Antipsychotic Use among Older Persons in Long-Term Institutional and Home Care

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ACADEMIC DISSERTATION
To be presented, with the permission of the Faculty of Medicine of the University of Tampere, for public discussion in the Main Auditorium of Pitkäniemi Hospital, on December 14th, 2007, at 12 o’clock.
To those I love
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LIST OF ORIGINAL PUBLICATIONS

The present dissertation is based on the following original publications, referred to in the text by the Roman numerals I-V. Some unpublished data are also presented.


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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>AD</td>
<td>Alzheimer’s disease</td>
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<tr>
<td>AdHOC</td>
<td>Aged in Home Care</td>
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<td>ADL</td>
<td>activities of daily living</td>
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<tr>
<td>ATC</td>
<td>Anatomical and Therapeutic Chemical classification of drugs</td>
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<td>BPSD</td>
<td>behavioural and psychological symptoms of dementia</td>
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<tr>
<td>ChEI</td>
<td>cholinesterase inhibitor</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<td>CVAV</td>
<td>cerebrovascular adverse event</td>
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<td>CVD</td>
<td>cardiovascular disease</td>
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<tr>
<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental disorders, fourth edition</td>
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<td>CPS</td>
<td>Cognitive Performance Scale</td>
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<td>DRS</td>
<td>Depression Rating Scale</td>
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<tr>
<td>EMEA</td>
<td>European Agency for the Evaluation of Medicinal Product</td>
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<tr>
<td>EPS</td>
<td>extrapyramidal symptoms</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>HC</td>
<td>home care</td>
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<td>ICD-10</td>
<td>International Classification of Disease, tenth edition</td>
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<td>LBD</td>
<td>Lewy body dementia</td>
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<td>LTCF</td>
<td>long-term care facility</td>
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<td>MDS</td>
<td>Minimum Data Set</td>
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<td>OR</td>
<td>odds ratio</td>
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<td>PD</td>
<td>Parkinson’s disease</td>
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<tr>
<td>RAI</td>
<td>Resident Assessment Instrument</td>
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<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
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<tr>
<td>STAKES</td>
<td>National Research and Development Centre for Welfare and Health</td>
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<td>TD</td>
<td>tardive dyskinesia</td>
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ABSTRACT

Background: Although antipsychotics are widely used in geriatric patients, there is a paucity of information about the use patterns of antipsychotic medication in home and long-term institutional care, especially among the oldest old and schizophrenic residents.

Aims: The purpose of the present study was to investigate the prevalence of use of antipsychotics and associated factors among elderly persons in long-term institutional and home care.

Materials and methods: The population data in the various studies (I-V) were drawn from the national Resident Assessment Instrument (RAI) database located in STAKES during the period 2001-2006. The data collection method was the Minimum Data Set (MDS) for long-term care facilities (MDS-LTC) and home care (MDS-HC).

Results: The prevalence of the use of antipsychotics in long-term institutional care decreased from 42% in 2001 to 39% in 2003. The overall confounder-adjusted decrease in antipsychotic use was not statistically significant. However, during the study period the use of antipsychotics decreased significantly among residents with wandering as a behavioural problem. However, the use of antipsychotics increased in those residents who concurrently received anxiolytics (Study I). Antipsychotic medication use among nonagenarians in long-term institutional care was also common (30%) and seemed in many cases to be associated with residents’ negative attitudes to others. The major finding was an increasing risk of antipsychotic use among querulous residents. However, this risk was lower among those residents with good social skills (Study II). Approximately 19% of the older residents in long-term institutional care with schizophrenia were not on antipsychotic medication. Any diagnosis of dementia,
severe underweight and severely impaired vision was associated with non-use of antipsychotics (Study III). Antipsychotic use among home care patients in Finland was lower (11.0%) than in long-term institutional care. Several predictive factors such as psychiatric diagnosis, delusions and cognitive impairment were associated with the use of antipsychotics, whereas there was a negative association between age and the use of antipsychotics (Study IV). Of home care patients in nine European countries, 6.2% received antipsychotic medication. Frequency of the use of one or more antipsychotic medications varied widely between study sites, ranging from 3.0% in Denmark to 12.4% in Finland. Certain factors such as delusions, hallucinations, depression, dementia and cognitive impairment as well as youngest age group and concomitant use of other psychotropics explained the use of antipsychotics. Residing in Finland or Italy was also a risk indicator (Study V).

**Conclusions:** Based on present results and the current literature it seems reasonable to conclude that the use of antipsychotic medication in home and long-term institutional care in Finland was among the highest in the world. The use of antipsychotics was approximately three times more common in long-term institutional care than in home care. The finding that the use of antipsychotics was more common among youngest age group, 65-74 years, contradicts some earlier reports. In many cases antipsychotics were not being prescribed based on clinical indication. The proportion of residents with schizophrenia without any antipsychotic medication was equal to that found in earlier studies.
TIIVISTELMÄ

Tausta: Psykoosilääkkeiden käytöstä vanhusten pitkäaikaisessa koti- ja laitoshoidossa on vähän tutkimustietoa, vaikka vanhusikäisillä käytetään psykoosilääkkeitä runsaasti. Tietoa puuttuu erityisesti kaikkein iäkkäimmien ja skitsofreniaa sairastavien vanhusten psykoosilääkkeiden käytöstä.

Tavoitteet: Tutkimuksen tarkoituksena oli selvittää psykoosilääkkeiden käytön yleisyyttä ja siihen vaikuttavia tekijöitä vanhusten pitkäaikaisessa laitosh- ja kotihoidossa.

Aineisto ja menetelmät: Tutkimusaineisto kerättiin eri tutkimuksiin Stakesissa olevasta vuosien 2001–2006 välisestä RAI (Resident Assessment Instrument) -tietokannasta. Laitoshoidossa tutkimusaineiston keräykseen oli käytetty MDS (Minimum Data Set)- LTC (Long-Term Care) ja kotihoidossa MDS-HC (Home Care) tiedonkeruumenetelmää.


INTRODUCTION

Population aging presents a challenge in all countries of the world, but it is thought that in Finland the changes will come more rapidly than in most other EU countries (Statistics Finland 2007a). It is estimated that by 2035, the proportion of the population aged 65 or over will increase from the current level of 16% to about 27% in Finland (Statistics Finland 2007b). Although an increasing number of older people enjoy good health longer than previously (Sulander et al. 2006), living independently and need no assistance and care, the aging of the population will increase pressure on social and health services.

Dementia affects over 6% of people age 65 and over worldwide (Wimo et al. 2003) and increases sharply with age (Lobo et al. 2000, Ferri et al. 2005). Although improvements in outpatient services, home nursing and home help services in particular, have also enabled to increasing numbers of elderly people with dementia continue to live at home, dementia is the major cause of long-term institutionalisation among older people. At the same time residents in long-term institutional care are ever more frail (Noro et al. 2005). According to earlier reports, about three-quarters of older people in nursing homes are suffering from dementia (Macdonald et al. 2002, Hosia-Randell and Pitkälä 2005).

The need for care is increasing not only by population ageing but also by the longer duration of different diseases. Dementias commonly lead to impaired functional capacity and greatly increase the need for services. Behavioural and psychological symptoms of dementia develop in most elderly patients at some stage (Lawlor 2004).

Older people with psychiatric disorders constitute a significant subgroup of elderly population. According to epidemiological studies the 12-month prevalence rate of any psychiatric disorder was 5.8% among community living
elderly people and 68-94% among elderly residents in long-term care settings (Rovner et al. 1990, Wancata et al. 1998, Hybels and Blazer 2003). The recent epidemiological The Health 2000 Study reported the lifetime prevalence of psychotic disorders to be 3.6% among elderly people in Finland (Perälä et al. 2007). However, the prevalence of schizophrenia is increasing in older individuals as the overall lifespan increases and more individuals with schizophrenia survive into later life. It has been estimated that the absolute number of older patients with schizophrenia will double over the next 30 years (Cohen et al. 2000).

Antipsychotics are widely used in geriatric disorders. The proportion of residents receiving antipsychotic medication in long-term institutional care has varied widely, 15-42% (Liperoti et al. 2003, Hosia-Randell and Pitkälä 2005). Excessive prescribing of antipsychotic therapy is a concern owing to their potential to cause serious adverse events.

In this dissertation the prevalence and associated factors of antipsychotic use among elderly people in long-term institutional and home care were studied.
1 REVIEW OF THE LITERATURE

1.1 Social and health services for older people

1.1.1 Older population proportions and trends

The proportions of older persons out of the total population are increasing in most countries. At the end of 2005, the number of over-65s accounted for 16% of the Finnish population, over-75s for 7.5% and over-85s for 1.7% (STAKES 2007). By 2035, the number of over-65s is estimated to grow to 27%. The population share over-75s will increase to 15% and over-85s at nearly 5%. The growth of the older population can partly be explained by the fact that people live longer than ever before.

Preliminary data for 2005 indicate that the average life expectancy of the Finnish population was 75.5 years for men and 82.3 years for women. By 2035, the life expectancy will rise to 81.3 years for men and 85.8 years for women (Statistics Finland 2006, STAKES 2007). With the worldwide aging of the population the number of disabled older persons in and out of institutions will approximately triple from 1985 to 2050 (Manton 1997).

