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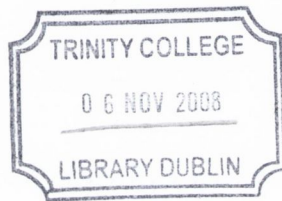
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**SUBSYNDROMAL DEPRESSION AND ANXIETY;
PREDICTORS, CONSEQUENCES AND TWO YEAR
OUTCOME IN THE IRISH ELDERLY**



**A thesis presented to the University of Dublin
for the degree of Doctor in Medicine**

by

Elaine Greene MB MRCPsych

**Mercer's Institute for Research in Ageing,
St James's Hospital, Dublin.
September 2008**

DECLARATION

I declare that the work contained in this thesis is entirely my own, except where credited in the acknowledgements. This thesis has not been submitted as an exercise for a degree to any other university. I agree that the library of the University of Dublin may lend or copy this thesis on request.

Data were collected between September 1999 and September 2001 and this work was completed in Mercer's Institute for Research on Ageing. The project was approved by the Federated Dublin Voluntary Hospitals ethics committee and informed consent was obtained from all participants.



Elaine Greene

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SUMMARY

Background

Depression is the commonest mental illness in late life and frequently occurs comorbidly with anxiety. While all levels of illness severity have been reported a significant proportion of older adults suffer with clinically significant symptoms which fall outside diagnostic criteria for 'caseness'. These subsyndromal mental disorders are gaining importance not only because they are more commonly observed than 'case-level' illness but also because they have a significant negative impact on morbidity, mortality and quality of life in this population. Furthermore the literature suggests that subsyndromal depression and anxiety may share similar risk factors and lie on a continuum with case-level depressive illness.

The main objective of this thesis was to examine the impact (in terms of service use), course and clinical significance (in terms of two-year outcome) of subsyndromal anxiety and depression in the Irish community dwelling elderly. A secondary objective was to identify risk factors for depression in late life using a longitudinal study design.

Methods used

Five hundred and eighteen community dwelling subjects over the age of 65 were recruited from three GP practices in the catchment area of St. James Hospital. All subjects were screened for mental disorders using AGECAT. Information on a comprehensive set of risk factors for depression based on literature review was collected contemporaneously. This included demographic details, social network and data on alcohol and tobacco use. Personal and family history of depression and other psychiatric illnesses were recorded. The number and type of positive and negative life-events was also recorded. Physical health details, including the presence of a number of medical conditions, cardiovascular risk factors, self and observer ratings of physical health status, the presence of chronic pain and pattern of medication use were recorded. Cognitive functioning was measured using the Mini Mental State Examination.

Major findings

1. Rates of subsyndromal anxiety and depression

Rates of subsyndromal anxiety were high affecting twenty four percent of the sample at baseline and exceeded the baseline rate of subsyndromal depression (fourteen percent).

2. Effects of subsyndromal anxiety and depression on service use

Subsyndromal anxiety did not directly increase the rates of service use whereas individuals with subsyndromal depression had significantly more frequent GP visits and showed a trend towards excessive service use.

3. Predictors of anxiety and depressive symptoms

Having a personal history of depression increased the risk of both subsyndromal depressive and anxiety symptoms. Additionally living alone significantly increased the risk of subsyndromal anxiety while being married conveyed a protective effect from subsyndromal depression.

4. Predictors of incident depression

Ten percent of the population at risk developed new depression over the course of the study. The presence of subjective memory complaints at baseline was the strongest predictor of depression in our sample. Baseline subsyndromal depression was predictive of incident depression while subsyndromal anxiety (including all subtypes of anxiety symptoms) was not. However, the presence of generalised anxiety symptoms at baseline was predictive of depression. All other factors which significantly predicted depression were health related variables.

5. Comorbidity of anxiety and depression

Our study findings strongly support the continuity hypothesis of depression and generalised anxiety disorder. Baseline generalised anxiety disorder symptoms were predictive of subsyndromal depression and baseline subsyndromal depression was predictive of subsyndromal anxiety. Additionally both subsyndromal depression and generalised anxiety symptoms were predictive of case level depression.

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List of abbreviations

AGECAT:	Automated Geriatric Examination for Computer Assisted Taxonomy
BDZ:	Benzodiazepine
CMC:	Chronic medical complaint
COPD:	Chronic obstructive pulmonary disease
CSO:	Central statistics office
DSM -IV:	Diagnostic and statistical manual for mental disorders, version 4
ECT:	Electroconvulsive therapy
EOD:	Early onset depression
ESRI:	Economic and Social Research Institute
GAD:	Generalised anxiety disorder
GMS:	Geriatric Mental State
GP:	General practitioner
LOD:	Late onset depression
LTC:	Long term care
MinD:	Minor depression
MDD:	Major depressive disorder
MMSE:	Mini-mental state examination
NCAOP:	National council for ageing and older people
SMC:	Subjective memory complaints
SPSS:	Statistical package for the social sciences
SS:	Subsyndromal
SSA:	Subsyndromal anxiety
SSD:	Subsyndromal depression
SSOrg:	Subsyndromal organic symptoms
WHO:	World health organisation

Chapter 1.

Introduction

1.1 Subsyndromal Depression and Anxiety in mixed age populations

Subsyndromal depression

In 1996 the World Health Organisation (WHO) reported that that unipolar depressive disorder was the fourth leading cause of disability worldwide. In addition their study projected that depression would be the second leading cause of disability in 2020 accounting for approximately 11% of the world's total disease burden (Murray 1996). In light of this prediction studies of the lifetime course of depressive illness have gained importance. Identifying 'prodromes' of major depressive disorder (MDD) is particularly important if preventative strategies are to be developed to reduce the projected burden of depression.

Earlier research had traditionally focussed on major depressive disorder which represents the tip of the iceberg in this illness (Judd, Akiskal et al. 1998) with subsyndromal disorders considered to be transient entities lacking the clinical importance of case-level illness. Much debate has generated around the categorical classification of depression (Sullivan, Kessler et al. 1998). Categorical classificatory systems such as the diagnostic and statistical manual for mental disorders, version 4 (DSM -IV) (APA 1994) assume that MDD, minor depression (MinD) and less severe depressive illnesses are diagnostically discrete entities, which are aetiologically different and thus appropriately classified as different disorders. The 'continuity hypothesis' of depression proposes that the distinction of depressive illness subtypes in DSM is artificial and far from being discrete entities such classification represents cross sectional views of a dynamic spectrum of depressive symptoms. Supporters of the continuity hypothesis have argued that superimposing a categorical diagnostic classification on a continuously distributed trait ultimately fails to represent adequately the underlying spectrum of depression (Angst and Merikangas 1997). The continuity hypothesis is supported by twin studies which suggest that unipolar MDD is a genetically homogenous disorder manifesting as a continuum of depressive symptoms over time (Kendler and Gardner 1998). In addition in a 12-year study of the weekly symptomatic course

of unipolar MDD Judd and colleagues found that MDD manifests as a continuum of depressive symptoms that vary in severity and duration over time (Judd, Akiskal et al. 1998). Thus SSD may be an antecedent or a sequela of major depressive disorder. As yet there are no consensus criteria for the diagnosis of SSD. It is generally held that SSD represents the presence of 'clinically significant' depressive symptoms, which fail to meet the threshold for a diagnosable depressive disorder (Sadek and Bona 2000). Most studies use cut points on depression scales to define the presence of clinically significant symptoms. As a result there is considerable variation in reported rates of SSD (Schotte and Cooper 1999), nevertheless all studies agree that the rate of SSD exceeds that of MDD.

Epidemiological studies of mixed age populations have demonstrated that subsyndromal depressive symptoms are highly prevalent in the general population (Broadhead, Blazer et al. 1990; Judd, Paulus et al. 1996). In addition primary care studies have highlighted the considerable negative impact of these subsyndromal syndromes in terms of magnitude of subjective suffering and impairment (Ormel, Oldehinkel et al. 1993). Naturalistic studies examining the course of unipolar depression show that SSD has prognostic significance, conveying a significantly increased risk of developing MDD (Angst and Merikangas 1997; Judd, Akiskal et al. 1998; Murphy, Nierenberg et al. 2002). SSD not only increases the risk of MDD but also significantly increases the risk of developing other medical illnesses. The risk of hypertension (Jonas, Franks et al. 1997), cardiovascular disease (Anda, Williamson et al. 1993) and stroke (Jonas and Mussolino 2000) are all increased with SSD. Furthermore, studies of SSD in mixed age populations have found that SSD is associated with significant social dysfunction (Judd, Paulus et al. 1996), disability (Broadhead, Blazer et al. 1990; Judd, Paulus et al. 1996) and functional impairment (Rapaport and Judd 1998). SSD has been associated with increased use of health services (Johnson, Weissman et al. 1992; Judd, Schettler et al. 2002) and has the characteristics of a clinically relevant depressive condition (Sherbourne, Wells et al. 1994; Akiskal, Judd et al. 1997). There is a compelling body of evidence suggesting that SSD is an important clinical entity whose presence greatly increases morbidity in the general population.

Subsyndromal anxiety in the general population; clinical significance and comorbidity with depression

Subsyndromal anxiety (SSA) is less well described in mixed age populations (Davidson, Hughes et al. 1994; Angst, Merikangas et al. 1997) and data are largely derived from co-morbidity studies. Anxiety and depression are highly comorbid throughout the life cycle (Kessler, Nelson et al. 1996; Angst 1997; Barbee 1998). There may be a common genetic predisposition to both conditions where the resulting illness is dependent on exposure to specific environmental stressors (Gillespie, Kirk et al. 2004). In addition, there are limited data which suggest that SSA may predict or precede depressive illness (Kessler, Nelson et al. 1996) and has been found to have a significant negative impact on the presentation, course and prognosis of MDD (Angst 1997; Barbee 1998). In addition the presence of SSA may significantly impact on the course of chronic medical conditions and has been associated with a poorer prognosis in COPD (Yohannes, Baldwin et al. 2000; Mikkelsen, Middelboe et al. 2004) and an increased risk of hypertension (Jonas, Franks et al. 1997). While the impact of SSA is not as extensively described as SSD available data suggest that it is highly prevalent and has significant associated morbidity.

1.2 Subsyndromal anxiety and depression in older adults

Research on SSD and SSA is relatively sparse in the elderly despite the fact that old age psychiatrists have long argued that diagnostic criteria such as DSM may not adequately capture mental illness in this age group (Beekman ATF 1999; Chopra, Zubritsky et al. 2005). It is evident from clinical practice that the presentation of mental illnesses in late life may be significantly different to that of younger adults (Gallo, Rabins et al. 1997; Gallo, Rabins et al. 1999). As a result many older adults with clinically significant symptoms fall below the threshold for case-level mental illness. This is reflected in epidemiological studies which suggest that SSD (Copeland JRM 1992; Beekman ATF 1999; Copeland JRM 1999; Arean and Alvidrez 2001) and SSA (Larkin, Copeland et al. 1992) are more prevalent than the nosological categories themselves. There has been much debate over how to accurately define subsyndromal disorders in late life (Rollman and Reynolds 1999; Geiselman and Bauer 2000; Hybels CF 2001; Flint AJ 2002). While some authors have suggested that creating a category of subsyndromal

mental illnesses adds little to our understanding of late life disorders (Royall 2004) most agree that ignoring this category excludes a large subgroup of the population with significant morbidity (Heun R 2000; Lavretsky, Kurbanyan et al. 2004). In general subsyndromal disorders are classified as clinically significant symptoms occurring in the absence of a diagnosable illness (Lyness, King et al. 1999; Lavretsky, Kurbanyan et al. 2004). With the projected increase of the elderly population it is increasingly important to move research upstream from major mental disorders to subsyndromal illness especially if preventative interventions are to be developed. Despite a lack of consensus on diagnostic criteria there is a growing body of literature describing the presentation, course and outcome of subsyndromal disorders in late life.

Late-life subsyndromal depression

It is well established that depression is the commonest mental illness in late-life however the prevalence of major depressive illness is quite low in this population with much higher proportions suffering with MinD or SSD (Copeland JRM 1999). Rates of SSD of 12 to 23% have been reported (Beekman ATF 1995; Copeland JRM 1999; Schoevers RA 2000). Not surprisingly the impact of subsyndromal depression in late-life has been found to be as severe as in younger adults. The continuity hypothesis for depression is also supported by data from older populations. SSD is both predictive of (Lyness, Caine et al. 2002; Chopra, Zubritsky et al. 2005) and occurs as a sequela of MDD in late-life (Sharma VK 1998; Gasto, Navarro et al. 2003). SSD has been found to have a serious impact on physical wellbeing in the elderly. Rates of physical and functional disability (Bruce, Seeman et al. 1994; Rollman and Reynolds 1999; Jin, Zisook et al. 2001; Lyness, Caine et al. 2002) are increased by depressive symptoms. Even more striking in late-life are the effects of SSD on medical comorbidity. SSD has been found to increase physical complaints (Beekman ATF 1995; Mossey, Gallagher et al. 2000) and as been associated with poorer outcomes in both heart disease (Sullivan, Newton et al. 2004) and COPD (Yohannes AM 2003). SSD has been found to increase the rate of heart failure in older women (Williams, Kasl et al. 2002) and increase the risk of stroke in both genders (Jonas and Mussolino 2000). Rates of service use are increased in SSD even after controlling for the effect of chronic medical conditions (Beekman ATF 1997; Lyness, Caine et al. 2002). The

outcome of SSD is bleak, mortality rates have been found to increase with increased levels of depression (Penninx, Geerlings et al. 1999; Schoevers, Geerlings et al. 2000; Penninx, Beekman et al. 2001; Schulz, Drayer et al. 2002; Lavretsky, Mistry et al. 2003). Depressive symptoms may impact on health behaviours increasing mortality risk (Schulz, Drayer et al. 2002) in addition SSD increases the mortality rate in mild dementia (Janning, Bouwens et al. 1999). Risk factors for SSD have not been extensively explored in late-life. As SSD may lie on a continuum with MDD many risk factors are shared. Vulnerability factors including a female gender, personal and family history of depression have all been associated with SSD. Similarly physical illness and disability are over-represented in this group. SSD may also arise de-novo in late-life as a result of exposure to profound life events such as spousal bereavement (Turvey C; Mendes de Leon CF 1994; Zisook, Paulus et al. 1997). There are few prospective studies examining predictors of SSD, most available data are cross sectional or derived from studies examining MDD in this age-group. Identifying risk factors for SSD is an important research prerogative, as preventative interventions are urgently needed to reduce the burden of illness in this age group.

Late-life subsyndromal anxiety

The course and outcome of anxiety disorders in late life have until recently received little attention. There are many reasons for this lack of research interest. It was previously assumed that anxiety disorders were less common in older adults as epidemiological studies had demonstrated decreasing prevalence with age (Lenze, Shear et al. 2002; Flint 2005). There is now clearcut evidence that this assumption is untrue (Wetherell, Maser et al. 2005). As with SSD there are no consensus criteria for describing SSA however SSA consistently appears to be more prevalent than case level anxiety in late-life (Larkin, Copeland et al. 1992; Flint and Rifat 2002). There are many reasons for this finding. Firstly the threshold argument again applies to this subgroup of illnesses, standardised diagnostic criteria may miss a significant proportion of older adults who suffer with debilitating anxiety symptoms (Fuentes and Cox 1997; Small 1997). Secondly those older adults with anxiety disorders may not actually present for treatment (Wetherell, Le Roux et al. 2003). Those who do present may present with non-specific somatic symptoms of anxiety as older adults are more likely to

somatise and less likely to reveal mental health concerns (Small 1997; Flint and Rifat 2002). Some authors have suggested that ageist attitudes may lead to under-recognition of anxiety in later life (Lindesay, Briggs et al. 1989). In addition many individuals with anxiety symptoms also have case level depression resulting in a 'hidden' subgroup in the community (Larkin, Copeland et al. 1992; Copeland, Beekman et al. 1999; Flint and Rifat 2002). Symptoms of anxiety tend to fluctuate over time (Larkin, Copeland et al. 1992; de Beurs, Beekman et al. 2000; Schuurmans, Comijs et al. 2005). Longitudinal studies suggest that SSA conveys an increased risk of developing both case level anxiety (Schuurmans, Comijs et al. 2005) or depression (Larkin, Copeland et al. 1992) in late-life. A recent study found that patients with SSA displayed similar levels of disability and reduced well-being as those with case level anxiety disorders (de Beurs, Beekman et al. 1999). In addition, the same authors found that SSA resulted in increased health service use even after controlling for medical co-morbidity (de Beurs, Beekman et al. 1999).

1.3 Subsyndromal Mental illness in the Irish elderly

There are limited data available on subsyndromal mental illness in the Irish elderly. A recent prevalence study (Kirby, Bruce et al. 1997) reported prevalence rates of SSD of 9.2% and SSA of 18.3%. SSA was noted to be frequently co-morbid with case-level depression, (64% of those with case-level depression had co-morbid SSA) which is consistent with international study findings (Larkin, Copeland et al. 1992; Copeland JRM 1999). The outcome of subsyndromal disorders in the Irish elderly has not been described. It is clear however from the data presented by Denihan et al on the outcome of depression in the Irish community dwelling elderly that anxiety symptoms are highly co morbid with depression (Denihan, Kirby et al. 2000). In addition the continuity hypothesis of depression is supported by the finding that 10% of those depressed at baseline were found to have SSD at two-year follow-up. Interestingly a further 10% of this study sample were found to have SSA alone at two-years highlighting the fluidity of diagnostic categories in late-life. Factors associated with SSA and SSD have not been described in the Irish elderly population. There is limited data on service use in the Irish elderly (Lyons, McCarthy et al. 1991; Kelleher 1998). These studies did not employ any measure of psychiatric co-morbidity and so the impact

of subsyndromal disorders cannot be extrapolated from this data. The studies found that in general that assessed need for services in the elderly far outweighed the demand, in that individuals were not accessing services appropriate to their needs. What existing studies focussing on psychopathology do tell us is that anxiety symptoms increase the likelihood of benzodiazepine prescription in the Irish elderly (Kirby, Denihan et al. 1999). In addition anxiety symptoms occurring co-morbidly with depression produce a 'louder' depression which leads to an increased likelihood of treatment (Kirby, Denihan et al. 1999) albeit with benzodiazepines. Another Irish study found that anxiety symptoms also increase the likelihood of referral to psychogeriatric day hospital services (Eustace, Denihan et al. 2001). On the basis of the above study findings anxiety symptoms appear to have a paradoxical effect. While co-morbid anxiety symptoms lead to a more severe presentation of depression, they also make depression more visible in primary care and more likely to receive treatment. Unfortunately these individuals are more likely to be treated with benzodiazepines rather than antidepressants which clearly creates its own problems.

Data on risk factors for depression are also markedly limited in the Irish elderly. Existing data derive from cross sectional studies and are of limited use as chronic depression may be over-represented. Risk factors identified in cross sectional studies may be prognostic rather than predictive and the direction of causality is unclear.

In summary on the basis of existing data we know that SSD and SSA are common in the Irish elderly (Kirby, Bruce et al. 1997) and may be the sequela of a depressive episode (Denihan, Kirby et al. 2000). Whether SSA and SSD predict depression in this setting has not been explored.

The clinical relevance of late-life subsyndromal anxiety and depression

The National Council for Ageing and Older People (NCAOP) recently reported that the proportion of Irish people over 65 years of age was 11% in 2002 and is projected to rise to 15% by 2021 (Connell 2004). There have also been significant socio-economic changes in the Ireland over recent years. While 'the Celtic Tiger' has benefited a significant proportion of the population its effects have not been altogether positive for the elderly. The adverse effects of this socio-economic change on the elderly population are both direct and indirect. The Economic and

Social Research Institute (ESRI) recently published a document tracking trends in poverty over a 6-year period encompassing the nascence of the Celtic Tiger. Relative income poverty rates have increased significantly in the elderly particularly in those with illness or disability over this period of time (Whelan 2005). According to the 2002 census figures 32% of older Irish adults suffer with a disability (NCAOP 2005). This means that a significant proportion of our elderly population are living near or below the poverty line. Socio-economic deprivation is well known to impact on mental wellbeing. This effect may be buffered by community and family support (Wenger and Tucker 2002). A recent study of the Irish community dwelling elderly found that depressed older adults relied heavily on family support displaying 'family dependent' social networks (Kirby et al 1999 unpublished data). With the 'Celtic Tiger' property prices have boomed and an increasing proportion of the younger population have had to move outside of the city limits to find affordable accommodation (CSO 1999). As a result the availability of family support has been reduced. In addition this problem is further compounded by the trend towards both spouses working further reducing the amount of actual time available to provide support to older family members. The net effect of these changes will be decreased family and informal caregiving support for older adults in the community and an increased dependence on already stretched social and community services. At present 4% of older adults provide informal unpaid care for friends or family members with illness or disability and it is likely that this figure will increase over time. (NCAOP 2005). A recent study of Irish elderly caregivers found that the rate of psychopathology in this population is high (Denihan, Bruce et al. 1998). The burden of illness is likely to increase in this subgroup. While the main effects of recent socio-economic changes may not be obvious at present it is likely that the effects will be magnified by the projected increase in the older adult population over the coming years.

Previous research in the Irish community dwelling elderly has shown that case-level mental illness is frequently missed in the community and that there is a significant degree of hidden morbidity that does not reach the attention of primary care physicians (Denihan, Kirby et al. 2000). It may seem futile to examine the clinical features, course and outcome of subgroups who may be even less likely to come to the attention of GPs. There are a number of reasons why this not the case.

Firstly there are no existing data on the predictors, course and outcome of subsyndromal mental disorders in the Irish elderly. While information from international studies can be utilised in identifying subgroups at risk, this data may not adequately reflect the Irish situation. Secondly existing data on subsyndromal mental disorders suggest that they are highly predictive of case-level illness. Thirdly there are no existing longitudinal studies of predictors of depression in the Irish elderly. Finally the recent socio-economic and projected sociodemographic changes within the Irish population will inevitably increase the burden on services for the elderly however there are little existing data to inform mental health service planners on specific areas of need.

Depression is the commonest mental illness in late life and carries with it a significant burden of disability. As SSD and SSA have been associated with increased risk of depression exploring the characteristics course and outcomes of these disorders is essential in order to develop preventative interventions to reduce the burden of illness over time. At present there are no longitudinal data available on subsyndromal mental illness in the Irish elderly. This thesis aims to explore SSA and SSD in an urban community based sample of older adults.

Chapter 2.

