alzheimer's Disease</td>
<td>Vascular Dementia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senile Dementia of Lewy Body type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 6 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0 1 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1 0 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0 0 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>0 0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0 2 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1 0 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>2 1 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 13.4

No. of months of Delusional Misidentification Amongst patients who Had at Least one Symptom of Delusional Misidentification at Baseline.

<table>
<thead>
<tr>
<th>No. of months of delusional misidentification during the 12 mth follow-up</th>
<th>DIAGNOSIS</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alzheimer’s Disease</td>
<td>Vascular Dementia</td>
<td>Senile Dementia of Lewy Body type</td>
</tr>
<tr>
<td>0</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Patients with unresolved psychosis were compared to patients who had psychosis at the time of the initial interview, but experienced three months or less of psychotic symptoms during the follow-up period. Significantly more of the patients with persistent psychotic symptoms had experienced at least three months of symptoms prior to the baseline interview (odds ratio 21.66, 95% confidence intervals 2.48, 190.57). There was also a trend for patients with persistent psychosis to have experienced symptoms at a frequency of at least daily (odds ratio 2.95, 95% confidence intervals 0.83, 10.49). There was no association between persistent psychotic symptoms and experiencing three or more psychotic symptoms at baseline (odds ratio 1.37, 95% confidence intervals 0.34, 5.42) or between persistent psychosis and either severe visual impairment (odds ratio 2.25, 95% confidence intervals 0.58, 8.67) or deafness (odds ratio 1.71, 95% confidence intervals 0.53, 5.58). Similarly there was no association between persistent psychotic symptoms and the baseline score on the total CAMCOG schedule (Mann-Whitney U test $u = 295.5 \ z = 0.60 \ p = 0.62$) or between persistent psychotic symptoms and the age of onset of the dementia (Mann-Whitney U test $u = 266.5 \ z = 0.35 \ p = 0.72$).

Patients with persistent delusions compared to those with brief delusions were significantly more likely to have experienced three months of psychotic symptoms prior to the baseline interview (Fisher's exact test $p = 0.01$) and were significantly more likely to have experienced symptoms at least daily (odds ratio 5.60, 95% confidence intervals 1.14, 27.39). There were no significant associations with experiencing three or more different psychotic symptoms at the time of the initial assessment (odds ratio 2.18, 95% confidence intervals 0.41, 11.59), deafness (odds ratios 1.67, 95% confidence intervals 0.40, 6.95), severe visual impairment (odds ratios 0.98, 95% confidence intervals 0.16,
5.99), the baseline CAMCOG score (Mann-Whitney U test \( u = 111.0 \) \( z = 0.75 \) \( p = 0.45 \)) or age at the onset of the dementia (Mann-Whitney U test \( u = 127.5 \) \( z = 0.16 \) \( p = 0.87 \)).

Patients with persistent compared to those with brief periods of visual hallucinations were significantly more likely to have experienced their psychotic symptoms at a frequency of at least daily at the time of the baseline assessment (Fisher’s exact test \( p = 0.04 \)). There was also a trend towards an association between persistent visual hallucinations and a higher initial score on the CAMCOG schedule (Mann-Whitney U test \( u = 21 \) \( z = 1.95 \) \( p = 0.05 \)). Persistent visual hallucinations were not however significantly associated with having three months of psychotic symptoms at baseline (Fisher’s exact test \( p = 0.32 \)), deafness (Fisher’s exact test \( p = 0.11 \)), severe visual impairment (Fisher’s exact test \( p = 0.13 \)), experiencing three or more psychotic symptoms (Fisher’s exact test \( p = 0.09 \)) or the age of onset of the dementia (Mann-Whitney U test \( u = 37.5 \) \( z = -0.62 \) \( p = 0.54 \)).

Persistent compared to brief delusional misidentification was also significantly associated with an initial frequency of psychotic symptoms of at least daily (Fisher’s exact test \( p = 0.048 \)) and a duration of psychotic symptoms of at least three months at the time of the initial assessment (Fisher’s exact test \( p = 0.01 \)). There were however no significant associations between persistent delusional misidentification and deafness (Fisher’s exact test \( p = 0.23 \)), severe visual impairment (Fisher’s exact test \( p = 0.36 \)), having three or more psychotic symptoms at baseline (Fisher’s exact test \( p = 0.42 \)), age of onset of the dementia (Mann-Whitney U test \( u = 41 \) \( z = -0.80 \) \( p = 0.42 \)) or the CAMCOG score at the time of the baseline assessment (Mann-Whitney U test \( u = 41 \) \( z = -0.79 \) \( p = 0.42 \)).
CHAPTER 14

RESULTS - PREVALENCE, ASSOCIATIONS AND SYMPTOMS OF DEPRESSION

Depression was diagnosed according to the DSMIIIR and RDC criteria. In addition, the distribution of Cornell Depression Scale scores for the whole sample are shown in Figure 14.1. Three discrete peaks are evident, perhaps reflecting normality, minor depression and major depression.

Twenty-one (16.9%) patients had DSMIIIR major depression, thirty-one (25.0%) patients fulfilled the criteria for RDC major depression whilst a further thirty-four patients (27.4%) fulfilled the RDC criteria for minor depression. The Kappa co-efficient for the correlation between DSMIIIR and RDC major depression was +0.63. Twelve patients who fulfilled the RDC criteria for major depression did not fulfil the DSMIIIR criteria for major depression, whilst two patients fulfilling the RDC criteria for minor depression fulfilled the DSMIIIR criteria for major depression.

Of the seventy-nine patients with dementia in contact with old age psychiatry services in Birmingham, twenty-six (32.9%) had RDC major depression, twenty-five (31.6%) had RDC minor depression and twenty-eight (35.4%) had no depression. This compared to only two out of twenty-five (8%) of the patients attending the memory clinic with RDC major depression, six (24%) with RDC minor depression and seventeen (68%) with no depression. Three (15%) of the patients in contact with the old age psychiatry services in Coventry had RDC major depression and three (15%) had RDC minor depression, whilst fourteen (70%) had no depression. There was a significant difference in the prevalence rate of RDC minor and major depression in the three settings (Chi² 14.7, 7df,
p < 0.05). The distribution of minor and major depression in the three settings is illustrated in Table 14.1.

Nine of the twenty patients (45%) with vascular dementia had RDC major depression and a further two (10%) had RDC minor depression. This compared to fifteen out of eighty-eight (17.0%) patients with probable or possible Alzheimer's disease with RDC major depression and twenty-eight out of eighty-eight (31.8%) with minor depression. Four of the twelve patients with Senile Dementia of Lewy Body Type fulfilled the criteria for RDC major depression (33%) and a further four (33%) fulfilled the criteria for RDC minor depression. Three (75%) of the four patients with unspecified dementia fulfilled the RDC criteria for major depression. The proportion of patients with major and minor depression in each of the diagnostic groups is shown in Figure 14.2.
Total Cornell Scores in the Overall Sample

Figure 14.1
Depression by Diagnosis

Figure 14.2
<table>
<thead>
<tr>
<th>Condition</th>
<th>%</th>
<th>%</th>
<th>%</th>
<th>Memory Clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate Depression</td>
<td>3</td>
<td>25</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Major Depression</td>
<td>3</td>
<td>26</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>18 (22.8%)</td>
<td>2</td>
<td>18</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1 (4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n = 20</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n = 79</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n = 25</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The One Month Prevalence Rates of Depression in the Memory Clinic and Psychiatric Services

**TABLE 4.1**
Patients with vascular dementia were significantly more likely to have RDC major depression than patients with Alzheimer's disease (odds ratio 3.98, 95% confidence intervals, 1.40, 11.25). There were however no significant differences between vascular dementia and Senile Dementia of Lewy Body Type (odds ratio 1.64, 95% confidence intervals 0.37, 7.24) or Senile Dementia of Lewy Body Type and Alzheimer's disease (odds ratio 2.43, 95% confidence intervals 0.65, 4.88) in the likelihood of having RDC major depression. There was a high correlation between the type of symptoms of depression experienced by patients with each of the three dementias (Alzheimer's disease vs Vascular Dementia, Spearman's $R = +0.91$, Alzheimer's disease vs Senile Dementia of Lewy Body Type, Spearman's $R = +0.85$, Vascular dementia vs Senile Dementia of Lewy Body Type, Spearman's $R = +0.81$).

The logistic regression analysis considering all the patients with dementia demonstrated that RDC major depression was significantly inversely associated with Alzheimer's disease (Wald 7.45 $p = 0.006$) and showed a strong trend towards a significant positive association with vascular dementia (Wald 3.80 $p = 0.05$). There was also a trend for those with severe visual impairment to be more likely to have RDC major depression (Wald 3.79 $p = 0.05$). When undertaking the same analysis looking at DSMIIIR major depression the same association with the type of dementia was confirmed. In addition deafness was significantly associated with DSMIIIR major depression (Wald 3.80 $p = 0.04$) and a past history of psychiatric disorder showed a trend towards a significant association (Wald 3.66 $p = 0.06$).
For the analysis of RDC minor depression, patients with RDC major depression were excluded, leaving ninety-three patients for evaluation. Deafness (Wald 4.91 p = 0.03) and physical health problems (Wald 6.59 p = 0.01) were the only factors significantly associated with RDC minor depression, although severe visual impairment showed a trend towards an association (Wald 3.94 p = 0.05). A more detailed description of the studied variables for RDC minor depression, RDC major depression and DSMIIIIR major depression is shown in Table 14.2 and the logistic regression analysis is shown in Table 14.3.
<table>
<thead>
<tr>
<th>Education</th>
<th>Physical Health Problems</th>
<th>Events</th>
<th>Male Gender</th>
<th>Depression</th>
<th>RDC Major</th>
<th>No Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 years or more</td>
<td>10</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Less than 10 years</td>
<td>13</td>
<td>28</td>
<td>3</td>
<td>12</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Vision Impaired</td>
<td>9</td>
<td>16</td>
<td>9</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Past History of Psychiatric Disorder</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>13</td>
<td>22</td>
<td>34</td>
</tr>
<tr>
<td>Physical Health Problems</td>
<td>7</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>Events</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>12</td>
<td>34</td>
<td>16</td>
</tr>
<tr>
<td>Male Gender</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Depression</td>
<td>8</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>RDC Major</td>
<td>2</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>No Depression</td>
<td>7</td>
<td>10</td>
<td>7</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

The associations of Depression - Descriptive Data (All Domains)

**TABLE 142**
<table>
<thead>
<tr>
<th>RDC Major Depression</th>
<th>BDI</th>
<th>RDC Major Depression</th>
<th>BDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>WAID</td>
<td>Depression</td>
<td>WAID</td>
</tr>
<tr>
<td></td>
<td>d</td>
<td></td>
<td>d</td>
</tr>
</tbody>
</table>

**Associations of Depression, a Logistic Regression Analysis - All Domains**

**Table 14.3**
A further logistic regression analysis was undertaken to look at the associations of RDC major depression in patients with Alzheimer's disease. Only visual impairment was significantly associated with RDC major depression (Wald 6.01 p = 0.01). Descriptive data are shown in Table 14.4 and the logistic regression analysis is shown in Table 14.5. There were only nine patients with DSMIIIR major depression and Alzheimer's disease, too few to undertake a logistic regression analysis. Using odds ratios and 95% confidence intervals however, deafness (odds ratio 9.00, 95% confidence intervals 1.86, 43.82) and visual impairment (odds ratio 6.61, 95% confidence intervals 1.67, 26.31) were significantly associated with the presence of DSMIIIR major depression. No association was seen for bereavement (odds ratio 3.19, 95% confidence intervals 0.73, 20.70; male gender odds ratio 0.49, 95% confidence intervals 0.05, 4.39; insight odds ratio 2.25, 95% confidence intervals 0.47, 11.02; life events odds ratio 2.63, 95% confidence intervals 0.21, 32.79; physical health problems odds ratio 1.29, 95% confidence intervals 0.22, 7.39; a past history of psychiatric disorder odds ratio 2.63, 95% confidence intervals 0.21, 32.79; living alone odds ratio 0.88, 95% confidence intervals 0.21, 3.71; education for ten or more years odds ratio 0.49, 95% confidence intervals 0.05, 4.39). A separate analysis was not undertaken for RDC minor depression as it occurred in only two patients with vascular dementia and four patients with Senile Dementia of Lewy Body Type.
<table>
<thead>
<tr>
<th>Major Depression</th>
<th>No Depression</th>
<th>Total</th>
<th>T-Test (2-tailed)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>7.6% (SD: 4.0)</td>
<td>17.0% (SD: 4.5)</td>
<td>0.04</td>
<td>0.64</td>
</tr>
<tr>
<td>6 months</td>
<td>7.7% (SD: 4.0)</td>
<td>17.0% (SD: 4.5)</td>
<td>0.04</td>
<td>0.64</td>
</tr>
<tr>
<td>3 months</td>
<td>7.7% (SD: 4.0)</td>
<td>17.0% (SD: 4.5)</td>
<td>0.04</td>
<td>0.64</td>
</tr>
</tbody>
</table>

**The Association of Depression with Major Depression**

**TABLE 14.4**
<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.71</td>
<td>1.40</td>
<td>Vertical Fluency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.88</td>
<td>0.20</td>
<td>Abstract Thinking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.41</td>
<td>0.0</td>
<td>Perception</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.40</td>
<td>0.71</td>
<td>Attention &amp; Calculation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.44</td>
<td>0.0</td>
<td>Remote Memory</td>
<td>2.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.29</td>
<td>1.3</td>
<td>Visual Memory</td>
<td>6.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.22</td>
<td>1.1</td>
<td>Recent Memory</td>
<td>5.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.45</td>
<td>8.8</td>
<td>Praxis</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>1.0</td>
<td>Expression</td>
<td>6.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.40</td>
<td>1.0</td>
<td>Comprehension</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.41</td>
<td>1.9</td>
<td>Orientation</td>
<td>8.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.43</td>
<td>0.0</td>
<td>Total CAMCOG Score</td>
<td>0.20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2 Logite regression analyses
- The associations of RDC Major Depression in Patients with Alzheimer's Disease

TABLE 145

\[ \text{Adjusted } (n = 16) \]
Nine patients with vascular dementia had RDC major depression. Although not sufficient to permit a logistic regression analysis, the numbers were large enough to allow comparison with patients who did not have depression, using Fisher's exact test. Using this method physical health problems were significantly associated with the presence of depression in vascular dementia (Fisher's exact test $p = 0.01$). None of the other variables were significantly associated with RDC major depression (bereavement Fisher's exact test $p = 0.35$, deafness Fisher's exact test $p = 0.42$, gender Fisher's exact test $p = 0.36$, insight Fisher's exact test $p = 0.35$, life events Fisher's exact test $p = 1.00$, a past history of psychiatric disorder Fisher's exact test $p = 0.13$, severe visual impairment Fisher's exact test $p = 0.14$, living alone Fisher's exact test $p = 0.36$, ten years or more of education Fisher's exact test $p = 0.50$). Descriptive data regarding these variables are shown in Table 14.6.