1.1.2 Long-term care for older people

The aim is to promote older people’s functional capacity and independent living, with the main aim that as many older people as possible can continue to live in their own homes and their familiar environments. In Finland services provided in the person’s home are provided by the social welfare authorities (home-help service units) or health care authorities (home-nursing units) either jointly or separately. At the end of 2005, living at home accounted for 89.6% of all over-75s. Of population aged 65 years and over 6.5% were having regularly home
care services, of population aged 75 and over 11.5% and of those aged 85 and over 20.9% (STAKES 2007).

At the same time as the older population is growing, an increasingly low proportion of older people live in long-term institutional care. Long-term institutional care for older people is mostly provided in residential homes and health-care inpatients wards. At the end of 2005 in Finland, those living at residential homes accounted for 2.2% and those living in inpatient care in health centres accounted for 1.3% for all over-65s (STAKES 2007). Results from long-term care facilities in 10 nations showed that institutionalization rates among the nations studied varied between 2% and 5% (Ribbe et al. 1997). In 2004 the proportions of over-65s in institutional care and housing services for older people in Nordic countries were: in institutional care in Finland 6.8%, in Sweden 7.3%, in Norway 11.8%, in Denmark 8.2% and in Iceland 9.4% (STAKES 2007). The proportions receiving home-help services were: 9.8% in Finland, 8.5% in Sweden, 14.1% in Norway, 21.6% in Denmark and 19.2% in Iceland.

1.2 Psychotic and organic mental disorders in later life

1.2.1 Psychotic symptoms and disorders

1.2.1.1 Epidemiology

For having at least one psychotic symptom, the estimated point prevalence in community living elderly people has been reported to be 3.2% to 5.7% (Henderson et al. 1998, Forsell et al. 2003). The prevalence rate of psychotic symptoms in individuals older than 85 without dementia has been found to be 10.1% (Östling and Skoog 2002). Two studies on individuals aged above 70 have reported a cumulative incidence of psychotic symptoms 4.8% (Henderson et al. 1998, Östling et al. 2007). Psychotic symptoms in older persons are important because of their clinical significance and social impact. According to
earlier studies there may be a twofold mortality risk in individuals above 70 years with psychotic symptoms (Henderson and Kay 1997).

The prevalence of psychotic disorders in the elderly has ranged from 0.1-5.1% in community based samples patients to 10%-63% in a nursing home population (Junginger et al. 1993, Copeland et al. 1998, Zayas and Grossberg 1998, Ritchie et al. 2004, Skoog 2004). The point prevalence of psychotic disorders seems to increase with age: 1.0% in the population aged 70 and 5.1% in the population aged 85 and more (Skoog 2004). The recent The Finnish Health 2000 Study reported that the lifetime prevalence of all psychotic disorders was 3.06% in general population (Perälä et al. 2007). The prevalence of psychotic disorders was highest in the age group 65 and over, 3.55% (2.80% in men, 3.98% in women). These prevalences accord with an earlier study by Ritchie et al. stating that lifetime prevalence of psychosis among elderly people was 4.7% (Ritchie et al. 2004). However, longitudinal epidemiological studies of psychiatric disorders in the very old are rare.

1.2.1.2 Risk factors for psychosis

The risk factors that are described as being associated with the development of psychotic symptoms in older people include the following: cognitive dysfunction, a higher level of social isolation than others in the community, being divorced or never married, being female, being old, having depressive symptoms and using psychotropic drugs (Forsell and Henderson 1998, Henderson et al. 1998, Zayas and Grossberg 1998). In the recent study hearing impairment in older people, however, was not a risk factor for psychosis (van der Werf et al. 2007), in contrast to previous reports (Prager and Jeste 1993, Stein and Thienhaus 1993, Almeida et al. 1995).
1.2.2 Schizophrenia

1.2.2.1 Diagnosis of schizophrenia

Schizophrenia is defined almost identically in the two major psychiatric classification systems, the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental disorders, 4th edition (DSM-IV; 1994) and the World Health Organization’s International Classification of Diseases, 10th edition (ICD-10; 1997). There are some differences between these criteria. In ICD-10, severe symptoms should have been present for 1 month, but DSM-IV requires 6 months’ duration (Schultz and Andreasen 1999).

Three broad types of symptoms characterize schizophrenia: positive symptoms, negative symptoms and cognitive impairment (Mueser and McGurk 2004). Positive or psychotic symptoms include extraordinary beliefs, delusions, hallucinations and incoherence or looseness of associations in thought and speech, grossly disturbed behaviour or affect. Long-term functioning is predominantly influenced by negative symptoms – such as flattening of affect, amotivation, anhedonia – and cognitive problems (Andreasen 1995). These cognitive deficits involve impaired executive functioning that affects planning, abstract thinking, rule flexibility, processing deficits, attention impairments and short- and long-term memory difficulties.

There are two distinct groups of individuals with late life schizophrenia. The first and larger group comprises patients with onset of schizophrenia early in life (early-onset schizophrenia) who are now elderly. The other group defined by onset of symptoms after age 40 or age 45 (late-onset schizophrenia) and onset of symptoms after age 60 (very-late-onset schizophrenia-like psychosis). Approximately 80% have early-onset schizophrenia (Cohen et al. 2000) with the remaining 20% including those with late-onset schizophrenia (Howard et al. 2000). However, this classification is included neither in ICD-10 nor in DSM-IV.
1.2.2.2 Prevalence of schizophrenia

Schizophrenia is among the most severe psychiatric disorders, affecting nearly 1% of the world’s population (Schultz and Andreasen 1999). For individuals over 65 years of age, community prevalence estimates for schizophrenia have been reported to vary from 0.1% to 0.6% (Nielsen and Nielsen 1989, Keith and Matthews 1991, Copeland et al. 1998). Other studies have suggested that the actual prevalence of schizophrenia in later life is higher, approximately 1.0% (Gurland and Cross 1982, Cohen 1990). In the recent population based Health 2000 study in Finland the lifetime prevalence of schizophrenia has been reported to be 0.92% among elderly people over 65 years of age (Perälä et al. 2007). It has been estimated that at least 0.1% of the world’s elderly population have a diagnosis of schizophrenia that started late in life (Arunpongpaaisal et al. 2003). Late onset schizophrenia accounts for about 15-23% of older adults with schizophrenia (Harris and Jeste 1988, Howard et al. 2000).

Approximately 85% of people with schizophrenia aged 65 and over are living in the community (Cohen et al. 2000). With the aging of the population and the downsizing of psychiatric institutions, nursing homes and equivalent settings have become increasingly common places of residence for patients with schizophrenia in the later stages of life. It has been reported that residents with schizophrenia account for 6-7% up to 12% of all nursing home residents (Gurland and Cross 1982, Tariot et al. 1993, McAlpine and Mechanic 2000, Snowdon et al. 2005).

1.2.2.3 Course of schizophrenia in later life

Mental disorders in general are life shortening (Hannerz et al. 2001). In addition to psychiatric symptoms, patients with schizophrenia often lack basic medical care and thus suffer from greater severity of comorbid medical disorders which may have a negative impact on both psychiatric and physical outcomes (Meyer et al. 2005). Compared with the general population, individuals with schizophrenia have an increased risk of death from medical causes and an up to 20% shorter lifespan (Harris and Jeste 1988). Mortality rates among people with
schizophrenia have been estimated to be two to four times higher than that in general population (Jeste et al. 1996). The prevalence of schizophrenia is increasing in older individuals as the overall lifespan increases and more individuals with schizophrenia survive into later life (Cohen et al. 2000).

Schizophrenia is an illness with a low rate of full recovery and characterised by considerable heterogeneity in symptomatology, course and outcome. For years it has been believed that in later life the severity of psychotic symptoms of schizophrenia is markedly reduced. There are essentially no long-term studies of the course of psychotic symptoms in schizophrenia that use formal assessments of symptom severity. In a cross-sectional study of patients with schizophrenia ranging in age from 25 to 95, all of whom were chronically institutionalized at the time of assessment, the severity of positive and negative symptoms was assessed (Davidson et al. 1995). The oldest patients in the study (aged 75 and over) still had considerable psychotic symptoms. By contrast, Jeste et al. have claimed an inverse association of age and the severity of psychotic symptoms (Jeste et al. 2003). Several longitudinal studies have shown that there is no evidence of improvement in psychotic symptoms with advancing age (Putnam et al. 1996, Harvey et al. 2003).

Because of sample heterogeneity, there is more controversy about improvement in negative symptoms; some investigators believe that negative symptoms dominate the picture in later life, whereas others contend that such symptoms remit (Cohen 1990, McGlashan and Fenton 1992, Davidson et al. 1995, Schultz et al. 1997, Cohen et al. 2000, Jeste et al. 2003). Cohen et al. note that in elderly schizophrenic patients negative symptoms may be difficult to identify because of the confounding effects of depression, medications and institutionalization (Cohen et al. 1996, Cohen and Talavera 2000). Negative symptoms have been found to correlate with cognitive deficits (Lindenmayer et al. 1997) and to be inversely correlated with functional status (Palmer et al. 2002). Institutionalized schizophrenic patients have demonstrated an age related pattern of cognitive change different from that observed for Alzheimer’s disease (AD) and healthy individuals (Friedman et al. 2001).
Cognitive impairment is a prominent feature of schizophrenia after the onset of psychosis and increases in severity and prevalence with age (Davidson et al. 1995, Harvey et al. 1995a, Harvey et al. 1995b). Although it has been reported that two thirds of elderly institutionalized patients with schizophrenia had cognitive impairments (Dwork et al. 1998), several studies have reported that AD and AD-like neuropathology does not occur more often in chronic schizophrenia than in general population (Dwork et al. 1998, Murphy et al. 1998, Purohit et al. 1998, Jellinger and Gabriel 1999). The prevalence of AD in elderly patients with chronic schizophrenia ranges from 2% to 9%, (Dwork et al. 1998, Murphy et al. 1998, Purohit et al. 1998, Jellinger and Gabriel 1999) showing that the frequency of AD may be equal or even less than in the general population.