Aims

The aims of the project were as follows;

1. To examine associations with subsyndromal depression and anxiety in older community dwelling adults.

Late-life anxiety and depression may share the same vulnerability factors and develop following exposure to specific stressors such as life-events. This study (chapter 5) examines the clinical and sociodemographic correlates of SSA and SSD in an older Irish population, and explores whether baseline associations are similar for the two groups.

2. To determine the impact of subsyndromal mental illness on health service use.

Studies suggest that subsyndromal anxiety and depression are associated with increased health service use in late-life. There are limited data available on the impact of mental illness on service use in the Irish community dwelling elderly. This study (chapter 6) examines rates of health service and medication use of patients with SSD and SSA and compares the rates with those of well subjects.

3. To identify predictors of changes in anxiety symptoms and report the two-year outcome of SSA.

Studies examining the outcome of anxiety symptoms in late-life have found a high degree of comorbidity with depressive symptoms and a tendency for symptoms to persist over time. In addition some studies suggest that anxiety disorders in older adults may precede or predict depressive illness. These studies (chapters 7 and 8) examine predictors of new anxiety symptoms and the naturalistic outcome of SSA in a sample of community-dwelling older Irish subjects over a 2-year period.

4. To identify predictors of change in depressive symptoms and report the two-year outcome of SSD.

The outcome of case-level depression in the Irish community dwelling elderly has been described. Little is known about the outcome of subsyndromal disorders in this population. These studies (chapters 9 and 10) examine predictors of onset, change and chronicity of SSD in a sample of community-dwelling Irish elderly subjects over a 2-year period.

5. To examine subsyndromal anxiety and depression as predictors of incident depression in older community dwelling Irish People.

Longitudinal studies of late-life depression have identified several risk factors. In addition SSA and SSD have been reported as predictors of depression in the elderly. There are no longitudinal studies of risk factors for depression in the Irish community dwelling elderly. This study (chapter 11) examines putative risk factors for depression over a 2-year period with particular focus on exploring the strengths of SSA and SSD as predictors of depression.

Chapter 3.

Methodology

Data presented in this thesis derive from a naturalistic study of mental disorders in older people in the Dublin south central area. This chapter will describe the core methodology employed in the project. Methodology specific to each study will be presented in the relevant chapters.

Baseline data included in this thesis were collected as part of an ongoing prevalence study of mental disorders in the community dwelling elderly. The follow-up studies were completed over two years. Hereafter baseline will be referred to as t0, the first year of follow-up as t1 and the second year of follow-up as t2. Studies presented in this thesis include data from t0, t1 and t2.

3.1 Sample selection

This project was performed in collaboration with three general practitioners whose practices are situated in the St James's Hospital catchment area in Dublin's south inner city.

All three general practitioners had participated in a previous study examining prevalence rates of mental disorders among the community dwelling elderly (Kirby, Bruce et al. 1997). The sample was selected on a 'convenience' basis. General practitioners whose patients were surveyed as part of an ongoing prevalence study during the preceding year were approached for involvement in the longitudinal project. All three practices agreed to participate.

Individuals aged 65 years and over living in the community were identified from practice lists (General Medical Services and private lists). Subjects who were deceased or had moved away and were still recorded on the practice lists were excluded. In addition those elderly people identified as living in residential care (nursing homes or long-stay hospital beds) were not included in the study.

Each person was sent an individually addressed and signed letter inviting them to participate in the project and giving a morning on which the interviewers would call. The letter included a brief description of the project and a contact address

and number for further information. Each person was invited to make contact with the project co-ordinator to confirm the suitability of the interview date or to make a written or verbal refusal. All individuals who had not made a refusal were visited and interviewed in their homes on the arranged date. If there was no answer at the person's home a note was left and a second letter was sent with another appointment. If contact was not made after two visits efforts were made to ascertain whether the person still resided at the address through contact with neighbours and the GP. If this was confirmed the individual was deemed to have refused participation. This process was followed at baseline (t0). A similar process was used at follow-up (t1 and t2) with letters sent to all baseline participants excluding those who had refused, died or moved away.

Description of catchment area and local health services

The St James's Hospital catchment area is urban, primarily working class and includes pockets of significant socioeconomic deprivation. This catchment area spans three Health Service Executive (HSE) community care areas. Each HSE community care area is served by separate teams of public health nurses and home-help providers. Additionally there are a limited number of day centres in each area, provided by both the HSE and voluntary bodies (e.g. Alzheimer's Ireland).

Psychiatry services are provided through St James's hospital catchment area service. At the time of completion of this study the St James's hospital Psychiatry for the Elderly service was multidisciplinary and led by a consultant psychiatrist. The service was primarily community based although a significant number of referrals also came through the general hospital (liaison and emergency presentations). The service included a day hospital facility based in St Patrick's hospital (a private psychiatric hospital in the catchment area) and a nine bedded acute admission unit within the general psychiatry clinic in St James's hospital. Referrals to the service came primarily from GP's.

The GP is the primary gatekeeper to a number of different health service providers within the Irish health system. While a percentage of individuals will enter the hospital system through the accident and emergency department the majority of older adults reviewed at hospital outpatient clinics are referred by GPs.

Public health nurses (PHN's) also play a pivotal role in accessing home help, day centre and community support from voluntary bodies. Public health nurses may be accessed through self referral by the individual or family, though the majority of PHN referrals come from GP's or general hospital doctors.

As the project sample was not randomly selected it cannot be assumed that the findings are generalisable to the broader older Irish population. However the age and gender profile of the sample reflected that of recent Dublin census findings giving a reasonable representative sample of the older urban Dublin population (see chapter 4).

All studies in this thesis were performed concurrently. Numbers included in the studies vary due to differential attrition and mortality rates experienced during the course of the study, the details of which are described in chapter 4.

3.2 The assessments

Diagnosis

Diagnosis was ascertained using the Geriatric Mental State Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) package (Copeland 1986) which has been adapted for use in the community. The GMS (Copeland, Kelleher et al. 1976; Gurland, Fleiss et al. 1976) is a semi-structured clinical interview for older adults formed from items extracted from the Present State Examination (Wing, Birley et al. 1967) and the Psychiatric Status Schedule (Spitzer, Fleiss et al. 1964). The GMS was designed to assess functional and organic illness in the elderly. Diagnoses are derived from the GMS when the AGECAT computerised diagnostic system is applied. The AGECAT system generates eight syndrome clusters for each subject: organicity, schizophrenia, mania, depression, hypochondriasis, phobias, obsessional and anxiety neuroses. A diagnostic confidence level is generated for each syndrome ranging from 0 (no symptoms) to 5 (severely affected). The programme then presents a hierarchically determined main diagnosis with levels of co-morbidity arising from secondary diagnoses. Confidence levels of three and above for any syndrome cluster indicate 'caseness' and correlate well with what psychiatrists would recognise as a case for treatment or intervention (Copeland, Beekman et al. 1999).

Diagnostic confidence levels of 1 or 2 are referred to as ‘subcase’ diagnoses and represent the presence of a substantial number of symptoms that fail to meet the diagnostic threshold for caseness. Those with ‘subcase’ diagnoses of depression have been found to differ significantly from ‘well’ subjects in the number of symptoms reported (Copeland, Beekman et al. 1999) and fall into the diagnostic category of subsyndromal or subthreshold depression (Schaub RT 2003). Subcase anxiety has also been found to reflect a clinically relevant degree of symptoms and can be considered to represent subsyndromal anxiety (Larkin, Copeland et al. 1992).

The validity of AGECAT diagnoses is well established. AGECAT diagnoses have been compared with psychiatrists diagnoses (Copeland 1986) and DSM -IV criteria (APA 1994) and have demonstrated good levels of agreement. Inter-rater and test-retest reliability have been established through international studies (Copeland, Prince et al. 2002). The GMS is reportedly the most widely used structured mental health assessment for older adults (Copeland, Prince et al. 2002) and GMS-AGECAT has been used to validate other measures of depression in late-life. The consistency and reliability of AGECAT allows cross-national comparisons to be made and outweighs the disadvantages of not using a psychiatrists diagnosis (Copeland, Beekman et al. 1999).

The GMS-AGECAT interview was administered by a trained interviewer (a doctor or research nurse) at all three waves of the study.

Cognitive impairment

Degree of cognitive impairment was assessed using the mini-mental state examination (MMSE) (Folstein, Folstein et al. 1975) (Appendix A) using a locally validated cut-point of 23 (Cullen, Fahy et al. 2005) to indicate cognitive impairment..

Sociodemographic details

Sociodemographic details including age, gender, religious denomination, marital status and living arrangement were collected using an adjunctive questionnaire developed for the MRC-ALPHA study. In addition social support network was examined using the network assessment instrument (Wenger and Tucker 2002) (Appendix B).

Psychiatric history

Past personal and family history of psychiatric illness and dementia were collected using the MRC ALPHA minimum dataset. Details of past treatment including ECT and a record of current psychotropic medications were recorded.

Life events

Reported life events experienced by the subjects in the preceding year were recorded using the list of threatening events (Brugha and Cragg 1990) (Appendix C).

Physical health data

Physical health data were collected using the MRC ALPHA minimum dataset. The presence or absence of a number of chronic medical conditions were recorded. In addition the presence or absence and site of pain was also recorded. Subjects perceived health was recorded on a five-point scale ranging from 1 (excellent physical health) to 5 (severe impairment). Subjects health was also objectively rated by the interviewer on a similar five- point scale. The presence or absence of self reported disability was recorded and further examined by recording whether the subject ever spent days confined to bed by disability. A list of current medications was also recorded.

Substance use

Details on the amount of alcohol consumed (in units per week) and smoking history were recorded.

Service use

Details of health and social service use were collected cross-sectionally at t1 using a form designed for the study (Appendix D).

3.3 Data Collection, data analysis and writing

GMS data were entered into the GMS-AGECAT programme on an IBM laptop computer at the time of interview. All other details and scales were recorded on paper. Data including AGECAAT diagnosis were entered into a Filemaker-Pro database and analysed using SPSS version 12 statistical package on a Dell laptop

computer. Specific details of statistical tests used are described under the heading methods in each chapter. The thesis was written in Microsoft word 2000 on a Dell laptop computer.

Chapter 4.

Baseline diagnoses and associations with attrition and mortality

4.1 Background

One of the greatest obstacles encountered in longitudinal studies is sample attrition. This may be even more pronounced in studies of the elderly where physical ill health and mortality rates are higher than that of the general population and significantly impact on retention of subjects.

Exploring factors associated with attrition is important for two reasons; firstly, selective attrition can bias results and secondly, identification of factors associated with attrition can inform future studies.

A number of statistical techniques are available to correct for sample attrition including multiple imputation methods and variable weighting. However before these techniques are applied the relationship of attrition with variables of interest must be explored. Where no significant association is found between variables of interest and attrition, attrition can be assumed to be random and statistical corrections are unnecessary.

Attrition may be defined by reasons for non-participation. Mortality, failure of contact, physical frailty or poor health and overt refusal due to lack of interest are all subtypes of attrition.

There are three main aims of this study. Firstly, to compare the age and gender distribution of our sample with recent population statistics. Secondly, to report baseline diagnoses and compare them to previous study findings. Finally, to explore attrition rates over the course of the project in order to identify patterns of attrition requiring statistical correction.

4.2 Methodology

Data collection methods are described in chapter 3. All subjects (n=518) are included in this study. Baseline diagnoses (diagnoses at t0) are described and compared with those of a previous prevalence study in a similar population. Age and gender distributions are compared with population statistics from the Central Statistics Office (CSO). For the purposes of this study attrition due to mortality and attrition for other reasons will be addressed separately. Those who died during the course of the study are described as the 'mortality' group and those who were lost to follow-up for other reasons are described as the attrition group. Subtypes of attrition are explored by year. Those recorded in this sample include 'non-participation due to physical ill health, moving away (to different address or long term care (LTC)), failure of contact (no reply) and direct refusal.

Univariate associations between types of attrition and year of study or mortality are explored using non-parametric statistics. Where Mann-Whitney-U tests are used to compare sample means, the test statistic is reported as 'MW'. All results reported are two-sided, alpha was set at 0.05 with Bonferroni corrections applied for multiple analyses.

4.3 Results

Initial response rate

1018 persons were invited to participate in this project and 518 consented to interview. Sixty-three percent of non-participants were female and there was no significant difference in gender proportions between those who declined and the project participants. The mean age of the non-participants was 76 (s.d.=10) and while there was a trend towards older age in non-participants the difference was not significant.

Age and Gender distribution of baseline sample

The age and gender distribution of participants at baseline differed from that reported by the CSO from the 2002 population census. As baseline data were collected in 1998-1999 it is likely that our samples characteristics may better reflect the 1996 population census statistics (table 1.). The proportion of older-old (70 years of age and above) in our sample is greater than that of both census reports. The mean age of our sample was 74 (s.d.=6, range 65-95).

Table 1.

Distribution of sample by age and gender

Age Group	Male n(%)	Female n(%)	Total n(%)	1996 Dublin Census %	2002 Dublin Census %
65-69	48(37)	83(63)	131(25)	35	39
70-74	61(40)	94(18)	155(30)	26	27
75-79	46(37)	78(15)	124(24)	20	18
80-84	22(30)	51(10)	73(14)	12	10
85+	11(31)	24(5)	35(7)	7	6
Total	188(36)	330(64)	518(100)	100	100

Baseline diagnoses

Diagnoses (as defined by AGECAT) are represented in table 2. The numbers in diagnostic categories differed slightly from those recorded in 1997. The rates of subsyndromal anxiety and subsyndromal depression were higher than those reported in 1997. In the case of depression subtypes however when cases and subsyndromal categories are combined the rates are remarkably similar. There were no diagnostic cases of schizophrenia in either sample. In addition there were no subjects with case level anxiety alone in the current sample, however n= 12 of the depressed individuals and n=1 of the subjects with organic illness (2.5 % of the total sample) had co-morbid case level anxiety. Anxiety and depression were highly co-morbid 88% of those with case-level depression (n=37) had co-morbid anxiety at case or subsyndromal level. 45% of all subjects (n=233) were well at baseline.

Table 2.
Distribution of diagnoses compared with previous Dublin study

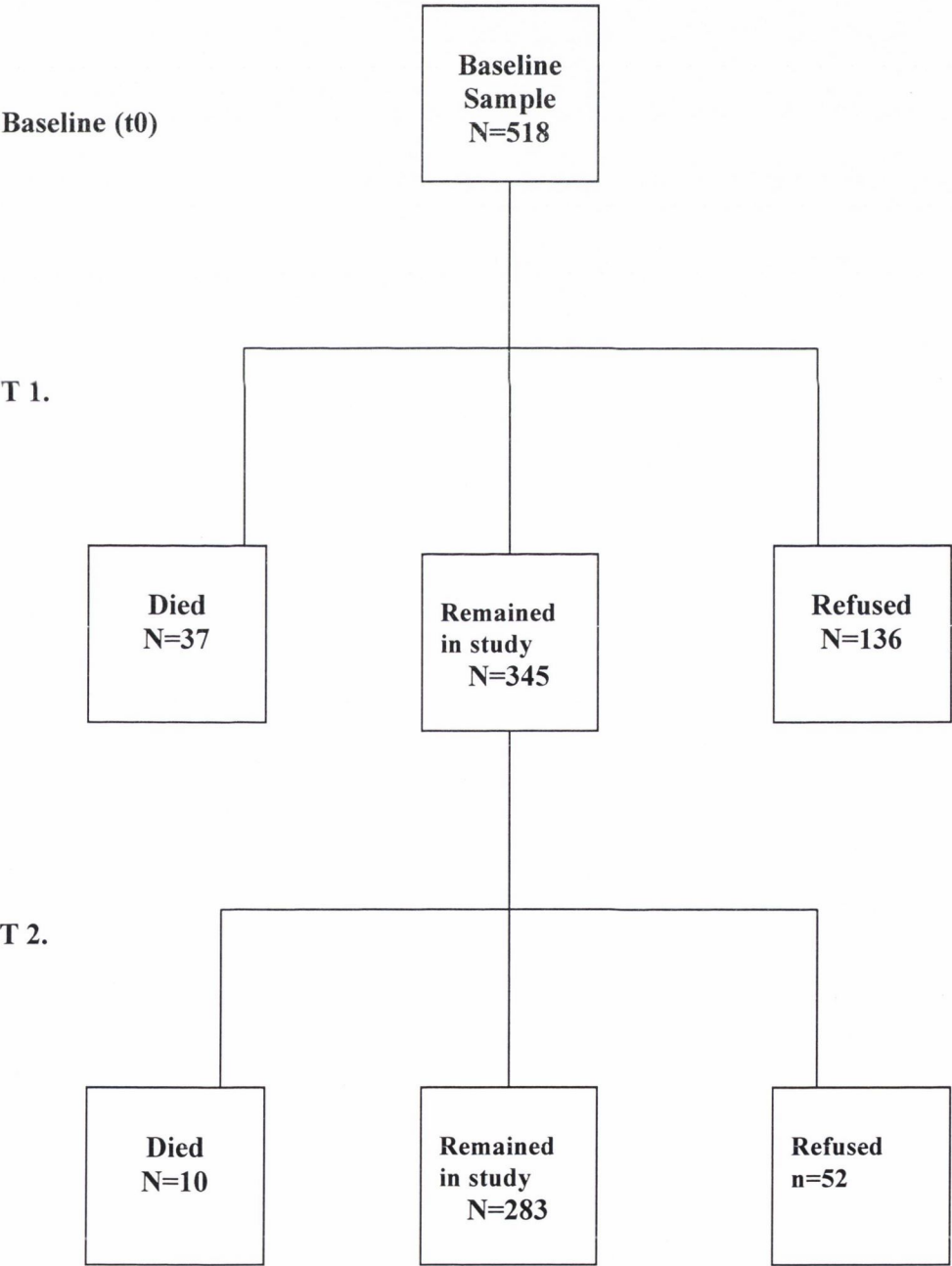
AGECAT Diagnosis	Current study (n=518)	Dublin 1997 (n=1232)
Organic Case n(%)	22(4)	50(4)
Organic Subcase n(%)	21(4)	Not available
Depression Case n(%)	42(8)	127(10)
Subsyndromal dep. n(%)	74(14)	113(9)
Total dep. case & SSD n(%)	116(22)	240(19)
Anxiety Case n(%)	0	12(1)
Subsyndromal Anxiety n(%)	125(24)	216(18)
Total Anx. case & SSA n(%)	125 (24)	240(19)
Schizophrenia Subcase n(%)	1(0.2)	5(0.4)

Sample attrition and mortality

A substantial proportion of our baseline sample (46%) were lost to follow-up over the course of the study. The retention of subjects and numbers lost to follow-up through attrition and mortality is presented graphically in figure 1.

Figure 1.

Sample attrition over the two-year study period.



4.31 Attrition

Loss to follow-up during the course of the project was due to a number of different reasons. 39 subjects had moved during the course of the study. This included nine who moved away (6 at t1 and 3 at t2) and 30 who moved into long term care (18 at t1 and 12 at t2).

Spousal bereavement was given as a reason for refusal by five subjects at t1 and one subject at t2. Interestingly the remaining subjects who refused follow-up included 32 married couples (28 at t1 and 4 at t2). Notably refusal in this group was not associated with significant psychopathology in one or other spouse. Reasons for attrition are described in table 3.

Table 3.

Reasons for loss to attrition by year

Year of study			
Reason	t1 n=136	t2 n=52	Total lost to attrition n=191
Moved n(%)	24(18)	15(29)	39(20)
No reply n(%)	30(22)	11(21)	41(21)
Refused n(%)	65(48)	19(37)	86(45)
Too unwell n(%)	17(12)	7(13)	25(14)

The association of diagnosis with attrition

Attrition at t1 was associated with having a baseline diagnosis of organic illness at case or subcase level ($\chi^2=17.987$, 3 d.f., $p<0.001$). Approximately one quarter of those in the depressive illness subgroup (case and subcase combined) were lost to follow-up over the course of the study however this was not significant. Table 4 shows attrition by diagnosis at both follow-up assessments (t1 and t2).

Table 4.
Attrition for reasons other than death by diagnosis

Diagnosis	t 0 Diagnosis (n=518) n(%)	t 1 Attrition (n=136) n(%)	t 1 Diagnosis (n=345) n(%)	t2 Attrition (n=52) n(%)	Total lost t0 –t2 (n=191) n(%)
SSD	74(21)	12(9)	39(11)	7(13)	19(10)
SSA	125(24)	38(28)	63(18)	13(25)	51(27)
Depressed	42(8)	15(11)	18(5)	4(8)	19(10)
Organic case	22(4)	10(7)	12(3)	5(10)	15(8)
SS organic*	21(4)	10(7)	4(1)	0	10(5.2)
SS schizophrenia*	1(0.05)	0(0)	1(0)	0	0
Well	233(45)	51(38)	152	23(44)	74(39)
Total	518(100)	136(100)	152(100)	52(100)	191(100)

*SS=subsyndromal

Attrition at t1 was associated with having an organic diagnosis. There was a trend towards higher attrition rates in those who were cognitively impaired, had lower MMSE scores and reported their health as poor but these associations were not significant. Table 5 shows the results of analyses for all variables at t1. Remarkably few of our sample 2.3% (n=12) had completed third level education. For the purposes of analysis those with second and third level education were grouped together and comprised 35% (n=183) of the complete study sample (n=518). Regarding marital status at baseline 73 (14%) were single, 242 (47%) married and 203 (39%) were widowed. 18% (n=94) of the total sample had a history of depression, this did not influence attrition rates.

Attrition at t2 was not significantly associated with any variable of interest. There was a trend, however to increased attrition rates in persons with lower MMSE scores, cognitive impairment and to a lesser extent, with having a lower level of education. Table 6 shows the results for all variables at t2.

The most consistent association with attrition over both years of the study was the trend towards increased attrition with increasing degree of cognitive impairment. The association was only statistically significant at t1 and at that assessment only associated with having a diagnosis of organic illness.

Table 5.

Univariate associations with attrition at t1

Variable of interest	Stayed in study n=345	Attrition n=136	2 group comparison	p
Organic diagnosis n%	15(13)	20(15)	$\chi^2 = 17.98$, 3 d.f.	<0.001*
Mean Age (s.d.)	74(6)	74(6)	MW $z = -1.3$	0.182
Female Gender n%	221(64)	90(66)	$\chi^2 = 2.82$, 2 d.f.	0.244
Marital status: Widowed n (%)	141(41)	47(35)	$\chi^2 = 10.76$, 6 d.f.	0.132
Lives alone n (%)	114(33)	40(29)	$\chi^2 = 2.436$, 2 d.f.	0.313
Primary education n (%)	228(66)	85(63)	$\chi^2 = 1.023$, 2d.f.	0.600
Mean MMSE score	26(3)	26(4)	MW $z = -1.7$	0.083
Cognitive impairment n (%)	43(13)	31(23)	$\chi^2 = 7.223$, 1 d.f.	0.007 ^Ψ
Poor self reported health n (%)	131(38)	66(49)	$\chi^2 = 4.071$, 1d.f	0.044 ^Ψ
Poor rated health n (%)	157(46)	74(54)	$\chi^2 = 2.752$, 1d.f.	0.097 ^Ψ
Disability n (%)	116(34)	40(29)	$\chi^2 = 0.609$, 2d.f.	0.435

* Significant at $\alpha < 0.005$ following Bonferroni correction.