Full CAMCOG data was available on one hundred and sixteen patients in the overall sample. Possible associations with CAMCOG sub-scores were evaluated for DSMIIIIR major depression, RDC major depression and RDC minor depression using the same logistic regression method. The only significant association was between DSMIIIIR major depression and less severe impairment of recent memory (Wald 5.7 $p = 0.02$). No other factors showed even a trend towards an association. The overall level of cognitive deficit was not significantly associated with depression diagnosed according to any of the criteria specified. Descriptive data are shown Table 14.7 and the logistic regression is shown in Table 14.8.
### TABLE 14.6
The Associations of Depression - Descriptive Data (Vascular Dementia)

<table>
<thead>
<tr>
<th></th>
<th>No RDC Depression (n = 9)</th>
<th>RDC Major Depression (n = 9)</th>
<th>DSMIIIR Major Depression (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of Onset</td>
<td>76.89 (S.D 5.25)</td>
<td>75.33 (S.D. 7.1%)</td>
<td>73.57 (S.D. 7.2%)</td>
</tr>
<tr>
<td>Bereavement</td>
<td>2 (22.2%)</td>
<td>3 (33.3%)</td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td>Deafness</td>
<td>2 (22.2%)</td>
<td>2 (22.2%)</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Male Gender</td>
<td>4 (44.4%)</td>
<td>4 (44.4%)</td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>Insight</td>
<td>2 (22.2%)</td>
<td>3 (33.3%)</td>
<td>2 (28.6%)</td>
</tr>
<tr>
<td>Life Events</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Physical Health Problems</td>
<td>0 (0%)</td>
<td>5 (55.6%)</td>
<td>4 (57.1%)</td>
</tr>
<tr>
<td>Past History of Psychiatric Disorder</td>
<td>1 (11.1%)</td>
<td>4 (44.4%)</td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>Severe Visual Impairment</td>
<td>2 (22.2%)</td>
<td>5 (55.6%)</td>
<td>4 (57.1%)</td>
</tr>
<tr>
<td>Lives Alone</td>
<td>4 (44.4%)</td>
<td>4 (33.3%)</td>
<td>3 (42.9%)</td>
</tr>
<tr>
<td>10 years or more of Education</td>
<td>1 (11.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>Verbal Fluency</td>
<td>Abstract Thinking</td>
<td>Perception</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------</td>
<td>-------------------</td>
<td>------------</td>
</tr>
<tr>
<td>0.91 22 28</td>
<td>1.17</td>
<td>0.84</td>
<td>0.70</td>
</tr>
<tr>
<td>1.90 20 19</td>
<td>1.97</td>
<td>1.31</td>
<td>1.81</td>
</tr>
<tr>
<td>1.96 25 46</td>
<td>1.88</td>
<td>2.49</td>
<td>1.89</td>
</tr>
<tr>
<td>1.97 1.70</td>
<td>1.74</td>
<td>2.96</td>
<td>2.48</td>
</tr>
<tr>
<td>1.88 2.90</td>
<td>2.77</td>
<td>1.36</td>
<td>1.44</td>
</tr>
<tr>
<td>1.30 6.60</td>
<td>3.27</td>
<td>3.28</td>
<td>3.44</td>
</tr>
<tr>
<td>1.10 8.03</td>
<td>7.34</td>
<td>4.72</td>
<td>8.26</td>
</tr>
<tr>
<td>5.24 2.89</td>
<td>3.17</td>
<td>4.28</td>
<td>6.07</td>
</tr>
<tr>
<td>4.98 1.70</td>
<td>4.80</td>
<td>1.85</td>
<td>2.71</td>
</tr>
<tr>
<td>2.71 4.34</td>
<td>4.27</td>
<td>2.04</td>
<td>1.77</td>
</tr>
</tbody>
</table>

**Note:** Values are shown for different conditions and measures.

**TABLE 14.7**

CAMCOG Sub-Scores in Patients with and without Depression

- All Denudans
<table>
<thead>
<tr>
<th>Domain</th>
<th>WAID</th>
<th>WAID</th>
<th>WAID</th>
<th>WAID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auditory Perception</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention &amp; Concentration</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Language Expression</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Language Comprehension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CACOC Score</td>
<td>1.35</td>
<td>0.25</td>
<td>0.88</td>
<td>1.33</td>
</tr>
</tbody>
</table>

**TABLE 14**

CACOC Score - All Domains
A further logistic regression analysis was undertaken to examine the cognitive profile of RDC major depression in patients with Alzheimer's disease. No significant associations were identified. The means and standard deviations of the CAMCOG subscales are shown in Table 14.9 and the logistic regression is shown in Table 14.10. The number of patients with DSMIIIR major depression were insufficient to undertake a logistic regression analysis but there was no significant difference in the total CAMCOG score between those with and those without DSMIIIR major depression (Mann-Whitney U test $u = 353.5 \ z = -0.03 \ p = 0.98$). Similarly there were too few patients with vascular dementia in any of the categories of depression to undertake a logistic regression analysis. There were however sufficient patients with vascular dementia to compare the total CAMCOG scores in patients with and without RDC major depression using the Mann-Whitney U test. No significant association was evident (Mann-Whitney U test $u = 29.5 \ z = 0.34 \ p = 0.33$).
<table>
<thead>
<tr>
<th>0.50</th>
<th>1.33</th>
<th>1.57</th>
<th>0.74</th>
<th>0.90</th>
<th>1.60</th>
<th>4.96</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.27</td>
<td>0.89</td>
<td>0.23</td>
<td>1.70</td>
<td>2.25</td>
<td>0.40</td>
<td>2.40</td>
</tr>
<tr>
<td>1.86</td>
<td>2.22</td>
<td>2.43</td>
<td>3.00</td>
<td>2.47</td>
<td>2.80</td>
<td>2.80</td>
</tr>
<tr>
<td>1.88</td>
<td>1.11</td>
<td>0.70</td>
<td>0.00</td>
<td>1.00</td>
<td>1.33</td>
<td>1.28</td>
</tr>
<tr>
<td>1.82</td>
<td>5.78</td>
<td>1.00</td>
<td>2.00</td>
<td>0.99</td>
<td>2.80</td>
<td>5.65</td>
</tr>
<tr>
<td>0.99</td>
<td>2.33</td>
<td>7.27</td>
<td>7.78</td>
<td>3.11</td>
<td>6.07</td>
<td>6.69</td>
</tr>
<tr>
<td>1.41</td>
<td>2.00</td>
<td>0.33</td>
<td>1.33</td>
<td>2.16</td>
<td>2.87</td>
<td>4.00</td>
</tr>
<tr>
<td>2.60</td>
<td>4.56</td>
<td>4.27</td>
<td>9.30</td>
<td>4.68</td>
<td>1.90</td>
<td>4.73</td>
</tr>
<tr>
<td>14.73</td>
<td>4.93</td>
<td>1.01</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DSMMR Major Depression</th>
<th>NO DSMMR Major Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
</tr>
</tbody>
</table>

TABLE 14.9

CAMCOG sub-scores in patients with and without depression with Alzheimer's disease.
<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensional Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Major Depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstract Thinking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention &amp; Calculation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Praxis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CAMCOG Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 14.10**

CAMCOG Sub-Scores in Patients with and without Depression.
The most common symptoms amongst the twenty-one patients with DSMIIIR major depression were depressed mood (95.2%), loss of interest (90.5%), anxiety (85.7%), irritability (71.4%), lack of energy (66.7%), suicidal thoughts (61.9%) and lack of mood reactivity (61.9%). Only diurnal mood variation (14.3%) and mood congruent delusions (4.8%) occurred in less than 33% of the patients with major depression. A fuller description is shown in Table 14.9. The Spearman’s Rank Correlation co-efficient between the rank order of symptoms in patients with DSMIIIR major depression and RDC major depression was $+0.87 (p < 0.0001)$. The rank order of symptoms amongst patients with RDC minor depression was also extremely similar to that seen in patients with RDC major depression ($R = +0.84, p = < 0.0001$) although most of the symptoms occurred at a lower frequency. Patients with RDC major depression had a mean of 12.7 symptoms of depression whilst patients with RDC minor depression had a mean of 7.0 symptoms.
<table>
<thead>
<tr>
<th>Percent Major Depressive</th>
<th>Percent Minor Depressive</th>
<th>Other Mental Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>60%</td>
<td>52%</td>
<td>59%</td>
</tr>
<tr>
<td>96%</td>
<td>96%</td>
<td>96%</td>
</tr>
<tr>
<td>88%</td>
<td>88%</td>
<td>88%</td>
</tr>
<tr>
<td>71%</td>
<td>71%</td>
<td>71%</td>
</tr>
<tr>
<td>58%</td>
<td>58%</td>
<td>58%</td>
</tr>
<tr>
<td>41%</td>
<td>41%</td>
<td>41%</td>
</tr>
<tr>
<td>38%</td>
<td>38%</td>
<td>38%</td>
</tr>
<tr>
<td>31%</td>
<td>31%</td>
<td>31%</td>
</tr>
<tr>
<td>26%</td>
<td>26%</td>
<td>26%</td>
</tr>
<tr>
<td>19%</td>
<td>19%</td>
<td>19%</td>
</tr>
<tr>
<td>16%</td>
<td>16%</td>
<td>16%</td>
</tr>
<tr>
<td>14%</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>12%</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>8%</td>
<td>8%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**TABLE 14.11**

Frequency of Individual Symptoms in Patients with Depression

---

**Note:** The table above details the frequency of symptoms related to depression, major depressive disorder, minor depressive disorder, and other mental disorders. The percentages indicate the prevalence of these conditions in a specified population or sample.
A principal components analysis was undertaken to investigate the possibility of identifying meaningful sub-types of depression. Examining all patients with RDC minor or major depression, the Kaiser Meyer Olkin measure of sampling adequacy was 0.54 and the Bartlett test of sphericity was 322.12. The two factor solution produced factors with eigenvalues of 2.87 and 2.21 which explained 15.1% and 11.6% of the variance respectively. Using the study definition, anxiety (+0.64), lack of re-activity to pleasant events (+0.60), lack of energy (+0.63) and loss of interest (+0.69) were encompassed within Factor one and difficulty falling asleep (+0.76) and multiple awakenings during sleep (+0.73) were encompassed within Factor two. When lowering the specified association to +0.5, depressed mood was also included within Factor one (+0.51) and early morning wakening was encompa
(+0.67). Factor three included self-deprecation (+0.74) and diurnal mood variation (+0.60). If the specified criteria were reduced to +0.50, no further symptoms were added to Factors one or two but irritability (+0.56) and suicidal thoughts (+0.53) were added to Factor three. Using this model forty patients were included within Factor one, five patients were included in Factor two and nine patients in Factor three. Only fifteen patients could not be classified. The correlations of each of the symptoms with the three factors are shown in Table 15.1.
### TABLE 15.1

Correlations With the Factors of Depression Derived from a Principal Components Analysis

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>0.68</td>
<td>0.13</td>
<td>0.22</td>
</tr>
<tr>
<td>Depressed Mood</td>
<td>0.61</td>
<td>0.15</td>
<td>0.39</td>
</tr>
<tr>
<td>Mood Reactivity</td>
<td>0.78</td>
<td>0.11</td>
<td>-0.01</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.20</td>
<td>0.19</td>
<td>0.56</td>
</tr>
<tr>
<td>Agitation</td>
<td>0.32</td>
<td>0.35</td>
<td>0.03</td>
</tr>
<tr>
<td>Retardation</td>
<td>0.44</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Complaints</td>
<td>0.28</td>
<td>-0.18</td>
<td>0.47</td>
</tr>
<tr>
<td>Loss of interest</td>
<td>0.63</td>
<td>0.01</td>
<td>0.28</td>
</tr>
<tr>
<td>Appetite Loss</td>
<td>0.49</td>
<td>0.16</td>
<td>-0.02</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>0.30</td>
<td>-0.22</td>
<td>0.13</td>
</tr>
<tr>
<td>Lack of Energy</td>
<td>0.60</td>
<td>-0.07</td>
<td>0.15</td>
</tr>
<tr>
<td>Diurnal mood variation</td>
<td>-0.14</td>
<td>0.25</td>
<td>0.60</td>
</tr>
<tr>
<td>Difficulty falling asleep</td>
<td>0.13</td>
<td>0.80</td>
<td>0.00</td>
</tr>
<tr>
<td>Multiple awakenings during sleep</td>
<td>0.11</td>
<td>0.77</td>
<td>-0.07</td>
</tr>
<tr>
<td>Early morning wakenings</td>
<td>0.04</td>
<td>0.67</td>
<td>0.14</td>
</tr>
<tr>
<td>Suicidal thoughts</td>
<td>0.09</td>
<td>0.10</td>
<td>0.53</td>
</tr>
<tr>
<td>Self depreciation</td>
<td>0.16</td>
<td>-0.07</td>
<td>0.74</td>
</tr>
<tr>
<td>Pessimism</td>
<td>0.28</td>
<td>-0.23</td>
<td>0.48</td>
</tr>
<tr>
<td>Mood congruent delusions</td>
<td>-0.13</td>
<td>0.04</td>
<td>0.30</td>
</tr>
</tbody>
</table>
For the whole sample, the Kaiser Meyer Olkin measure of sampling adequacy was 0.67 and the Bartlett test of sphericity was 632.54. The three factor solution identified the same three factors. The only difference was that depressed mood (+0.61) was added to the symptoms associated with Factor one.