Schizophrenia in general is a chronic debilitating disease that is often characterized by frequent relapses associated with exacerbation of psychosis and the need for psychiatric rehospitalization. Only 8% of schizophrenic patients (40-70 years) living independently met the criteria for sustained remission (Auslander and Jeste 2004). Sustained remission was recently defined as a state in which patients have experienced an improvement in core sign and symptoms such as psychoticism, disorganization and negative symptoms to the extent that any remaining symptomatology is of such low intensity that it no longer interferes significantly with behaviour (Andreasen et al. 2005). It is below the threshold typically utilized in justifying an initial diagnosis of schizophrenia. With regard to symptom severity, these experts defined a score of mild or better [the Positive and Negative Syndrome Scale (PANSS): ≤3, the Brief Psychiatric Rating Scale (BPRS): ≤3, the Scale for the Assessment of Positive Symptoms (SAPS): ≤2 and the Scale for the Assessment of Negative Symtoms (SANS): ≤2)] simultaneously on all these items as representative of an impairment level consistent with symptomatic remission of illness. Six months was identified as the minimum period that a patient had to sustain this low level of symptomatology to be considered as in remission (Andreasen et al. 2005).

Most patients with schizophrenia are at very high risk of relapse in the absence of antipsychotic treatment. Unfortunately, there is no reliable indicator
to differentiate the minority who will not from the majority who will relapse without contained medication (Lehman et al. 2004). Antipsychotics can reduce the risk of relapse in the stable phase of illness to less than 30% per year (Gilbert et al. 1995, Leucht et al. 2003). Without maintenance treatment, 60-70% of patients relapse within 1 year, and almost 90% relapse within 2 years. While many of these studies included younger adults with schizophrenia, the rates of relapse following withdrawal of antipsychotics seemed to be comparable in those studies that included elderly patients (Jeste et al. 1993).

1.2.3 Dementia

It is estimated that there are over 24 million people with dementia worldwide (Ferri et al. 2005). The prevalence of dementia varies between 5.9% and 9.4% in European populations aged over 65 (Lobo et al. 2000, Berr et al. 2005) and increases sharply with age: it doubles every five years, being 0.8-1.5% in the age group of 65-69 years, and 24.8-28.5% in the age group of 85 years and older (Lobo et al. 2000, Ferri et al. 2005). In Finnish population-based studies a prevalence of 6.7-9.6% for all dementia has been reported (Sulkava et al. 1985, Koivisto 1995, Löppönen et al. 2003). In a recent study in Finland the prevalence of dementia was 22.8% in subjects aged over 75 years (Rahkonen et al. 2003). It has been reported that the prevalence of dementia among nonagenarians varied 26.7% to 38.6% (Juva et al. 1993, Juva et al. 2000, Polvikoski et al. 2001) and among centenarians 51-58% respectively in population based studies (Sobel et al. 1995, Andersen-Ranberg et al. 2001).

Dementia is an incurable disease with marked effects on cognition, activities of daily living and behaviour and it is a major cause of long-term institutionalization among older people. Dementia affects approximately three-quarters of older people in specialist nursing homes in UK and at least one third of residents had severe cognitive impairment (Macdonald et al. 2002). Figures of between 61 and 78% have been reported from Canada, Denmark and Australia (Brodaty et al. 2001, Sorensen et al. 2001, Hagen et al. 2005). Accordingly, in an previous study in Finland approximately 70% of the residents in nursing homes had been diagnosed with dementia (Hosia-Randell and Pitkälä 2005).
1.2.3.1 Behavioural and psychological symptoms and signs

Although cognitive dysfunction is the hallmark of dementia, behavioural and psychological symptoms of dementia (BPSD), such as psychosis, aggression, sleep disturbance, agitation, and mood disorders, develop in most elderly patients at some stage (Lawlor 2004). Agitation is a descriptive term applied to nonspecific physical and verbal behaviours that are commonly found in nursing home residents with dementia: these include symptoms of aggression, wandering, irritability, restlessness, shouting and pacing, usually in the context of distress and anxiety (Cohen-Mansfield and Billig 1986, Howard et al. 2001).

The prevalence of BPSD in both community and clinical settings is very high. In community-dwelling patients with dementia, more than 80% exhibit some BPSD from the onset of cognitive impairment, with apathy (45.3%), depression (43.6%), and agitation/aggression (40.1%) showing the highest cumulative prevalence (Lyketsos et al. 2002). For up to 60% of these patients, the level of BPSD will be in the clinically significant range (Lyketsos et al. 2002). The prevalence of clinically significant BPSD rises more than 80% for residents in nursing homes (Brodaty et al. 2001, Margallo-Lana et al. 2001, Pitkälä et al. 2004, Zuidema et al. 2007). Prevalence estimates for BPSD vary widely because of the heterogeneity of patients populations studied in terms of settings and type of dementia and the different definitions used for BPSD.

Psychotic symptoms develop in about half (30-60%) of patients with Alzheimer’s disease during the course of their dementia (Zayas and Grossberg 1998, Jeste and Finkel 2000, Ballard et al. 2001, Brodaty et al. 2001, Paulsen et al. 2000, Wilson et al. 2000). Delusions and hallucinations are prevalent in patients with dementia in 12-49% and 5-39% respectively (Wagner et al. 1995, Margallo-Lana et al. 2001, Pitkälä et al. 2004, Zuidema et al. 2007). Psychotic symptoms in dementia are variable, but may be persistent, with lasting symptoms present in 39-62% after 3 months and in 43-57% after 1 year (Schneider and Dagerman 2004). Psychotic symptoms have a clinical impact because psychotic symptoms in dementia may impair functional ability (Schneider et al. 2003) and
predict earlier institutionalization (Gonzalez-Salvador et al. 1999, Lopez et al. 1999, Pang et al. 2002).

Most of these symptoms and behaviours do not occur in isolation but tend to occur together in clusters or syndromes. For example, delusions have been associated with agitation, aggression and insomnia (Lachs et al. 1992, Gormley et al. 1998), while depression has been associated with psychotic symptoms (Lyketsos et al. 1999).

Moreover, the development of BPSD is a major risk for caregiver burden (Coen et al. 1997, Gonzalez-Salvador et al. 1999) and may be more important in this regard than are cognitive deficits of the disease process (Steele et al. 1990). The development of BPSD is also associated with a poorer prognosis, a more rapid rate of cognitive decline, illness progression (Paulsen et al. 2000), greater impairment in activities of daily living (Lyketsos et al. 1997) and impaired quality of life (Gonzalez-Salvador et al. 2000). In addition, it has been shown that BPSD adds significantly to the direct and indirect costs of care (Jönsson et al. 2006).

1.3 Antipsychotic medications

1.3.1 Definitions of antipsychotic medications

Antipsychotic medications are the mainstay of treatment for psychotic illnesses. Antipsychotic medications are broadly derived into conventional or typical neuroleptics and newer or atypical antipsychotics depending on their pharmacological profile. Conventional neuroleptics include e.g. haloperidol, chlorpromazine, thioridazine, block dopamine-D₂ receptors, and atypical antipsychotics e.g. clozapine, risperidone, olanzapine and quetiapine block both dopamine –D₂ and serotonin-5HT₂ receptors.

Atypical antipsychotics have suggested to work more effectively than conventional neuroleptics for treating the negative symptoms of schizophrenia.
and for treating patients who show treatment-resistance and do not respond to conventional neuroleptics (Salokangas et al. 2001).

1.3.2 Indications for using antipsychotics in older patients

According to the Expert Consensus Guidelines (US 2004), antipsychotics in the elderly are indicated for disorders with psychotic symptoms, that is schizophrenia, mania with psychosis, agitated dementia with delusions, psychotic major depression and delusional disorder (Alexopoulos et al. 2004). Experts have suggested that antipsychotics are sometimes indicated for mania without psychosis, delirium, and agitated dementia without delusions. By contrast, they do not recommend antipsychotics for irritability and hostility in the absence of a major psychiatric syndrome, non-psychotic major depression without severe anxiety, generalized anxiety disorder, panic disorder, hypochondrias or insomnia/sleep disturbance without a major psychiatric syndrome, severe nausea and vomiting, neuropathic pain or motion sickness. For patients with dementia and elderly patients with schizophrenia atypical antipsychotics are recommended (Salokangas et al. 2001, Alexopoulos et al. 2004, Lehman et al. 2004). Most “good practice” guidelines recommend non-pharmacological interventions as the first-line treatment approach for behavioural and psychiatric symptoms in people with dementia (Lawlor 2004, Pirttilä et al. 2006).