^Ψ Trend only

Table 6.

Univariate associations with attrition at t2.

	Stayed in study n=283	Attrition n=52	2 group comparison	p
Organic diagnosis n%	16(6)	5(10)	$\chi^2 = 0.731$, df 1	0.393
Mean Age (s.d.)	74(26)	75(6)	MW z = -0.18	0.565
Female Gender n%	175(62)	38(73)	$\chi^2 = 1.936$,df1	0.164
Marital: Widowed n%	113(40)	23(44)	$\chi^2 = 0.747$ 2df	0.898
Lives alone n%	90(49)	21(40)	$\chi^2 = 1.46$,1df	0.295
Primary education n%	180(63)	41(79)	$\chi^2 = 4.547$,df1	0.088
Mean MMSE score	27(3)	26(3)	MW z = -1.2	0.011*
Cognitive impairment n%	31(11)	12(23)	$\chi^2 = 4.738$,df 1	0.019*
History of depression	43(15)	12(23)	$\chi^2 = 1.456$, df1	0.228
Poor self reported health n%	104(37)	20(38)	$\chi^2 = 0.055$, df 1	0.937
Poor rated health n%	129(46)	21(40)	$\chi^2 = 0.293$, df 1	0.545
Disability n%	97(34)	14(27)	$\chi^2 = 0.766$,df 1	0.382

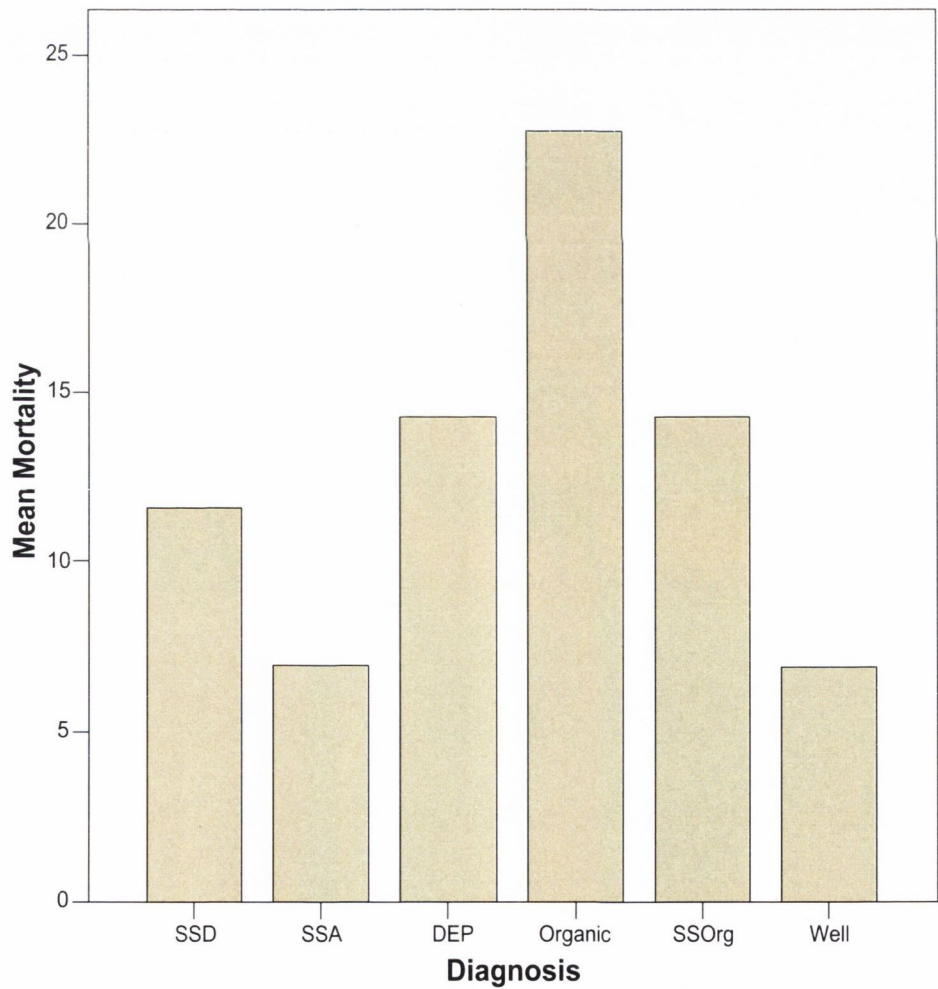
* Trend only, $\alpha < 0.005$ following Bonferroni correction.

4.32 Mortality over the course of the study

Forty-seven subjects died during the course of the study giving an overall mortality rate of 9%. The association between baseline diagnosis and mortality rates is represented in figure 2. Mortality rates were highest amongst the group of patients with an organic diagnosis at baseline 22% of this group died during the course of the study. The effect of depression on mortality rates was also notable with 14% of those with a baseline diagnosis of case-level depression and 12% of those with SSD dying over the course of the study.

Figure 2.

Mortality rate (%) by diagnosis



Having a baseline organic diagnosis at case level was significantly associated with mortality. Not surprisingly cognitive impairment and poor physical health were also significantly associated with mortality. Table 7 shows the associations between baseline factors and mortality over the course of the study. In the interest of preserving power as only 10 subjects had died between t1 and t2 of the study associations with mortality were not examined separately at each timepoint.

Table 7.

Association between baseline factors and mortality

Baseline variables	Alive n=471	Died n=47	2 group comparison	p
Organic diagnosis n%	35(7)	8(17)	$\chi^2 = 5.16,$ 1 d.f.	0.046 ^ψ
Mean Age (s.d.)	74(6)	77(7)	MW z = -3.2	0.002*
Female Gender n%	303(64)	27(57)	$\chi^2 = 0.604,$ 1 d.f.	0.437
Marital: Widowed n%	178(38)	20(43)	$\chi^2 = 0.863,$ 1 d.f.	0.834
Lives alone n%	151(32)	11(23)	$\chi^2 = 1.114,$ 1 d.f.	0.291
Mean MMSE score	27(3)	24(5)	MW z = -3.8	0.000*
Cognitive impairment n%	74(16)	15(32)	$\chi^2 = 6.78,$ 1 d.f.	0.009 ^ψ
Poor self rated health n%	190(40)	36(77)	$\chi^2 = 21.39,$ 1 d.f.	0.000*
Poor I. rated health n%	224(48)	39(83)	$\chi^2 = 21.45,$ 1 d.f.	0.000*

* Significant at $\alpha < 0.006$ following Bonferroni correction.

^ψ Trend only.

4.4 Discussion

The age distribution of our sample differs from that reported in the 2002 census (CSO 2002). This difference may be related to the time frame during which baseline data were collected (1998-1999) thus direct comparison may not be appropriate. In addition the gender distribution of our sample more accurately reflects that of the previous census (64% female and 36% male). The likelihood of a divergence from population norms is to be expected however as ours was a convenience sample, neither randomly selected nor stratified by age. Nevertheless, as incidence and prevalence figures will not be calculated from this study it is not essential that the sample be 'epidemiologically sound'. In addition, the over-representation of older-old may prove to be advantageous, as it will provide valuable information about a growing proportion of the Irish population. Despite the sampling issues referred to above in general the distribution of diagnoses was remarkably similar to that of a previous study in a similar population (Kirby, Bruce et al. 1997). The presence of higher numbers in the subsyndromal groups is useful as it provides good baseline samples of SSA and SSD, the key diagnoses of interest in this study.

A substantial proportion of our sample (46%) were lost to follow-up over the three years of the study. The mortality rate of 9% reflects that reported in census figures. The attrition rate for reasons other than mortality was high at 39%. However when the reasons for attrition are considered these rates are less alarming (that is, only 17% actually 'refused' follow up) and reflect those reported in other studies.

Few longitudinal studies of older adults have specifically examined attrition. Those which have frequently report that the main differences between participants and drop-outs tend to lie in their sociodemographic and health characteristics. The latter 'tend to be older, have lower levels of education, poorer health and poorer cognitive functioning at baseline' (Chatfield, Brayne et al. 2005). We found few such associations in our study at the level of statistical significance. The only factor which appeared to be related to attrition was having an organic diagnosis and this factor was only significant at the second wave. We did however identify a trend towards higher attrition rates in those with poor health at baseline which is well described (Launer, Wind et al. 1994; Matthews, Chatfield et al. 2004).

Many studies have reported an association between attrition and increasing age however this was true only in relation to mortality in our sample (Chatfield, Brayne et al. 2005). The over-sampling of older-old at the outset of our study may have resulted in less of an age effect.

One notable observation was that where one member of a couple refused the other concurred. Clearly this contributed greatly to the rate of attrition, accounting for 74% of those who gave an overt 'refusal' and 34% of the overall attrition rate. As this trend was not associated with the presence of significant psychopathology in either partner it is possible that ongoing participation by one partner would prove too uncomfortable when the other refused.

The trend towards both attrition and mortality in those with an organic diagnosis is a well documented finding (de Graaf, Bijl et al. 2000; Jacomb, Jorm et al. 2002; Van Beijsterveldt, van Boxtel et al. 2002). These authors suggest that persons with cognitive impairment may be unable to co-ordinate interviews due to executive dysfunction. In addition where the individual has some awareness of their deficits continued participation in a study may prove too confronting for them.

The associations between increasing age, poor physical health and mortality in our sample are unremarkable and well documented.

While mortality rates for those with a baseline diagnosis of depression were high at 14% they were not as high as those reported in a previous Irish study of depressed older adults (Denihan, Kirby et al. 2000). The follow-up period in our study was shorter however, which may explain this divergence. Mortality rates were also increased in those with SSD at baseline, this finding will be explored in more detail in chapter 8.

It is important to explore whether we could have taken any measures to reduce attrition during the course of this study. We found no consistent statistically significant association with attrition across the timepoints of this study. In other words it seems that attrition was random and as a result we can only speculate as to why dropouts occurred. The only factor that showed a consistent trend towards increased rates of both attrition and mortality was having a diagnosis of organic illness. A recent meta-analysis of attrition from longitudinal studies of older adults suggested methods for reducing the likelihood of attrition (Chatfield, Brayne et al. 2005). One suggestion was that in order to reduce attrition due to cognitive

impairment, a shorter interview or a proxy interview could be performed. This would not have been feasible in our study. A substantial minority (30%) of our subjects lived alone, which would make it difficult to identify collaborative informants. In addition, using a shortened interview would have led to important information being missed. Finally, as the case finding instrument used in this study (AGECAT) is designed for 'subject' assessment imputation of responses from a collaborative informant would have introduced bias in the results.

Another factor which may impact on attrition is the length of the interview (Van Beijsterveldt, van Boxtel et al. 2002). In the case of this study the interview was not overly taxing most subjects taking approximately one hour to complete both the AGECAT interview and associated questionnaire.

Attrition due to mortality is inevitable in studies of elderly subjects and as such is difficult to control for at the outset of the study. Furthermore, those factors which were significantly associated with mortality also increased the likelihood of attrition in our study. In light of this, it is unlikely that baseline 'over sampling' of frailer more cognitively impaired individuals would have impacted on overall retention rates.

Despite the high attrition rate we managed to retain 54% of our sample and have complete three-year data for a substantial group of 283 elderly subjects. In addition as attrition was found to be random no statistical corrections are indicated. As the sample size was significantly reduced by attrition it is possible that this will impact on power in at least some of the subsequent studies in this thesis. This will be discussed in more detail where it arises.

Chapter 5.

Co-morbidity of anxiety and depressive symptoms and baseline associations with subsyndromal anxiety and depression

5.1 Background

Anxiety and depression are highly comorbid throughout the life cycle (Devanand 2002). They may lie on a continuum and represent different expressions of the same underlying condition. This may be particularly true of the association between generalised anxiety disorder and depression (Kessler, McGonagle et al. 1994). It has also been suggested that GAD and depression share genetic vulnerabilities and that environmental exposure determines the development of either condition (Kendler 1996). Studies examining anxiety and depression in late-life have demonstrated significant levels of comorbidity of the two conditions and evidence of commonality of risk factors (de Beurs, Beekman et al. 2001; Schoevers, Beekman et al. 2003; Schoevers, Deeg et al. 2005). Conversely anxiety and depression may be separate entities with mutually exclusive risk factors. There are two purposes of this study. Firstly, to examine the degree of comorbidity of anxiety and depression at baseline. Secondly, to explore baseline associations with SSD and SSA. We hypothesise that there will be few differences in associations between the two disorders.

5.2 Methodology

The methodology employed is described in chapter three. All subjects interviewed at baseline are included in this study. As AGECAT generates diagnoses on a hierarchical level, comorbid symptoms are also described. The group with SSD was not ‘diagnostically pure’ as it contained individuals with comorbid subsyndromal anxiety. In addition a substantial proportion of the groups with depression and organic diagnoses were also found to have comorbid anxiety symptoms at case or subsyndromal level. For descriptive purposes the SSD group were split into those with depression alone (Dep) and those with depression and anxiety (D&A) and descriptives are presented by subgroup. Thereafter in order to preserve power, all subjects with SSD (with and without comorbid anxiety) are included in analyses as one group. Associations with a number of vulnerability and risk factors were explored. Vulnerability factors include age, gender and history of depression (personal and family). Risk factors include environmental conditions (sociodemographic variables), cognitive status, health variables and life events.

Statistical analysis

A group with comorbid anxiety and depressive symptoms were identified and the relationship between anxiety and depressive symptoms was explored using Spearman’s Rank order Correlation. The degree of shared variance (coefficient of determination) was calculated from Rho and two tailed results are reported.

The complete sample (n=518) was split into four groups based on diagnosis; SSD (depressive symptoms alone (Dep) and depressive and anxiety symptoms (D&A)), SSA, ‘well’ and ‘other psychopathology’. Associations with baseline variables between these four groups were explored using chi squared and Kruskal Wallis tests. Between group differences for SSA and SSD were then explored using non-parametric statistics. All reported associations are two-sided and Bonferroni corrections are applied for multiple analyses.

Specifically regarding the Bonferroni corrections; subgroups of variables were identified and Bonferroni corrections applied where the number of variables in each group exceeded three.

Sociodemographic variables included age, gender, marital status, social network, living arrangement and level of education. For these analyses alpha was set at 0.008. Cognitive variables included MMSE score, and the presence of subjective memory complaints (Subj. Memory complaints). For these analyses alpha was set at 0.01.

For health related variables including self rated health, interviewer rated health, disability, pain and arthritis alpha was set at 0.008.

5.3 Results

Diagnoses were described in chapter 4. In brief the sample consisted of 518 community dwelling elderly subjects of whom 233 were well, these subjects comprised the 'well' group. The 'other psychopathology' group (hereafter referred to in tables and text as 'other') included 45 subjects with an organic diagnosis (case or subcase), 42 subjects with case level depression and one with subsyndromal symptoms of schizophrenia.

The SSA group comprised 125 subjects. Regarding the quality of subsyndromal anxiety symptoms n=17 had phobic symptoms, n=98 had symptoms of generalised anxiety and n=10 had a combination of symptoms, specifically generalised anxiety and obsessional symptoms n=3 and generalised anxiety and phobic symptoms n=7. In addition one member of the SSA group had phobic and subsyndromal organic symptoms.

The group with SSD included two subgroups; n= 25 with 'pure SSD' and n=49 with comorbid anxiety symptoms where SSD took diagnostic precedence. Regarding the quality of comorbid anxiety symptoms n=37 had subsyndromal generalised anxiety disorder, n=9 had a combination of phobic and generalised anxiety, 1 had comorbid obsessional symptoms and n=2 had comorbid generalised anxiety and organic symptoms.

Of those who were depressed (case level) at baseline n=37 had comorbid anxiety symptoms at case or subcase level. Regarding the type of comorbid anxiety symptoms 12 subjects with depression had comorbid case level generalised anxiety disorder and a further 25 had subsyndromal generalised anxiety.

One subject with case level organic illness also had case level depression and case level generalised anxiety.

Comorbidity of anxiety and depression

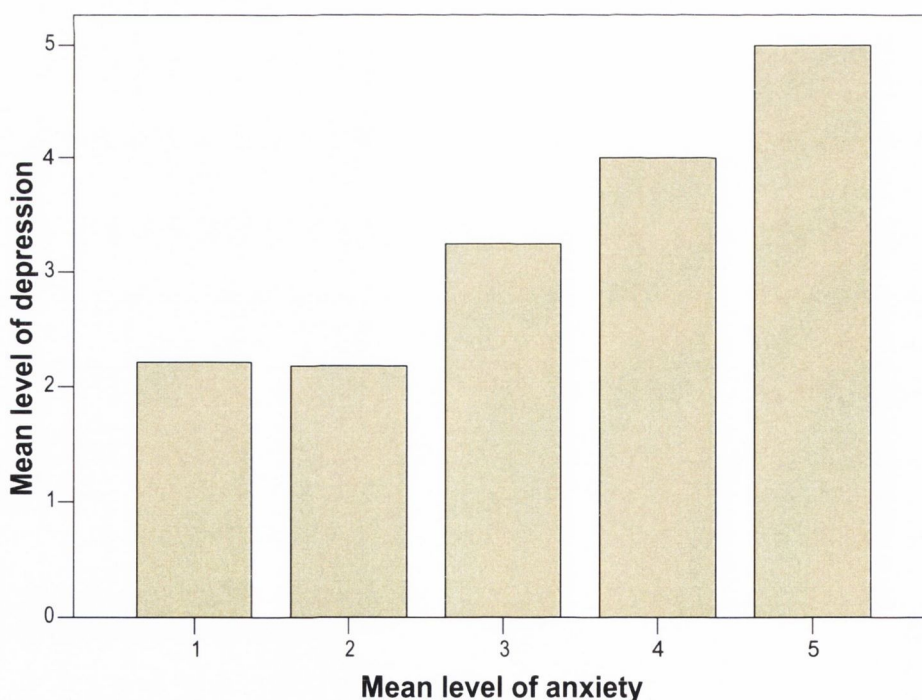
17% (n=87) of subjects had comorbid anxiety and depression at case or subcase level. This group included n=37 subjects with depression, n=1 subject with organic caseness and n=49 with 'mixed' SSD.

There was a moderate, positive correlation between anxiety and depression (Spearman's $\rho=0.392$, $n=87$, $p=0.002$). Higher levels of depressive symptoms were associated with the presence of higher levels of anxiety symptoms with a coefficient of determination of 0.154. The relationship between levels of anxiety and depressive symptoms is represented graphically in figure 3.

Figure 3.

Comorbidity of anxiety and depression at baseline

Co-occurrence of depression and anxiety (n=87)



Levels of 1 & 2 are subsyndromal

Levels of 3 and above are case level

Associations with subsyndromal psychopathology(4 group analysis)

Regarding sociodemographic variables, no association was found between age, marital status (table 8), living arrangement or level of education and diagnosis. Remarkably few subjects had completed tertiary education (table 9). There was a significant association between social network and diagnostic group ($\chi^2 = 34, 15$ df, $p=0.003$) with the majority of subjects with psychopathology at any level displaying a family dependent style of social network (see table 10). Being female was associated with having a subsyndromal diagnosis ($\chi^2 = 16.33, 3df, p=0.001$).

Table 8.

Distribution of marital status by diagnosis

Diagnosis								
Marital status	SSA n=125			SSD n=74		Other n=86	Well n=233	Total n=518
	GAD n=98	Phobic n=17	Mixed n=10	Dep n=25	D/A n=49			
Single	12 (12)	3 (18)	1 (10)	2 (8)	5 (10)	8 (9)	42 (18)	73 (14)
Married n (%)	52 (53)	10 (59)	5 (50)	12 (48)	22 (45)	35 (40)	107 (46)	242 (47)
Widow n (%)	34 (35)	4 (24)	4 (40)	11 (44)	22 (45)	43 (51)	85 (37)	203 (39)

Table 9.

Distribution of Level of Education by diagnosis

Diagnosis								
Level of Education	SSA n=125			SSD n=74		Other n=86 n(%)	Well n=233 n(%)	Total n=518 n(%)
	GAD	Phobic	Mixed	Dep	D/A			
	n=98	n=17	n=10	n=25	n=49			
	n(%)	n(%)	n(%)	n(%)	n(%)			
Primary	58 (59)	15 (88)	7 (70)	17 (68)	31 (63)	65 (75)	142 (61)	335 (65)
Secondary	39 (40)	2 (12)	3 (30)	8 (32)	18 (37)	20 (24)	81 (35)	171 (33)
Tertiary	1(1)	0	0	0	0	1(1)	10(4)	12(2.3)

Table 10.

Distribution of Social Network by diagnosis

Diagnosis								
Social network	SSA n=125			SSD n=74		Other n=86 n(%)	Well n=233 n(%)	Total n=518 n(%)
	GAD n=98 n(%)	Phobic n=17 n(%)	Mixed n=10 n(%)	Dep n=25 n(%)	D/A n=49 n(%)			
Family dependent	19 (19)	5 (30)	1 (10)	5 (20)	15 (31)	28 (33)	31 (13)	104 (20)
Locally integrated	69 (70)	11 (65)	7 (70)	16 (64)	31 (63)	49 (58)	183 (78)	366 (70)
Local self-contained	6 (6)	0	1 (10)	1 (4)	0 (0)	4 (5)	7 (3)	19 (4)
Community focused	3 (3)	0	1 (10)	1 (4)	0 (0)	0 (0)	9 (4)	14 (3)
Private	1 (1)	0	0	1 (4)	2 (4)	3 (4)	1 (1)	8 (2)
In transition	0	1 (6)	0	1 (4)	1 (2)	1 (1)	3 (1)	7 (1)

Figure 4.