Undertaking a logistic regression analysis to look at the patients assigned to sub-group one, a past history of psychiatric disorder (Wald 6.67 \( p = 0.01 \)) and severe visual impairment (Wald 5.29 \( p = 0.02 \)) were significantly positively associated with symptom group one depression. Sub-groups two and three were too small to meet the study criteria for a logistic regression analysis. Using Fisher's exact test, subgroup two depression was not significantly associated with any of the studied variables (bereavement Fisher's exact test \( p = 0.39 \), deafness Fisher's exact test \( p = 0.23 \), gender Fisher's exact test \( p = 0.32 \), insight Fisher's exact test \( p = 0.25 \), life events Fisher's exact test \( p = 0.85 \), physical health problems Fisher's exact test \( p = 0.42 \), a past history of psychiatric disorder Fisher's exact test \( p = 0.78 \), severe visual impairment Fisher's exact test \( p = 0.41 \), living alone Fisher's exact test \( p = 0.16 \), ten years or more of education Fisher's exact test \( p = 0.23 \), diagnosis of Alzheimer's disease versus vascular dementia Fisher's exact test \( p = 0.49 \), a diagnosis of Alzheimer's disease versus Senile Dementia of Lewy Body Type Fisher's exact test \( p = 0.34 \), a diagnosis of vascular dementia versus a diagnosis of Senile Dementia of Lewy Body Type Fisher's exact test \( p = 0.36 \), age at the onset of the dementia Mann-Whitney U test \( u = 474.5 \, z = -0.15 \, p = 0.88 \)).

Factor three depression was significantly associated with bereavement (Fisher's exact test \( p = 0.02 \)) but no significant associations were seen for any of the other variables.
(deafness Fisher's exact test \( p = 0.21 \), gender Fisher's exact test \( p = 0.29 \), insight Fisher's exact test \( p = 0.30 \), life events Fisher's exact test \( p = 0.75 \), physical health problems Fisher's exact test \( p = 0.17 \), past history of psychiatric disorder Fisher's exact test \( p = 0.65 \), severe visual impairment Fisher's exact test \( p = 0.31 \), living alone Fisher's exact test \( p = 0.25 \), education Fisher's exact test \( p = 0.32 \), diagnosis of Alzheimer's disease versus vascular dementia Fisher's exact test \( p = 0.39 \), diagnosis of Alzheimer's disease versus Senile Dementia of Lewy Body Type Fisher's exact test \( p = 0.41 \), diagnosis of vascular dementia versus a diagnosis of Senile Dementia of Lewy Body type Fisher's exact test \( p = 0.48 \), age at the onset of the dementia Mann-Whitney U test \( u = 370, z = 0.96, p = 0.34 \)).

Descriptive data relating to the studied variables are shown in Table 15.2 and the logistic regression analysis for subgroup one is shown in Table 15.3.

Examining the associations with CAMCOG sub-scores, there was a significant association between Sub-group one depression and higher scores on the recent memory sub-scale (Wald 4.65 \( p = 0.03 \)). There were too few patients in sub-groups two and three to undertake a logistic regression analysis but there were no significant differences in the total CAMCOG scores between patients in either of the sub-groups and those without RDC major depression (sub-group two Mann-Whitney U test \( u = 262, z = 0.04, p = 0.97 \), sub-group three Mann-Whitney U test \( u = 441, z = 0.19, p = 0.85 \)). Descriptive data regarding the mean sub-scale scores are shown in Table 15.4 and the logistic regression analysis is shown in Table 15.5.
# TABLE 15.2

**Associations of Depression in Depression Subgroups 1, 2 & 3**
- Descriptive Data

<table>
<thead>
<tr>
<th></th>
<th>Sub group 1 (n = 40)</th>
<th>Sub group 2 (n = 5)</th>
<th>Sub group 3 (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Onset</strong></td>
<td>76.03 (SD 6.80)</td>
<td>81.00 (SD 3.94)</td>
<td>78.78 (SD 5.97)</td>
</tr>
<tr>
<td><strong>Bereavement</strong></td>
<td>8 (20%)</td>
<td>1 (20%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td><strong>Deafness</strong></td>
<td>16 (40%)</td>
<td>2 (40%)</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td><strong>Male Gender</strong></td>
<td>9 (22.5%)</td>
<td>2 (40%)</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td><strong>Insight</strong></td>
<td>14 (35%)</td>
<td>2 (40%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td><strong>Life Events</strong></td>
<td>3 (7.5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Physical Health Problems</strong></td>
<td>13 (32.5%)</td>
<td>1 (20%)</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td><strong>Past History of Psychiatric Disorder</strong></td>
<td>8 (20%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Severe Visual Impairment</strong></td>
<td>14 (35%)</td>
<td>0 (0%)</td>
<td>2 (22.2%)</td>
</tr>
<tr>
<td><strong>Living Alone</strong></td>
<td>15 (37.5%)</td>
<td>1 (20%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td><strong>10 years or more of Education</strong></td>
<td>4 (10%)</td>
<td>2 (40%)</td>
<td>1 (11.1%)</td>
</tr>
</tbody>
</table>
### TABLE 15.3

**Associations of Sub-Group 1 Depression - A Logistic Regression Analysis**

<table>
<thead>
<tr>
<th>Sub-group 1</th>
<th>Wald</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset of dementia</td>
<td>3.34</td>
<td>0.07</td>
</tr>
<tr>
<td>Bereavement</td>
<td>0.12</td>
<td>0.73</td>
</tr>
<tr>
<td>Deafness</td>
<td>3.21</td>
<td>0.07</td>
</tr>
<tr>
<td>Education</td>
<td>1.20</td>
<td>0.27</td>
</tr>
<tr>
<td>Gender</td>
<td>0.28</td>
<td>0.60</td>
</tr>
<tr>
<td>Insight</td>
<td>0.91</td>
<td>0.34</td>
</tr>
<tr>
<td>Lives alone</td>
<td>3.47</td>
<td>0.06</td>
</tr>
<tr>
<td>Other Life Events</td>
<td>0.87</td>
<td>0.35</td>
</tr>
<tr>
<td>Past Psychiatric History</td>
<td>6.67</td>
<td>0.01*</td>
</tr>
<tr>
<td>Physical Health</td>
<td>3.22</td>
<td>0.07</td>
</tr>
<tr>
<td>Type of dementia</td>
<td>4.12</td>
<td>0.25</td>
</tr>
<tr>
<td>Visual Impairment</td>
<td>5.29</td>
<td>0.02*</td>
</tr>
<tr>
<td>Subgroup 1</td>
<td>Subgroup 2</td>
<td>Subgroup 3</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>SD</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>Mean</td>
</tr>
</tbody>
</table>

CAMCOG Sub-scores in Patients with Sub-group 1, 2 & 3 Depression

TABLE 15.4
TABLE 15.5

Cognitive Associations of Sub-Group 1 Depression, A Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Cognitive Function</th>
<th>Sub-group 1</th>
<th>Wald</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CAMCOG Score</td>
<td>1.47</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td>0.67</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Language Comprehension</td>
<td>0.30</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>Language Expression</td>
<td>0.07</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Praxis</td>
<td>0.36</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Recent Memory</td>
<td>4.65</td>
<td>0.03*</td>
<td></td>
</tr>
<tr>
<td>Visual Memory</td>
<td>1.97</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Remote Memory</td>
<td>1.65</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>Attention &amp; Calculation</td>
<td>0.47</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td>3.05</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Abstract thinking</td>
<td>0.69</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>1.38</td>
<td>0.24</td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER 16

RESULTS - DEPRESSION, FOLLOW-UP DATA

Sixteen of the eighty-nine patients who completed the one year of follow-up had DSM IIIR major depression at the time of the initial assessment, whilst twenty-one patients had RDC major depression and a further twenty-one patients had fulfilled the RDC criteria for minor depression. Three of the patients with DSM IIIR major depression did not experience either RDC major or RDC minor depression during any of the twelve months of follow-up. Only nine (56.3%) of these patients suffered three or more months of depression, combining the number of months of RDC major and RDC minor depression, and only two (12.5%) patients had depression for at least six months. One (6.3%) patient was still depressed after one year. During the follow-up year the sixteen patients had a mean of 1.5 months of RDC major depression and 2.93 months of depression, when RDC major and RDC minor depression were combined.

The twenty-one patients who initially fulfilled the criteria for RDC major depression had a mean of 1.52 months of RDC major depression over the follow-up year which increased to a mean of 3.24 months combining the number of months of RDC major and RDC minor depression. Twelve (57.1%) of the patients suffered from three or more months of RDC major or minor depression, whilst four (19%) had depression for at least six months. Two (9.5%) patients suffered from RDC major depression which did not resolve during the follow-up year.

Only two of the twenty-one patients with RDC minor depression at baseline had any months of RDC major depression during the follow-up year. In total however, these
twenty-one patients had a mean of 2.43 months of RDC major or minor depression. Six (28.6%) of the patients had three or more months of depression, whilst five (23.8%) were depressed for at least six months. In total, only two patients who fulfilled the diagnosis for any type of depression did not have a resolution of their symptoms during the year of follow-up, but nine patients experienced at least six months of depression (Table 16.1).

Of the fifteen patients with DSMIIIR major depression which resolved during the follow-up year; three (20%) had further episodes of RDC major depression and one patient (6.7%) had an episode of RDC minor depression. Of the nineteen resolved cases of RDC major depression, four (21.1%) had new episodes of RDC major depression, whilst three (15.7%) had new episodes of RDC minor depression. There were twenty-one resolved cases of RDC minor depression, of whom four (19.0%) had further episodes of RDC minor depression but none had an episode of RDC major depression. Resolved major depression recurred in about 20% of patients which ever definition of major depression was used. The recurrence rate of RDC minor depression was similar. The majority of further episodes of depression amongst patients with major depression were also of major depression and all of the episodes of recurrent depression amongst patients with RDC minor depression were also of minor depression.
TABLE 16.1

Outcome of Depression (all dementias)

<table>
<thead>
<tr>
<th>Baseline Diagnosis</th>
<th>0 - 2 (RDC major and minor Depression)</th>
<th>3 - 5</th>
<th>≥ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSMIIIIR major depression</td>
<td>7(43.8%)</td>
<td>7(43.8%)</td>
<td>2(12.5%)</td>
</tr>
<tr>
<td>(n = 16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDC major depression</td>
<td>9(42.9%)</td>
<td>8(38.1%)</td>
<td>4(19.0%)</td>
</tr>
<tr>
<td>(n = 21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDC minor depression</td>
<td>15(71.4%)</td>
<td>1(4.8%)</td>
<td>5(23.8%)</td>
</tr>
<tr>
<td>(n = 21)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Combining RDC major and RDC minor depression, nine (33.3%) of the twenty-seven depressed patients with Alzheimer's disease were depressed for three or more months and three patients (11.1%) were depressed for at least six months. The picture was very different for the six depressed patients with vascular dementia, all of whom were depressed for at least three months and three of whom were depressed for six months or more. Three (42.9%) of the seven patients with Senile Dementia of Lewy Body Type were depressed for at least three months, all of whom were depressed for six months or more. Comparing patients with three or more months of depression between each of the diagnostic groups using the Fisher's exact test, patients with vascular dementia were significantly more likely to have at least three months of depression than patients with Alzheimer's disease (vascular dementia versus Alzheimer's disease, Fisher's exact test $p = 0.005$). There was also a trend for patients with vascular dementia to be more likely to have three or more months of depression than patients with Senile Dementia of Lewy Body Type (vascular dementia versus Senile Dementia of Lewy Body Type, Fisher's exact test $p = 0.05$). There was no significant difference between the number of patients with three or more months of depression comparing patients with Senile Dementia of Lewy Body Type to those with Alzheimer's disease (Senile Dementia of Lewy Body Type versus Alzheimer's disease, Fisher's exact test $p = 0.30$). The number of months of depression experienced by patients with the different dementias is shown in Table 16.2.
### TABLE 16.2

Outcome of Depression In Patients With Different Types Of Dementia

<table>
<thead>
<tr>
<th>No. of months of Depression Episode (RDC major and minor depression combined)</th>
<th>0 - 2</th>
<th>3 - 5</th>
<th>≥ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease (n = 27)</td>
<td>18(66.7%)</td>
<td>6(22.2%)</td>
<td>3(11.1%)</td>
</tr>
<tr>
<td>Vascular dementia (n = 6)</td>
<td>0(0%)</td>
<td>3(50%)</td>
<td>3(50%)</td>
</tr>
<tr>
<td>Senile Dementia of Lewy Body Type (n = 7)</td>
<td>4(57.1%)</td>
<td>1(14.3%)</td>
<td>2(28.6%)</td>
</tr>
</tbody>
</table>
There were no significant correlations between the number of months of depression experienced and the baseline CAMCOG score (Pearson's R = +0.07), the age of the patient at the onset of the dementia (Pearson's R = -0.05), gender (Pearson's R = -0.24), deafness (Pearson's R = 0.06), number of years of education (Pearson's R = -0.15), insight (Pearson's R = -0.10), living alone (Pearson's R = +0.12), physical health problems (Pearson's R = 0.23), a past history of psychiatric disorder (Pearson's R = -0.03), bereavement (Pearson's R = -0.04) or severe visual impairment (Pearson's R = -0.06).

Forty seven patients who did not have RDC major or minor depression at the time of the baseline interview were followed up for one year. Twenty-eight (59.6%) of these patients did not develop depression in any of the follow-up months whilst five (10.6%) had new episodes of RDC major depression and fourteen (29.8%) had new episodes of RDC minor depression. Of the thirty-six patients with Alzheimer's disease, twenty-one (58.3%) did not develop any depression over the year of follow-up, four (11.1%) developed RDC major depression and eleven (30.6%) developed RDC minor depression. Only one (11.1%) of the nine patients with vascular dementia who were not depressed at baseline developed RDC major depression over the course of the year. One (11.1%) further patient developed RDC minor depression. Two of the patients with Senile Dementia of Lewy Body Type followed up for the year were not depressed at baseline, both developed RDC minor depression during the year. The annual incidence rates are shown in Table 16.3.
<table>
<thead>
<tr>
<th></th>
<th>I1 (%)</th>
<th>I1 (30.6%)</th>
<th>I4 (29.8%)</th>
<th>5 (10.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alzheimer's</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Patients</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline

In patients not depressed at

No. of New cases of Depression

Annual Incidence Rate of Depression

TABLE 163
Clearly the sample is not representative of all patients with dementia. Given the high participation rate of those approached, it should be representative of patients with mild to moderate dementia in contact with psychiatric services and a memory clinic service respectively, although unfortunately no information is available regarding patients who did not meet the DSMIII-R criteria for dementia or refused to participate. Each patient was assessed using a detailed standardised interview which allowed standardised diagnostic criteria to be applied. In addition, detailed information was collected concerning psychotic symptoms, depression and cognitive functioning using structured instruments.