These guidelines also recommend limiting antipsychotic treatment of people with dementia to the short-term treatment (up to three months) of severe neuropsychiatric symptoms associated with severe distress or serious risk (Alexopoulos et al. 2004, Ballard and Howard 2006). American experts recommend a duration of antipsychotic treatment after response before trying to discontinue the antipsychotic in agitated dementia with and without delusions – tapering should start at 3-6 months to determine the lowest effective maintenance dose. In the same guidelines they recommend that the lowest effective dose of antipsychotics may continue indefinitely time among older patients with schizophrenia (Alexopoulos et al. 2004).
1.3.3 Use of antipsychotic medications among elderly people

1.3.3.1 Use of antipsychotics in the home-dwelling elderly

Epidemiological studies in general population from different countries have shown the use of antipsychotics to vary from 1.0% to 1.4% (Alonso et al. 2004, Percudani et al. 2005, Trifiro et al. 2005) and to increase progressively with increasing age (Percudani et al. 2005, Trifiro et al. 2005). The proportion of patients taking antipsychotics among the home-dwelling elderly has ranged 3-11% in Europe (Giron et al. 2001, Linjakumpu et al. 2002, Fahey et al. 2003, Hartikainen et al. 2003b, Linden et al. 2004, Rapoport et al. 2005) being as low as 1.8% rates in the United States (Aparasu et al. 2003).

The use of antipsychotics has been found to be six times more common in demented individuals than among non-demented subjects (Giron et al. 2001, Hartikainen et al. 2003b). The associations between the use of antipsychotics and the level of cognitive functioning as well as the activities of daily living in elderly patients have been ether negative or positive (Sorensen et al. 2001, Craig et al. 2003, Lindesay et al. 2003). There are some reports of antipsychotic medication use in nondemented elderly people without any clear clinical indications such as psychotic symptoms (Hartikainen et al. 2003b).

1.3.3.2 Use of antipsychotics in long-term institutional care

Surveys have documented a high use of antipsychotic medication (15-42%) among elderly people in long-term institutional care (Liperoti et al. 2003, Hosia-Randell and Pitkälä 2005). Studies on antipsychotic use in long-term institutional care are presented in Table 1.
Table 1. Prevalence of antipsychotic use in long-term care facilities in various countries since 2000.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Age (years)</th>
<th>Country</th>
<th>Mean % of residents taking antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furniss L et al. (2000)</td>
<td>330</td>
<td></td>
<td>UK</td>
<td>28</td>
</tr>
<tr>
<td>Van Dijk KN et al. (2000)</td>
<td>2355</td>
<td>65+</td>
<td>The Netherlands</td>
<td>35</td>
</tr>
<tr>
<td>Draper B et al. (2001)</td>
<td>647</td>
<td>24-111</td>
<td>Australia</td>
<td>21.3</td>
</tr>
<tr>
<td>Margallo-Lana M et al. (2001)</td>
<td>231</td>
<td>-</td>
<td>UK</td>
<td>41</td>
</tr>
<tr>
<td>Sorensen L et al. (2001)</td>
<td>288</td>
<td>65+</td>
<td>Denmark</td>
<td>21</td>
</tr>
<tr>
<td>Ruths S et al. (2001)</td>
<td>1552</td>
<td>39-111</td>
<td>Norway</td>
<td>23</td>
</tr>
<tr>
<td>Osborne CA et al. (2002)</td>
<td>934</td>
<td>65+</td>
<td>UK</td>
<td>24.5</td>
</tr>
<tr>
<td>Macdonald A et al. (2002)</td>
<td>445</td>
<td>65+</td>
<td>UK</td>
<td>15.3</td>
</tr>
<tr>
<td>Fahey T et al. (2003)</td>
<td>172</td>
<td>65+</td>
<td>UK</td>
<td>28</td>
</tr>
<tr>
<td>Holmquist I et al. (2003)</td>
<td>225</td>
<td>65+</td>
<td>Sweden</td>
<td>16</td>
</tr>
<tr>
<td>Liperoti R et al. (2003)</td>
<td>139 714</td>
<td>65+</td>
<td>USA</td>
<td>15</td>
</tr>
<tr>
<td>Lindenay J et al. (2003)</td>
<td>4226</td>
<td>65+</td>
<td>UK</td>
<td>21.9</td>
</tr>
<tr>
<td>Nyaarda HA et al. (2003)</td>
<td>1027</td>
<td>65+</td>
<td>Norway</td>
<td>21.9</td>
</tr>
<tr>
<td>Bronskill SE et al. (2004)</td>
<td>19 870</td>
<td>65+</td>
<td>Canada</td>
<td>24</td>
</tr>
<tr>
<td>Briesacher BA et al. (2005)</td>
<td>1096</td>
<td>65+</td>
<td>United States</td>
<td>27.6</td>
</tr>
<tr>
<td>Hosia-Randell H and Piikilä K (2005)</td>
<td>1987</td>
<td>65+</td>
<td>Finland</td>
<td>42.6</td>
</tr>
<tr>
<td>Champoux N et al. (2005)</td>
<td>2460</td>
<td>65+</td>
<td>Canada</td>
<td>25.2</td>
</tr>
<tr>
<td>Snowdon J et al. (2005)</td>
<td>2302</td>
<td>-</td>
<td>Australia</td>
<td>25.1</td>
</tr>
<tr>
<td>Rochon PA et al. (2007)</td>
<td>47 322</td>
<td>66+</td>
<td>Canada</td>
<td>32.4</td>
</tr>
</tbody>
</table>

1.3.3.3 Use of antipsychotics among the oldest old

Only a few studies have reported on the overall prevalence of antipsychotic medication use in the oldest old (85 years and older). In a Swedish study the use of antipsychotics among individuals 85 years and older has been reported to be 10.4% among those living in institutions and 4.8% living in the community (Skoog et al. 1993). Of those oldest-old elderly with psychotic disorders only 8.7% received antipsychotics (Skoog et al. 1993). In another study among individuals at 85 years of age with psychotic symptoms (hallucinations or delusions) one fifth were prescribed neuroleptics. In addition those oldest-old with no psychotic symptoms 5.1% were taking antipsychotics (Östling and Skoog 2002).
1.3.3.4 Use of antipsychotics in older patients with schizophrenia

Antipsychotic medications are the key role of treatment for schizophrenia. It has been reported that in Australian nursing homes 6.1% of patients had been diagnosed as having schizophrenia and to 81% of them were prescribed antipsychotic medications (Snowdon et al. 2005). Some earlier studies on older schizophrenic residents in nursing homes have shown that 15-19% were not receiving any antipsychotic medication (Bowie et al. 2001, Snowdon et al. 2005).

Elderly patients with schizophrenia are more sensitive to the adverse effects of antipsychotic medications than younger patients and they are also more likely to be taking other medications that may increase the likelihood of adverse drug interactions. It is challenging for the clinician to decide whether or not to continue antipsychotic treatment: continued use of the drug is associated with serious adverse effects such as tardive dyskinesia (TD) and metabolic syndrome while discontinuing the drug can bring about a schizophrenic relapse.

1.3.3.5 Use of antipsychotics among patients with dementia

The behavioural and psychological symptoms of dementia (BPSD) are very common and antipsychotic medications are widely used to control these symptoms. Surveys have documented a frequent use of antipsychotics (23-48%) among patients with dementia in nursing homes (Lindsey et al. 2003, Nygaard et al. 2003, Hosia-Randell and Pitkälä 2005, Kim and Whall 2006, Raivio et al. 2007). Pitkälä et al. have stated that of the patients with dementia in acute geriatric wards and nursing homes in Helsinki, 42% were on conventional antipsychotics and 13% were on atypical antipsychotics (Pitkälä et al. 2004). In contrast to schizophrenia, no medications have been specifically approved for the psychotic or behavioural manifestations of dementia. Studies on randomized controlled trials (RCT) and meta-analysis of RCTs antipsychotic use in patients with dementia are presented in Table 2.
### Table 2. Principal studies of typical and atypical antipsychotics: study characteristics.

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Patients</th>
<th>Study Design</th>
<th>Length of Study</th>
<th>Drug</th>
<th>Patient residence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stotsky, 1984</td>
<td>358</td>
<td>RCT</td>
<td>4 wk</td>
<td>Thioridazine</td>
<td>Nursing home and hospital</td>
</tr>
<tr>
<td>Schneider et al. 1990</td>
<td>252</td>
<td>Meta-analysis of 7 RCTs</td>
<td>3-8 wk</td>
<td>Haloperidol, thioridazine, thiothixene clorpromazine, trifluoperazine, acetophenazine</td>
<td>Mostly nursing home</td>
</tr>
<tr>
<td>Lonergan et al. 2002</td>
<td>573</td>
<td>Meta-analysis of 5 RCTs</td>
<td>3-16 wk</td>
<td>Haloperidol</td>
<td>Community and nursing home</td>
</tr>
<tr>
<td><strong>Atypical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Deyn et al. 1999</td>
<td>229</td>
<td>RCT</td>
<td>12 wk</td>
<td>Risperidone</td>
<td>Nursing home</td>
</tr>
<tr>
<td>Katz et al. 1999</td>
<td>625</td>
<td>RCT</td>
<td>12 wk</td>
<td>Risperidone</td>
<td>Nursing home</td>
</tr>
<tr>
<td>Street et al. 2000</td>
<td>206</td>
<td>RCT</td>
<td>6 wk</td>
<td>Olanzapine</td>
<td>Nursing home</td>
</tr>
<tr>
<td>Clark rt al. 2001</td>
<td>206</td>
<td>RCT</td>
<td>6 wk</td>
<td>Olanzapine</td>
<td>Nursing home</td>
</tr>
<tr>
<td>Brodaty et al. 2003</td>
<td>345</td>
<td>RCT</td>
<td>12 wk</td>
<td>Risperidone</td>
<td>Nursing home</td>
</tr>
<tr>
<td>De Deyn et al. 2004</td>
<td>652</td>
<td>RCT</td>
<td>10 wk</td>
<td>Olanzapine</td>
<td>Nursing home</td>
</tr>
<tr>
<td>De Deyn et al. 2005</td>
<td>208</td>
<td>RCT</td>
<td>10 wk</td>
<td>Aripiprazole</td>
<td>Community living</td>
</tr>
<tr>
<td>Zhong et al. 2007</td>
<td>333</td>
<td>RCT</td>
<td>10 wk</td>
<td>Quetiapine</td>
<td>Mostly nursing home</td>
</tr>
</tbody>
</table>

RCT = randomized controlled trial

### 1.3.4 Adverse effects of antipsychotics

The adverse effects of antipsychotic medications, which can cause difficulties in any patient population, are particularly troublesome in elderly patients, who experience many age-related changes that may exacerbate the adverse effects of medication (Masand 2000). Alterations in pharmacokinetics and pharmacodynamics, however, complicate pharmacotherapy in older patients. Moreover, elderly patients frequently have comorbid illnesses, such as cardiovascular disease and dementia, and take multiple medications. In comparison with younger patients, geriatric patients show an increased
variability of response and an increased sensitivity to medication (Salzman 1990, Avorn et al. 1992).