Mean mini-mental state examination score by diagnosis

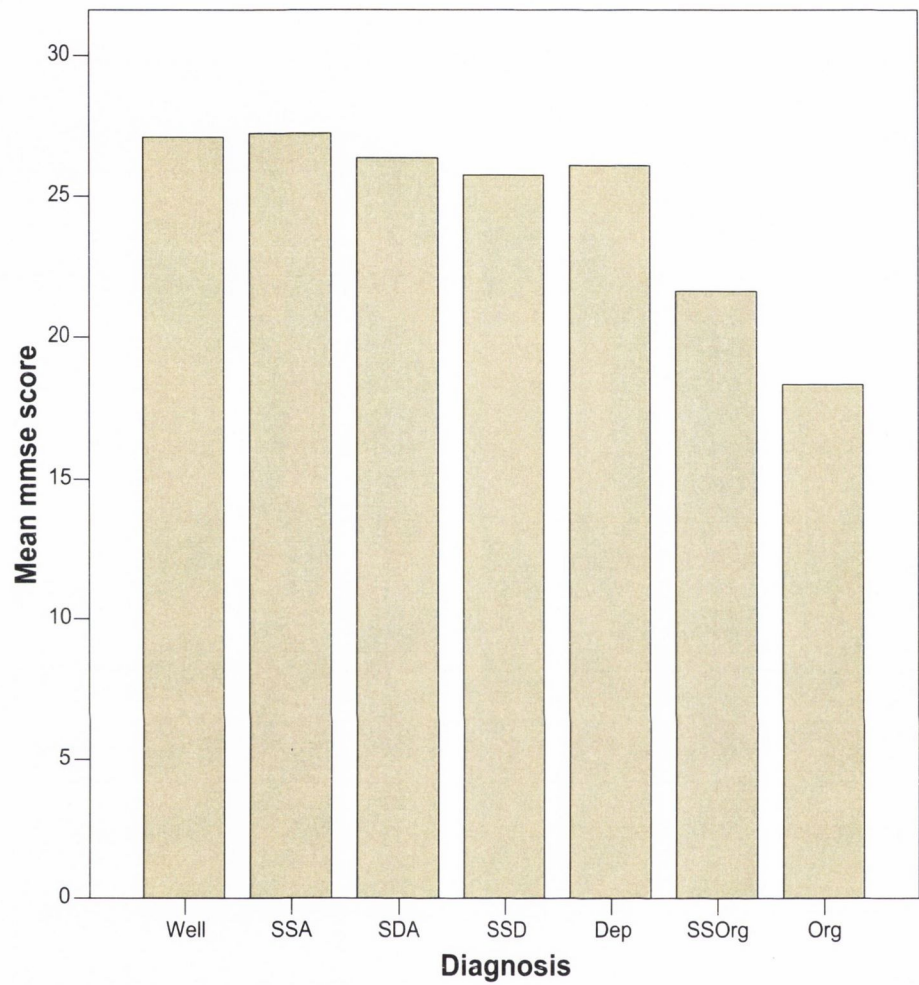
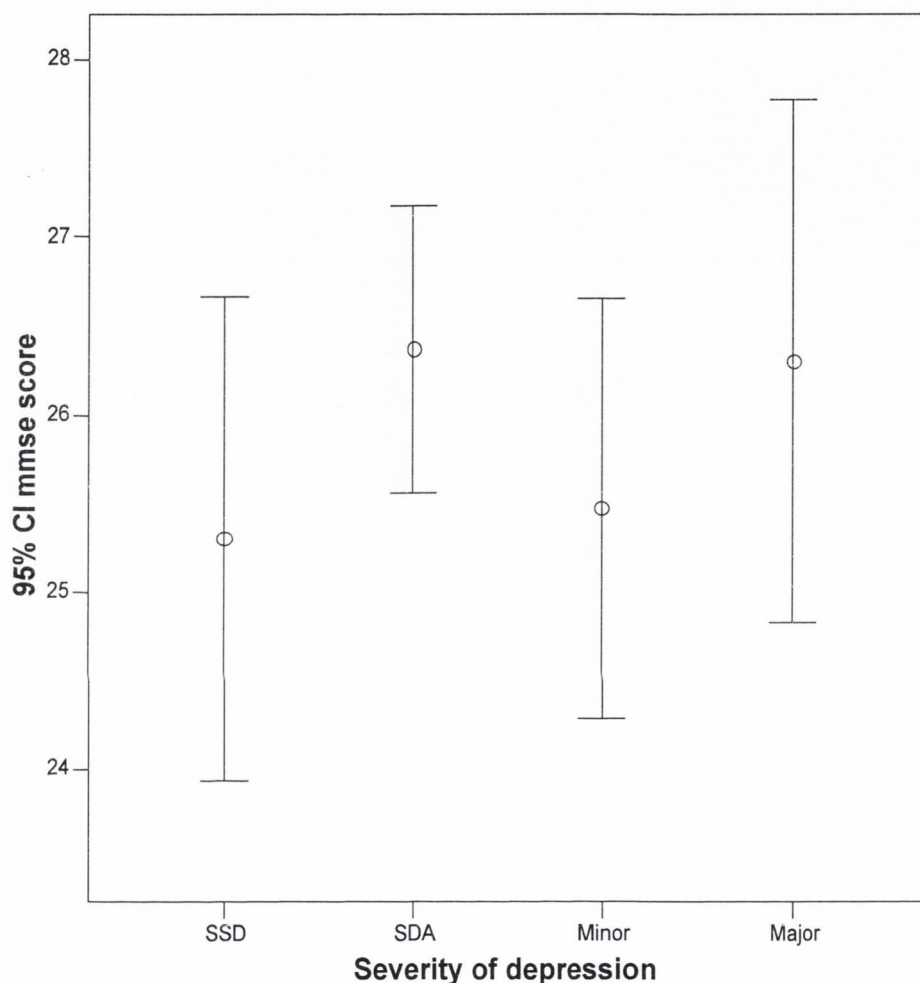


Figure 5.

Mean MMSE scores by severity of depression



Regarding cognitive variables, significant between group differences were found for mean MMSE scores (KW $\chi^2 = 75$, 3df, $p=0.000$). Differences in cognition appeared to lie between the group with ‘other psychopathology’ and the remainder of the sample. When mean MMSE scores are examined by diagnosis (figure 4) the mean scores for case and subcase organic diagnoses are lowest. Amongst the other diagnoses mean MMSE scores are lowest for the SSD group. When specific subtypes of SSD and case level depression are explored the group with pure SSD have lower scores than all other subgroups of depressive severity (figure 5). In addition, those with psychopathology at any level were more likely

to report subjective memory complaints than the well group ($\chi^2 = 30.9$, 3df, $p=0.000$).

There was also a significant between group difference for mean number of negative life events (KW $\chi^2 = 22.3$ df, $p=0.000$) this difference appeared to lie between the group with SSD and the remainder of the sample. In addition, a significant difference was found in reporting more than two negative life events in the preceding year between diagnoses ($\chi^2 = 26.11$, 3df, $p=0.000$) again, this difference appeared to lie between those with SSD and the remainder of the sample.

Regarding health related variables, significant between group differences were found for all four health variables and the differences appeared to lie between those with any degree of psychopathology and the well group.

Mean weekly alcohol consumption also differed significantly between diagnostic groups (KW $\chi^2 = 8.34$, 3df, $p=0.039$). On the basis of raw data it appeared that those who were either well, or had the mixed (anxiety and depression) subtype of SSD were more likely to consume more alcohol than the remainder of the sample.

Results for all univariate analyses are presented in table 12.

Between group differences for subsyndromal diagnoses (2 group analyses)

Those with SSD were more cognitively impaired than the group with SSA having significantly lower mean MMSE scores (MWU 3478, $z=3$, $p=0.003$) and showed a trend towards having decreased mean Sunderland CDT scores (MWU 3758, $z=2$, $p=0.07$). While having a family history of depression was not associated with either diagnosis, SSD was associated with having a personal history of depression ($\chi^2 = 4.2$, 1df, $p=0.04$). The association between history of depression and psychopathology is represented in figure 6.

The group with SSD reported a significantly greater number of negative life events in the preceding year than those with SSA (MWU 3673, $z=0.25$, $p=0.01$) and consequently were also significantly more likely to have experienced two or more life events in the preceding year ($\chi^2 = 10.17$, 1df, $p=0.001$). The group with SSD also showed a trend towards having poorer self-reported and observer rated health than those with SSA, but not to a statistically significant extent. Complete results of analyses are presented in table 12. Associations between negative life

events and subsyndromal diagnoses are presented in table 11. Statistical associations are limited as the cell sizes for all but one variable were too small to complete chi-squared analysis. The most notable between group difference on a descriptive level was that a greater proportion of those with ‘pure’ SSD reported recent bereavement. There were no associations between specific life events and SSA.

Table 11.

Associations between negative life events and subsyndromal diagnoses

Life Event	Diagnosis					
	SSA n=125			SSD n=74		2 group χ^2 analysis 1 d.f.
	GAD n=98 n(%)	Phobic n=17 n(%)	Mixed n=10 n(%)	Dep n=25 n(%)	D&A n=49 n(%)	
New Health problem	6(6)	2(12)	0	9(36)	22(45)	not applicable
Bereaved	38(39)	7(41)	5(50)	16(54)	18(38)	$\chi^2=5.6$, p=0.06*
Had something stolen	6(6)	2(12)	0	5(20)	9(18)	not applicable
Upset by other factors	27(28)	1(6)	1(10)	7(28)	16(33)	not applicable
Financial problems	0	0	0	1(4)	2(4)	not applicable
Moved house	0	0	0	0(0)	2(4)	not applicable

* trend only $\alpha=0.008$

Figure 6.

Relationship between history of depression and diagnosis

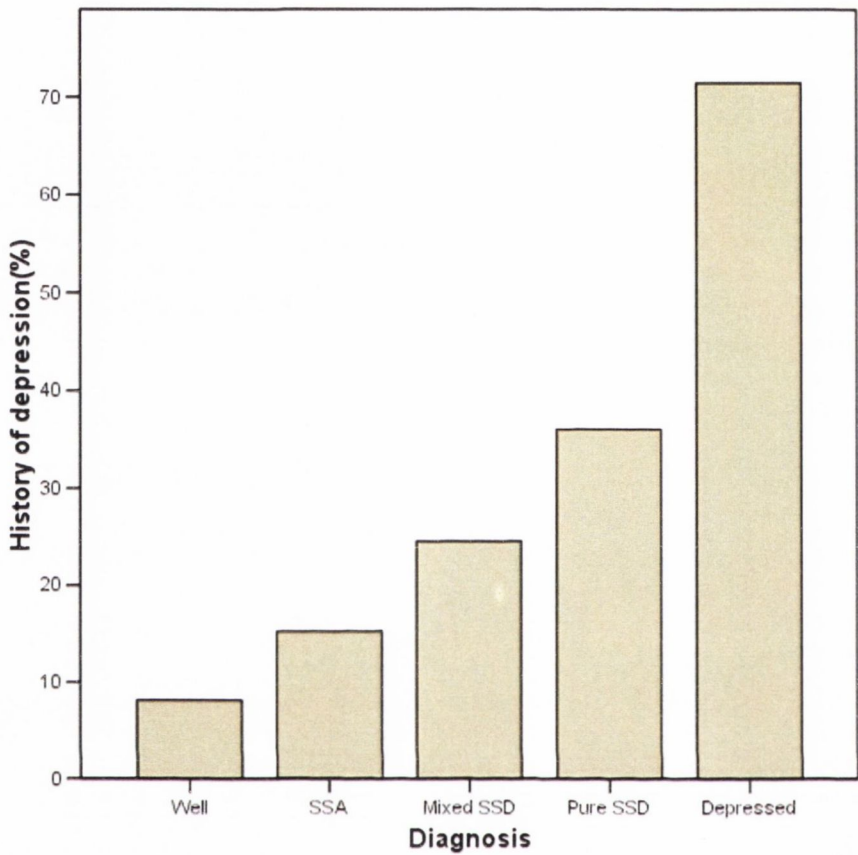


Figure 7.

Relationship between diagnosis and mean number of negative life events

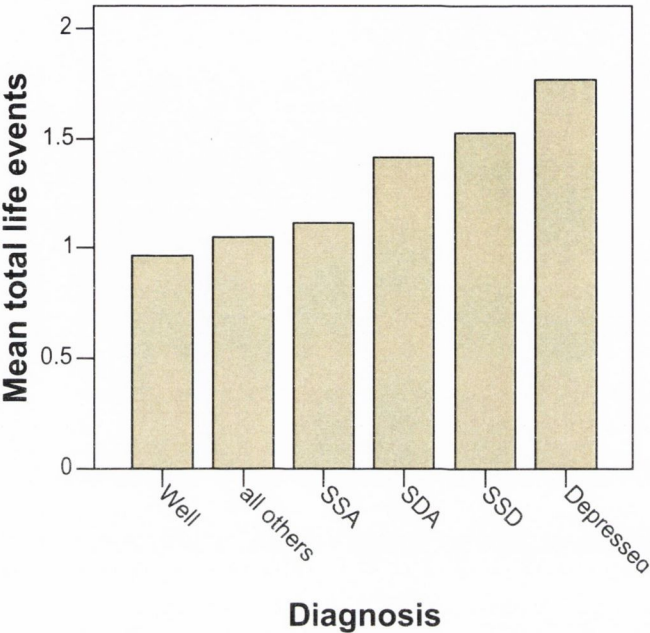


Table 12. Baseline associations with SSA and SSD.

	SSA n=125 n(%)	SSD n=74		Other n=86 n(%)	Well n= 233 n(%)	4 group analysis n=518	2 group analysis (SSA vs SSD) n=199
		Dep n=25 n(%)	D&A n=49 n(%)				
Age; mean (s.d.)	73(6)	75(6)	73(5)	76(8)	74(6)	KW $\chi^2 = 6.98$, 3df, p=0.07	MW z = 0.62, p=0.54
Gender; female	93(74)	16(64)	39(80)	51(60)	131(56)	$\chi^2 = 16.33$, 3df, p=0.001*	$\chi^2 = 0.0$, 1df, p=1
Marital status; single	16(13)	2(8)	5(10)	8(9)	42(18)	$\chi^2 = 12$, 6df, p=0.06	$\chi^2 = 2.5$, 2df, p=0.29
Lives alone	39(31)	10(40)	19(39)	24(28)	70(30)	$\chi^2 = 2.7$, 3df, p=0.44	$\chi^2 = 0.99$, 1df, p=0.32
Family dependent	25(20)	5(20)	15(31)	28(33)	31(13)	$\chi^2 = 34$, 15 df, p=0.003*	$\chi^2 = 7.5$, 5df, p=0.18
Primary education	80(64)	17(68)	31(63)	64(75)	143(61)	$\chi^2 = 5.52$, 3df, p=0.137	$\chi^2 = 0.01$, 1df, p=1
Mean MMSE (s.d.)	27(3)	26(3)	26(3)	23(5)	27(3)	KW $\chi^2 = 75$, 3df, p=0.000*	MWz = 3, p=0.003*
Cognitive impairment	10(8)	3(12)	3(6)	29(34)	19(8)	$\chi^2 = 44.5$, 3df, p=0.000*	$\chi^2 = 0.001$, 1df, p=1
Subj. Memory complaints	19(16)	6(24)	13(27)	29(35)	23(10)	$\chi^2 = 30.9$, 3df, p=0.000*	$\chi^2 = 2.6$, 1df, p=0.11
History of depression	19(15)	9(36)	12(26)	35(41)	19(8)	$\chi^2 = 52$, 3df, p=0.000*	$\chi^2 = 4.2$, 1df, p=0.04*
Family history depression	16(13)	2(8)	12(25)	12(14)	25(11)	$\chi^2 = 3.51$, 3df, p=0.32	$\chi^2 = 0.923$, 1df, p=0.34
Mean Neg. life events(s.d.)	1(1)	2(1)	1(1)	1.4(1)	1(1)	KW $\chi^2 = 22$, 3df, p=0.000*	MWz = 0.25, p=0.01*
>2 negative life events	7(6)	5(20)	10(20)	13(15)	9(4)	$\chi^2 = 26.11$, 3df, p=0.000*	$\chi^2 = 10.17$, 1df, p=0.001*
Poor self rated health	50(40)	12(48)	31(63)	58(68)	74(31)	$\chi^2 = 41.65$, 3df, p=0.000*	$\chi^2 = 5.41$, 1df, p=0.02 [†]
Poor observer rated health	56(45)	13(52)	33(67)	69(81)	91(39)	$\chi^2 = 50.27$, 3df, p=0.000*	$\chi^2 = 4.9$, 1df, p=0.03 [†]
Disability	45(36)	11(44)	20(41)	46(54)	57(24)	$\chi^2 = 57$, 3df, p=0.000*	$\chi^2 = 0.457$, 1df, p=0.49
Pain	44(35)	10(40)	18(38)	32(38)	42(18)	$\chi^2 = 22.31$, 3df, p=0.000*	$\chi^2 = 0.049$, 1df, p=0.83
Arthritis	44(35)	9(36)	16(33)	27(32)	40(17)	$\chi^2 = 18.8$, 3df, p=0.000*	$\chi^2 = 0.002$, 1df, p=0.96
Mean alcohol units (s.d.)	5(10)	5(12)	6(21)	3(7)	6(11)	KW $\chi^2 = 8.34$, 3df, p=0.039*	MWz = 0.7, p=0.5

* Statistically significant, [†] Trend only

5.4 Discussion

Anxiety and depression were highly comorbid in our sample both at case and subcase level. This is a well documented finding (Lindesay, Briggs et al. 1989; Kirby, Bruce et al. 1997; Beekman, de Beurs et al. 2000; Lenze, Mulsant et al. 2002). There was only a moderate correlation between levels of anxiety and depressive symptoms that is, a linear association between levels of depression and anxiety was only present in 15% of those with comorbidity. This has been described previously where comorbidity levels between depression and anxiety appear to rise along a gradient of severity of symptoms (Schoevers, Beekman et al. 2003). While the inclusion of subjects with comorbid anxiety symptoms in both the SSD and 'other psychopathology' groups may have diluted our findings, retaining these subjects allows a more accurate representation of the community dwelling elderly.

Despite the heterogeneity of our diagnostic groups a number of baseline variables were found to be significantly associated with subsyndromal psychopathology. In addition, consistent with our baseline hypothesis we found few differences in associations between the two disorders.

Variables which were significantly associated with subsyndromal diagnosis on four group analysis but not on two group analysis (SSA vs SSD) can be assumed to represent shared vulnerability or risk factors. Gender proved to be the strongest common vulnerability factor with females comprising 74% of the groups with subsyndromal diagnoses. This replicates other study findings, most epidemiological studies of depression and anxiety in late life have found increased rates in females (de Beurs, Beekman et al. 2001). Other vulnerability factors including personal and family history of depression were not found to be shared between the subsyndromal groups. Having a history of depression significantly increased the risk of SSD alone. It is interesting to note the association between proportions of subjects reporting a history of depression and diagnosis (represented in figure 6). While a shared vulnerability was not found for personal history of depression the proportions alone suggest the likelihood of commonality of this vulnerability factor. It is possible that the association between history of depression and SSA may have been stronger if a larger sample (i.e. greater than n=518) were included in this study. Health related variables specifically the

presence of disability, pain and arthritis were associated with both SSA and SSD. As this is a cross sectional study the direction of causality is unclear. Disability and pain can increase depression and anxiety and the opposite is also the case (Mossey, Gallagher et al. 2000; Beekman, Penninx et al. 2002; Braam, Prince et al. 2005; van Gool, Kempen et al. 2005). In the case of arthritis however it is likely that the presence of arthritis increased the risk of both SSA and SSD in our sample. In addition the group with SSD showed a trend towards increased rates of poor self and observer rated health over and above that of those with SSA.

There were few baseline variables whose associations distinguished SSA from SSD. Where differences occurred they lay in the realm of cognitive function and life events. One of the most striking findings was that the group with SSD had significantly lower mean MMSE scores than those with SSA. Anxiety symptoms are well described in the context of dementia however community based studies of older adults have reported no association between anxiety symptoms and cognition (Lindesay, Briggs et al. 1989; van Balkom, Beekman et al. 2000). The association between SSD and MMSE score could not be explained by cognitive impairment alone as equal proportions (8%) of both groups were cognitively impaired. It is possible that SSD affected cognition through attentional or executive pathways however specific deficits on the MMSE were not explored in detail in this study. Differences in cognition were not explained solely by the presence of depressive symptoms as evidenced by the comparison (graph) of mean MMSE scores across a spectrum of severity of depressive symptoms. It is possible that the group with 'pure' SSD represent a group with organic brain changes or MCI. In addition having a history of depression was associated with lower MMSE scores at baseline and this may have contributed to the differences between SSA and SSD. Whether cognitive deficits in this subgroup represents a pre-dementia state will be explored in more detail in a further chapter reporting on the two-year outcome of SSD. The differences in mean MMSE scores were reflected in the proportions of individuals reporting memory complaints. Subjects with SSD were more likely to report memory complaints (27% SSD vs 24% SDA vs 16% SSA) but not to a statistically significant degree.

Negative life events were associated with SSD but not SSA. In addition the mean number of negative life events reported differed by diagnosis with subjects diagnosed with depression reporting the greatest number of life events in the

preceding year. Those with SSD reported a significantly greater number of negative life events than subjects with SSA. This association may be explained in part by recall bias which cannot be outruled in a cross sectional study (Devanand, Kim et al. 2002). The subjective impact of life events has been reported to differ between individuals (Mazure, Maciejewski et al. 2002) particularly where there is a pre-existing vulnerability such as having a history of depression or personality based coping style (Ormel, Oldehinkel et al. 2001; de Beurs, Comijs et al. 2005). Some studies have suggested that the nature and quality of life events may have a causative role to play in increasing the likelihood of anxiety or depressive symptoms (Kendler, Karkowski et al. 1998; de Beurs, Beekman et al. 2001) however when the types of negative life events were explored in this sample no convincing patterns emerged. Earlier studies have reported an association between anxiety and both loss events (Beekman, Bremmer et al. 1998) and the presence of major illness in a spouse (i.e. threat or stress) (de Beurs, Beekman et al. 2001) however in more recent studies no association was found between the development of anxiety and the type of life events reported (Schuurmans, Comijs et al. 2005).

Being female is associated with increased likelihood of suffering with a subsyndromal condition in our sample. As this was a cross sectional study we can only speculate as to the direction of causality of other associations. These associations will be explored further on a longitudinal basis in chapters 7 and 9.

Chapter 6.

The influence of subsyndromal anxiety and depression on health and social service use

6.1 Background

The influence of depressive symptoms on health service use is well described (Beekman, Deeg et al. 1997; Beekman, Penninx et al. 2002). More recent studies have found that subsyndromal anxiety (SSA) also influences service use in older adults (de Beurs, Beekman et al. 1999; Schuurmans, Comijs et al. 2005).