Although the method for diagnosing the individual dementias was novel, good agreement between the interviews of different raters was achieved. The diagnostic information was collected on the GMS/HAS schedules, which are well validated standardised instruments (Dewey et al 1992) and well validated diagnostic criteria were used to diagnose Alzheimer's disease and vascular dementia. The criteria used to diagnose Senile Dementia of Lewy Body Type (McKeith et al 1992) have been validated retrospectively but not prospectively. They are however the most widely used diagnostic system and achieved satisfactory concurrent validity with the only other published set of operational criteria (Byrne et al 1991). Even so, to consider Senile Dementia of Lewy Body Type as a disorder in its own right is largely a matter of personal opinion. The condition has for example been described as a variant of Alzheimer's disease by some groups (Hansen et al 1990). The majority of cases of Senile Dementia of Lewy Body Type would have
fulfilled the NINCDS ADRDA criteria for possible Alzheimer's disease. An alternative approach would have been to allow patients to have multiple diagnoses with many patients satisfying both criteria. This would have minimised differences between the two categories. The group of patients fulfilling the criteria for Senile Dementia of Lewy Body Type did appear to have a distinct outcome which offers some support for considering them separately, although this argument becomes rather circular.

The Burns' Psychotic Symptom Checklist was designed specifically for the current study, in the absence of any other suitable schedules. Although the schedule has not been validated, it contains a comprehensive list of symptoms, which were described in as much detail as possible. Visual hallucinations, delusions and delusional misidentification were then diagnosed by one of the raters according to the study criteria.

Symptoms of depression were assessed using one of the only two scales validated for the assessment of depression in dementia sufferers, the Cornell Depression Scale (Alexopolous et al 1988). The guidelines were slightly modified to cover a one month and not a one week period. The diagnosis of depression was made according to DSMIIIIR (American Psychiatric Association 1987) and RDC criteria (Spitzer et al 1978), enabling the comparison of criteria and the study of mild depression. The omission of the criterion that patients with depression caused by organic disorders cannot be diagnosed as suffering from DSMIIIIR major depression was waived in the current study. Although this procedure has not been formally validated, the method has been widely used in previous work. Seven of the twelve follow-up interviews were conducted over the telephone using only carers information about symptoms of depression. The absence of direct observational data and the patients own account of their symptoms may have led
to some discrepancy between the reporting of symptoms in different months, although satisfactory agreement was achieved for psychotic symptoms and depression between the baseline and month one interviews and between the month one and month two interviews respectively.

Cognitive assessments were undertaken using the CAMCOG, a well validated schedule which has been widely used (Roth et al 1986, Blessed et al 1991). The current study did however use a slightly different configuration of sub-scales, based on the work of Hooper and Bucks (1993).

The demographic comparisons between the three service settings revealed only one significant difference, a greater degree of cognitive impairment amongst patients in contact with the Coventry service compared to either of the other settings. Although the demographic characteristics of the three samples appear similar, important between sample differences may have occurred. This is likely to be of most relevance when considering the prevalence rates of depression, which varied widely between the different services. The Memory Clinic patients were initially recruited with the aim of increasing the number of patients with mild dementia, an objective not achieved.

When the results are considered in total, a large number of statistical comparisons were made. Statistical techniques were chosen with the aim of minimising false positive results, although given the large number of tests some may have occurred. It is therefore important to interpret the results in conjunction with previous research findings and to examine their internal consistency with other results from the current study.
CHAPTER 18
DISCUSSION - PSYCHOTIC SYMPTOMS

The current study supports previous studies utilising purpose designed instruments for the ascertainm ent of psychotic symptoms in suggesting that the prevalence rate exceeds 60% (Merriam et al 1988, Flynn et al 1991, Devanand et al 1992, Förstl et al 1993). The prevalence rate of psychotic symptoms was similar amongst patients attending a memory clinic service and those in contact with old age psychiatry services. Delusions occurred in 48.4% of patients, a rate comparable to other studies using purpose designed instruments (Reisberg et al 1987, Förstl et al 1993). The 35.5% prevalence of visual hallucinations was similar to Förstl's estimate of 32% (Förstl et al 1993) but higher than several other studies (Patterson et al 1990, Devanand et al 1992, Deutsch et al 1991). Auditory hallucinations occurred in 12.9% of subjects, a prevalence rate similar to several other studies (Förstl et al 1993, Deutsch et al 1991), although even amongst studies using structured instruments there has been considerable variation. Delusional misidentification has been reported by fewer studies. The prevalence rate of 29.0% in this sample is similar to the estimates of 34% (Förstl et al 1993) and 30% (Deutsch et al 1991) in other studies but higher than the 17.1% found by Reisberg et al (1987). There is a reasonable degree of concordance amongst studies which have used structured instruments to measure the prevalence rate of psychotic symptoms in general, delusions and delusional misidentification. The prevalence rates of visual hallucinations are however less consistent. The prevalence rates of all symptom categories are considerably higher than estimated by earlier studies.

The rank order of individual symptoms reported in the current study is similar to the
approximate estimate of rank prevalence made by Ballard & Oyebode (1995) based on the previous literature, with delusions of reference, delusions of theft, delusions of strangers in the house, visual hallucinations of strangers and delusions of persecution as the most commonly occurring symptoms. One patient experienced a Fregoli syndrome and one a delusion of partition, both of which were previously undescribed in dementia subjects. Delusional misidentification of one’s house, which was reported as common by groups using the BEHAVE AD instrument (Reisberg et al 1987), occurred in only two subjects.

Some degree of distress was reported by 61.4% of subjects with psychotic symptoms although the distress was only marked for 16.9%. The total number of subjects distressed by their symptoms was rather higher than the 30% reported by Gilley et al (1991). Interestingly it seems that the number and frequency of symptoms are better predictors of distress than their type. Eighty per cent of subjects had no insight into the abnormal nature of their psychotic experiences, although only one third of these actually acted on the abnormal beliefs. The type of symptoms experienced were not related to the degree of insight, but an increased number of symptoms and a greater frequency of symptoms were associated with reduced insight. Perhaps greater exposure to the psychotic symptoms acts to reinforce the reality of the belief systems.

Over 90% of patients with Senile Dementia of Lewy Body Type experienced at least one psychotic symptom. They were significantly more likely to experience visual hallucinations and delusional misidentification than patients with Alzheimer’s disease, although this is rather a tautology as visual hallucinations are amongst the diagnostic criteria for Senile
Dementia of Lewy Body Type. Patients with Senile Dementia of Lewy Body Type also experienced more different types of psychotic symptom at a greater frequency than patients with Alzheimer's disease or vascular dementia. The rank order of individual psychotic symptoms in the three dementias was however similar. Patients with vascular dementia were significantly more likely to experience visual hallucinations than patients with Alzheimer's disease, although the likelihood of experiencing delusions or delusional misidentification was not significantly different in the two dementias. This perhaps explains the failure to identify an association between vascular dementia and psychotic symptoms in previous studies (Cummings et al 1987, Binetti et al 1993). The strongest associations identified for psychotic symptoms in the logistic regression analyses were deafness, visual impairment, the type of dementia, the severity of agnosia and the impairment of expressive language skills. A separate analysis focusing just on patients with Alzheimer's disease did not reveal any additional associations. Deafness, visual impairment and agnosia could all isolate patients from accurate sensory information. Females with vascular dementia were significantly more likely to experience psychotic symptoms than males. None of the other factors associated with psychotic symptoms in patients with Alzheimer's disease were associated with these symptoms in patients with vascular dementia. Patients with psychotic symptoms in the context of vascular dementia did show a trend towards greater overall impairment on the CAMCOG schedule, particularly patients with visual hallucinations. The hypothesis that there may be a different pattern of associations between psychotic symptoms and vascular dementia requires further study.
The data offer support to the supposition that delusions and visual hallucinations have a different pattern of associations. Delusions were associated with deafness, whereas visual hallucinations were associated with visual impairment and vascular dementia. Patients who suffered from delusions were significantly more likely to have experienced a life event, but the same association was not reported for patients with visual hallucinations. Patients with delusions had significantly greater impairment of recent memory but the same was not true of patients with visual hallucinations.

It has been demonstrated that visual impairment is common amongst other groups of patients with visual hallucinations, such as those suffering from the Charles Bonnet Syndrome (Gold & Rabins 1989). In addition, Perry et al (1990) suggested an association between occipital lobe cholinergic deficits and visual hallucinations. This would be consistent with a model where deficits at any stage of the perception of visual data could predispose to the development of visual hallucinations. The association between visual impairment and visual hallucinations, both in the overall sample and amongst patients with Alzheimer’s disease, fits in well with this model and so could be considered as a putative aetiological factor.

Deafness was significantly associated with the presence of delusions both for the sample as a whole and for patients with Alzheimer’s disease. This makes sense in view of the association between deafness and psychosis amongst patients with paraphrenia (Kay & Roth 1961). The association can therefore be considered as a putative aetiological factor. The finding also has potential treatment implications as hearing aids can substantially improve the level of symptomatology in patients with paraphrenia and auditory
impairment (Almeida 1993). Similarly the association between delusions and life events has a parallel in the literature pertaining to functional psychosis (Brown & Birley 1968), and this too could be considered as a putative aetiological factor. Only a small number of patients actually experienced life events however and they may only be important for a minority of patients. Nevertheless it is an important area for further study, which should perhaps make use of more sensitive instruments to detect a broader range of stresses.

Gray (1982) proposed a "comparator" system responsible for monitoring sensory information from the outside world and comparing this with internal perceptual configurations. It is not difficult to see how deafness could increase the number of potential discrepancies between the internal and external configurations as well as leading to increased ambiguity regarding the intent of others. Patients who experienced delusions had significantly greater impairment of recent memory, which is primarily a reflection of the extent of hippocampal damage. This is of interest as it is consistent with Zubenko's et al (1991) study suggesting an increase of plaques and tangles in the hippocampus of patients with psychotic symptoms. It is also the proposed location of Gray's (1982) comparator. Life events do not fit clearly into the same model. Zubenko et al (1991) reported an association between psychosis in dementia sufferers and an imbalance of the noradrenaline to 5-hydroxytryptamine ratio. The neuro-endocrine response to a stressful situation could well augment such an imbalance.

Older age was associated with delusions and a later age of onset was associated with visual hallucinations in the overall sample, whilst delusions were significantly associated
with a later age of onset amongst patients with Alzheimer’s disease. The two variables were highly correlated and probably measure the same dimension. The correlations between age and both visual impairment and deafness respectively were weak and are unlikely to explain the association between age and delusions in the context of a logistic regression analysis. It is possible that some of the patients with a later onset represent a discrete group with a different symptom pattern and course.

The significant association between psychotic symptoms and Senile Dementia of Lewy Body Type is difficult to interpret in view of the diagnostic criteria of this condition. The possibility of an increased frequency of visual hallucinations amongst patients with vascular dementia compared to those with Alzheimer’s disease is however of interest and requires further study. There was no association between psychotic symptoms and a tendency to confabulate. Although some of the theoretical difficulties of distinguishing confabulation from delusions have been discussed (Flint 1991), this would suggest that there is no substantial overlap.

None of the variables studied showed a significant association with delusional misidentification, although in the analysis of cognitive subscales a trend towards an association with greater impairment of receptive language function was evident. On excluding patients with the phantom boarder delusion, there was also a trend towards an association with agnosia. This is consistent with the picture identification difficulties previously described amongst these patients ( Förstl et al 1991) and makes sense for symptoms such as the mirror image and television misidentification where the primary abnormality appears to be a difficulty in accurately identifying images with secondary
delusions. There is no support however for Förstl's et al (1991) finding of an association between delusional misidentification and frontal lobe impairment. Symptoms such as delusional misidentification of television and mirror images represent a failure to correctly identify the nature of a visual phenomenon, followed by a delusional elaboration. This seems fundamentally different from the Capgras phenomenon and delusional misidentification of one's house where the core element is an altered sense of familiarity. The phantom boarder delusion is again different, often representing a delusional elaboration of a visual hallucination. Further nosological refinement of delusional misidentifications may help to delineate a pattern of associations.

Patients with psychotic symptoms were significantly more cognitively impaired than patients without. This concurs with the findings of most previous studies (Rockwell et al 1994, Devanand et al 1992). The findings were similar to those of Jeste et al (1992), in suggesting that although cognitive functions were significantly more impaired in those with psychotic symptoms, there was a clustering of scores within the moderate to severe range. In the current study patients tended to have CAMCOG scores between twenty-one and forty. The absence of a significant difference in the overall level of cognitive impairment from the rest of the sample for patients with delusions and delusional misidentification is also consistent with previous work. The current study is however different in not finding a greater degree of cognitive impairment amongst patients with visual hallucinations. This is probably explained by the average level of cognitive functioning for the sample as a whole, which was substantially lower than in previous reports. The absence of any significant associations in the analysis focusing upon patients with Alzheimer's disease was probably a consequence of the reduced sample size.
The principal components analysis is consistent with the conclusions drawn from the logistic regression calculations that visual hallucinations, delusions and delusional misidentification should be considered as separate symptom groups. The best solution from the principal components analysis identified four distinct factors. Three closely replicated the symptom groups visual hallucinations, delusions and delusional misidentification, although the phantom boarder syndrome was found to be associated with visual hallucinations and not delusional misidentification. The fourth symptom group was an entirely distinct cluster of symptoms consisting of visual hallucinations of relatives and delusions concerning relatives being in the house. This category could be seen as a collection of comfort phenomena, a notion supported by the significant inverse association between this symptom group and emotional distress. Léger & Clément (1991) suggest that delusions arise as part of a mechanism to protect the individual from the uncertainties of cognitive decline. This in some ways parallels the role of pseudo-hallucinations in the recently bereaved (Clayton 1979). Dementia patients commonly talk of parents as a way of promoting security (Miesen 1993). It would not be a great jump to envisage hallucinatory or pseudo-hallucinatory experiences of parents or other familiar figures in the same way. This is an important observation for these individuals, as some of the symptoms may be an adaptive coping strategy and not a pathological condition.