Adverse effects of particular concern in the older individuals include anticholinergic toxicity/reactions (which can lead to urinary retention, constipation, dry mouth, worsening of glaucoma, and confusion), neurological symptoms [e.g. extrapyramidal symptoms (EPS) and tardive dyskinesia (TD)], orthostatic hypotension, cardiac conduction disturbances (e.g. corrected QT interval prolongation), reduced bone mineral density, sedation, and cognitive slowing (Masand 2000). In a recent systematic review antipsychotic drug as a group seemed to be associated with an increased risk of falling (Hartikainen et al. 2007). Both conventional and atypical antipsychotics have been reported to increase the risk of fractures (Takkouche et al. 2007) and to increase the risk of hospitalization for femur fracture in institutionalized elderly patients (Liperoti et al. 2007). In the 1990s, the newer atypical antipsychotic therapies were introduced. These agents were thought to be safer than the earlier conventional antipsychotic therapy, leading to widespread use of atypical agents in nursing homes (Bronskill et al. 2004, Briesacher et al. 2005).

1.3.4.1 Neurological

Extrapyramidal symptoms include parkinsonism, akathisia and dystonia. Older individuals are particularly prone to develop parkinsonism (Wilson and MacLennan 1989), which is a frequent neuroleptic adverse effect that has a triad of symptoms: resting tremor, rigidity, and bradykinesia. Akathisia is characterized by increased restlessness, psychomotor activity, and agitation, an inability to sit still.

Tardive dyskinesia is a movement disorder characterized by involuntary, irregular or repetitive abnormal movements more frequently observed in the peribuccal, periocular areas, but also perceptible in the hands, legs, and feet. Tardive dyskinesia, one of the most serious adverse effects of treatment with conventional antipsychotics, is 5 to 6 times more prevalent in older than in younger adults (Caligiuri et al. 1999, Jeste et al. 1999). In addition to age, other
risk factors for tardive dyskinesia include early EPS, cumulative amounts of antipsychotics, duration of antipsychotics treatment, and history of alcohol abuse and/or dependence (Jeste et al. 1999, Jeste et al. 2000). Severe TD can be especially troublesome to the elderly, because orofacial TD can impair eating and swallowing and also result in dental problems that may progress to mouth infection and/or unintelligible speech. The gait disturbances of patients with severe limbtruncal dyskinesia may lead to falls and injuries (Jeste et al. 2000).

Although atypical antipsychotics have lower ability for EPS than conventional antipsychotics, atypical antipsychotics have been reported to be associated with parkinsonism (Rochon et al. 2005), other movement disorders (Lee et al. 2005) and are likely to also have low potential for tardive dyskinesia (Jeste et al. 2000), despite the paucity of controlled studies in elderly people. However, in younger patients with schizophrenia the prevalences for antipsychotic-induced movement disorders in schizophrenia patients are usually in the range 29% to 74% (Van Harten et al. 1996, Muscettola et al. 1999, Modestin et al. 2000). In an Estonian patient sample of 99 chronic schizophrenia patients in a state nursing home aged 18-65 years (mean age 49.7 years), nearly two-thirds suffered from a antipsychotic-induced movement disorder (Janno et al. 2004). The prevalence of antipsychotic-induced movement disorders in the patients receiving clozapine was 35% and in those receiving conventional antipsychotics 68%.

1.3.4.2 Metabolic
Antipsychotic medication may contribute to the development of metabolic syndrome by causing weight gain (Allison et al. 1999, Koponen et al. 2002), lipid abnormalities (Koro et al. 2002, Casey 2004) and abnormalities in glucose regulation (Haupt and Newcomer 2002, Leslie and Rosenheck 2004). In a Finnish study Suvisaari et al. showed that typical antipsychotic medications were associated with high prevalence of metabolic syndrome (Suvisaari et al. 2007). However, the prevalence among those aged 55 and over did not differ from that in the general population. A recent meta-analysis showed that clozapine and
olanzapine were consistently associated with increased risk for diabetes, in contrast to risperidone and quetiapine treatment (Scheen and De Hert 2007). The estimate for new-onset diabetes mellitus in the 10-year naturalistic study in clozapine-treated patients has been reported to be approximately 43% (Henderson et al. 2005).

In elderly patients with dementia atypical antipsychotics have been not shown to be associated with weight gain, glucose intolerance, diabetes or hyperlipidaemia (Gurevitz et al. 2004, Herrmann and Lanctot 2006). In the Clinical Antipsychotic Trial of Intervention Effectiveness study for Alzheimer's disease (CATIE-AD), patients with AD gained weight with olanzapine and risperidone and lost weight with placebo (Schneider et al. 2006). Schneider et al. have suggested that the possibility that antipsychotics cause metabolic syndrome in the elderly requires further investigation (Schneider et al. 2006).

1.3.4.3 Cardiovascular

The metabolic syndrome (obesity, dyslipidemia, impaired glucose tolerance and hypertension) has been shown to be an important risk factor in the development of both type 2 diabetes mellitus and cardiovascular disease (the combination of cerebrovascular disease, coronary heart disease, and peripheral vascular disease). Cardiovascular disease is the leading cause of death in patients with schizophrenia (Brown 1997).

Some antipsychotics have been suspected to of causing increased risk of ventricular arrhythmias and sudden cardiac death (Shader and Greenblatt 1998, Straus et al. 2004). Users of antipsychotics are over-presented in registries of sudden death (Mehtonen et al. 1991). Recently, epidemiological studies have reported a direct relationship between conventional antipsychotics and the risk of sudden death (Ray et al. 2001, Hennessy et al. 2002). A QTc interval > 500 ms (as measured in ECG) increases the risk of potentially lethal arrhythmias such as torsades pointes and sudden death (Roden 2004). Both typical and atypical antipsychotics have been associated with cardiac conduction abnormalities, with
the magnitude of QTc prolongation being slightly smaller with atypical antipsychotics (Herrmann and Lanctot 2006). A large case-controlled study of patients >65 years of age using antipsychotics examined the risk of hospitalisation for ventricular arrhythmias or cardiac arrest (Liperoti et al. 2005). There was no increase risk associated with treatment with atypical antipsychotics compared with no use, while treatment with typical antipsychotics increased the risk by 86% compared with no use and more than doubled the risk compared with treatment with atypical antipsychotics. However, it has been reported that antipsychotic-treated elderly psychiatric inpatients did not have a higher rate of cardiac morbidity compared to patients who had not received antipsychotics (Barak et al. 2007).

In 2005, responding to several studies (De Deyn et al. 1999, Katz et al. 1999, Street et al. 2000, Brodaty et al. 2003, De Deyn et al. 2004), the Food and Drug Administration (FDA) and European Agency for the Evaluation of Medicinal Products (EMEA) issued a warning regarding atypical antipsychotic medications, noting that the drugs might increase the risk of cerebrovascular adverse events (CVAEs) in elderly patients with dementia-related behaviour disturbances. There is limited evidence regarding the long-term safety of atypical antipsychotics in elderly patients with dementia. The potential for increased risk of stroke and mortality is a serious concern (Carson et al. 2006). Conventional antipsychotics have been shown in a meta-analysis to have modest efficacy in BPSD (Schneider et al. 1990), but their contribution to CVAEs has not so far been examined.

1.3.4.4 Mortality

Atypical antipsychotics have also been linked to death among elderly patients with dementia (Schneider et al. 2005, Wang et al. 2005). In a recent study Gill et al. stated that the use of atypical antipsychotics was associated with an increased risk for death compared with non-use among older adults with dementia (Gill et al. 2007). However, the risk for death may be greater with conventional antipsychotics than with atypical antipsychotics. In a population-based study in
Canada the risk of death associated with conventional antipsychotic medications was comparable to the risk of death associated with atypical antipsychotics (Schneeweiss et al. 2007). In a Finnish study in patients with dementia Raivio et al. stated that neither the use of atypical antipsychotics nor the use of conventional neuroleptics increased mortality. The use of restrain doubled the mortality (Raivio et al. 2007).
2 AIMS OF THE STUDY

The general purpose of the present study was to investigate the prevalence of antipsychotic use among older persons in long-term institutional and home care.

The specific aims of the present study were:

1 To investigate the use of antipsychotic medications, change over time and associated factors in a three-year follow-up among residents in long-term institutional care in 2001-2003 (Study I).

The main question was: Is there any change of the prevalence of antipsychotic use during the study period and which factors would explain the change?

2 To investigate the use of antipsychotic medications and associated factors among nonagenarian residents in long-term institutional care in 2003 (Study II).