While both disorders are associated with excess service use appropriate care is often not provided (Goldberg and Bridges 1988; de Beurs, Beekman et al. 1999). There are many different reasons for this finding. Older adults may be less likely to seek help for psychiatric problems and when they do present their symptoms are frequently under-recognised in primary care. In addition the presentation of both depression and anxiety can differ in late-life where the preponderance of somatic symptoms further reduces the likelihood of diagnosis (Goldberg and Bridges 1988; Small 1997).

Extraneous factors may also impact on service use and must be taken into consideration when rates of service use are explored. A number of models have been developed for conceptualising pathways to care (Andersen and Newman 1973; Gater, de Almeida e Sousa et al. 1991). One such model which has been used in a similar study exploring service utilisation in late-life distinguishes predisposing, enabling and need-for-care factors (de Beurs, Beekman et al. 1999). Predisposing factors include age, level of education and awareness of services. Enabling factors include conditions which facilitate entry into healthcare including the availability of services and financial resources. Need for care factors include the signs and symptoms of disease and disability, which influence the decision to seek help. As increasing age is associated with an increase in chronic medical conditions the rate of service use will be expected to increase with age.

The combination of chronic medical conditions with comorbid anxiety or depression may further increase health service use. It is unclear however whether SSA and SSD have similar effects on service use in late-life. The purpose of this study is to compare the effect of SSA and SSD on the types and rates of health service use in community dwelling older adults.

6.2 Methodology

The sample was derived from the first timepoint of the longitudinal study (t1) (n=345). In addition to the basic data collected at all timepoints of the project (detailed in chapter 3) extra information was acquired for this study as follows;

Details of health service use: For the purposes of this study all participants (n=345) were administered a self report questionnaire enquiring about details of health and social service use in the preceding year (Appendix D).

Details of chronic medical conditions: The number of currently treated chronic medical conditions was recorded using a checklist (including arthritis, hypertension, hypercholesterolaemia, diabetes, cerebrovascular disease, ischaemic heart disease, parkinsons disease, thyroid disease and chronic respiratory disease) and verified by examining current medication use.

Statistical analysis

Univariate associations with the use of different services were examined using non-parametric statistics; chi squared analysis for categorical variables and Kruskal-Wallis or Mann Whitney U tests for continuous variables. High service use was defined as the sample mean number of services plus one standard deviation. Univariate associations with high service use were then examined using non-parametric statistics. The relationships between variables of interest and diagnosis and degree of interaction between variables were explored using non-parametric statistics. A series of logistic regression analyses were designed controlling for interactions. Factors associated with high service use were entered into backwards-stepwise logistic regression analyses with high service use as the dependent variable. Independent variables entered into separate models were as follows 1; SSD, MMSE score and disability 2; SSA and CMCs 3; gender and poor interviewer rated health 4; age and poor self-rated health. Results of Kruskal-Wallis tests are reported as KW χ^2 , and results of Mann Whitney U tests as MW . Results of the logistic regression analyses are reported as odds ratios with associated confidence intervals. Bonferroni corrections were applied for multiple analyses and all reported statistics are two-tailed.

6.3 Results

Sample description

The initial sample consisted of 345 subjects (total t1 sample). Data on service use were missing for $n=26$ subjects. Diagnoses in the remaining 319 subjects were as follows; well $n=167$, SSD $n=44$, SSA $n=79$, depressed $n=4$, organic case $n=11$, organic subcase $n=4$. As the main purpose of this study was to examine service use in relation to SSA and SSD only those with a diagnosis of SSA, SSD or well were included ($n=290$). In addition numbers in the depressed and organic subgroups were too small to allow meaningful exploration of associations with service use.

The mean age of the sample was 75 (Range 66-92, $s.d.=5.7$), those with SSA showed a trend towards being younger than the remainder of the sample ($KW\chi^2=6.396$, 2 d.f., $p=.041$). 63% of the sample were female. Gender was significantly associated with subsyndromal diagnosis, female subjects being over-represented in the subsyndromal groups ($\chi^2=12.724$, 2d.f., $p=0.002$). Regarding marital status, 14% of the sample were single, 42% married and 44% widowed. 35% of subjects lived alone. The majority of our subjects had completed primary level education only ($n=231$). The mean MMSE of our sample was 27 (range 18-30, $s.d.=3$). There was no association between marital status, living arrangement, MMSE score or level of education and diagnosis. 12% ($n=35$) reported a history of depression and this was associated with SSD ($\chi^2=9.895$, 2d.f., $p=0.007$).

Regarding physical health variables 52% ($n=151$) of the sample reported poor physical health, 51% ($n=149$) were rated to have poor health by interviewers, 30% ($n=86$) reported disability and 36% ($n=105$) reported experiencing pain. SSD showed a significant association with poor self rated health ($\chi^2=11.641$, 2 d.f., $p=0.003$) and a trend towards increased frequency of poor interviewer rated health ($\chi^2=8.541$, 2 d.f., $p=0.014$). In addition, there was a trend towards increased complaints of pain in the group with SSA ($\chi^2=7.162$, 2d.f., $p=0.028$). The mean number of CMCs for the sample was 1.2 (range 0-5, $s.d. 1.2$) and while those with SSD had a marginally higher mean number of CMCs (1.39) this was not significant.

Use of health services and psychotropic medications

285 subjects (98% of the sample) had seen their GP with 54 (19%) reporting 6 or more visits in the preceding year. Those subjects with SSD showed a trend towards greater frequency of GP visits ($\chi^2 = 7.134$, 2d.f., $p = 0.028$). The use of psychiatry services was remarkably low with only three subjects attending psychiatry outpatient services. Very few subjects reported using health related social services, 7 (2%) received meals on wheels, 20 (7%) received home help and 11 (4%) attended a day centre. The mean number of services used by the whole sample in the previous year was 3.21 (Range 0-9, s.d.= 1.8) and there was no association between mean number of services used and diagnosis. Regarding psychotropic medication usage only 10 subjects (3%) were receiving antidepressant treatment. 82 subjects (28%) were using benzodiazepines. The use of benzodiazepines was significantly associated with SSA ($\chi^2 = 18.03$, 2 d.f., $p < 0.000$). Univariate associations with service use are represented in table 13.

Table 13.

Use of health services and psychotropic medications by diagnosis

Services used in past year	SSA (n=79) n%	SSD (n=44) n%	Well (n=167) n%	Univariate Analysis (2.d.f.)
GP	79(100)	43(98)	163(98)	n/a
>5 GP visits	15(19)	14(32)	24(14)	$\chi^2=7.134$, p=0.028*
Hospitalised	16(20)	10(23)	28(17)	$\chi^2=1.008$, p=0.604
Outpatient attendance	43(54)	20(45)	69(41)	$\chi^2=3.719$, p= 0.516
Public health nurse	19(24)	14(32)	46(28)	$\chi^2=0.879$, p=0.645
Chiropodist	35(44)	18(41)	71(43)	$\chi^2=0.143$, p=0.931
Dentist	6(8)	8(18)	22(13)	$\chi^2=3.122$, p=0.210
Other health professional	45(57)	21(48)	82(50)	$\chi^2=1.553$, p=0.460
Physiotherapist	9(11)	7(16)	10(6)	$\chi^2=4.983$, p=0.083
Meals on wheels	1(1)	3(7)	3(2)	n/a
Home help	3(4)	4(9)	13(8)	n/a
Day centre	2(3)	5(12)	4(2)	n/a
Day hospital	1(1)	1(2)	0	n/a
Mean total services used(s.d.)	3.29(2)	3.55(2)	3.08(2)	KW $\chi^2=2.107$, p=0.349
Antidepressant use	4(5)	3(7)	3(2)	n/a
Benzodiazepine use	30(38)	13(30)	24(14)	$\chi^2=18.03$, p<0.001 ^ψ

n/a= not applicable due to small cell size.

^ψ Significant at $\alpha<0.001$

* Trend only

Associations with high use of services.

High service use defined as the use of >5 services in the past year (sample mean +1 s.d.). 40 subjects used 6-9 services in the preceding year. Notably 25% of those with SSD had used 6 or more services in the preceding year. The only variables which predicted high service use were poor self reported and observer rated health. In addition those who were older, had a greater number of CMCs, reported disability and had a diagnosis of SSD showed a trend towards high service use (table 14).

Table 14. Associations with high service use

Variable of interest	Number of services used		Univariate analysis	Logistic regression analysis (1 d.f.)
	0-5 (n=250) n(%)	6-9 (n=40) n(%)		
Gender (Female)	159(64)	24(60)	$\chi^2=0.068$, 1 d.f., $p=0.79$	ns
Mean Age (s.d.)	75(6)	77(6)	MW $z=-2.2$, $p<0.05^*$	Wald 4.8, $p=0.028^*$, OR=1.1, 95% CI=1-1.14
Marital status; Single	36(14)	7(18)	$\chi^2=2.781$, 1 d.f., $p=0.25$	
Living alone	86(34)	15(38)	$\chi^2=0.041$, 1 d.f., $p=0.84$	
Mean MMSE (s.d.)	27(3)	27(2)	MW $z=-2.8$, $p=0.62$	ns
Primary level of education	200(80)	31(78)	$\chi^2=0.361$, 1 d.f., $p=0.84$	
History of depression	30(12)	5(13)	$\chi^2=0.008$, 1 d.f., $p=0.93$	
Subsyndromal Anxiety	70(28)	9(23)	$\chi^2=0.285$, 1 d.f., $p=0.6$	
Subsyndromal Depression	33(13)	11(28)	$\chi^2=4.424$, 1 d.f., $p<0.05^*$	Wald 4.341, $p=0.037^*$, OR=2.4, 95% CI=1.1-5.3
Well	147(58)	20(50)	$\chi^2=0.763$, 1 d.f., $p=0.38$	
Poor self reported health	118(47)	33(83)	$\chi^2=15.832$, 1 d.f., $p<0.001^\Psi$	Wald 14.6, $p<0.001^\Psi$, OR=5.3, 95% CI= 2.2-12
Poor observer rated health	117(47)	32(80)	$\chi^2=13.9$, 1 d.f., $p<0.001^\Psi$	Wald 13.3, $p<0.001^\Psi$, OR= 4.5, 95% CI=2-10
Self reported disability	78(31)	22(55)	$\chi^2=7.6$, 1 d.f., $p<0.01^*$	Wald 8.4, $p=0.004^*$, OR=2.8, 95% CI=1.4-5.6
Self reported pain	93(37)	12(30)	$\chi^2=0.494$, 1 d.f., $p=0.48$	
Mean No. of CMC's(s.d.)	1.15(1)	1.65(1)	MW $z=-0.5$, $p<0.01^*$	Wald 5.21, $p<0.05^*$, OR=1.4, 95% CI= 1.04-1.77

$^\Psi$ Significant at the $\alpha < 0.003$ level.

* Trend only

6.4 Discussion

For the purposes of clarity our results will be discussed within the framework of the model for determinants of care.

Predisposing factors such as sociodemographic variables, level of education and cognitive status did not influence service use in our sample. While gender was associated with the presence of subsyndromal diagnoses this association did not translate to increased service use.

Enabling factors may have contributed to the overall rate of service use in our sample. Healthcare for the general public in Ireland is provided free of charge, as such financial constraints should not influence access. In addition the entire sample fell within the catchment area of a large public general hospital with a well-established old age psychiatry service. This may have contributed to the rate of general medical and surgical outpatient and inpatient service use, however the availability of old age psychiatry services did not have any influence on the rates of mental health service use. Only three patients reported seeing a psychiatrist in the preceding year. In addition all three had been seen on an outpatient basis, one subject (with SSA) in the day hospital setting and two others (with SSD) at outpatient clinics. The effect of age on mental health service use has been explored previously and it seems that elderly subjects are less likely to utilise mental health services for a number of reasons including lack of awareness of services and fear of stigmatisation (Klap, Unroe et al. 2003; Li, Proctor et al. 2005). As referrals to the old age psychiatry service in this area are largely made by GPs this may have been a rate-limiting factor. The majority of our subjects (98%) had seen their GP (often on more than one occasion) in the preceding year however this did not increase the likelihood of referral to psychiatry services. The under-recognition of late-life mental illness by primary care clinicians is well documented and as the groups we describe fell below the threshold for caseness this is likely to have further reduced their detection and referral.

Need-for-care factors exerted the greatest influence on service use in our sample. As expected those subjects with a greater number of CMCs showed a trend towards high service use. Increasing age was also associated with a trend towards high service use which has been described previously (Livingston, Thomas et al. 1990; Dening, Chi et al. 1998). From a diagnostic viewpoint the rate of service use in SSD was elevated above those with other diagnoses but not to a statistically

significant extent. The impact of SSD on service use is well described. While intermediary factors may play a role, the trend towards high service use in SSD in our sample was independent of age, number of chronic medical conditions and disability.

SSA on the other hand appeared to exert little effect on service use. This may be attributable in part to the fact that the group with SSA was diagnostically heterogeneous. In addition, it is well documented that older subjects with phobic symptoms in particular may be less likely to seek medical help. The most striking effect of SSA was on benzodiazepine prescription, with one in three subjects with SSA being treated with benzodiazepines. This is a common finding (de Beurs, Beekman et al. 1999) and has been described in an Irish setting previously (Kirby, Denihan et al. 1999).

The factor which had the greatest impact on service use in our sample was self-rated physical health. Where subjects perceived their health as poor they were 5 times more likely to be high users of services than their peers. It seems that estimations of self-rated health were not overly inflated in our sample as there was a high degree of correlation between self and observer rated poor health. In addition those with poor observer rated health were 4.5 times more likely to be high users of services.

While SSD and SSA did not predict high service use they may have had an indirect effect on service use at the level of physical health perception. Depressive symptoms have been reported to exert a negative effect on perception of health (Denning, Chi et al. 1998; Levinson and Druss 2005) and disability (Beekman, Penninx et al. 2002; Chopra, Zubritsky et al. 2005). Furthermore, a recent study (de Beurs, Beekman et al. 1999) found that anxiety symptoms were associated with increased disability in older adults to the extent of anxiety disorders themselves. These effects are reflected by our study findings. In chapter 5 we found that SSD was associated with a trend towards poor self and interviewer rated health and that both SSA and SSD were associated with disability. In the current study sample SSD was significantly associated with poor self-rated health and in addition a greater proportion of those with SSA reported disability (41%). Whether interventions at the level of subsyndromal psychopathology would have a net effect of reducing 'inappropriate' service use in late-life is unclear and will be discussed in greater detail in subsequent chapters.

Chapter 7.

The two-year outcome of subsyndromal anxiety

7.1 Background

Subsyndromal anxiety is common in the elderly and frequently occurs comorbidly with other diagnoses (as described in chapter 6). Existing studies which have reported on the course and outcome of anxiety symptoms in late life tend to focus primarily on anxiety disorders. Those studies which comment on the outcome of SSA have produced divergent results. Some have demonstrated that SSA lies on a continuum with depressive spectrum disorders, others suggest that SSA may be a clinically distinct entity which follows a different course to depressive illnesses. Most existing longitudinal studies have large time intervals between waves thus the course of SSA is largely unknown.

There are two main purposes of this study. Firstly, to describe the course of SSA over a two-year period specifically focussing on the rates of conversion of symptoms and mortality rates in this period. Secondly to explore predictors of chronicity and recovery in this group.

7.2 Methodology

All subjects with a baseline diagnosis of SSA will be described in this chapter. Changes in anxiety symptoms will be presented graphically. Outcomes will be described using descriptive statistics.

Statistics

For the purposes of this study two specific groups were the focus of statistical analysis, that is, those who recovered over the two-year period (became well) and those who were experienced persistent or relapsing SSA. Univariate associations with recovery or persistence were explored using non-parametric statistics.

A series of logistic regression analyses were designed with recovery versus chronicity as the dependent variable. Independence of variables of interest were established using non-parametric statistics. This allowed the formation of groups of independent variables which were entered into separate regression models. Variables were grouped as follows; 1) marital status t0, pain t0, history of depression and gender, 2) self rated health, family history of depression, level of education, living alone t0, 3) age t0, alcohol consumption t0, poor observer rated health t0, 4) MMSE t0, disability t0 (α was set at 0.05).

7.3 Results

The baseline (t0) sample included n=125 subjects with SSA of whom n=98 had generalised anxiety symptoms (GAD), n=17 had phobic symptoms and n=10 had mixed symptoms. 9 subjects died during the course of the study, 7 subjects with GAD, one with phobic symptoms and one with mixed symptoms. In addition a total of n=45 subjects with SSA were lost to attrition over the course of the study 33 GAD, 9 phobic and 3 mixed.

As mortality is considered an outcome variable the final study sample includes n=80 subjects. Regarding the quality of anxiety symptoms the group of 80 includes n=65 with GAD, n= 8 with phobic symptoms and n=7 with mixed symptoms. Two year outcome data for the final sample of n=80 are presented in table 15.

Table 15: Two-year Outcome of Subsyndromal Anxiety (n=80)

Anxiety Subtype t0	t1 Outcome by diagnosis		SSA			SSD	SDA	Anx	SOrg	Org	Dep	Well	RIP
			GAD	Phobic	Mixed								
Generalised Anxiety n=65	SSA n=31	GAD n=28	15	0	0	0	2	0	0	0	4	6	1
		Mixed n=3	0	0	0	1	1	0	0	0	0	1	0
	SSD n=1		0	0	0	0	0	0	0	0	0	0	1
	SDA n=7		6	0	0	0	1	0	0	0	0	0	0
	Anxiety case n=1		0	0	0	0	1	0	0	0	0	0	0
	SOrg n=1		0	0	0	0	0	0	0	1	0	0	0
	Depressed n=2		0	0	0	0	0	1	0	0	0	1	0
	Well n=18		4	1	0	0	1	0	1	0	0	10	1
	RIP n=4		0	0	0	0	0	0	0	0	0	0	4
Phobic n=8	SSA n=6	GAD n=1	0	1	0	0	0	0	0	0	0	0	0
		Phobic n=3	0	3	0	0	0	0	0	0	0	0	0
		Mixed n=2	1	1	0	0	0	0	0	0	0	0	0
	SDA n=1		0	0	0	0	1	0	0	0	0	0	0
	RIP n=1		0	0	0	0	0	0	0	0	0	0	1
Mixed n=7	SSA n=3	GAD n=1	1	0	0	0	0	0	0	0	0	0	0
		Phobic n=2	1	0	0	0	0	0	0	0	0	1	0
	SOrg n=1		0	0	0	0	0	0	0	1	0	0	0
	SDA n=1		0	0	0	0	0	0	0	1	0	0	0
	Well n=1		1	0	0	0	0	0	0	0	0	0	0
	RIP n=1		0	0	0	0	0	0	0	0	0	0	1
Outcome (n=80) by t2 diagnosis n(%)			29(36)	6(8)	0	1(1)	7(9)	1(1)	1(1)	3(4)	4(5)	19(24)	9(11)

Associations with chronicity and recovery

35 subjects remained at the SSA level at t2 and 19 subjects were well. One of the well subjects had developed case-level depression at t1 and recovered at t2 and was excluded from analysis. The total sample included n=53 subjects, n=35 with SSA at t2 and n=18 who had recovered. 74% of those with chronic SSA had GAD at baseline, 17% phobic and 9% mixed. Of those who recovered 94% had GAD at baseline and 6% had mixed symptoms. Table 16 shows univariate associations with chronicity and recovery.

Table 16.

Baseline associations with chronicity of and recovery from SSA.

Baseline Variable	Chronic n=35 n(%)	Recovered n=18 n(%)	Univariate analysis
Mean Age (s.d.)	72(5)	77(7)	MW $z = -1.6$, $p=0.105$
Gender (Female)	27(77)	9(50)	$\chi^2=2.8$, 1 d.f., $p=0.09$
Married	23(66)	10(56)	$\chi^2=1.6$, 2 d.f., $p=0.447$
Living alone	9(26)	5(28)	$\chi^2=0.00$, 1 d.f., $p=1$
Primary education	24(69)	10(56)	$\chi^2=0.401$, 1 d.f., $p=0.53$
Mean MMSE (s.d.)	27(2)	28(1)	MWz $=-1.6$, $p=0.1$
Cognitive impairment	2(5.7)	0(0)	n/a
History of depression	6(17)	0	n/a
Family history of depression	7(20)	2(11)	n/a
Mean Alcohol (s.d.)	3(5)	12(18)	MW $z = -1.3$, $p=0.180$
Poor self rated health	10(29)	5(28)	$\chi^2=0.00$, 1 d.f., $p=1$
Poor observer rated health	12(34)	7(39)	$\chi^2=0.001$, 1 d.f., $p=0.98$
Disability	10(28)	7(39)	$\chi^2=0.204$, 1 d.f., $p=0.65$
Pain	14(40)	5(28)	$\chi^2=0.33$, 1 d.f., $p=0.564$
Benzodiazepines	17(49)	6(33)	$\chi^2=0.589$, 1 d.f., $p=0.44$
Antidepressants	2(6)	0	n/a

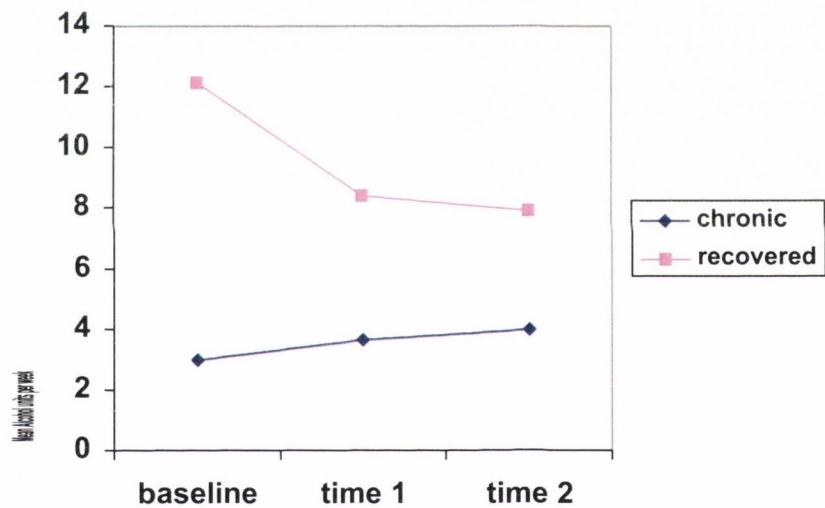
Table 17.

Changes in benzodiazepine treatment (t0-t2) by outcome

Treatment	Chronic n=35	Recovered n=18	Total n=53
BDZ stopped	4(12)	3(17)	7(14)
New BDZ commenced	3(9)	1(6)	4(8)
BDZ continued	14(38)	3(17)	17(31)

Figure 8.