No support is provided for the findings of Drevets & Rubin (1989), Rosen & Zubenko (1991) or Förstl et al (1993). Each of these groups found a greater speed of cognitive deterioration amongst Alzheimer's disease patients with psychotic symptoms. A significant but weak correlation between the degree of cognitive deterioration and the number of months during which psychotic symptoms were experienced was however
demonstrated. The severity of cognitive impairment was less severe in each of the three previous studies than in the current sample. It is hence possible that the most pronounced cognitive deterioration amongst patients with psychotic symptoms occurs in the earlier stages of the dementing process, reaching a plateau thereafter. In the present study, half of the patients with Senile Dementia of Lewy Body type had an enormous deterioration of more than thirty points on the CAMCOG schedule. It is not uncommon for patients with Senile Dementia of Lewy Body type to fulfil the NINCDS ADRDA criteria for probable Alzheimer's disease (Burns et al 1990b). It is conceivable that patients with Senile Dementia of Lewy Body Type could be included in a sample diagnosed according to these criteria and may substantially alter the apparent pattern of deterioration. Further work is needed to tease out the correct explanation.

The significant association between the number of months during which psychotic symptoms were experienced and the degree of cognitive deterioration could be interpreted as suggesting that psychotic symptoms have a direct influence on cognitive deterioration, rather than indicating a sub-group of patients with a more malignant dementia process. Such an effect could potentially be mediated by the production of cortisol or similar chemicals in response to the distress felt by these patients.

During the course of the follow-up year, 73% of patients experienced resolution of their delusions, 61% experienced resolution of their visual hallucinations and 65% experienced resolution of their delusional misidentification. Combining all categories of psychotic symptoms, resolution occurred in 53% of patients, although approximately 25% suffered a further episode. Recurrence of symptoms occurred most frequently amongst patients with delusions and least frequently amongst patients with visual hallucinations, delusional
misidentification (in the absence of the phantom border syndrome) and comfort phenomenon. The number of months of psychotic symptoms experienced by patients followed a bimodal distribution with a cluster of patients experiencing brief psychotic episodes of three months or less and a further cluster experiencing symptoms for at least nine months of the year. Although there were some minor differences between the different categories of psychotic symptoms, persistent psychosis in most categories was associated with at least three months of psychosis at the time of the baseline interview and a baseline frequency of psychotic symptoms of at least daily. Neither deafness nor severe visual impairment, which were both significantly associated with the presence of psychotic symptoms, were associated with persistent psychosis. There was a trend for persistent visual hallucinations to be associated with lower baseline CAMCOG scores. This association was not evident for the other categories of psychotic symptoms. As this was only a trend and seven variables were investigated for three different categories of psychotic symptoms, the results must be interpreted cautiously. It is however of potential importance and merits further investigation.

The bimodal pattern of brief and persistent psychotic disorders was seen in all three of the dementias studied, although no patients with vascular dementia had more than nine months of delusions. Patients with Senile Dementia of Lewy Body type were significantly more likely to have persistent visual hallucinations than patients with Alzheimer’s disease. Whilst it is not surprising that patients with Senile Dementia of Lewy Body type should commonly experience visual hallucinations as they are included within the diagnostic criteria, the increased likelihood of persistence provides support for the argument that the nature of visual hallucinations is different amongst these patients. Even amongst
patients with persistent psychotic symptoms, new symptoms commonly arose and the
collection of psychotic symptoms experienced by individual sufferers was far from
static.

Only one previous study has reported an annual resolution rate of psychotic symptoms.
Rosen & Zubenko (1991) found only 2.2% of psychotic symptoms to resolve.
Standardised instruments were not used for the detection of psychotic symptoms and no
intermediate follow-ups were undertaken. The symptoms occurring most frequently
would be the most likely to be identified, and brief psychotic episodes may remain
undetected. The resolution rate of psychotic symptoms in the current study was
substantially higher at 53%. This figure is more likely to be accurate in view of the
monthly follow-up regime, which made use of a standardised instrument. There were
however twenty-seven patients with persistent psychotic symptoms. Perhaps an annual
resolution rate of approximately 2% is realistic for this group, although this requires
further study. These findings can be used to inform treatment decisions. As the
resolution rate of new psychotic symptoms is high, it is probably unhelpful to instigate
treatment until symptoms have persisted for at least three months. If the level of distress
is such that it is difficult to avoid treating the symptoms before this time, it would be
appropriate to discontinue treatment after the symptoms have resolved. A treatment trial
would seem indicated for patients who have experienced three months or more of
psychotic symptoms, particularly if the symptoms occur at least once a day. As 75% of
recovered cases do not relapse, a trial of treatment discontinuation would again be
useful.
The annual incidence rate of psychotic symptoms was 46.7%. New cases of delusional misidentification excluding the phantom boarder syndrome, comfort phenomena and visual hallucinations occurred in 11.8%, 12.5% and 15.8% of patients respectively. New cases of delusional misidentification including the phantom boarder syndrome occurred in 24.4% of patients and new cases of delusions arose in 30.4% of patients. More than 80% of patients experienced at least one psychotic symptom during the study. Previous estimates of the annual incidence rate varied from 1% (Burns et al 1990) to 5.3% (Chen et al 1991). A considerably higher annual incidence rate is seen in the current study. The increased frequency of follow-up assessments, undertaken with a standardised instrument is likely to have improved symptom detection. The incidence rate reported in the current study is therefore likely to be accurate for a sample of patients in contact with clinical services. A longer period of follow-up would be necessary to determine the incidence rate of persistent psychosis amongst those with newly developed symptoms. It is however a tenable hypothesis that the incidence rate of persistent psychosis, which is probably what has been identified in previous studies, is much lower. The incidence rate of delusions and visual hallucinations did not differ significantly between the different dementias. Patients with both Senile Dementia of Lewy Body type and vascular dementia were however significantly more likely to develop new cases of delusional misidentification (not including the phantom boarder syndrome). The incidence rate of these symptoms was between 25% and 35% for vascular dementia and Senile Dementia of Lewy Body Type, whilst it only just exceeded 5% for patients with Alzheimer's disease. The sample size in the current study was too small to identify more subtle differences in the incidence rates of different psychotic phenomena. This is clearly an area requiring further study.
CHAPTER 19
DISCUSSION - DEPRESSION

The 16.9% prevalence rate of DSMIIIR major depression is within the 15% to 30% range suggested by previous work (Burns 1991a), although there is a wide discrepancy between the prevalence rates of depression in the different settings, which mirrors the variability of reported prevalence rates from different clinical services. The demographic characteristics of the three patient populations were generally similar, although the Coventry patients had a significantly greater degree of cognitive impairment. The severity of cognitive impairment has been linked to the likelihood of suffering from depression in some studies (Cooper et al 1990, Teri & Wagner 1991). No association between depression and the severity of cognitive impairment was however evident in the current sample and this is unlikely to have been a major confounding factor. There were also a slightly higher proportion of patients with non-Alzheimer dementias in the memory clinic sample, which if anything should have biased the results in the opposite direction by elevating the prevalence rate in the memory clinic. None of the sample differences can hence explain the disparate prevalence rates. Henderson (1990) has suggested that concurrent depression in patients with dementia leads to differential referral to hospital services. Differential referral of depressed patients to psychiatric services but not memory clinic services would be consistent with the current findings.

The correlation between DSMIIIR and RDC major depression was reasonably high, with a Kappa value of 0.63. Despite this the DSMIIIR criteria were more restrictive. Thirty-nine percent of cases fulfilling the criteria for RDC major depression did not fulfil the DSMIIIR criteria. There were also a considerable number of patients, thirty-four (27.4%)
in total, who fulfilled the RDC criteria for minor depression. Patients with RDC major depression had a mean of 12.7 depressive symptoms whilst patients with minor depression had a mean of 7.0 symptoms. All patients with minor depression and 90.3% of patients with RDC major depression experienced a sustained low mood, whilst 11.8% and 45.2% respectively had frequent suicidal thoughts. There are therefore a number of patients who do not fulfil the restrictive criteria for DSMIIIR major depression but do fulfil the criteria for RDC minor or major depression and have significant psychiatric morbidity, emphasising the importance of less severe depressive disorders amongst dementia sufferers.

The common symptoms of depression amongst patients with DSMIIIR major depression were similar to those described in other patient populations (Blazer et al 1987). One exception was the low prevalence of diurnal mood variation which occurred in only 14.3% of patients with DSMIIIR major depression. This has not been reported in previous studies of depression amongst dementia sufferers. The current data did not support the supposition that patients with dementia and depression have less intrapsychic symptoms (Merriam et al 1988) with 33.3% of patients exhibiting these symptoms. The findings do support the work of Cummings (1988) and Ballard et al (1993b) in suggesting that suicidal thoughts are common.

Examining the aetiologies of DSMIIIR major depression, RDC major depression and RDC minor depression separately may have had the effect of increasing the chance of spurious associations. Alzheimer's disease was significantly inversely associated with both DSMIIIR major depression and RDC major depression, whilst vascular dementia was
significantly associated with DSMIIIR major depression and showed a trend towards an association with RDC major depression. These findings are also consistent with previous literature (Reding et al 1985, Greenwald et al 1989, Cummings et al 1987) and so the association could be considered as a putative aetiological factor. Depression is of course one of the items included in the Hachinski scale, although it only contributes one point to the scale and is unlikely to be an important confounding factor. Thirty-three percent of the patients with Senile Dementia of Lewy Body Type had RDC major depression, confirming that depression is common in this condition.

Deafness was significantly associated with DSMIIIR but not RDC major depression in the sample as a whole and in patients with Alzheimer's disease. The finding therefore has to be interpreted cautiously, although deafness is associated with functional depression in the elderly (Carabellese et al 1993) and merits further consideration. A past history of psychiatric disorder showed a trend towards an association with DSMIIIR but not RDC major depression in the overall sample but was not significantly associated with depression diagnosed according to either set of criteria amongst patients with Alzheimer's disease. Although there is only very limited evidence to support the association in the current study, a past history of psychiatric disorder has been significantly associated with depression in previous reports (O'Connor et al 1990ab, Rovner et al 1989). Visual impairment was significantly associated with both DSMIIIR and RDC major depression amongst patients with Alzheimer's disease and showed a trend towards a significant association with RDC major depression when all dementia sufferers were considered. Visual impairment has been the subject of only very limited previous enquiry and the current results must be interpreted with care, particularly as
they derive from a number of different analyses. The link between depression and both deafness and visual impairment amongst dementia sufferers is an important area for future study. Larger studies are needed to confirm these putative associations.

The current report supports the findings of previous studies (Verhey et al 1993, Ott & Fogel et al 1992) in suggesting that retention of insight is not an important factor in the development of major depression. It is also consistent with previous work in finding that neither demographic factors nor physical health problems (Ballard et al 1993b) are associated with major depression. The data do not support Cohen’s et al (1993) proposal that living alone is an important association of major depression.

The overall level of cognitive impairment was not significantly associated with depression. The literature is fairly equally divided between studies which suggest that severity of cognitive impairment is important (Cooper et al 1990, Pearson et al 1989, Reifler et al 1982, Teri & Wagner 1991, Reifler et al 1989) and those which do not (Reding et al 1985, Mackenzie et al 1989, Pozzi et al 1993, Ott & Fogel 1992, Verhey et al 1993, Fitz & Teri 1994, Fischer et al 1990, Cummings et al 1987, Cummings 1988, Swearer et al 1988, Breen et al 1984). The current study supports the latter view. The findings for patients with Alzheimer’s disease are consistent with previous reports (Burns et al 1990c, Fitz & Teri 1994) suggesting that there is no association between the presence of depression and any specific pattern of cognitive impairments, although the better performance of depressed patients in the overall sample on tasks of recent memory could be interpreted as offering support to Förstl’s et al (1992) finding that there is less severe hippocampal involvement in patients with concurrent depression and dementia.
A significant association between the presence of RDC major depression and physical health problems was identified in patients with vascular dementia. This is congruent with the literature pertaining to depression in the elderly without dementia (Philpot 1990) and supports Cummings’ (1988) proposal that physical health difficulties may predispose to depression in this patient group. Physical health problems could therefore be considered to be a putative aetiological factor for the development of major depression amongst patients with vascular dementia. The possibility emerges that the aetiology of depression in patients with vascular dementia differs from that of patients with Alzheimer’s disease. A larger sample of patients with vascular dementia is required to test this hypothesis.

RDC minor depression was significantly associated with the presence of physical health problems and deafness. Both have been reported as associations of depression in the absence of cognitive impairment (Philpot 1990, Carabellese et al 1993, Thomas 1981, Mahapatra 1974) and hence merit further study. There were similar prevalence rates of RDC minor depression amongst patients in old age psychiatry services and those attending the memory clinic. Perhaps the pattern of differential referral postulated to occur for more severe depressions does not apply to milder conditions. Milder depression may have a different aetiology to more severe depression. It would be interesting to take this work further and examine whether patients with milder depression have similar patterns of monamine loss in the brain stem nuclei as patients with major depression (Zweig et al 1988, Zubenko & Moossy 1988).

The most satisfactory solution from a principal components analysis was the three factor solution. The same factors were identified in patients fulfilling Research Diagnostic
Criteria for depression and patients in the sample as a whole. Factor one included the symptoms anxiety, lack of energy, decreased mood reactivity and loss of interest; Factor three included the symptoms irritability, suicide, self deprecation and diurnal mood variation whilst Factor two consisted entirely of sleep items. Factor one is similar to the apathy factor identified by Forsell et al (1993). The other cluster identified by Forsell et al (1993) included the items frequent suicidal thoughts and guilt. Factor three included both of these symptoms but not dysphoria, which was associated with the factor in Forsell’s et al (1993) study. In the current sample dysphoria was common amongst all patients with depression. Factor two, which consisted entirely of sleep items, has not been identified in any previous work. Sleep disturbance is a core symptom of depression and occurs frequently in dementia sufferers (Rabins et al 1982). It is hence an important possibility that sleep disturbance may be the central feature of a distinct depressive subtype, although caution must be exercised as the symptom group may represent an artefact due to the greater reporting of sleep symptoms by carers living with patients.