The main question was: What is the prevalence of antipsychotic use among nonagenarian institution residents and which factors associate such use?

3 To investigate the factors associated with non-use of antipsychotics among older residents with schizophrenia in long-term institutional care in 2006 (Study III).

The main question was: What is the prevalence of older residents with schizophrenia not having any antipsychotics at the time of the data gathering and which factors are associated with non-use of antipsychotics?

4 To investigate the use of antipsychotic medications and factors associated with such use in elderly patients in home care in Finland in 2004 (Study IV).

The main question was: What is the prevalence of antipsychotic use among home care patients in Finland and which factors are associated with such use?

5 To investigate the use of antipsychotic medications and associated factors in nine European countries in 2001-2002 (Study V).

The main question was: Is there any variation in antipsychotic use among home care patients in nine European countries and which factors contribute to such variation?
3 MATERIALS AND METHODS

Multidimensional functional assessment is the basis of individualized care. It is especially important in the care of elderly, with complex symptoms and often with cognitive impairment. An assessment instrument for elderly people used in this study is the Resident Assessment Instrument (RAI), which was developed in the United States in the late 1980s to improve individual care planning and the quality of care in nursing homes (Morris et al. 1990). In addition, it was designed to estimate the need for resources and develop the payment system. The RAI consists of three basic components: 1. a questionnaire (Minimum Data Set, MDS), 2. a help tool for care planning (Residents’ Assessments Protocol, RAPs) and 3. a user manual. Since 1990, interRAI (www.interrai.org), a non-profit international research organisation, has been copyright holder and developer of this system. The interRAI assessment instruments have been introduced in over 30 countries.

The “Benchmarking and the Implementation of the RAI System in Elderly Care” project was launched in Finland in 2000 on the initiative of STAKES (National Research and Development Centre for Welfare and Health) and the Chydenius Institute in collaboration with the staff of private and public service housing facilities and residential homes and with public health centre wards (Noro et al. 2005).

3.1 Materials

The population data in the various studies (I-V) were drawn from the national RAI database located in STAKES for the period 2001 to 2006.
Every unit in the RAI database joined on a voluntary basis. The recruitment process was through web-page announcements by STAKES and the common interest of the units to improve their caring patterns. Only long-term elderly care units were included in the data. Long-term institutional care includes only hospital-based long-term care units (non-acute ward) and residential homes. All types of institutional setting were included: small and large, urban and rural.

In 2001 there were 16 hospital-based long-term institutions and 25 residential homes that comprised approximately 17% of long-term institutional care for the elderly. In 2006, the data consisted of a total of 24 hospital-based long-term care institutions (103 wards) and 52 residential homes (239 wards). Units in 29 municipalities located in different parts of Finland with 7611 resident assessments represent approximately a crude third of all residents in long-term institutional care. During the study period the same long-term care units remained, only a small proportion was different. The data of each study were derived from the latest available complete national database.

Home care patients in the present study include only regular home-care clients who received home nursing or both home nursing and home help services and also had a valid service and care plan. For each of the home care units, each patient who had one assessment was included in the dataset. In order to present reliable outcomes from home care, assisted living was excluded. In addition, the data were derived only from areas where all or almost all patients had been assessed.

### 3.1.1 Long-term institutional care

The only exclusion criterion was age ≤65 years, except that the Study II exclusion criterion was ≤90 years. Every person residing in the unit was assessed. Since assessments were part of the care process there were no resident refusals. For each resident only one assessment was included in the dataset. In Finland the semi-annual data collection was adapted as optimal to monitor changes in caring patterns.
3.1.1.1 Three-year follow-up (I)

The population data were derived from 16 hospital-based long-term care institutions (55 wards) and 25 residential homes (102 wards) in 14 municipalities. The data were derived from three different timepoints representing the same services. Firstly, the units in the database during the period 1 July to 31 December, 2001 were identified and the individual assessments for relevant parts were included in the analysis. Secondly the same units with their current assessments were identified during the periods 1 July to 31 December, 2002 and 2003. In the study, instead of residents, the units were followed with varying numbers of individuals in each year.

3.1.1.2 Nonagenarians (II)

The population data were derived from 23 hospital-based long-term care institutions (69 wards) and 43 residential homes (190 wards) in 26 municipalities. Every resident aged 90 or older was included in the extracted set. The extracted dataset covered the period from 1 January to 30 June 2003.

3.1.1.3 Residents with schizophrenia (III)

The population data were derived from 7,611 total assessments, of which 2,629 (34.5 %) were hospital-based long-term care institutions (103 wards) and 4,982 (65.5%) residential homes (239 wards) in 29 municipalities. Every resident with a diagnosis of schizophrenia aged 65 years or more was included in the extracted set. Data from all residents with a diagnosis of schizophrenia were gathered and these data comprised 53 hospital-based long-term care wards and 108 residential home wards in 22 municipalities. The extracted data set covered the period from 1 January to 30 June 2006.

3.1.2 Home care

The population data were derived from home care units caring for patients in a certain geographical area in Finland and also in several European countries. The
exclusion criterion was aged <65 years. In addition, those who were no longer resident in their original homes or temporarily residing in institutional settings at the time of the assessment were excluded.

3.1.2.1 Home care in Finland (IV)

The data were derived from 5 home care units in 4 municipalities located in different parts of Finland. The extracted dataset covered the period from 1 July to 31 December in 2004. The data were derived from the latest available full database.

3.1.2.2 Home care in nine European countries (V)

The study population consisted of a random sample of elderly people admitted to the home care programmes in 11 different European Home Health Agencies between 2001 and 2003 and who participated in the The Aged in Home Care (AdHOC) project, under the sponsorship of the European Union (Carpenter et al. 2004). The AdHOC project analysed the structure and organisational characteristics of home care services in 11 European countries along with the clinical and functional characteristics of their patients.

The population data of Study V were derived from AdHOC Study during the September 2001 – January 2002 11 European countries, from which the data from two countries (Sweden and France) were excluded due to lack of data on medication or inconsistent recording of antipsychotics. The AdHOC Study was designed to compare outcomes of different models of community care using a structured comparison of services and a comprehensive standardised assessment instrument. The samples in each of the countries were gathered from identified municipalities providing formal home care services and a population considered representative of the country’s urban area was selected. The participating home care patients were randomly selected from home care agencies serving a certain geographical area. This register led to the creation of a cross-national population-based data set in nine European countries (the Czech Republic, Denmark,
Finland, Germany, Iceland, Italy, the Netherlands, Norway and the United Kingdom).

3.2 Methods

The data collection method was RAI with its care assessment component known as the Minimum Data Set (MDS) for Long-Term Care Facilities (LTCF) and Home Care (HC).

3.2.1 Minimum Data Set (MDS)

The MDS is a standardized primary screening and comprehensive assessment tool for the health care status of residents in nursing homes (Hawes et al. 1995). It was introduced in the United States in response to the United States Congress in the Omnibus Budget Reconciliation Act of 1987. It consists of 18 sections, with items including defined codes concerning physical, psychological and psychosocial functioning. All parts of the RAI are described in the Training Manual (Morris et al. 1995), which gives additional information and precise instructions on how to carry out the assessment.

The MDS was intended for clinical, quality assurance and research purposes. The MDS has been tested for validity and reliability in the US (Hawes et al. 1995) and in other countries such as Sweden and Denmark (Sgadari et al. 1997) and also in Finland (Björkgren et al. 1999). The use of the MDS: the instrument is intended to facilitate communications across disciplines, to inquire about the patient’s status over a relevant time period, e.g. seven or 90 days, and to use multiple sources of information from the patient himself/herself, relatives, staff and from medical and nursing records. The assessment is recommended to be originated by nurse, based on interactions between patient and staff in daily contacts, with conversation and the observations of the patient, and performed in co-operation between different professions. On average the assessment takes 60-90 minutes to complete, depending on factors such as the complexity of the patients needs and ability to communicate. The personnel conducting the MDS
assessments on each of the wards and home care units had received a minimum of 20 hours’ standardized education that included assessments step-by-step according to the training manual (Morris et al. 1995) and the use of software (Boholm 2005).

In addition to interviews with and observations of patients, data were collected from the medical and nursing documents, and from the patients’ caregivers including the home care professionals. The diagnoses (ICD-10) were taken from the medical records as recorded by treating physicians (mostly GPs). Due to the high prevalence of dementia in long-term care facilities and in order to ascertain the prevalence of the psychiatric diseases not linked with dementia, the psychiatric diagnoses available in the database were reclassified into a hierarchical order as follows (Studies I-III): 1) all residents with any diagnosed form of dementia, 2) residents without dementia and with schizophrenia, 3) residents without dementia and without schizophrenia but with diagnoses of mood disorders and 4) residents without the above diagnoses but with a diagnosis of anxiety. Medical diagnoses were noted if they were the subject of active treatment or monitoring or if they affected the patient’s current condition.