Association between alcohol consumption and outcome of SSA



Predictors of chronicity and recovery

Backwards stepwise logistic regression analysis identified female gender as a predictor of chronicity ($p=0.05$, $OR=3.4$, $CI=1.1-11.38$) and higher mean baseline alcohol consumption as a predictor of recovery ($p=0.027$, $OR=1.08$, $CI=1.01-1.17$).

7.4 Discussion

The outcome of SSA over two years was poor. 44% had an outcome of SSA, 11% had died and only 24% (n=19) had recovered (became well) at t2. A further 14% who had recovered at t1 had relapsed at t2. It is clear that SSA is a highly labile diagnosis, only 23 subjects (29%) remained at SSA level throughout the whole study period. The rate of conversion of symptoms from subcase to case anxiety was low with only two subjects developing case level anxiety (2.5%) both of whom developed case level GAD. There was little transition across subtypes of anxiety symptoms, such transition occurring mainly in the mixed subtype. In addition 4% of subjects developed organic caseness over the course of the study.

The degree of transition of diagnoses, particularly across the depressive spectrum was remarkable and lends some weight to the hypothesis that anxiety and depression may lie on a continuum. 7.5% (n=6) developed case level depression, two at t1 and four at t2. The transition to case level depression occurred only in those with the GAD subtype of SSA. Previous studies of case level GAD in late life have demonstrated high rates of comorbidity with and transition to depression (Schoevers, Deeg et al. 2005). The conversion of SSA (GAD subtype) to depression has not been described previously. It is possible that the GAD subtype of SSA may represent individuals in the recovery phase of GAD or depression. In addition as case level anxiety may be underdiagnosed by AGE-CAT (Larkin, Copeland et al. 1992) these individuals may be closer to the case threshold of GAD than their diagnosis suggests.

Specifically regarding the subtype of anxiety symptoms there was little transition across diagnostic categories apart from the mixed type of symptoms.

The low rate of recovery from SSA reflects that of previous studies of anxiety in older adults where recovery rates of between 19 and 31% have been reported (Larkin, Copeland et al. 1992; de Beurs, Beekman et al. 2000; Schuurmans, Comijs et al. 2005). It is important to note that these studies focussed mainly on case level anxiety and not pure SSA, in addition, these studies included individuals with depressive symptoms. The rate of chronicity or persistence of symptoms was also remarkably similar to existing data on anxiety disorders (Schuurmans, Comijs et al. 2005).

We did not identify any significant baseline associations with recovery or relapse. It seems likely however that our analyses were limited by the small group size.

Treatment with benzodiazepines seemed to have little impact on the outcome of SSA over two years. 62% of our sample were on benzodiazepine treatment at baseline and a higher proportion of those displaying a chronic course remained on treatment throughout the study. Studies of the outcome of anxiety disorders in late-life have found that benzodiazepine treatment is not associated with recovery (Schuurmans, Comijs et al. 2005). In light of the small sample size the results of the regression analysis must be interpreted with caution. Being female was predictive of persistent anxiety, this is consistent with previous study findings (Larkin, Copeland et al. 1992; de Beurs, Beekman et al. 2000). In addition we found that having a higher mean baseline alcohol consumption was predictive of recovery. While the odds ratio was small (1.08) it is important to note that alcohol consumption was a continuous variable (measured in units of alcohol per week) meaning that the odds ratio is 1.08 for every one unit difference in mean alcohol consumption. This is an interesting finding and suggests that our sample may be self-medicating with alcohol to reduce anxiety. This has been reported in studies of younger adults where anxiety and alcohol misuse have been found to be strongly correlated (Regier, Farmer et al. 1990). Data on the association of anxiety disorders and alcohol misuse in late life are lacking. Studies which have addressed this issue have found no association in older adults (Krystal, Leaf et al. 1992; van Balkom, Beekman et al. 2000) however these studies specifically focussed on panic disorder. Some have suggested that the elderly tend to preferentially seek relief from anxiety through benzodiazepine use (van Balkom, Beekman et al. 2000). In our sample levels of both alcohol and benzodiazepine use were high. A previous study examining alcohol misuse in this sample found that excessive consumption was associated with being male and widowed. There were a greater proportion of males in the recovered group which may possibly have contributed to the higher recorded levels of alcohol use. When the pattern of alcohol consumption is examined in detail it appears that the level of alcohol consumption increases steadily in the chronic group over the two years of the study while it is decreasing in the recovered group. Recovery was not, however associated with a decrease in alcohol consumption. This anomaly may be explained by examining the raw data which demonstrates that at all three time points (t0, t1 and t2) the level of consumption in the recovered group is elevated above that of the chronic group supporting the likelihood of self medication.

On the basis of our study findings so far it seems that being female is associated with both the presence (chapter 5) and chronicity of SSA in late-life. Alcohol consumption appears to be associated with the remission of anxiety symptoms. In addition we found a strong relationship between having GAD symptoms at baseline and developing case level depression. The significance of SSA as a predictor of depression will be explored in a future chapter.

Chapter 8.

Predictors of new anxiety symptoms

8.1 Background

Few studies have examined predictors of anxiety in late-life (Beekman, Bremmer et al. 1998; de Beurs, Beekman et al. 2000; Le Roux, Gatz et al. 2005; Lenze, Mulsant et al. 2005). Much of the existing data on predictors of anxiety are derived from co-morbidity studies where depression was the primary focus of the study (Beekman, de Beurs et al. 2000; de Beurs, Beekman et al. 2001; Flint and Rifat 2002; Lenze, Mulsant et al. 2005; Steffens and McQuoid 2005). Most studies are based on clinical populations which may not appropriately represent the community dwelling elderly. In addition many studies examining risk factors for anxiety are cross sectional and may not accurately identify risk factors as chronic anxiety may be over-represented. So far we have explored variables associated with the presence of anxiety symptoms at baseline, the co-morbidity of anxiety and depression, the impact of SSA on service use and the two-year outcome of SSA. The purpose of this study is to identify predictors of new anxiety symptoms in a community dwelling elderly cohort.

8.2 Methodology

Subjects who were anxiety free at baseline and had complete two-year follow-up data (i.e. complete data from t1 and t2) were identified. Association with a number of putative vulnerability and risk factors for anxiety were explored. A number of new variables were derived from the data which represent measures of changes in symptoms over the two years of the study. Spousal bereavement was recorded and dichotomised as 'newly widowed' over the course of the study or not. Changes in self and observer rated health and disability were calculated and converted into categorical variables namely 'no change', 'improved' and 'worsened'. The presence of chronic pain was assessed and expressed as a dichotomous variable. The occurrence of new pain (reported at t1 or t2 in the absence of t0 pain) was dichotomised into present or absent. Changes in alcohol consumption were calculated and converted into a dichotomous variable namely 'no change or decreased consumption' or 'increased consumption'. Changes in MMSE scores were calculated and converted into a categorical variable namely 'significantly increased MMSE', 'no significant change' and 'significantly decreased MMSE'. Significant change was deemed to have occurred where the change in MMSE was greater than 1 standard deviation above or below the baseline mean MMSE score (i.e. a change of $> \pm 3$ points). Unlike the preceding studies in this thesis examining SSA in this study risk factors for all new anxiety symptoms were explored, that is, the group with new anxiety symptoms includes subjects who develop SSA, and new co-morbid anxiety symptoms (SDA).

Statistical analyses

The two-year course of symptoms is described in a tabular format and reported as descriptive statistics. In order to preserve power and avoid confounding any subjects who had developed new anxiety at t1 and recovered (became well) at t2 were excluded from analyses. The sample was split into two groups on the basis of the development of new anxiety symptoms. Univariate associations with development of anxiety symptoms were explored using non-parametric statistics. Bonferroni corrections were applied for multiple analyses and all reported findings are two-tailed. Independence of putative risk factors were explored using

non-parametric statistics. Four regression analyses were designed with outcome of new anxiety as the dependent variable. Factors entered into separate regression models were as follows; 1) gender, widowed during course of study (t0-t2), change in MMSE (t0-t2), history of depression, level of education and change in self reported health (t0-t2) (α set at 0.006), 2) baseline marital status, change in alcohol consumption (t0-t2), poor self rated health t0, change in disability (t0-t2), chronic pain(t0-t2)(α set at 0.01), change in living arrangement (t0-t2), family history of depression, change in observer rated health (t0-t2), new pain (t0-t2) (α set at 0.05), 4) living alone t0, poor observer rated health t0, age t0(α set at 0.05). Significant risk factors for anxiety are reported as odds ratios with associated 95% confidence intervals.

8.3 Results

Sample description

At baseline 56% of subjects (n=293) were completely anxiety free. Of this group 44% were lost to follow-up, n=26 through death and n=103 through attrition for other reasons (for a full description of all subjects and attrition refer to chapter 4).

The study sample included n=164 subjects with complete three year data. 56% of the sample were female and the mean age of the sample was 74 (s.d.=6, range=65-88). The mean MMSE was 27 (s.d.=3, range =15-30).

Baseline diagnoses and course of symptoms are shown in table 18. A total of n=37 developed new anxiety symptoms over the course of the study. This group included n=21 who developed new anxiety symptoms at t1 (SSA n=18, SDA n=3) and n=16 who developed new anxiety symptoms at t2 (SSA n=11, SDA n=5). Of this group n=10 had recovered at t2.

Regarding the subtype of new anxiety symptoms n=34 developed GAD symptoms and n=3 developed mixed GAD and Phobic symptoms.

Table 18.

Development of new anxiety symptoms t0-t2

Diagnosis								
t0	t1	t2						
		Dep.	SSD	SDA	SSA	Org	SSO	Well
Depressed n=1	SSA n=1 Φ	-	-	-	1	-	-	-
SSD n=13	Dep. n=1	-	-	1*	-	-	-	-
	SSD n= 4	1	1	1*	1*	-	-	-
	SSA n= 3 Φ	-	-	-	2	-	-	1 ^Ψ
	Well n= 5	-	-	1*	2*	-	-	2
Organic n= 2	Organic n=2	-	-	-	-	2	-	-
SSO n=6	Organic n=1	-	-	-	-	1	-	-
	Well n=5	1	-	-	-	-	1	3
SSchiz n=1	SSchiz N=1	-	-	1*	-	-	-	-
Well n=141	Dep. n=1	-	-	-	1*	-	-	-
	SSD n=6	1	-	1*	1*	-	-	3
	SDA n=3 Φ	-	-	-	1	-	-	2 ^Ψ
	SSA n=14 Φ	1	-	1	4	-	1	7 ^Ψ
	Organic n= 2	-	-	-	-	2	-	-
	SSOrg n=2	-	-	-	-	-	1	1
	Well n=113	3	3	0	6*	2	2	97

Φ= new anxiety symptoms t1 (n=21), * = new anxiety symptoms t2 (n=16),
Ψ = recovered at t2 (n=10)

Baseline associations with new anxiety (n=164)

Factors which were found to be associated with the occurrence of new anxiety symptoms during the course of the study on univariate analysis included living alone at baseline ($\chi^2=4.06, 1 \text{ d.f.}, p=0.044$) and having a history of depression ($\chi^2=5.05, 1 \text{ d.f.}, p=0.025$). Baseline associations with new anxiety are represented in table 19.

Table 19.

Association of baseline variables with new anxiety (n=164)

Baseline Variable	No anxiety n=127 n(%)	New anxiety n=37 n(%)	Univariate analysis
Mean Age (s.d.)	75(6)	73(5)	MWz = -1.22, p=0.222
Gender (female)	66(52)	26(70)	$\chi^2=3.19, 1 \text{ d.f.}, p= 0.074^\Psi$
Married	55(43)	13(38)	$\chi^2=0.437, 2 \text{ d.f.}, p=0.804$
Living alone	34(27)	17(46)	$\chi^2=4.06, 1 \text{ d.f.}, p=0.044^*$
Education primary	78(61)	22(60)	$\chi^2=0.001, 1 \text{ d.f.}, p=0.98$
Mean MMSE(s.d.)	27(3)	27(3)	MWz = -0.13, p=0.9
Cognitively impaired	10(8)	4(11)	$\chi^2=0.052, 1 \text{ d.f.}, p=0.82$
History of depression	9(7)	8(22)	$\chi^2=5.05, 1 \text{ d.f.}, p=0.025^*$
Family Hx depression	17(13)	4(11)	$\chi^2=0.018, 1 \text{ d.f.}, p=0.814$
Poor self rated health	36(28)	10(27)	$\chi^2=0.000, 1 \text{ d.f.}, p=1$
Poor observer rated health	50(39)	15(35)	$\chi^2=0.075, 1 \text{ d.f.}, p=0.78$
Disability	34(27)	9(24)	$\chi^2=0.007, 1 \text{ d.f.}, p=0.93$
Pain	26(21)	5(14)	$\chi^2=0.508, 1 \text{ d.f.}, p=0.48$
Mean alcohol units (s.d.)	6(11)	4(11)	MWz = -1.35, p=0.18

* Significant association ($\alpha = 0.05$)

$^\Psi$ Trend only ($\alpha = 0.05$)

Table 20.

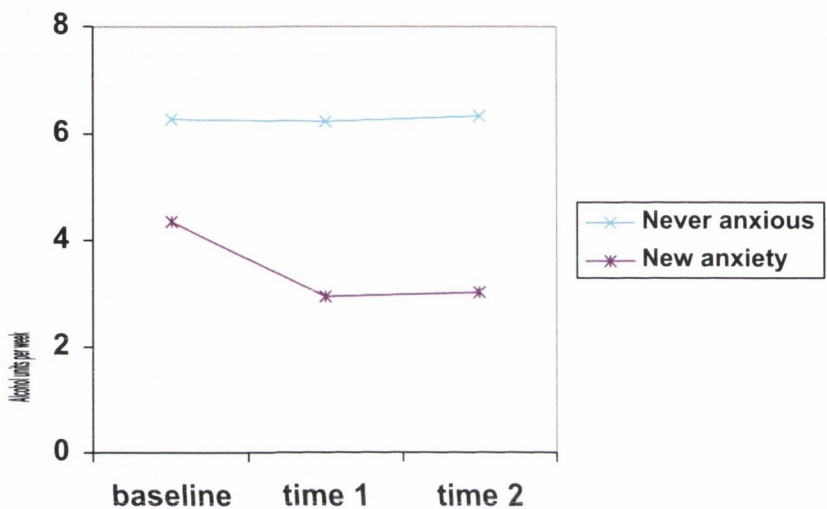
Distribution of baseline social network by outcome (n=154)

Social Network	No Anxiety n=127	New Anxiety n=27
	n(%)	n(%)
Family dependent	17(13)	1(4)
Locally integrated	99(78)	24(89)
Local self-contained	2(2)	0
Wider community focussed	5(4)	1(4)
Private	1(1)	0
In transition	3(2)	1(4)

In a previous study we found that the chronicity of SSA was associated with increased mean alcohol consumption at baseline (see chapter 7). In order to further explore the relationship between alcohol consumption and anxiety symptoms the change in mean alcohol consumption by year was examined by outcome and is represented in figure 9.

Figure 9.

Association between development of new anxiety symptoms and changes in mean alcohol consumption t0-t2 (n=154)



Vulnerability and risk factors for new anxiety symptoms

10 subjects who developed new anxiety symptoms at t1 had recovered (become well) at t2. The regression analysis examining risk factors for new anxiety was limited to those who developed new anxiety and had not recovered at t2.

Table 21 represents factors which predicted new anxiety symptoms over the course of the study.

Table 21.

Risk factors for new anxiety symptoms (n=154)

Risk Factor	No Anxiety n=127 n(%)	New Anxiety n=27 n(%)	Wald	p	O.R.	95% C.I.
History of depression	9(7)	6(22)	5.224	0.022*	3.75	1.2-11.6
Living alone t0	34(27)	14(52)	6.191	0.013	2.95	1.3-6.9
New pain (t0-t2)	42(33)	15(56)	4.487	0.034	2.64	1.1-6.5

* Trend only $\alpha=0.006$

8.5 Discussion

New anxiety symptoms were common in our sample. Of a total of 164 subjects at risk 23% developed new anxiety symptoms over the course of the study. In addition all of these subjects developed GAD symptoms with three having co-morbid phobic symptoms. While we can only comment on the one year outcome of a proportion of this 'new anxiety' group it is clear that of those who developed new anxiety at t1 (n=21) only 48% (n=10) reverted back to being well at t2, the remainder having persistent anxiety symptoms or developing other psychopathology. It must be borne in mind that the recovery rate of 48% recovery is likely to have been inflated by the attrition and mortality rates in this sample.

While we found in previous chapters that being female was associated with the presence of SSA at baseline and predictive of experiencing chronic anxiety symptoms female gender did not increase the risk of developing anxiety symptoms to a statistically significant degree. This highlights the importance of not lending too much weight to risk factors derived from cross sectional studies. It seems on the basis of our findings that the gender association at t0 was attributable to chronic cases being over-represented. Many studies examining risk factors for anxiety in late life report that being female conveys significant risk (Fuentes and Cox 1997; Beekman, Bremmer et al. 1998) however these studies are cross sectional in design. Of existing longitudinal studies some report increased risk in females (de Beurs, Beekman et al. 2001) while others report no gender differences (Lenze, Shear et al. 2002; Le Roux, Gatz et al. 2005; Wetherell, Maser et al. 2005). When the raw data is examined it is clear that females are over-represented in the group who become anxious when compared to those who never develop anxiety (70% vs 52%). In addition there is a trend towards increased risk in females ($p=0.051$) on regression. It seems likely that being female conveys increased vulnerability to anxiety in our sample but that other factors (e.g. new pain, living arrangement) are actual risk factors and have more predictive power.

Those with a history of depression showed a trend towards having a greater risk of developing anxiety symptoms. It was possible that the association failed to gain significance as a predictor as we excluded those who had recovered at t2. Repeating the analysis including those who had recovered did not change the

findings significantly ($p=0.015$, $O.R.=3.6$, $C.I. =1.3-10$). Previous studies examining the comorbidity of GAD and depression in late life have found significantly increased risk of GAD in those with a history of depression (de Beurs, Beekman et al. 2001; Schoevers, Beekman et al. 2003; Schoevers, Deeg et al. 2005). In addition incident anxiety symptoms in individuals with baseline depression have been found to predict a chronic resistant subtype of depression (Schoevers, Beekman et al. 2003). It is likely that a stronger relationship with having a history of depression was found in these studies as case level disorders were examined. Nevertheless the trend highlights the probability that GAD and depression lie on a continuum even at the subsyndromal level.

Those who lived alone at t_0 were almost three times more likely to develop anxiety symptoms than their peers. Those who live alone clearly exist in a 'less supported' environment than those who live with others, however the effect of living alone was not buffered by social network. We can only speculate as to why living arrangement conveyed increased risk. Living alone may convey an increased risk through a number of different pathways. Those who live alone may possibly experience more 'loneliness' or be less likely to have a close confidant or significant other to support them psychologically. In addition living alone may possibly increase feelings of insecurity and anxieties about safety and coping ability in late life. As data on loneliness and coping are not available in our sample we are unable to examine this finding in more detail.

Those who developed new pain over the course of the study were 2.6 times more likely to develop new anxiety whereas chronic pain did not affect risk. Studies of pain and anxiety disorders in late life are few, most of the data available describe younger subjects. A recent study examining the relationship between 'affect' and pain in older adults found that state anxiety was associated with acute pain but that the association was greater in individuals with baseline trait anxiety (Feeney 2004). Cross sectional studies have found evidence to support the increased perception of pain in anxiety states and also increased anxiety in the context of pain (Romano and Turner 1985). In a more comprehensive review of available data Pilowsky 1988 found that depression was associated with chronic pain and anxiety associated with acute pain. In our earlier cross sectional study at baseline we found that those with SSA reported experiencing more pain than the group who were well (35% vs 18%) however the rate of self reported pain did not differ

across different groups with psychopathology and a marginally greater proportion of the group with SSD (40%) complained of pain.

We have identified two significant predictors of new anxiety symptoms, living alone and experiencing new pain. In addition being female and having a history of depression appear to increase vulnerability to anxiety in late life. Whether these groups can be targeted for preventative interventions will be discussed in chapter 12.

Chapter 9.

The two-year outcome of subsyndromal depression

9.1 Background

Few studies have examined the course and outcome of SSD in late life. On the basis of existing data it seems that the outcome is generally poor and may reflect that of case level depression.

Existing studies have found that a substantial proportion of people with SSD will progress to develop case-level depression (Lyness, Caine et al. 2002; Chopra, Zubritsky et al. 2005). SSD has also been associated with increased mortality rates, particularly in subjects with pre-existing cognitive impairment (Janzing, Bouwens et al. 1999; Lavretsky, Mistry et al. 2003). There is little available data on the naturalistic course of SSD in the community dwelling elderly. Available data are largely derived from studies which primarily address the outcome of case level depression (Beekman, Geerlings et al. 2002).

Little is known of the course and outcome of SSD in the community setting and no studies have addressed its course in the Irish elderly. The aims of this chapter are to describe the naturalistic course and outcome of SSD in a community dwelling Irish elderly sample.

9.2 Methodology

This chapter will focus on those with SSD at baseline (n=74). A sample will be identified which includes subjects with SSD at baseline who have complete two-year follow-up data (i.e. complete data from t1 and t2) available. The symptomatic course will be described as change in diagnosis by year. The two year outcome will be described by diagnosis and factors associated with persistence and remission will be explored. As the numbers included in this study are small outcomes will be explored using descriptive statistics only.

9.3 Results

The baseline sample for this study included 74 subjects with SSD. This included n=49 with subsyndromal depression and comorbid anxiety ('D&A' subgroup) and n=25 with 'pure' SSD ('D only' subgroup). 31% of the baseline sample were lost to follow-up through attrition during the course of the study, n=13 refused at t1 and n=10 refused at t2. The remaining sample of n=51 subjects with complete two-year follow-up data will be the focus of this study.

Changes in diagnosis by year are described in table 22. 30% had persistent SSD over two years (n=3 D only and n=12 D&A) and a further 16% converted to SSA (GAD subtype) over the two years of the study. The two-year outcomes of SSD by diagnosis are represented in figure 10.