Symptom group one depression was significantly associated with severe visual impairment, a past history of psychiatric disorder and better retention of recent memory; hence displaying notable overlap with the associations of DSMIIIR major depression. Symptom group three depression on the other hand was significantly associated with bereavement, but did not show even a trend towards an association with any of the variables associated with Symptom group one depression. Almost half of the patients in this group had experienced a recent bereavement. The data do not support Forsell’s et al (1993) suggestion that the overall severity of the dementia shows any different pattern of associations with any of the sub-groups identified. It is an interesting possibility that
a sub-set of patients may be particularly prone to a cluster of symptoms including self
deprecation and suicidal thoughts and that this may be associated with bereavement. This
would suggest that the bereavement reactions of dementia sufferers are an important
area for future research and that including patients with severe depression in the context
of a bereavement in aetiological studies of depression may distort the results.

An initial diagnosis of DSMIIIIR major depression or RDC major depression predicted
a similar course of disorder. For patients diagnosed according to either set of criteria
approximately 55% had at least three months of depression, 12-19% had at least six
months of depression and 5-10% of cases remained unresolved after one year. In
addition the recurrence risk of RDC major depression in resolved cases of both
DSMIIIIR and RDC major depression was approximately 20%. Combining RDC major
and minor depression, only one third of patients with Alzheimer's disease had three or
more months of depression and 11% had depression for at least six months, whilst all six
patients with vascular dementia had at least three months of depression and 50% of
these patients suffered depression for six months or more. The course of depression in
patients with Senile Dementia of Lewy Body type was intermediate with three out of the
seven patients experiencing at least three months of depression, all of whom experienced
depression for six months or more. Although the numbers in the vascular dementia group
were small, these patients were significantly more likely to suffer from at least three
months of depression than patients with Alzheimer's disease.

Although requiring confirmation in studies with a larger numbers of patients suffering
from vascular dementia, depression amongst these patients appears to be persistent.
Based upon these findings it would seem appropriate to treat major depression in patients with vascular dementia as soon as it is identified, using antidepressant medication. Patients with Alzheimer's disease on the other hand had a much less persistent course of depression, with two-thirds of cases resolving in the first three months. It would be difficult to recommend treating these disorders by pharmacological means when first identified, especially as a pharmacological approach might take a month or more to effect an improvement. The relatively high rate of spontaneous resolution might explain the findings of Reifler et al (1989), where improvement of depression occurred in both the treatment and control groups. Only one third of the patients who were depressed for three months continued to be depressed for a further three months. It would not be helpful to suggest a duration of three months as an appropriate point to instigate pharmacological treatment. Two of the three cases which did persist for six months however, continued unresolved for one year. It would therefore seem appropriate to commence drug treatment amongst this group of patients.

RDC major depression was recurrent in a quarter of cases, these patients probably represent a further group of patients who may benefit from pharmacological treatment, although the follow-up period was not sufficiently long to document the longer term course of depression amongst these individuals. Only three of the patients with Senile Dementia of Lewy Body type were depressed for three or more months, but all of these patients continue to be depressed for six months. Although the numbers are very small, it may be appropriate to instigate treatment slightly earlier in these patients, perhaps after three months of depression.
RDC minor depression had a very different course. Only a quarter of the patients had three or more months of depression, although almost all of these patients continued to be depressed for six months. Hence for the majority of patients minor depression is a brief disorder but for a substantial minority it is a persistent disorder, perhaps akin to dysthymia. It is therefore important to identify persistent RDC minor depression, perhaps commencing treatment if it persists for three months or more.

As only two of the patients with Senile Dementia of Lewy Body Type who were followed up for one year, were not depressed at baseline, the study tells us little about the incidence rate of depression in these patients. There were however thirty-eight patients followed up for one year with Alzheimer's disease, who were not depressed at the time of the initial interview. Ten percent of these patients developed RDC major depression and an additional 30.6% developed RDC minor depression. A further nine patients with vascular dementia, who did not suffer from depression at the time of the initial assessment, were followed up for one year. The 11.1% annual incidence rate of major depression was similar to the incidence rate for patients with Alzheimer's disease. As these figures are based on regular monthly interviews with a standardised instrument, they are likely to be accurate annual incidence figures.
CHAPTER 20

PSYCHOTIC SYMPTOMS AND DEPRESSION - EXPANDED THEORETICAL MODELS

Psychotic Symptoms

Perhaps the most obvious point to emerge from the current study is the importance of considering visual hallucinations and delusions as separate phenomena. Visual hallucinations were associated with visual impairment. Precedents for this link are seen in the Charles Bonnet syndrome, where visual impairment is a common predisposition (Gold & Rabins 1989) and the association between late paraphrenia and ocular pathology (Cooper & Porter 1976). It has also been suggested by Perry et al (1990) that occipital lobe deficits are important in the genesis of visual hallucinations. We are therefore left with a model where either peripheral visual impairment or visual impairment caused by cortical degeneration is linked to visual hallucinations. Recanzone et al (1992) demonstrated in animal experiments that if a cortical area was damaged, a topographical reorganisation occurred with broadening of the receptive field. The perceptive role of some of the damaged cells was taken over by the surrounding areas. Some of the cells were however found to discharge spontaneously. Rabins (1994) has suggested that this theory might explain the link between peripheral visual problems and visual hallucinations amongst the elderly. This model is particularly applicable to dementia sufferers where impairment of visual processing can occur at a number of different levels, any of which could theoretically lead to altered function of receptive brain areas, possibly with spontaneous discharge of cells leading to the perception of visual images by the patient.
Delusions emerged as a separate group of symptoms which were associated with deafness and short term memory deficits, the latter suggesting prominent hippocampal involvement. This is intriguing in view of the identified association between hippocampal dysplasia and schizophrenia (Heckers et al 1991). Although none of the patients in the present study exhibited any first rank symptoms of Schneider, delusions of reference and delusions of persecution were common, both of which do arise frequently in patients with schizophrenia. Gray (1982) argues that the hippocampus acts as a "comparator" which continually monitors sensory data from the outside world and compares this with expected perceptual configurations. If discrepancies are identified, a control process then alters the internal working model of the world to accommodate the mismatches. Among dementia sufferers this comparator function is put under particularly severe stresses in view of the difficulty of maintaining a temporally correct, clear representation of the outside world. A sudden realisation, for example that an item is missing will not be consistent with the persons representation of where they believe the item to be and will create a mismatch. This would necessitate a re-alignment of either the internal model or the model of the outside environment. It seems likely that the way in which the comparator system undertakes the re-alignments will determine the likelihood of experiencing delusions. Frith (1992) expands Gray’s (1982) theory suggesting that self monitoring of actions is also important in the genesis of positive symptoms of schizophrenia and that this function is centred around the pre-frontal cortex. If correct, the pre-frontal cortex and the hippocampus are both involved in the genesis of first rank symptoms of schizophrenia, this perhaps explains the absence of first rank symptoms in patients with dementia and delusions, where it is mainly the hippocampal system which is impaired.
Deafness was also strongly associated with delusions. This is certainly consistent with the literature pertaining to paraphrenia (Kay & Roth 1961) but can perhaps also be seen as linking into Gray's (1982) model. Auditory stimuli are an important source of information about the outside world giving important cues about the emotions and intent of other people. Without these stabilising inputs it is far more likely that discrepancies between the internal and external models will be attributed to the malevolence of others.

The third major group of psychotic symptoms are those of delusional misidentification. It is probably best to focus on the core symptoms, delusional misidentification of mirror images and delusional misidentification of television images which were part of the delusional misidentification symptom group identified by principal components analysis.

The literature concerning the Capgras syndrome and the Fregoli syndrome amongst patients without cognitive impairment emphasises the importance of frontal lobe deficits and the presence of an altered sense of familiarity (Ellis & Young 1990). The mirror and television misidentifications symptoms however have a different quality, where the failure to correctly identify the nature of images leads to a series of delusional beliefs. Hence there are two distinct processes involved, firstly abnormal identification and secondly the genesis of secondary delusions. The group of misidentification symptoms (excluding the phantom boarder syndrome) were associated with agnosia. This is consistent with the work of Förstl et al (1991) and explains the first part of the model, where failure of correct identification is essential. There are no clear explanations for the second part of the process leading to the genesis of secondary delusions from the current data, although one could postulate that a similar process to that seen for delusions would be in operation. Misidentifications of this kind would put great pressure on the comparator.
system which may generate secondary delusions as the best fit model when trying to align incompatible internal and external representations.

Depression

The evidence from the studies of Förstl et al (1992), Zweig et al (1988) and Zubenko et al (1991) suggesting an association between lesions in the locus coeruleus and depression amongst patients with Alzheimer’s disease is compelling, perhaps in some ways too compelling, which may have discouraged investigation of potentially important psychosocial factors.

Although the application of DSMIIIR criteria could in some ways be regarded as creating a category fallacy, it would appear that a group of patients with dementia can be identified who suffer from symptoms of depression which are very similar to those experienced by people with depression in the absence of cognitive impairment. Furthermore the association with factors such as physical health problems, a past psychiatric history, a family history of psychiatric disorder and major life events such as bereavement also closely parallel the type of aetiological factors known to be important in patients with “functional” depression.

This produces a dilemma. On the one hand Zubenko et al (1991) have suggested that the neuropathological changes in the locus coeruleus can explain cases of depression amongst Alzheimer disease patients with 95% specificity and sensitivity, whilst on the other hand there is evidence that a variety of other factors may be important. It is also rather incongruent that different patterns of neurochemical association are evident in
patients with depression in the context of dementia, but that the other associations are similar to those seen in "functional depression". Perhaps the most curious anomaly is the association between depression and a past history of psychiatric disorder and depression, if there is a specific organic basis to depression in dementia sufferers.

The results of the current study may help to clarify the situation. Depression associated with bereavement was identified as a separate symptom group. It was also evident that factors such as deafness and physical health problems may be more important in patients with milder depression. A tenable hypothesis would therefore be that a distinct group of patients with severe depression have markedly increased cell loss in the locus coeruleus. Other patients with psycho-social precipitants or a genetic vulnerability to depression may be vulnerable to the development of affective disorder with a broader range of symptom severity. Some degree of overlap may be expected in the pattern of symptoms seen amongst patients who have experienced severe psycho-social stresses such as a bereavement. A model suggesting two distinct aetiologies fits better with the apparent inconsistencies of the two scenarios than an interactive model. This hypothesis could be tested by systematically following up a cohort of patients with dementia, collecting detailed information about symptoms of depression, life events and a personal or family loading for affective disorder. Post-mortem neurochemical study would then be able to compare patients with depression who had cell loss in the locus coeruleus to those who did not.

What is perhaps more intriguing is the situation that occurs in Senile Dementia of Lewy Body Type and vascular dementia. It seems that the prevalence rate of depression in
both of these disorders exceeds that seen in Alzheimer's disease. Could a similar dichotomous model of depression explain the situation seen in these disorders? In the absence of hard data this has to be speculative. Obviously patients with vascular dementia may be more prone to a whole series of physical disabilities which could increase the risk of "psycho-social" depression. An organic link between depression and vascular dementia in some patients could also be possible, perhaps amongst patients with left frontal lobe vascular lesions, subcortical lesions or vascular lesions in the locus coeruleus.

Patients with Senile Dementia of Lewy Body Type are particularly prone to falls and sensitivity reaction to neuroleptics, both of which may lead to an increased number of life events. It is unlikely however that this alone could explain the increased prevalence rate. Perhaps some patients have a distinct distribution of plaques, tangles and Lewy bodies which increases their vulnerability to severe depression. Obviously the brainstem aminergic nuclei are a candidate region. These hypotheses should be testable in a similar manner to the Alzheimer's disease model.
CONCLUSIONS

1. The one month prevalence rate of psychotic symptoms amongst dementia sufferers was almost 70% and the one year prevalence was in excess of 80%. The majority of patients experienced distress because of their psychotic symptoms and few had insight into the abnormal nature of their experiences. The number of different psychotic symptoms and the frequency with which they occurred were better predictors of both distress and insight than the type of individual psychotic symptoms.

2. Deafness, severe visual impairment and more severe impairment on the total CAMCOG scale were significantly positively associated with the presence of psychotic symptoms. Evidence was presented suggesting that delusions, visual hallucinations and delusional misidentification had a pattern of associations which were independent of one another. In addition, the results of a principal components analysis were consistent with this hypothesis.

3. A new category of psychotic symptom, comfort phenomenon was suggested. These symptoms included visual hallucinations of relatives and delusions that relatives were in the house. They were inversely associated with distress. It is suggested that they may be a psychological coping mechanism rather than a pathological phenomenon.

4. Approximately 50% of patients who did not have psychotic symptoms at the time of the baseline interview developed them over the ensuing year. Of those who did have psychotic symptoms approximately 50% resolved over the year of follow-up. The pattern
of resolution was bimodal, with a group of patients experiencing brief psychotic symptoms which resolved after a month or two and a further group experiencing highly persistent symptoms which continued for the majority of the year.

5. Patients with psychotic symptoms at the time of the baseline interview did not have a significantly greater cognitive deterioration over the year of follow up. There was however a significant positive correlation between the magnitude of deterioration and the number of months during which psychotic symptoms were experienced.

6. The one month prevalence of DSM IIIR major depression was 16.9%, the one month prevalence of RDC major depression was 25% and the one month prevalence of RDC minor depression was 27.4%. RDC major depression was significantly more frequent in patients in contact with psychiatric services than those in contact with the memory clinic and significantly more frequent in patients with vascular dementia than patients with Alzheimer’s disease. A subgroup of depressed patients with dementia may be suffering from bereavement reactions.