Information on drug use was collected for 7 days prior to the assessment and included the ACT codes (Anatomical and Therapeutic Chemical code) of antipsychotics N05A, anxiolytics N05B, antidepressants N06A (with the exception of lithium) and hypnotics N05C. Only regularly used prescription drugs were included in the analysis. In addition Studies IV-V included the name and ATC code, formulation, dosage, frequency and mode of administration. Apart from medications for dizziness and/or nausea and lithium, all medications with an ATC code of N05A were coded as antipsychotics. After that the antipsychotics were divided into two categories, conventional (chlorpromazine, chlorprotixene, fluphenazine, flupentixol, haloperidol, levomepromazine, melperone, perphenazine, periciazine, sulpiride, thioridazine, zuclopenthixol) and atypical (clozapine, olanzapine, quetiapine, risperidone). In addition, chlorpromazine equivalents of antipsychotics were calculated using a table as published by Schatzberg (Study IV).
3.2.1.1 Assessment system for the Long Term Care Facility

The first assessment system created by the members of interRAI was the Long Term Care Facility (LTCF). The interRAI LTCF was originally developed in 1988-90 under the US Health Care Financing Administration. The development of MDS/RAI was mandated by the 1987 Nursing Home Reform Law, which also required that it be implemented in all US nursing homes. The MDS-LTCF is a 6 page tool consisting of core screening and assessment items in the following areas: sociodemographic information, prior customary routine, cognition, communication/hearing, vision, mood and behaviour, psychosocial well-being, physical functioning and structural problems, bladder and bowel continence, disease diagnoses, health conditions, oral/nutritional status, dental status, skin condition, activity pursuits, medications, special treatments and procedures, and discharge potential. The condition is coded for whether present or not. The usability of the variables has been tested and validated (Casten et al. 1998, Lawton et al. 1998).

3.2.1.2 Assessment system for Home Care

The Home Care assessment system was developed in 1993-94 to provide a common language for assessing the health status and care needs of frail elderly and disabled individuals living in the community (www.interRAI.org). The system was designed to be comparable with the Long Term Care Facility system. The HC was designed to highlight issues to functioning and quality of life for community-residing individuals. It consists of the Minimum Data Set for Home Care (MDS-HC) and Client Assessment Protocols (CAPs).

The MDS-HC tool is a 5-page tool designed to collect standardized information on a broad range of domains critical to caring for individuals in the community, including items related to cognition; communication/hearing, vision, mood and behaviour, social functioning, informal support services, physical functioning, continence, disease diagnoses, health conditions, preventive health measures, nutrition/hydration, dental status, skin condition, environment/home safety, service utilization, medications and socio-demographic/background information.
The reliability and validity of the MDS-HC data elements and its embedded scales have been demonstrated through a series of on-going international studies (Landi et al. 2000, Morris et al. 1997). In addition to interviewing and observing the patients, data were collected from the medical and nursing documents, and from the patients’ caregivers including the home care professionals.

3.2.1.3 Scales

The Cognitive Performance Scale (CPS) was combined within the hierarchical seven-category from five of the RAI/MDS items from different sections MDS with the levels 0-6 (intact-very severe impairment) (Morris et al. 1994, Hartmaier et al. 1995). The CPS includes the RAI/MDS items: short-term memory, cognitive skills for daily decision-making, ability to be understood by others, self-performance in eating, and comatose. The CPS has been evaluated against two standard cognitive assessment tools, The Mini Mental State Examination (MMSE) (Folstein et al. 1975) and the Test for Severe Impairment (TSI) (Albert and Cohen 1992), with a high degree of reliability (Morris et al. 1994, Hartmaier et al. 1995, Paquay et al. 2007).

The Activities of Daily Living Hierarchy Scale (ADL) groups activities of daily living according the stage of the disablement process in which they occur. The ADL Hierarchy Scale ranges from 0 (low impairment) to 6 (total dependence) (Morris et al. 1999). The four items used to score the hierarchical ADL-scale (0-6) are personal hygiene, toileting, locomotion and eating. Early loss ADL`s (e.g. dressing) are assigned lower scores than late loss ADL`s (e.g., eating)

The Depression Rating Scale (DRS) was used to screen for depression in nursing home residents where at least 3 points refer to probability of depression (Burrows et al. 2000). The 7-item scale was derived from mood and behavioural items in the Minimum Data Set. The DRS validated against two interview-based criterion measures, the Hamilton Depression Rating Scale and the Cornell Scale for Depression in Dementia, both of which have been tested and validated in geriatric populations (Burrows et al. 2000). The DRS items are: 1. residents
made negative statements 2. persistent anger and irritability with self and others 3. expression of what appear to be unrealistic fears 4. repetitive health complaints 5. repetitive anxious complaints/concerns (non-health-related) 6. sad, pained, worried facial expressions 7. crying, tearfulness.

3.3 Statistical methods

In all studies the associations of the use of antipsychotics with selected explanatory variables were tested using chi-square tests for the dichotomous variables and t-tests for the continuous variables. Continuous variables were first categorized and then dichotomized to form 0 or 1 dummy variables. The associations between these variables and the use of antipsychotics were then tested using chi-square test. Statistically significant factors according to univariate tests were included one by one in the multiple logistic regression model to test the independently associated factors.

Specifics of different studies are given:

Study I. After identifying the significant associates of use of antipsychotics in 2001, these variables were entered into a multiple logistic regression model that represented 2001 only. The following step was to separately test this model using the same variables that provided significance in 2001, using data from 2002 and then data from 2003. R-square for variance explanation was recorded in each of the multiple logistic regression analyses. Finally, the interactions between the independent variables and time-points were tested for the whole population to identify the most potent predictors of use of antipsychotics (see e.g. Häkkinen et al. 1996, Häkkinen 2002). Changes over time (i.e. level of prevalence of antipsychotics use compared to 2001) were estimated in the multiple logistic regression model using data from all three time-points and creating dummy variables for each of the years and each of the predictors identified for use of antipsychotics, which thus allowed the monitoring of confounder adjusted changes. All the procedures were performed step by step.
Study II. In addition to existing variables a summary scale was formed in which the new dichotomous variables was 0 if no sign in any individual item of entities “sense of initiative/involvement” or “unsettled relationships” was found and 1 if any of them was present. These new variables were likewise first tested separately.

Study III. All associations in both dichotomous and continuous variables as well as multivariate analysis were calculated for non-use of antipsychotics.

Study IV. The significant dichotomous and continuous variables were also analysed in multivariate model separately within the groups of both atypical and conventional antipsychotics.

Study V. The site at which the frequency of antipsychotic use was lowest was used as a reference. After testing for the associations between chosen variables and total number of antipsychotics, the same tests (dichotomous, continuous and multivariate) were performed using typical and atypical antipsychotics separately as dependent variables.

p-values less than 0.05 were considered statistically significant. The data was analysed at STAKES and all statistical analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, North Carolina, USA).

3.2 Ethical considerations

The study was conducted according to the guidelines of the Declaration of Helsinki, and the Ethical Commitee of Tampere University Hospital. The STAKES Ethical Commitee and the Ministry of Social Welfare and Health have approved the RAI data collection.
4 RESULTS

4.1 Long-term institutional care (I, II, III)

4.1.1 Characteristics of residents

Sociodemographic and main clinical background data of the residents in Studies I-III are given in Table 3 and Table 4.

Table 3. Sociodemographic characteristics of residents in long-term institutional care according to Studies I-III.