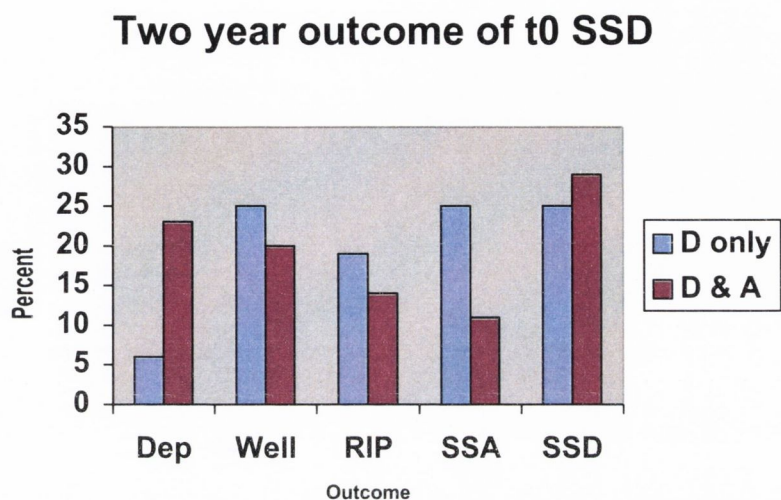
Table 22.

Changes in diagnosis by year of baseline SSD (n=51)

Diagnosis t0 (SSD)	Diagnosis t1	Diagnosis t2						
		Dep	SSD		SSA GAD	SOrg	Well	RIP
			D only	D/A				
D only n=16	Depressed n=1	-	-	1	-	-	-	-
	SSD n=4	-	1	1	1	-	-	-
	SSA n=3	-	-	-	1	-	2	-
	Well n=5	-	-	1	2	-	2	-
	RIP n=3	-	-	-	-	-	-	3
D&A n=35	Depressed n=2	1	1	-	-	-	-	-
	D only n=1	1	-	-	-	-	-	-
	D&A n=12	4	1	5	-	1	1	-
	SSA n=9	-	-	4	3	-	1	1
	Well n=7	1	-	-	1	-	5	-
	RIP n=4	-	-	-	-	-	-	4
Outcome t2 by diagnosis (n=51)		7 (14)	3 (6)	12 (24)	8 (16)	1 (2)	11 (22)	8 (16)

Figure 10.

Two-year outcome by baseline subtype of SSD (n=51)



8 subjects died giving a mortality rate of 16% in this subgroup. 18% (n=9) developed case level depression during the course of the study, (n=3 at t1 and n=6 at t2). Of those who developed case level depression at t1, one remained depressed at t2, one reverted to SSD and the other reverted to SDA (with comorbid GAD symptoms). 32% continued to suffer with SSD at t2 (n=3 with pure SSD and n=12 with SDA). 16% developed SSA (all GAD subtype) at t2. Only 22% had recovered (become well) at t2.

As the groups who recovered and experienced persistent symptoms were very small this precluded any meaningful statistical analysis. Associations are explored using descriptive statistics only described in table 23.

Table 23.

Associations (descriptive) with chronicity and recovery of SSD (n=34)

Variable	Persistent SSD n=23	Recovered (Well) n=11
Gender (female)	17(74)	7(64)
Mean age(s.d.)	74(5)	73(6)
Married t0	13(57)	3(27)
Newly widowed t0-t2	2(9)	0
Living alone t0	9(39)	5(46)
Mean MMSE t0	26(3)	27(2)
Cognitively impaired t0	4(17)	0
Decreased MMSE t0-t2	0	2(18)
Subjective memory complaints	7(30)	1(10)
Primary education	17(74)	6(55)
Mean alcohol t0(s.d.)	5(9)	7(17)
Increased alcohol t0-t2	1(4)	0
Mean life events t0-t2 (s.d.)	3.4(2)	3(2)
History of depression	9(39)	2(18)
Family hx depression	6(26)	1(9)
Poor self rated health t0	14(61)	5(55)
Poor observer rated health t0	13(56)	7(64)
Pain t0	11(48)	4(36)
Disability t0	12(52)	9(82)
On benzodiazepines t0	6(26)	3(27)
On antidepressants t0	3(13)	1(9)
New antidepressants t0-t2	0	0

9.4 Discussion

The outcome of SSD was poor in our sample with only 22% recovered at follow-up. In addition 32% continued to experience SSD at t2. A substantial proportion had died during the course of the study (16%). The effect of depressive symptoms (even at subsyndromal level) on mortality have been described previously (Lavretsky, Mistry et al. 2003). The mortality rate was slightly higher in those with 'depression only' (19%) than those with mixed symptoms (14%) at baseline. The elevated rate may have occurred as a result of medical comorbidity in our sample in that a greater proportion of those who died reported poor physical health at baseline (94% vs 60%) however this could not be explored statistically. The increased mortality rate did not seem to be associated with cognitive impairment as equal proportions of those who died and those who survived were cognitively impaired. A recent study examining the effects of SSD on mortality rates in late life found that SSD may actually convey a protective effect in females (Hybels CF 2002). This was not true of our sample.

Rates of incident depression were high in both groups with an overall conversion rate of 18%. This is higher than the rate of 7% reported by Lyness et al (Lyness, Caine et al. 2002) however theirs was a one year follow-up study. Our findings reflect more closely those reported by Chopra et al who reported conversion rates from SSD to diagnosable depression of 24% over a three-month period (Chopra, Zubritsky et al. 2005) this was a clinical sample in which elevated rates above those observed in the community would be expected. It is interesting to note the differential rates of conversion to depression in our sample. The presence of comorbid anxiety symptoms resulted in a substantially increased rate of conversion to depression. Only six percent of the group with pure depressive symptoms converted to depression during the course of the study whereas 23% of those with mixed depression anxiety symptoms converted. It is likely that the presence of comorbid anxiety symptoms meant that the 'D&A' subgroup were closer to the threshold of depression. Conversely, studies have found that where depression and anxiety exist comorbidly at case level a more severe illness is likely with a consequent poorer prognosis (Barbee 1998). It seems that the same may be true at the subsyndromal level.

A substantial proportion of our sample converted to SSA over the course of the study (16%). All of these subjects had developed generalised anxiety symptoms. This finding confirms that of previous studies (chapters 7 and 8) where we have found high rates of conversion across subsyndromal categories. Depression and anxiety in our sample are highly comorbid and appear to lie on a continuum. The results of this study must be interpreted with caution and may not be generalisable as the numbers were too small to allow meaningful statistical analysis. Nevertheless our findings reflect those reported in existing studies of SSD outcome. The strength of SSD as a predictor of case level depression will be explored in a future chapter.

Chapter 10.

Predictors of new subsyndromal depression

10.1 Background

While many studies have commented on the course and outcome of SSD few have examined risk factors for the development of new subsyndromal depressive symptoms. It is likely that risk factors for SSD are similar to or the same as those for case-level depression. Some studies have found that SSD can arise de-novo that is, in the absence of a history of depression (Angst, Merikangas et al. 1997; Chopra, Zubritsky et al. 2005). Other studies suggest that SSD represents a prodrome to or a partially resolved depressive illness (Judd, Akiskal et al. 1998). By exploring predictors of new SSD we can shift the focus upstream from case-level mental illness and identify at-risk groups for whom preventative interventions can be developed.

So far we have explored associations with SSD at baseline, the effects of SSD on service use, the two-year outcome of SSD and predictors of change in SSD symptoms. In this chapter we will examine predictors of new SSD over a two-year period.

10.2 Methodology

This study included only those subjects who had complete two-year follow-up data (i.e. complete data from t1 and t2) and excluded those with SSD at baseline (n=74). The study sample included 240 subjects. 34 subjects in total developed new SSD over the course of the study. Changes in diagnosis over the two years of the study were explored in the group who developed SSD. Table 20 represents baseline diagnoses and progression to SSD.

Statistical analyses

As a number of subjects who develop SSD at t1 will have recovered at t2 in order to preserve power only baseline predictors of SSD are explored. A number of putative predictors of new SSD were derived from the previous studies and the literature and univariate associations with new SSD were explored using non-parametric statistics.

Relationships between variables of interest were explored using non-parametric statistics and a series of backwards stepwise logistic regression analyses were designed with an outcome of SSD as the dependent variable.

Factors entered into the regression analyses were as follows 1) Marital status, history of depression, disability and level of education, 2) gender, family history of depression, pain, age and MMSEt0 3) case level depression t0, living alone t0, 4) poor self rated health t0, baseline GAD symptoms, 5) poor interviewer rated health t0, baseline SMCs.

10.3 Results

34 subjects (14% of the population at-risk) developed new SSD over the course of the study. This group included n=5 who were depressed at baseline, n=15 with SSA, 1 with subsyndromal schizophrenia, and 13 well subjects (see table 24).

Ten subjects with new SSD at t1 progressed to SSA at t2, one subject developed case-level depression and one developed case-level organic illness. In addition six subjects who developed SSD at t1 had recovered (become well) at t2.

Table 24.

Changes in diagnosis by year in those who developed new SSD (n=34)

Diagnosis t0 n=34	Diagnosis t1	Diagnosis t2					
		Dep	SSD	SDA	SSA	Org	Well
Depressed n=5	SSD n=1 ^Φ	-	-	-	-	-	1 ^Ψ
	SDA n=3 ^Φ	-	-	1	2	-	-
	Well n=1	-	-	1*	-	-	-
SSA n=15	SDA n=9 ^Φ	-	-	2	6	1	-
	SSA n=4	-	1*	3*	-	-	-
	CA n=1	-	-	1*	-	-	-
	Well n=1	-	-	1*	-	-	-
SSchiz n=1	SSchiz n=1	-	-	1*	-	-	-
Well n=13	SSD n=6 ^Φ	1	-	1	1	-	3 ^Ψ
	SDA n=3 ^Φ	-	-	-	1	-	2 ^Ψ
	SSA n=1	-	-	1*	-	-	-
	Well n=3	-	3*	-	-	-	-

^Φ = New SSD t1 (n=22)

* = New SSD t2 (n=12)

^Ψ = Recovered t2 (n=6)

Table 25.

Relationship between history of early onset vs late onset depression and new SSD

History of depression	No SSD (n=206) n(%)	New SSD (n=34) n(%)
No history	169(82)	23(65)
Early onset (<50yoa)	10(5)	3(9)
Late onset (>50yoa)	27(13)	8(24)

Table 26. Associations with and predictors of new SSD (n=240)

Baseline Variable	No SSD n=206 n(%)	New SSD n=34 n(%)	Univariate analysis	Logistic regression Analysis
Mean Age(s.d.)	74(6)	75(6)	MW z = -1, p=0.288	ns
Gender (female)	120(58)	25(74)	$\chi^2=2.25$, 1 d.f., p=0.134	ns
Marital Status (Married)	102(50)	10(30)	$\chi^2=5.2$, 2 d.f., p=0.074 ^Ψ	p=0.025, O.R.=0.4, CI=0.172-0.892*
Living alone	56(27)	15(44)	$\chi^2= 3.2$, 1 d.f., p=0.072 ^Ψ	ns
Primary Education	128(62)	20(71)	$\chi^2=0.571$, 1 d.f., p=0.470	ns
Mean MMSE (s.d.)	27(3)	27(2)	MWz = -0.8, p=0.404	ns
History of depression	26(13)	9(27)	$\chi^2=3.4$, 1 d.f., p=0.063 ^Ψ	p=0.048, O.R.=2.4, CI= 1.01-5.8*
Family History	30(15)	2(6)	na	ns
Subj. Memory Complaints	32(16)	9(27)	$\chi^2=1.9$, 1 d.f., p=0.162	ns
Baseline GAD symptoms	56(27)	18(53)	$\chi^2=7.9$, 1 d.f., p=0.005*	p=0.043, O.R. = 2.2, C.I.=1.02-4.7*
Baseline depression	11(5.3)	5(15)	na	ns
Poor self rated health	68(33)	14(41)	$\chi^2=0.540$, 1 d.f., p=0.462	ns
Poor observer rated health	89(43)	16(47)	$\chi^2=0.054$, 1 d.f., p=0.816	ns
Disability	62(30)	12(35)	$\chi^2=0.166$, 1 d.f., p=0.684	ns
Pain	54(26)	11(32)	$\chi^2=.289$, 1 d.f., p=0.591	ns

na= not applicable due to small cell size, ns= non-significant

*= significant at $\alpha=0.05$

^Ψ = trend

Predictors of new SSD

Associations with and predictors of new SSD are represented on table 26. Factors significantly predictive of new SSD were as follows; having a history of depression ($p=0.048$, O.R.=2.4, CI= 1.01-5.8) and having GAD symptoms at baseline ($p=0.043$, O.R. = 2.2, C.I.=1.02-4.7). In addition being married conveyed a protective effect ($p=0.025$, OR=0.4 CI=0.172-0.892). This did not however translate into an increased risk in those who were single or widowed. When a more indepth exploration of marital status as a predictor of new SSD was completed with marital status as separate dichotomous variables (i.e. single vs others, widowed vs others, and married vs others) being married remained the only significant finding.

10.4 Discussion

The incidence of SSD was high with 14% of subjects developing new SSD over the course of the study. Despite significant univariate associations few factors were predictive of SSD.

Being married conveyed a protective effect against the development of SSD. This effect has been described previously in studies of case level depression (Schoevers, Beekman et al. 2000; Beekman, Deeg et al. 2001). Having a partner may convey a protective effect through having a close confidant or supportive relationship and reducing loneliness in late-life (Grace and O'Brien 2003).

Those with a history of depression were 2.4 times more likely to develop SSD over a two-year period than those without. The proximity of the most recent depressive episode to the onset of SSD (i.e. recency of depression) did not convey increased risk as baseline case-level depression was not predictive of SSD in this sample. Some studies have suggested that SSD may represent unresolved depression (Gasto, Navarro et al. 2003). When raw data are examined the proportion of subjects in whom 'new SSD' may actually represent a partially resolved depression was 15%. While having a history of depression conveyed an increased risk a substantial proportion of those who developed SSD (63%) had no history of depression. This suggests that SSD may arise de-novo in late-life and is not entirely accounted for by long standing vulnerability (Chopra, Zubritsky et al. 2005). Having baseline anxiety symptoms, specifically symptoms of generalised anxiety disorder significantly increased the risk of developing SSD. Those with baseline GAD symptoms were twice as likely to develop SSD over the course of the study than those without. The association between GAD and depression has been described previously, having a history of GAD significantly increases the risk of developing case level depression (Livingston, Watkin et al. 1997; Lenze, Mulsant et al. 2005; Schoevers, Deeg et al. 2005). On the basis of our findings the same pattern seems to be true of GAD and depression at subsyndromal level.

This lends further weight to the continuity hypothesis of depression and anxiety in late-life. We have already demonstrated an increased rate of SSA in subjects with a history of depression or SSD, in addition it seems that baseline SSA (GAD subtype) increased the risk of SSD. The relative strengths of SSA and SSD as predictors of depression will be explored in chapter 11.

Chapter 11.

Subsyndromal anxiety and depression as predictors of incident depression

11.1 Background

In preceding chapters we discovered a relationship between SSA and SSD. In our sample SSA predicted SSD and SSD predicted SSA. Furthermore when the two-year outcome of SSA and SSD was examined a substantial proportion of both groups developed case-level depression. Existing data indicates that the presence of SSD substantially increases the risk of case-level depression over time. In addition generalised anxiety disorder may precede case level depression in some subjects where the two disorders lie on a continuum. It is unclear whether the same is true of the SSA or symptoms of GAD itself. Whether the increased rate of depression in the groups with SSA and SSD is attributable to other factors common to both disorders remains to be seen. The relationship may arise as a result of having individuals in either group with poor physical health or disability, both factors being associated with an increased risk of depression.

In this chapter the importance of SSA and SSD as predictors of depression are explored.

11.2 Methodology

This study included only those subjects who had complete two-year follow-up data (i.e. complete data from t1 and t2). In order to exclusively explore risk factors for new depression those subjects with case level depression at baseline (n=42) are excluded. A number of subjects who developed new case level depression over the course of the study were identified. Subjects who developed depression between follow-up assessments (i.e. between t0 and t1, and between t1 and t2) and had been treated or recovered prior to the following visit were only included as incident cases of depression if they had been actively treated (by their GP or psychiatrist) with antidepressants between assessments. In order to preserve power only baseline predictors of depression are explored. This meant that year-by-year differences did not need to be accounted for and reduced the effect of attrition. Subtypes of new depression were classified by AGE CAT diagnoses. Diagnoses of DN3 and above were classified as 'neurotic depression', and where there was comorbid anxiety symptoms 'mixed anxiety depression'. Diagnoses of DP3 and above were classified as 'psychotic depression'. Where AGE CAT diagnoses were not available (i.e. where individuals had become depressed between waves and recovered at the time of the diagnostic interview) the subtype of depression was retrospectively assigned according to treatment used, that is, where antipsychotic medication had been prescribed the diagnosis of 'psychotic depression' was assumed.

Statistical analysis

The data was split into two groups according to the presence or absence of incident depression. A number of putative risk factors for depression were explored. The association between baseline variables and incident depression were explored using non-parametric statistics. Relationships between variables of interest were explored and a number of logistic regression analyses were designed with the presence or absence of incident depression as the dependent variable. Results are described as odds ratios and associated 95% confidence intervals.

11.3 Results

The sample included n=267 subjects who were not depressed at baseline. Diagnoses were as follows; well n=141, subcase Schizophrenia n=1, organic case n=5, organic subcase n=6, SSD n=43 (pure ssd n=13, D&A subtype n=30), SSA n=71 (n=52 GAD subtype, n= 7 phobic and n=12 mixed). A total of n=82 had GAD symptoms at baseline (n= 58 SSA (n=52 pure and n=6 mixed) and n=24 SSD).

Twenty-six subjects developed case level depression during the course of the study. This included n=6 who developed case level depression at t1, n= 17 at t2 and n= 3 between assessments. Of this group n=4 developed ‘neurotic depression’, n= 10 developed ‘mixed anxiety depression and n=12 developed ‘psychotic depression’ (of whom n=4 had comorbid anxiety symptoms).

Sixty-two percent of the sample were female. The mean age was 74 (s.d.=6, range=65-92). The mean MMSE score was 27 (s.d.=3, range=15-30) and the sample included n=28 (11%) with cognitive impairment.

The relationship between new depression and baseline marital status is represented in table 27.

Table 27.

Distribution of baseline marital status and incident depression (n=267)

	No depression n=241 n(%)	New depression n=26 n(%)	Total Sample n=267 n(%)
Single	35(15)	1(4)	36(14)
Married	112(47)	14(54)	126(47)
Widowed	94(39)	11(42)	105(39)

Figure 11.

Rate of Incident depression by baseline diagnosis

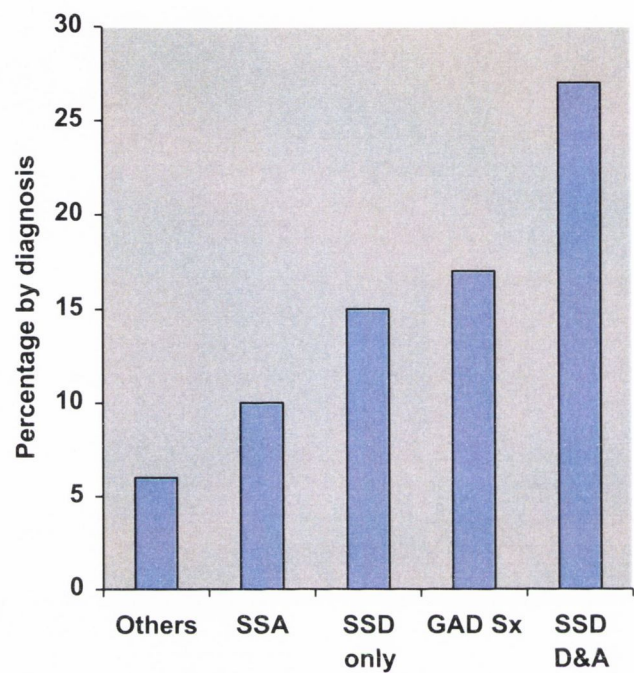


Table 28.

Subtype of new depression by baseline diagnosis

Baseline Diagnosis	Neurotic depression n=4 n(%)	Mixed anxiety depression n=10 n(%)	Psychotic depression n=12 n(%)
SSA	2(50)	2(20)	3(25)
SSD (D only)	0	1(10)	1(7.5)
GAD Sx	3(75)	6(60)	5(40)
SSD (D&A)	1(25)	4(40)	3(25)
Other Dx	1(25)	3(30)	5(40)
Total by subtype	4(100)	10(100)	12(100)

Of those who became depressed during the course of the study $n=8$ had a history of depression of whom $n=3$ had early onset depression (EOD) (onset <50 years of age) and $n=5$ had late onset depression (LOD) (onset at > 50 years of age). The remainder of the sample who became depressed ($n=18$) in the absence of a history of depression were defined as 'late-onset'. All three subjects with EOD and 9 subjects with LOD reported SMCs. Regarding the subtypes of depression noted those with EOD ($n=3$) developed mixed anxiety depression, of those with LOD $n=3$ developed 'neurotic depression', $n=7$ mixed anxiety depression and $n=12$ psychotic depression. Rates of incident depression by baseline diagnosis are compared in figure 11. Subtypes of new depression by baseline diagnosis are represented in table 28.

Factors associated with and predictive of depression are represented on table 29. The strongest predictor of depression in our population was the presence of subjective memory complaints at baseline. From a diagnostic viewpoint both SSD and generalised anxiety symptoms at baseline were strong predictors of depression. Disability, poor self reported health, pain and arthritis were all predictors.

Table 29. Baseline associations and predictors of depression (n=267)

Baseline Variable	No depression n=241 n(%)	New depression n=26 n(%)	Univariate analysis	Logistic regression analysis
Mean Age (s.d.)	74(6)	74(5)	MWz = 0.15, p=0.879	ns
Gender (Female)	146(61)	19(73)	$\chi^2=1.06$, 1 d.f., p=0.301	ns
Marital status (Married)	112(47)	14(54)	$\chi^2=3.01$, 2 d.f., p=0.222	ns
Living alone	75(31)	8(31)	$\chi^2=0.000$, 1 d.f., p=1.00	ns
Primary Education	148(61)	18(69)	$\chi^2=0.323$, 1 d.f., p=0.57	ns
Mean MMSE	27(3)	27(2)	MWz = -0.12, p=0.903	ns
Mean weekly alcohol (s.d.)	5(11)	7(15)	MWz = -1.4, p=0.169	ns
Subjective memory complaints	30(13)	12(46)	$\chi^2=17.29$, 1 d.f., p=0.000*	p=0.000, O.R.=5.7, C.I.=2.3-14.2
History of depression	25(10)	8(31)	$\chi^2=7.23$, 1 d.f., p=0.007*	p=0.005, O.R.=4, C.I.=1.5-10.6
Family history of depression	35(15)	2(8)	$\chi^2=0.434$, 1 d.f., p=0.5	ns
Poor self-reported health	76(32)	15(58)	$\chi^2=6.03$, 1 d.f., p=0.014*	p=0.010, O.R.=3, C.I.=1.3-6.7
Poor observer-rated health	98(41)	16(62)	$\chi^2=3.37$, 1 d.f., p=0.066	ns
Disability	72(30)	17(65)	$\chi^2=11.76$, 1 d.f., p=0.001*	p=0.001, O.R.=4.5, C.I.=1.9-11
Pain	61(25)	12(46)	$\chi^2=4.13$, 1 d.f., p=0.042*	p=0.027, O.R.=2.5, C.I.=1.1-5.8
Arthritis	58(24)	12(46)	$\chi^2=4.83$, 1 d.f., p=0.028*	p=0.03, O.R.=2.7, C.I.=1.09-6.6
Baseline SSA	64(27)	7(27)	$\chi^2=0.000$, 1 d.f., p=1.00	ns
Baseline SSD	33(14)	10(39)	$\chi^2=8.9$, 1 d.f., p=0.003*	p=0.019, O.R.=3.1, C.I.=1.2-7.8
Baseline GAD symptoms	68(28)	14(54)	$\chi^2=6$, 1 d.f., p=0.014*	p=0.017, O.R.=2.7, C.I.=1.2-6.3

11.4 Discussion

The rate of incident or new depression was high in our sample with 10% of the population at risk developing new depression over the course of the study.