7. The annual incidence rate of RDC major depression was 10.6%. RDC major depression was a relatively brief disorder amongst patients with Alzheimer’s disease where only 33.3% of sufferers experienced symptoms for three months or more and only 11.1% were depressed for as long as six months. Depression was much more persistent amongst patients with vascular dementia where all six patients experienced at least three months of depression and three experienced depression for six months or more. The implications for pharmacological treatment were discussed.
8. Although only 28% of patients with RDC minor depression experienced depression for three months or more during the follow-up year, 83% of these patients continued to experience depression for six months or longer. It is suggested that a substantial minority of patients with RDC minor depression have a disorder akin to dysthymia which merits treatment.
References


227


Roth, M. & Morrissey, J.D. (1952) Problems in the Diagnosis and Classification of Mental Disorder in Old Age; with a study of case material. J Mental Science. 98, 66-80.


229


### APPENDIX A

**BURNS’ SYMPTOM CHECKLIST - INFORMANTS QUESTIONNAIRE**

<table>
<thead>
<tr>
<th>Key</th>
<th>Frequency</th>
<th>Emotion</th>
<th>Insight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>x1 - x3 per month</td>
<td>0 - No unpleasant emotion</td>
<td>0 - none, acts on</td>
</tr>
<tr>
<td>2</td>
<td>weekly</td>
<td>1 - some unpleasant emotion</td>
<td>1 - none, doesn’t act on</td>
</tr>
<tr>
<td>3</td>
<td>x2 - 6 per week</td>
<td>2 - Marked unpleasant emotion</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>daily</td>
<td></td>
<td>2 - partial</td>
</tr>
<tr>
<td>5</td>
<td>&gt; x2 per day</td>
<td></td>
<td>3 - complete</td>
</tr>
</tbody>
</table>

**Frequency**

0
1
2
3
4
5

No. of months belief held for.

**a)** Does he/she ever comment that someone or something may be controlling his/her thoughts, feelings, actions?

**Detailed examples:**

b) Does he/she ever comment that someone/something may be interfering with his/her thoughts? [Who? How? etc]

c) Does he/she ever believe that he/she has special talents/powers or is a special person? [What powers? Why believes it? etc]

d) Does he/she ever think that people are laughing at him/her or talking about him/her? [Who? Why? etc]

e) Is he/she suspicious? Does he/she ever believe that people are deliberately trying to harm or annoy him/her? [Who? What are they doing? Why?]

f) Does he/she ever believe that someone is trying to hide or steal his/her things? [Who? Why? How?]

g) Does he/she ever think that there might be people in the house when alone? [Who? Why? How? Does he/she ever actually see them? How does he/she know?]

h) Does he/she ever feel that people on the television or in photographs might be real? [Prompts - feels that people on TV in room]
i) Does he/she ever look in the mirror and believe the reflection to be someone else? [Who? What’s explanation?]

j) Does he/she ever feel that people he/she meets might be different from usual in some way or might be imposters? [In what why? Who? Why? What’s the explanation]

k) Has he/she been inclined to blame him/herself of feel unreasonably guilty or poor? [over what?]

l) Does your relative smell strange odours/tastes that others do not notice? [Prompts Gas, Poison, Chemicals etc]

m) Does your relative hear things that other people cannot hear? [Noises, Voices, whom familiar/unfamiliar, adults/children, where from? 2nd person/3rd person]

n) Does your relative have visions or see things that are invisible to other people? [Colours/lights/formed images, who - familiar or unfamiliar, adults or children, objects/animals]

o) Has your relative ever thought that
   a) people
   b) animals
   c) materials/things
   d) Radiation
   can pass through or influence him/her through walls, doors, ceilings or floors?

p) Has your relative ever thought that their home is not their own? [Who’s home? What’s explanation? - Is it delusional not just failure to recognise home?]
APPENDIX B

Scoring System

\[ \begin{align*}
   a & = \text{unable to evaluate} & 1 & = \text{mild or intermittent} \\
   0 & = \text{absent} & 2 & = \text{severe}
\end{align*} \]

Ratings should be based on symptoms and signs occurring during the week prior to the interview. No score should be given if symptoms result from physical disability or illness.

A. Mood Related Signs

1. ANXIETY
   anxious expression, ruminations, worrying
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

2. SADNESS
   sad expression, sad voice, tearfulness
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

3. LACK OF REACTIVITY TO PLEASANT EVENTS
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

4. IRRITABILITY
   easily annoyed, short tempered
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

B. Behavioural Disturbance

5. AGITATION
   restlessness, handwringing, hairpulling
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

6. RETARDATION
   slow movements, slow speech, slow reactions
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

7. MULTIPLE PHYSICAL COMPLAINTS
   (score 0 if G1 symptoms only)
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

8. LOSS OF INTEREST
   less involved in usual activities (score only if changed occurred acutely, i.e. in less than one month)
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]

C. Physical Signs

9. APPETITE LOSS
   eating less than usual
   \[ \begin{align*}
   a & = 0 & 1 & 2
   \end{align*} \]
10. WEIGHT LOSS
(score 2 if greater than 5 lbs in one month)

11. LACK OF ENERGY
fatigues easily, unable to sustain activities (score only if changed occurred acutely, ie, in less than one month)

D. Cyclic Functions

12. DIURNAL VARIATION OF MOOD
symptoms worse in the morning

13. DIFFICULTY FALLING ASLEEP
later than usual for this individual

14. MULTIPLE AWAKENINGS DURING SLEEP

15. EARLY MORNING AWAKENING
earlier than usual for this individual

E. Ideational Disturbance

16. SUICIDE
feels life is not worth living, has suicidal wishes, or makes suicide attempts

17. SELF-DEPRECIATION
self-blame, poor self-esteem, feelings of failure

18. PESSIMISM
anticipation of the worst

19. MOOD CONGRUENT DELUSIONS
delusions of poverty, illness, or loss

236
APPENDIX C

Orientation - Day of week, date, month, year, season, county, city, 2 streets near home, floor of building, address of current place.

Language Comprehension - Nod head, touch right ear with left hand, before look at ceiling look at floor, tap each shoulder twice with 2 fingers keeping eyes shut, is this place a hotel, are villages larger than towns, was there radio before TV, reading - close your eyes, if you are older than 50 put your hands behind your head.

Language Expression - Name pictures - shoe, typewriter, scales, suitcase, barometer, lamp; definitions - what would you do with a hammer, where would you buy medicine, what is a bridge, what is an opinion.

Praxis - Copy pentagon, copy spiral, copy 3d house, draw clock face, ideational - fold piece of paper, put in envelope, ideomotor - show how to wave goodbye, show how to cut with scissors, show how to brush teeth.

Recent memory - What were the pictures you saw, what's been in news the last 2 weeks, remember name and address.

Visual memory - Which of these pictures seen before.

Remote memory - Date 1st world war started, 2nd world war started, leader of Germans, leader of Russians, what was Mae West famous for, name of King/Queen, who next to throne, name of Prime Minister, name of flyer who's son was kidnapped.

Attention & Calculation - Count backwards from 20, 7 from 100 - continue subtracting 7, add 10p + 5p, take 15p from £1.

Perception - Identify objects - pen, watch, identify pictures, Queen, Pope; identify pictures from unusual angles - spectacles, shoe, purse, cup and saucer, telephone, pipe.

Abstract thinking - similarity between - apple and banana, shirt and dress, table and chair, plant and animal.

Verbal fluency - Name as many different kinds of animals as you can in 1 minute.
APPENDIX D

a) CAMDEX Criteria for Mild and Moderate Dementia

Mild Dementia

Difficulty in acquiring new information and recalling recent events. Belongings are therefore lost or misplaced and information recently imparted intermittently forgotten or totally lost.

Orientation for date, day of week, place are impaired to a limited extent or in a patchy and inconsistent manner.

Impairment is evident in activities demanding problem solving or reasoning.

Speech shows mild defect in respect of clarity of meaning.

Defects in knowledge of names of prominent figures, important events, simple geographical information.

Impairment of skills in daily living, errors and confusion of tasks in everyday work, mistakes in housework, cooking (inappropriate ingredients or other errors). More conspicuous errors of judgement and inappropriate conduct in those in professional, highly skilled or socially responsible activities.

Self care mildly impaired or not at all. There may be occasional errors in dress, limited decline from usual standards of tidiness and cleanliness.

Emotional responsiveness may be well retained or mildly impaired according to type of dementia. There may be blunting or lability of emotion or both.

Clinical examination at this stage shows social facade well reserved but systematic enquiry reveals indubitable cognitive deficits and emotional or personality changes.

Moderate Dementia

Severe impairment in the retention and the retrieval of new information and recently experienced events and activities. Recent events are rarely remembered and then usually in a transient manner. Well learned or very familiar material may be better retained but also defective.

Amnesia for recent events which may be associated with confabulation.

Impairment of most or all indices of orientation.

Capacity for reasoning and problem solving severely impaired.

Language unclear or incoherent but not invariably to a marked extent.
Competence at work and in daily living severely affected. Unable to function independently at work, housework, shopping, handling money.

Inability to dress or eat meals unaided partly or intermittently affected.

Marked impairment in self care, severe deterioration in personal standards of cleanliness and methods of eating and intermittent incontinence of sphincters.

Clinical examination reveals indubitable dementia though limited aspects of 'cognitive function', personality and also language and certain well established skills (e.g. musical ability) may be relatively intact.

b) DSMIIIR CRITERIA FOR DEMENTIA

A. Demonstrable evidence of impairment in short- and long-term memory. Impairment in short-term memory (inability to learn new information) may be indicated by inability to remember three objects after five minutes. Long-term memory impairment (inability to remember information that was known in the past) may be indicated by inability to remember past personal information (e.g., what happened yesterday, birthplace, occupation) or facts of common knowledge (e.g., past Presidents, well-known dates).

B. At least one of the following:

1. Impairment in abstract thinking, as indicated by inability to find similarities and differences between related words, difficulty in defining words and concepts, and other similar tasks
2. Impaired judgement, as indicated by inability to make reasonable plans to deal with interpersonal, family, and job-related problems and issues
3. Other disturbances of higher cortical function, such as aphasia (disorder of language), apraxia (inability to carry out motor activities despite intact comprehension and motor function), agnosia (failure to recognise or identify objects despite intact sensory function), and "constructional difficulty" (e.g., inability to cope three-dimensional figures, assemble blocks, or arrange sticks in specific designs)
4. Personality change, i.e., alteration or accentuation of premorbid traits.

C. The disturbance in A and B significantly interferes with work or usual social activities or relationships with others.

D. Not occurring exclusively during the course of Delirium.

E. Either (1) or (2):

1. There is evidence from the history, physical examination, or laboratory tests of a specific organic factor (or factors) judged to be etiologically related to the disturbance

239
(2) in the absence of such evidence, an etiologic organic factor can be presumed if the disturbance cannot be accounted for by any nonorganic mental disorder, e.g., Major Depression accounting for cognitive impairment.

c) NINCDS ADRDA CRITERIA FOR PROBABLE AND POSSIBLE ALZHEIMER'S DISEASE

I. The criteria for the clinical diagnosis of PROBABLE Alzheimer's disease include:

- dementia established by clinical examination and documented by the Mini Mental Test, "Blessed Dementia Scale", or some similar examination, and confirmed by neuropsychological tests:
  
- deficits in two or more areas of cognition:
  
- progressive worsening of memory and other cognitive functions:
  
- no disturbance of consciousness;
  
- onset between ages 40 and 90, most often after age 65; and
  
- absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition.

II. The diagnosis of PROBABLE Alzheimer's disease is supported by:

- progressive deterioration of specific cognitive functions such as language (aphasia), motor skills (apraxia), and perception (agnosia);

- impaired activities of daily living and altered patterns of behaviour;

- family history of similar disorders, particularly if confirmed neuropathologically; and

- laboratory results of:
  
- normal lumbar puncture as evaluated by standard techniques;

- normal pattern or nonspecific changes in EEG, such as increased slow-wave activity, and

- evidence of cerebral atrophy on CT with progression documented by serial observation.
III. Other clinical features consistent with the diagnosis of PROBABLE Alzheimer's disease, after exclusion of causes of dementia other than Alzheimer's disease, include:

- plateaus in the course of progression of the illness;
- associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations, catastrophic verbal, emotional, or physical outbursts, sexual disorders, and weight loss;
- other neurologic abnormalities in some patients, especially with more advanced disease and including motor signs such as increased muscle tone, myoclonus, or gait disorder.
- seizures in advanced disease; and
- CT normal for age.

IV. Features that make the diagnosis of PROBABLE Alzheimer's disease uncertain or unlikely include:

- sudden, apoplectic onset;
- focal neurologic findings such as hemiparesis, sensory loss, visual field deficits, and incoordination early in the course of the illness; and
- seizures or gait disturbances at the onset or very early in the course of the illness.

V. Clinical diagnosis of POSSIBLE Alzheimer's disease:

- may be made on the basis of the dementia syndrome, in the absence of other neurologic, psychiatric, or systemic disorders sufficient to cause dementia, and in the presence of variations in the onset, in the presentation, or in the clinical course;
- may be made in the presence of a second systemic or brain disorder sufficient to produce dementia, which is not considered to be the cause of the dementia; and
- should be used in research studies when a single, gradually progressive severe cognitive deficit is identified in the absence of other identifiable cause.

VI. Criteria for diagnosis of DEFINITE Alzheimer's disease are:

- the clinical criteria for probable Alzheimer's disease and
histopathologic evidence obtained from a biopsy or autopsy.

VII. Classification of Alzheimer’s disease for research purposes should specify features that may differentiate subtypes of the disorder, such as:

- familial occurrence;
- onset before age of 65;
- presence of trisomy-21; and
- coexistence of other relevant conditions such as Parkinson’s disease.

d) THE HACHINSKI ISCHEMIA SCORE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrupt onset</td>
<td>2</td>
</tr>
<tr>
<td>Stepwise progression</td>
<td>1</td>
</tr>
<tr>
<td>Fluctuating course</td>
<td>2</td>
</tr>
<tr>
<td>Nocturnal confusion</td>
<td>1</td>
</tr>
<tr>
<td>Relative preservation of personality</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>1</td>
</tr>
<tr>
<td>Emotional incontinence</td>
<td>1</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1</td>
</tr>
<tr>
<td>History of strokes</td>
<td>2</td>
</tr>
<tr>
<td>Evidence of associated atherosclerosis</td>
<td>1</td>
</tr>
<tr>
<td>Focal neurologic symptoms</td>
<td>2</td>
</tr>
<tr>
<td>Focal neurologic signs</td>
<td>2</td>
</tr>
</tbody>
</table>

e) McKEITH OPERATIONAL CRITERIA FOR SENILE DEMENTIA OF LEWY BODY TYPE

- Fluctuating cognitive impairment affecting both memory and higher cortical functions (such as language, visuospatial ability, praxis, or reasoning skills). The fluctuation is pronounced, with both episodic confusion and lucid intervals, as in delirium, and is evident either on repeated tests of cognitive function or by variable performance in daily living skills.