The presence of subjective memory complaints (reported in 16% of subjects) was found to be the strongest predictor of depression in our sample. Those with baseline memory complaints were almost six times more likely than their peers to develop depression over a two-year period. The association between memory complaints and depressive symptoms has been described previously in both cross-sectional (McGlone, Gupta et al. 1990; O'Connor, Pollitt et al. 1990; Bolla, Lindgren et al. 1991; Jorm, Christensen et al. 1994) and longitudinal studies (Tobiansky, Blizard et al. 1995; Schmand, Jonker et al. 1997). Existing data suggests that subjective memory complaints may more accurately reflect the affective state rather than the cognitive ability of the complainant. Follow-up studies of subjects with SMCs have demonstrated an increased risk of depression over time (Tobiansky, Blizard et al. 1995; Schmand, Jonker et al. 1997). SMCs may more accurately represent a prodrome to depression rather than heralding cognitive decline. While those with SMCs are more likely to have depressive symptoms at any level of severity, some longer term follow-up studies have demonstrated that SMCs may be predictive of Alzheimer's disease. In our sample, those individuals with SMCs who developed new depression in the absence of a history of 'early onset' depression also had marginally lower mean baseline MMSE scores than the remainder of the group who became depressed (26 vs 27). It is possible that in this subgroup of our sample where depressive symptoms arose concurrently with SMCs the combined symptoms may reflect a vascular type of depression. There was no significant relationship between SMCs and cognitive decline in our sample however the follow-up period was short (2 years) and significant decline would not be expected over this period of time.

Subjects with SSD at baseline were 3 times more likely to become depressed over the course of the study. This is in keeping with previous studies of both younger (Judd, Akiskal et al. 1998) and older adults (Lyness, Caine et al. 2002; Chopra, Zubritsky et al. 2005). It is likely that SSD lies on a continuum with major depressive illness. Having SSA at baseline was not predictive of depression at follow-up. This is likely to be due to the diagnostically heterogeneous nature of this

group. When GAD symptoms were examined separately a relationship was found, those with GAD symptoms being almost three times as likely to develop depression. The presence of GAD symptoms significantly increased the risk of depression in SSD in our sample. When data were reanalysed with the subtypes of SSD entered separately into regression analyses the odds ratio of developing depression with the mixed 'D&A' subtype of SSD increased to 4.4 ($p=0.002$, C.I.=2-11) and SSD (D alone) was no longer predictive of depression ($p=0.487$, O.R.= 1.7, C.I.= 0.4-8.4). Mixed anxiety and depression at case level in late life has been recognised as a more severe subtype of depression. It is possible that the presence of both depressive and anxiety symptoms results in a more 'severe' subtype of SSD. Conversely, the increased risk of depression where GAD symptoms and SSD occur concurrently may be attributable to a greater symptom load resulting in these individuals being closer to the threshold for case-level depression.

All other factors which significantly predicted depression were health related variables. Poor self-rated health, pain, disability and arthritis all increased the risk of depression in our sample. These associations have been described previously.

We have identified four modifiable predictors of depression; SSD, generalised anxiety symptoms, pain and arthritis. Intervention at the level of SSD may reduce the risk of depression particularly where there are co-morbid generalised anxiety symptoms. Active management of pain symptoms particularly where they arise in the context of arthritis may also reduce the risk of depression over time.

Chapter 12.

Conclusion and recommendations

12.1 Background

In this thesis we have explored the impact and outcome of subsyndromal anxiety and depression in the Irish Community dwelling elderly. This is the first time that subsyndromal mental disorders have been explored in the Irish setting, in addition this thesis includes the only existing prospective study of predictors of depression in an Irish community dwelling elderly cohort. Furthermore the naturalistic longitudinal design of our study has allowed us to observe the course and outcome of these disorders in detail. The results are unique on a number of levels and will have an important role to play in the planning and provision of mental health services for the Irish elderly.

There are a number of limitations to our study. Firstly, as the sample were neither randomly sampled nor stratified for age we cannot provide accurate prevalence figures for SSA and SSD. In addition as the attrition rate was high some of our statistical analyses have been limited by power issues. Data were collected in the homes of older adults living in the Dublin South Central area (between September 1998 and September 2001). As the sample consisted entirely of urban dwelling older adults the findings may not be generalisable to the rural Irish setting. At the very least there are significant differences in accessibility of health and social services between urban and rural settings. However as the majority of older Irish adults live in the urban setting the representative sample and study findings give a good reflection of the mental health status of a substantial proportion of older Irish adults. This also increases the relevance of our data in health service planning for older adults in the urban setting.

Despite these limitations we have complete two-year follow-up data on 283 subjects and our studies have produced some interesting and significant findings. In this chapter the strengths and weakness of our studies will be discussed under a number of headings, comparisons with local and international data will be made and conclusions and recommendations drawn.

12.2 Subsyndromal anxiety in the Irish elderly

Prevalence and detection of anxiety disorders in late-life

Anxiety disorders were traditionally considered to be less common in late life (Lenze, Shear et al. 2002) more recent study findings have disputed this assumption. The rates of anxiety disorders and anxiety symptoms in particular may exceed those of depressive illnesses in this age group (Beekman, Bremmer et al. 1998). In addition rates of SSA in particular may exceed rates observed in younger adults (Salzman 2004). The results of our study support these findings. Baseline rates of subsyndromal anxiety were high at 24% however the rates of 'case level anxiety' were considerably lower and all baseline cases occurred comorbidly with depression or other diagnoses. If we consider the rates of anxiety symptoms occurring at any level (case or subcase or comorbid) at baseline the rates were almost doubled at 41%.

Reported prevalence rates of anxiety vary hugely between studies. Discrepancies may arise as a result of differences in both screening tools and populations studied. In the case of population based studies anxiety is frequently 'hidden' by comorbid depression and may be under-reported. Other factors may also play a role in the under-recognition of late-life anxiety. Patients with long standing anxiety disorders are unlikely to present for the first time in later life, having either been treated by general adult services or having coped with their symptoms over time. Anxiety may present differently in late life where somatic symptoms predominate. Older adults who develop new phobias are likely to remain undetected in the community. Furthermore, some authors have suggested that therapeutic nihilism and ageist attitudes further contribute to the under-recognition of anxiety in later life (Lindesay, Briggs et al. 1989). The rates of benzodiazepine prescription in our sample with SSA suggest that at least some anxiety symptoms are recognised at the primary care level. The use of benzodiazepines as a first line treatment option is clearly hazardous in this population however and as our outcome study showed, has little impact on the resolution of symptoms.

Accuracy of our definition of SSA

There are no consensus criteria for diagnosing SSA. It is generally accepted that SSA describes patients with clinically significant anxiety symptoms who fail to reach the threshold for caseness on specific diagnostic criteria. The level and quality of symptoms required for caseness may differ from one scale to another. Even diagnostic packages designed for use in the elderly population may underdiagnose anxiety disorders. Larkin and colleagues have acknowledged that the 'threshold level' for caseness defined within the AGE CAT package may underestimate case level anxiety in this population (Larkin, Copeland et al. 1992). This was reflected in our findings particularly in relation to the GAD subtype of SSA where we found that the patterns of outcome and comorbidity were remarkably similar to those described in studies of 'case-level' GAD in late life. Nevertheless the AGE CAT package accurately captures degrees of comorbidity that may not be readily identifiable by the use of specific anxiety or depression scales in this population (Copeland, Prince et al. 2002).

On the basis of our study findings it is clear that our sample with SSA represented a diagnostically heterogeneous group. This was evident when the outcomes of specific SSA subtypes were examined. While there was a degree of fluidity and transition across subtypes of SSA (particularly with the GAD and mixed subtypes) those with phobic symptoms showed little transition. In addition the GAD subtype of SSA carried with it the poorest prognosis of those with SSA in our sample.

Impact of SSA on wellbeing in late life

SSA had a significant effect on wellbeing and disability which is consistent with previous study findings (de Beurs, Beekman et al. 1999). Those with SSA at baseline reported significantly more disability than those without. Disability has been reported as a risk factor for anxiety (Lenze, Shear et al. 2002). However in our sample the direction of causality was not as expected in that SSA increased the subjective perception of disability. In addition disability was not found to be a significant predictor of anxiety.

SSA has been reported to increase rates of service use (de Beurs, Beekman et al. 1999). When this study is examined in more detail the reported effect of SSA is

primarily on rates of benzodiazepine prescription and not service attendance per se. SSA was significantly associated with increased benzodiazepine use in our sample. SSA did not directly increase the rates of service use however it is likely that SSA exerted an indirect effect through increased disability.

The overall prognosis of SSA was poor with only 25% recovering over the study period. In addition 44% continued to experience anxiety symptoms at two-year follow-up. Not surprisingly the use of benzodiazepines had no effect on the outcome of SSA (Schuurmans, Comijs et al. 2005). This underlines the need to consider alternative interventions for anxiety symptoms in late life. Serotonin specific reuptake inhibitors (SSRIs) have been found to be more effective and safer than benzodiazepines for the treatment of anxiety in the elderly, their use was markedly limited in our cohort. However, as our study focussed on subsyndromal disorders the rate of detection and treatment would be expected to be lower than for case level illness. In addition there are limited data on the efficacy of SSRIs in the treatment of SSA. It is more of a concern that anxiety symptoms at subsyndromal level are being detected, but treated with medication whose risks outweigh its benefits in this age group.

Not only was the prognosis for SSA poor but GAD symptoms at any level in our sample (i.e. occurring in the context of SSA or comorbidly) conveyed a significantly increased risk of depression over time. This is an important finding and highlights the fact that anxiety symptoms and their effects are not negligible in late life.

12.3 Subsyndromal depression in the Irish elderly

Prevalence and detection of SSD in late-life

Depression is the commonest mental illness in late-life (Copeland, Beekman et al. 1999). Rates of minor and subsyndromal depression far exceed the rates of major depression in this age group (Beekman, Geerlings et al. 2002). SSD is a relatively recent concept, its importance has been well documented in younger adults (Judd, Akiskal et al. 1998) and more recently in the elderly (Lyness, King et al. 1999; Hybels CF 2001; Lavretsky, Kurbanyan et al. 2004). The rate of SSD in our sample was high at 14% and was higher than rates reported in a previous Irish

prevalence study (Kirby, Bruce et al. 1997). However the cumulative rates of depressive spectrum disorders in both studies are remarkably similar.

Accuracy of our definition of SSD

The lack of consensus criteria for SSD has resulted in a broad range of reported prevalence figures across studies. Our study used the AGECAAT package to define SSD. While the AGECAAT diagnoses of case level depression (DN3 and DP3 and above) have been validated against DSM depression diagnoses AGECAAT subcase diagnoses have received little attention (Gurland, Fleiss et al. 1976). The diagnosis of subcase depression denotes the presence of a clinically significant number of symptoms over and above that which would be considered 'normal' variant in the community (Copeland, Beekman et al. 1999). It is possible that our definition was overinclusive and encompassed a broad spectrum of 'subsyndromal severity. Nevertheless the use of a computerised diagnostic interview reduced the possibility of observer bias and our diagnostic 'criterion' (i.e. AGECAAT 'subcase' depression) seems to have had little effect on the predictive ability of this subgroup in our sample.

Impact of SSD on wellbeing in late life

SSD was associated with significant impairment in our study. SSD at baseline was associated with increased life-events, poor self perceived health, disability and pain. In addition we found that individuals with SSD had significantly more frequent GP visits and showed a trend towards excessive service use.

The prognosis of SSD was poor, 50% of our sample continued to experience depressive symptoms at any level at two-year follow-up (32% SSD and 18% depressed). We found a 16% mortality rate in the SSD cohort which is lower than that reported in case-level depression in a similar population (30%) (Denihan, Kirby et al. 2000) but is elevated above that which would be expected for subjects of similar age. The association between depression and mortality is complex (Cuijpers and Schoevers 2004). A recent study has suggested that the association between depression and mortality may be attributable to subjective perception of poor health rather than the number or severity of depressive symptoms per-se (Blazer and Hybels 2004). Poor health may have contributed to the mortality rate

in our sample also as those with SSD were more likely to report poor health than those without. We can only speculate on the basis of raw figures as to the associations with both recovery and remission. Those with persistent SSD were more likely to have personal and family histories of depression and were also more likely to have experienced spousal bereavement over the course of the study than those who recovered. This reflects the findings of Denihan et al who found that similar factors influenced persistence of depression (Denihan, Kirby et al. 2000). Thus the profile and outcome of SSD is remarkably similar to but not as severe as that of case level illness in this population.

12.4 Predictors of anxiety and depressive symptoms in the Irish elderly

We examined a number of putative vulnerability and risk factors for both SSA and SSD in our sample. Shifting the focus ‘upstream’ may be invaluable in identifying individuals at-risk.

One of the most commonly cited vulnerabilities for psychopathology in late life is female gender. Existing data indicate that females may be at greater risk of developing anxiety symptoms or disorders in late-life (Beekman, de Beurs et al. 2000; de Beurs, Beekman et al. 2001; Flint 2005; Le Roux, Gatz et al. 2005). In addition, many studies have reported an increased risk of depression in female subjects. Being female was associated with an increased likelihood of both SSA and SSD at baseline and was also predictive of chronicity of anxiety symptoms but was not predictive of developing either new SSD or anxiety symptoms. The lack of a predictive relationship between gender and SSA and SSD in our sample may be attributable in part to power as a greater proportion of both groups were indeed female. However the association between gender and both baseline and chronicity of anxiety symptoms highlights the possibility that at baseline the association was likely contributed to by over-representation of chronic ‘female’ cases. This has been highlighted in more comprehensive detail in a recent meta analysis of risk factors for depression in late life which reported that many studies did not find evidence for increased risk of depression in females (Cole and Dendukuri 2003).

Having a personal history of depression increased the risk of both SSD and anxiety symptoms (particularly the GAD subtype). Family history was not found

to be significantly associated with either disorder nor did the raw data demonstrate any trend which may have been masked by power issues.

When we examined 'recent' psychiatric history or baseline diagnosis as predictors of either disorder we found that baseline GAD symptoms were predictive of SSD and that baseline SSD was predictive of SSA. This association has been described previously in the context of case level disorders (Lenze, Mulsant et al. 2005) but not, to our knowledge, at the subsyndromal level. We found a complex relationship between depression and anxiety in our sample which will be discussed in more detail below.

While SSD was associated with an increased number of life events at baseline neither the number or the quality of life events were predictive of either SSA or SSD. This diverges from studies of case level disorders in this population (de Beurs, Beekman et al. 2001). The lack of a relationship may be attributable in part to the severity of symptoms studied (i.e. case level versus subsyndromal disorders). When studies of life events as predictors of anxiety or depression are examined in more detail it seems that the individual personality style has a crucial role in the perception, impact and ultimate outcome following exposure to life events (Ormel, Oldehinkel et al. 2001). For example De Beurs et al report that having an external locus of control significantly increases the risk of developing anxiety symptoms in late life (de Beurs, Comijs et al. 2005). It is possible that an association between life events and psychopathology exists even at the subsyndromal level but we may have missed this association through failure to collect data on personality and coping styles.

We found that living alone significantly increased the risk of SSA while being married conveyed a protective effect from SSD. On the basis of these findings we can infer that social support has an important role to play both as a predictor of and protective factor against the development of subsyndromal disorders in late life. However as the type of social network did not buffer these effects it may be the quality of these social relationships that have a predictive or protective effect. Lack of a close confidant is a well documented risk factor for depression throughout the life cycle.

12.5 Comorbidity of anxiety and depression and the implications thereof

The impact of anxiety on the presentation course and outcome of depression is well described. The presence of co-morbid anxiety and depression leads to a more severe presentation of illness with increased levels of suicidality, a slower and poorer response to antidepressant treatment (Flint and Rifat 2002) and an increased likelihood of drop-out from treatment (Mulsant and Ganguli 1999). Anxiety has also been associated with a chronic course of depression in older depressed individuals (Schoevers, Beekman et al. 2003). In a recent study Steffens and McQuoid reported that older depressed patients with symptoms of generalised anxiety were less likely to remit than those without (Steffens and McQuoid 2005). In contrast Lenze and colleagues described good treatment outcomes for patients with co-morbidity with early intervention (Lenze, Mulsant et al. 2003). Previous Irish studies have found that anxiety may 'unmask' depression in the community leading to a 'louder' depression (Kirby, Denihan et al. 1999). In addition in the Irish setting those with co-morbidity are more likely to receive treatment (Kirby, Denihan et al. 1999; Eustace, Denihan et al. 2001). Anxiety symptoms may also increase the risk of relapse of depression (Schoevers, Deeg et al. 2005). This effect was evident in our study of predictors of depression where we found that those with GAD symptoms were at increased risk of developing case level depression.

The possibility that GAD and depression may lie along a continuum has been a source of debate in the literature (Schoevers, Deeg et al. 2005). There have been few longitudinal studies of the course of anxiety and depressive symptoms in late life and these studies have produced conflicting results. Some authors have found compelling evidence to support a continuity hypothesis (Lenze 2003; Schoevers, Beekman et al. 2003; Schoevers, Deeg et al. 2005), others have concluded that GAD and depression are discrete entities (Beekman, de Beurs et al. 2000; de Beurs, Beekman et al. 2001). Our study findings strongly support the continuity hypothesis of depression and GAD. SSA was predictive of SSD, SSD predictive of SSA and both SSD and GAD symptoms were predictive of case level depression.

12.6 Conclusion and recommendations

On the basis of our findings we can conclude that subsyndromal depression and anxiety have a serious impact in the Irish elderly. Far from representing inconsequential symptoms these disorders are associated with significant morbidity in the community. In addition, when anxiety and depressive symptoms occur comorbidly they present a more severe picture and the risk of case level depression is significantly increased.

The above findings highlight the need to identify and monitor individuals with subsyndromal symptoms closely. While few if any studies of interventions for SSD and SSA exist closer follow-up may allow earlier and more appropriate intervention should case level psychopathology develop. In addition early intervention may decrease functional disability and reduce the burden both on sufferers and services (Lenze, Mulsant et al. 2003; Flint 2005). With the greying of the population it has become increasingly important to identify vulnerable subgroups and attempt to intervene before the burden of their illness increases.

Future studies should focus on developing preventative interventions for these individuals.

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Appendix A: *Mini-Mental State Examination (MMSE)*

<i>Orientation</i>		Score
What is the	year?	1
	Season?	1
	Date?	1
	Day?	1
	Month?	1
Where are we	Country?	1
	County?	1
	City?	1
	Floor?	1
	Address?	1
Registration		
Name three objects and ask the subject to repeat the list.		
Repeat the list until the subject learns all three.		3
Attention and Calculation		
Spell world backwards		5
Recall		
Ask the subject to recall the three objects learnt.		3
Language		
Naming: Ask the subject to name a pen and a watch		2
Repetition: Ask the subject to repeat “no ifs ands or buts”		1
Three stage command: Ask the subject to take a piece of paper in their right hand, fold it in half and put it on the floor.		3
Ask the subject to read and obey “close your eyes”		1
Ask the subject to write a sentence		1
Ask the subject to copy intersecting pentagons		1
<i>Total score</i>		/30

Appendix B: *The support network assessment instrument*

Questions

1. How far away, in distance does your nearest child or other relative live?
Do not include spouse.
2. If you have any children, where does your nearest child live?
3. If you have any living sisters or brothers, where does your nearest sister or brother live?
4. How often do you see any of your children or other relatives to speak to?
5. If you have friends in this community/neighbourhood, how often do you have a chat or do something with one of your friends?
6. How often do you see any of your neighbours to have a chat with or do something with?
7. Do you attend any religious meetings?
8. Do you attend meetings of any community/neighbourhood or social groups, such as old peoples clubs, lectures or anything like that?

Responses

Questions one to six have six response categories each, categories seven and eight have three response categories.

Scoring

Each network receive a score of zero or one for each question, depending on the response. The network type with the highest score from the eight questions is the individual's network.

Appendix C: *List of threatening events.*

1. **Health problem** (e.g. major physical illness, injury or accident), which has started or significantly worsened in the previous two years

Not causing disability or distress 0

Currently causing disability or distress 1

2-3. Bereavement

Death of a close friend or relative other than spouse in previous two years

Death of spouse in previous two years (either =1)

4. Loss or theft of a valuable

Loss or robbery of objects of personal or actual value (e.g. wedding ring, cherished pet, money equivalent to one weeks income) in previous two years 1

5. Other serious upset

Other seriously upsetting event in previous two years 1

6. Financial difficulty

Moderate or major financial difficulties which have started or significantly worsened in previous two years 1

7-8. Move of residence

Moves of residence which have seriously upset the person in previous two years 1

9. Pleasant event

Pleasant life event within the previous two years 1

Appendix D: *Service Utilisation Questionnaire*

S1. Have you seen any of the following health professionals in the past year?

GP _____
Public health Nurse _____
Chiropodist _____
Dentist _____
Physiotherapist _____
Other Health Prof. _____

S2. How often do you see or speak to your GP?

Less than once a year _____
At least once a year _____
2 or 3 times a year _____
At least once a month _____
Other _____ (Frequency _____)

S3. Have you been hospitalised over the past year? _____ (If no, skip to S5)

S4. What reason were you hospitalised for?

Medical _____
Surgical _____
Psychiatry _____
Rehab _____
Respite _____

S5. Do you attend the hospital outpatient department? _____

S6. Do you receive any of the following services?

Meals on wheels _____
Home help _____
Day centre _____

S7. Do you attend a day hospital? _____