- At least one of the following: Visual or auditory hallucinations or both, which are usually accompanied by
secondary paranoid delusions
Mild spontaneous extrapyramidal features or neuroleptic sensitivity syndrome - that is, exaggerated adverse responses to standard doses of neuroleptics

- Despite the fluctuating pattern the clinical features persist over a long period (weeks or months), unlike delirium, which rarely persists as long. The illness progresses, often rapidly, to an end stage of severe dementia
- Exclusion by appropriate examination and investigation of any underlying physical illness adequate to account for the fluctuating state
- Exclusion of past history of confirmed stroke or evidence of cerebral ischaemic damage, or both, on physical examination or brain imaging.

**f) BYRNE CRITERIA FOR DEMENTIA ASSOCIATED WITH CORTICAL LEWY BODIES**

Diagnostic criteria for dementia associated with Cortical Lewy bodies: A, B, C, and D should be present to make a diagnosis of *probable* dementia associated with Cortical Lewy bodies.

A. Either 1, 2 or 3: (1) Gradual onset of dementia syndrome (which fulfils DSMIIIIR criteria) with prominent attentional deficits or the appearance early in the course of apparent acute confusional states for which no underlying toxic metabolic infective or other cause is identified, or 'classical' Parkinson's (defined as levodopa-responsive parkinsonism) disease at onset with the later emergence of dementia syndrome (as described in (1) or (3) the simultaneous occurrence at onset of dementia (as described in 1) and parkinsonism.

B. Both 1 and 2 should be fulfilled: (1) the absence of any unequivocal history of stroke (2) no focal signs other than parkinsonism (note: the Hachinski score is not reliable in this respect).

C. Three or more of the following should be present: (1) tremor; (2) rigidity; (3) postural change; (4) bradykinesia; (5) gait abnormality. These symptoms may be mild and may develop late in the course of the illness and abnormal involuntary movements resulting from levodopa treatment are unusual in Parkinsonism with Cortical Lewy bodies.

D. Other causes of dementia syndrome or parkinsonism have been excluded (e.g. boxer's encephalopathy, chronic phenothiazine poisoning) after thorough clinical and laboratory investigation.

A, B, C and D should be present to make a diagnosis of *possible* dementia.
associated with Cortical Lewy bodies.

A. Either 1 or 2: (1) Dementia (as described above) with acute onset and rapid course, sometimes associated with plateaux (periods where the symptoms do not progress) and frequently associated with psychiatric symptoms (depression or delusional states) or (2) dementia (as described above) with late presentation of parkinsonian symptoms which fulfil B.

B. One or two of the following: (1) tremor; (2) rigidity; (3) bradykinesia; (4) postural change; (5) gait abnormality.

C. (1) The absence of any unequivocal history of stroke; (2) no focal signs other than parkinsonism. Both should be fulfilled (note: the Hachinski score is not reliable in this respect).

D. Other causes of dementia syndrome and parkinsonism have been excluded, after thorough clinical and laboratory investigation.

g) RDC MAJOR AND MINOR DEPRESSION

Major Depressive Disorder

This category is for episodes of illness in which a major feature of the clinical picture is dysphoric mood or pervasive loss of interest or pleasure accompanied by the depressive syndrome. This category is distinguished from less severe disturbances of mood which are not accompanied by the full syndrome.

This category may be superimposed on or follow any other existing disorder with the exception of Schizophrenia, Residual Subtype, which should be recorded as previously noted. This category can be used for subjects who have had a complete recovery from a schizophrenic or schizo-affective episode.

A through F are required for the episode of illness being considered.

A. One or more distinct periods with dysphoric mood or pervasive loss of interest or pleasure. The disturbance is characterised by symptoms such as the following: depressed, sad, blue, hopeless, low, down in the dumps, "don't care anymore", or irritable. The disturbance must be prominent and relatively persistent but not necessarily the most dominant symptom. It does not include momentary shifts from one dysphoric mood to another dysphoric mood, e.g., anxiety to depression to anger, such as are seen in stages of acute psychotic turmoil.

B. At least five of the following symptoms are required to have appeared.

1. Poor appetite or weight loss or increased appetite or weight gain.
2. Sleep difficulty or sleeping too much.
3. Loss of energy, fatigability, or tiredness.
(4) Psychomotor agitation or retardation (but not mere subjective feeling of restlessness or being slowed down).

(5) Loss of interest or pleasure in usual activities, including social contact or sex (do not include if limited to a period when delusional or hallucinating). (The loss may or may not be pervasive).

(6) Feelings of self-reproach or excessive or inappropriate guilt (either may be delusional).

(7) Complaints or evidence of diminished ability to think or concentrate, such as slowed thinking, or indecisiveness (do not include if associated with marked formal thought disorder).

(8) Recurrent thoughts of death or suicide, or any suicidal behaviour.

C. Duration of dysphoric features at least one week beginning with the first noticeable change in the subject's usual condition (definite if lasted more than two weeks, probable if one to two weeks).

D. Sought or was referred for help from someone during the dysphoric period, took medication, or had impairment in functioning with family, at home, at school, at work, or socially.

E. None of the following which suggest Schizophrenia is present:

(1) Delusions of being controlled (or influenced), or of thought broadcasting, insertion, or withdrawal (as defined in this manual).

(2) Non-affective hallucinations of any type (as defined in this manual) throughout the day for several days or intermittently throughout a one week period.

(3) Auditory hallucinations in which either a voice keeps up a running commentary on the subject's behaviours or thoughts as they occur, or two or more voices converse with each other.

(4) At some time during the period of illness had more than one month when he exhibited no prominent depressive symptoms but had delusions or hallucinations (although typical depressive delusions such as delusions of guilt, sin, poverty, nihilism, or self-deprecation, or hallucinations with similar content are not included).

(5) Preoccupation with a delusion or hallucination to the relative exclusion of other symptoms or concerns (other than typical depressive delusions of guilt, sin, poverty, nihilism, self-deprecation or hallucinations with similar content).

(6) Definite instances of marked formal thought disorder (as defined in this manual), accompanied by either blunted or inappropriate affect, delusions or hallucinations of any type, or grossly disorganised behaviour.

F. Does not meet the criteria for Schizophrenia, Residual Subtype.

RDC MINOR DEPRESSIVE DISORDER

This category is for non-psychotic episodes or periods of illness in which the most
prominent disturbance is a relative sustained mood of depression without the full depressive syndrome that characterises Major Depressive Disorder. This category is distinguished from Generalised Anxiety Disorder in which there is a clear predominance of anxious mood, and from Labile Personality in which the depressed mood rarely lasts more than a few hours or days at a time.

The condition may be chronic in that the period may be of very long duration or may have continued up until the onset of another superimposed disorder such as Schizophrenia, Major Depressive Disorder, Manic Disorder, etc. If the subject has had Minor Depressive Disorder for at least two years prior to the onset of a superimposed disorder, both disorders should be noted for the present illness and the duration noted for each.

A through F are required for the episode of illness being considered.

A. An episode of illness in which a relatively persistent depressed mood dominates the clinical picture (or is coequal with anxiety). The depressed mood may be described as depressed, sad, blue, hopeless, low, or down in the dumps.

B. Two or more of the symptoms listed below have appeared as part of the episode:

   1. Poor appetite or weight loss or increased appetite or weight gain (change of one lb. a week over several weeks or ten lbs. a year when not dieting).
   2. Sleep difficulty or sleeping too much.
   3. Loss of energy, fatigability, or tiredness.
   4. Psychomotor agitation or retardation (but not mere subjective feeling of restlessness or being slowed down).
   5. Loss of interest or pleasure in usual activities, including social contact or sex (do not include if limited to a period when delusional or hallucinating).
   6. Feelings of self-reproach or excessive or inappropriate guilt (either may be delusional).
   7. Complaints or evidence of diminished ability to think or concentrate, such as slowed thinking, or indecisiveness (do not include if associated with obvious formal thought disorder).
   8. Recurrent thoughts of death or suicide, or any suicidal behaviour.
   9. Nonverbal manifestations of depression such as tearfulness or sad face.
   10. Pessimistic attitude.
   11. Brooding about past or current unpleasant events.
   12. Preoccupation with feelings of inadequacy.
   13. Resentful, irritable, angry, or complaining.
   14. Demandingness or clinging dependency.
   15. Self-pity.
   16. Excessive somatic concern.

C. Duration of episode at least one week for probable, two weeks for definite.

D. The episode of illness being considered does not meet the criteria for Major Depressive Disorder; Schizophrenia; Schizo-affective Disorder, Manic or Depressed Type; Briquet's Disorder (Somatisation Disorder); Unspecified Functional Psychosis;
Manic Disorder; Cyclothymic Personality; labile Personality; or Intermittent Depressive Disorder. (If the condition, Minor Depressive Disorder, has been chronic (i.e. two or more years), an episode of Major Depressive Disorder, Schizo-affective Disorder, or Manic Disorder may be superimposed. In that case, both disorders are noted for the present illness and the duration noted for each).

E. The episode of illness may be superimposed on another pre-existing psychiatric disorder, for example, Alcoholism, Phobic or Obsessive Compulsive Disorder. This category should be given as an additional diagnosis only if the depressed mood, by virtue of its intensity or effect on functioning, can be clearly distinguished from the subject's usual condition.

F. When the episode of illness is not superimposed on another pre-existing psychiatric disorder, it must result in either impairment in functioning with family, at home, at school, at work, or socially, taking medication, or seeking or being referred for help from someone.
h) DSMIIIIR CRITERIA FOR MAJOR DEPRESSION

Note: A "Major Depressive Syndrome" is defined as criterion A below.

A. At least five of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood, or (2) loss of interest or pleasure. (Do not include symptoms that are clearly due to a physical condition, mood-incongruent delusions or hallucinations, incoherence, or marked loosening of associations).

1. depressed mood (or can be irritable mood in children and adolescents) most of the day, nearly every day, as indicated either by subjective account or observation by others
2. markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated either by subjective account or observation by others of apathy most of the time)
3. significant weight loss or weight gain when not dieting (e.g. more than 5% of body weight in a month), or decrease or increase in appetite nearly every day (in children, consider failure to make expected weight gains)
4. insomnia or hypersomnia nearly every day
5. psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. fatigue or loss of energy nearly every day
7. feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. 

1. It cannot be established that an organic factor initiated and maintained the disturbance
2. The disturbance is not a normal reaction to the death of a loved one (Uncomplicated Bereavement).

Note: In the current study no judgement was made concerning whether the dementia 'caused' the depression, but the diagnosis of dementia did not in anyway preclude a diagnosis of major depression.

C. At no time during the disturbance have there been delusions or hallucinations for as long as two weeks in the absence of prominent mood symptoms (i.e. before the mood symptoms developed or after they have remitted).
D. Not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder NOS.

i) PSYCHOTIC SYMPTOMS

Delusional beliefs had to be false, firmly held and impervious of evidence to the contrary not to be explicable entirely by cognitive failure and to have been experienced at least twice, on occasions more than one week apart. Hallucinations were considered to be present if described by the patient or if clearly described to the informant by the patient. Delusional misidentification encompassed the symptoms: delusional misidentification of mirror images, television images, people, objects, ones house and the phantom boarder syndrome. Symptoms also had to fulfil the criteria for a delusion. Delusional misidentification of television images focuses upon the delusional belief that people in the television set are real and exist in the environment of the patient. Patients often express secondary delusional beliefs where perceived ill-intent is attributed to the images. The delusional misidentification of mirror images describes the delusional belief that the reflection seen in a mirror is a different person from the individual whose reflection it is, and that the person exists in a tangible sense. Patients often harbour related beliefs pertaining to a world behind the mirror or believe that the mirror represents a door to a different room. Again perceived ill-intent is often attributed to the image. To be considered as a delusional misidentification the belief that ones' house was not ones' home had to be more than failure to recognise ones own house, delusional explanations had to be given. Examples of such delusional beliefs include "I went for a walk and when I came back someone had changed the house" or "when I came back from the day centre I had moved into a neighbours house". People often comment upon the similarity of the house to their own, but identify minor differences. The delusional misidentification of people and objects have the same characteristics as the Capgras syndrome in younger adults.
APPENDIX E

Personal Contribution to the Project - I designed the study and wrote the Protocol, having sought advice widely. I planned and monitored the training package for the other participants to learn how to use the necessary schedules. I obtained ethical approval for the study, liaised with a number of clinicians and was personally responsible for recruitment and consent of the study participants. I supervised the work of the other participants and co-ordinated the assessment programme. I undertook 58 of the 125 initial assessments, 20 complete follow up assessments (240 interviews) and an additional 45 month 12 assessments. I organised and co-ordinated the inter-rater reliability study. I was solely responsible for the literature search and for writing the project, with the supervision of Dr Oyebode.
ACKNOWLEDGEMENTS

I would like to thank Professor J. Lindesay, Professor A. Burns, Professor J. Copeland, Professor R. Levy, Dr. P. Saunders and Dr. M. Dewey for their help in designing the study and Dr. C. Graham, Dr. C. Bannister, Dr. B. Coope, Dr. K. Saad, Dr. M. Gahir, Dr. F. Abid and Dr. M. Solis for their help with data collection and organisation. I would also like to thank Dr T Hughes and Dr P Davies for their statistical advice.

I would especially like to thank Dr. F. Oyebode for supervising the project, Professor G. Wilcock for his help and encouragement, Mrs. J. Baker for her secretarial input and Dr R Thavasothy for his encouragement with early research projects.