<table>
<thead>
<tr>
<th></th>
<th>Three-year follow-up,</th>
<th>Three-year follow-up,</th>
<th>Three-year follow-up,</th>
<th>Nonagenarian residents,</th>
<th>Residents with schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2001 (I)</td>
<td>2002 (I)</td>
<td>2003 (I)</td>
<td>2003 (II)</td>
<td>2006 (III)</td>
</tr>
<tr>
<td>N</td>
<td>3662</td>
<td>3969</td>
<td>3867</td>
<td>1334</td>
<td>356</td>
</tr>
<tr>
<td>Mean age in years</td>
<td>82.9 ±7.74</td>
<td>83.0 ±7.56</td>
<td>83.1 ±7.69</td>
<td>92.9 ± 2.7</td>
<td>78.2 ± 7.5</td>
</tr>
<tr>
<td>Age group, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>16.0</td>
<td>14.9</td>
<td>14.7</td>
<td>-</td>
<td>32.9</td>
</tr>
<tr>
<td>75-84</td>
<td>38.6</td>
<td>39.6</td>
<td>39.1</td>
<td>-</td>
<td>46.9</td>
</tr>
<tr>
<td>85-94</td>
<td>40.0</td>
<td>40.5</td>
<td>40.8</td>
<td>76.0 (90-94 y)</td>
<td>13.2</td>
</tr>
<tr>
<td>95+</td>
<td>5.4</td>
<td>5.0</td>
<td>5.4</td>
<td>24.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>75.5</td>
<td>75.4</td>
<td>75.9</td>
<td>87.8</td>
<td>77.5</td>
</tr>
<tr>
<td>Previous mental health history</td>
<td>12.6</td>
<td>11.0</td>
<td>10.0</td>
<td>5.5</td>
<td>72.2</td>
</tr>
<tr>
<td>Arrived from a psychiatric hospital</td>
<td>4.9</td>
<td>4.2</td>
<td>3.6</td>
<td>1.5</td>
<td>23.9</td>
</tr>
</tbody>
</table>
Table 4. Clinical data of residents in long-term institutional care according to Study I-III.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Documented diagnoses, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any dementia</td>
<td>54.9</td>
<td>57.4</td>
<td>57.5</td>
<td>58.6</td>
<td>24.2</td>
</tr>
<tr>
<td>Schizophrenia (^a)</td>
<td>4.6</td>
<td>3.9</td>
<td>3.9</td>
<td>1.0</td>
<td>100(^1)</td>
</tr>
<tr>
<td>Depression (^b)</td>
<td>15.3</td>
<td>15.6</td>
<td>15.7</td>
<td>11.5</td>
<td>8.4(^1)</td>
</tr>
<tr>
<td>Anxiety disorder (^c)</td>
<td>2.2</td>
<td>2.4</td>
<td>2.0</td>
<td>2.2</td>
<td>2.5(^1)</td>
</tr>
<tr>
<td><strong>Psychiatric and behavioural symptoms, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delusions</td>
<td>10.4</td>
<td>10.6</td>
<td>10.5</td>
<td>9.5</td>
<td>37.4</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>14.7</td>
<td>14.4</td>
<td>14.4</td>
<td>12.8</td>
<td>40.5</td>
</tr>
<tr>
<td>Reason to suspect depression (DRS= 3+) (^5)</td>
<td>22.0</td>
<td>22.9</td>
<td>21.9</td>
<td>21.1</td>
<td>21.6</td>
</tr>
<tr>
<td>Wandering</td>
<td>18.0</td>
<td>19.0</td>
<td>18.4</td>
<td>15.1</td>
<td>17.4</td>
</tr>
<tr>
<td>Verbally abusive</td>
<td>21.3</td>
<td>20.2</td>
<td>19.2</td>
<td>14.8</td>
<td>35.7</td>
</tr>
<tr>
<td>Physically abusive</td>
<td>11.6</td>
<td>11.6</td>
<td>11.3</td>
<td>9.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Socially disruptive</td>
<td>22.9</td>
<td>22.4</td>
<td>21.9</td>
<td>20.7</td>
<td>36.8</td>
</tr>
<tr>
<td>Resists care</td>
<td>30.0</td>
<td>30.5</td>
<td>30.0</td>
<td>30.7</td>
<td>43.3</td>
</tr>
<tr>
<td>Recurring anxious complaints</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>21.9</td>
<td>27.5</td>
</tr>
<tr>
<td>Recurring physical movements</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>28.9</td>
<td>35.7</td>
</tr>
<tr>
<td><strong>Cognition and physical functions, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPS (^#) 0</td>
<td>9.1</td>
<td>8.1</td>
<td>7.1</td>
<td>8.8</td>
<td>6.2</td>
</tr>
<tr>
<td>CPS 1-2</td>
<td>21.0</td>
<td>18.9</td>
<td>19.4</td>
<td>19.5</td>
<td>32.3</td>
</tr>
<tr>
<td>CPS 3-6</td>
<td>69.9</td>
<td>72.0</td>
<td>73.5</td>
<td>71.4</td>
<td>61.5</td>
</tr>
<tr>
<td>ADL (^##) 0</td>
<td>7.2</td>
<td>8.1</td>
<td>7.1</td>
<td>6.2</td>
<td>7.9</td>
</tr>
<tr>
<td>ADL 1-2</td>
<td>18.1</td>
<td>18.9</td>
<td>19.4</td>
<td>15.2</td>
<td>26.4</td>
</tr>
<tr>
<td>ADL 3-6</td>
<td>74.7</td>
<td>73.0</td>
<td>73.5</td>
<td>78.6</td>
<td>65.7</td>
</tr>
<tr>
<td><strong>Psychotropic medication, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>41.6</td>
<td>40.4</td>
<td>38.6</td>
<td>29.5</td>
<td>81.5</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>41.6</td>
<td>42.4</td>
<td>41.5</td>
<td>33.8</td>
<td>27.3</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>35.0</td>
<td>34.6</td>
<td>32.8</td>
<td>26.4</td>
<td>46.6</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>41.0</td>
<td>37.5</td>
<td>33.2</td>
<td>33.7</td>
<td>21.9</td>
</tr>
</tbody>
</table>

\(^a\) without dementia, \(^b\) without dementia and schizophrenia, \(^c\) without dementia, schizophrenia and depression, \(^*\): Concomitant with schizophrenia, \(^\$\) DRS: Depression Rating Scale >3 indicates depression, \(^#\) CPS: Cognitive Performance Scale: 0 no cognitive impairment, 1-2 mild cognitive impairment, 3-6 moderate to severe cognitive impairment, \(^##\) ADL: Activities of Daily Living Scale: 0 no dependence on assistance with daily living, 1-2 mild degree of dependence on assistance with daily living, 3-6 moderate to severe degree of dependence on assistance with daily living.
4.1.2 Prevalence of antipsychotic use

The prevalence of antipsychotic use was 41.7% in 2001, 40.4% in 2002, and 38.6% in 2003 (I). However, the overall confounder-adjusted decrease in antipsychotic use was not statistically significant. The proportion of nonagenarian residents prescribed one or more antipsychotics was 29.5% of the study population in 2003 (II). The prevalence of antipsychotic use among older schizophrenia residents in 2006 was 81.5%, thus 18.5% of residents with schizophrenia were not on antipsychotic medication (III).

4.1.3 Multivariate results

In 2001-2003 the use of antipsychotics decreased with among residents who had wandering as a behavioural problem [odds ratio (OR) 0.79, 95%CI 0.63-0.99] and increased among residents with concomitant use of anxiolytic medications (OR 1.23, 95%CI 1.03-1.48) (I).

Factors independently associated with the use of antipsychotics among nonagenarian residents were: socially inappropriate or disruptive behavioural symptoms (OR 1.86, 95%CI 1.36-2.54), concomitant anxiolytic medication (OR 1.83, 95%CI 1.39-2.42), recurring anxious complaints (OR 1.61, 95%CI 1.17-2.22), recurring physical movements (OR 1.43, 95%CI 1.08-1.91) and unsettled relationships (OR 1.35, 95%CI 1.15-1.57) (II). A good sense of initiative or involvement were significantly less likely to be associated with antipsychotics (OR 0.86, 95%CI 0.80-0.94). There were no associations between any psychiatric diagnoses or symptoms and the use of antipsychotics.

Factors independently associated with non-use of antipsychotics among residents with schizophrenia were: severe degree of functional impairment (OR 3.21, 95%CI 1.61-6.42), severely impaired vision (OR 2.62, 95%CI 1.26-6.61), any diagnosis of dementia (OR 2.58, 95%CI 1.38-4.81) and severe underweight (OR 2.20, 95%CI 1.15-4.17) (III). There was a negative association between non-use of antipsychotics and a factor “had arrived from a psychiatric hospital” (OR 0.31, 95%CI 0.12-0.81).
4.2 Home care (IV, V)

4.2.1 Characteristics of patients

The sociodemographic and main clinical background data of the patients in Studies IV-V are given in Table 5.

4.2.2 Prevalence of antipsychotic use

The prevalence of antipsychotic use was 11.0% among home care patients in Finland in 2004 (IV). Of the home care patients in nine European countries (the Czech Republic, Denmark, Finland, Germany, Iceland, Italy, the Netherlands, Norway and the United Kingdom) 6.2% received antipsychotic medication (V). The prevalence of the use of one or more antipsychotics varied widely between study sites, ranging from 3.0% in Denmark to 12.4% in Finland.

4.2.3 Multivariate results

Factors independently associated with the use of antipsychotics in Finland were: any psychiatric diagnosis (OR 6.62, 95%CI 4.19-10.45), delusions (OR 4.19, 95%CI 2.22-7.90), parkinsonism (OR 3.08, 95%CI 1.07-8.87), not at ease interacting with others (OR 1.88, 95%CI 1.06-3.36), and moderate to severe cognitive impairment (OR 1.47, 95%CI 1.06-2.04) (IV). By contrast, patients 85 years and older were significantly less likely to be taking antipsychotics (OR 0.59, 95%CI 0.43-0.81). The use of atypical antipsychotic medication was associated in the logistic regression model with delusions (OR 4.05, 95%CI 2.01-8.17), parkinsonism (OR 3.66, 95%CI 1.10-12.19), any psychiatric diagnosis (OR 3.06, 95%CI 1.66-5.63), moderate to severe cognitive impairment (OR 2.0, 95%CI 1.32-3.03) and age 85 and older (OR 0.66, 95%CI 0.44-0.99).
Table 5. Sociodemographic characteristics and main clinical data of patients in home care according to Studies IV and V.

<table>
<thead>
<tr>
<th></th>
<th>Home care in Finland (IV)</th>
<th>Home care in nine European countries (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1106</td>
<td>3251</td>
</tr>
<tr>
<td>Mean age in years</td>
<td>81.2 (±6.9)</td>
<td>82.2 (±7.3)</td>
</tr>
<tr>
<td>Age group, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>15.8</td>
<td>17.7</td>
</tr>
<tr>
<td>75-84</td>
<td>51.5</td>
<td>44.8</td>
</tr>
<tr>
<td>85-94</td>
<td>31.0</td>
<td>38.1 (85+ y)</td>
</tr>
<tr>
<td>95+</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>74.4</td>
<td>74.4</td>
</tr>
<tr>
<td>Documented diagnoses, %</td>
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<td></td>
</tr>
<tr>
<td>Any dementia</td>
<td>17.5</td>
<td>12.3</td>
</tr>
<tr>
<td>Any psychiatric</td>
<td>13.1</td>
<td>13.2</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>2.0</td>
<td>4.9</td>
</tr>
<tr>
<td>Psychiatric and behavioural symptoms, %</td>
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<td></td>
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<tr>
<td>Delusions</td>
<td>5.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>3.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Reason to suspect depression (DRS= 3+)</td>
<td>17.5</td>
<td>16.1</td>
</tr>
<tr>
<td>Wandering</td>
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<td>0.8</td>
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<tr>
<td>Verbally abusive</td>
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<td>0.7</td>
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<tr>
<td>Physically abusive</td>
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<td>0.3</td>
</tr>
<tr>
<td>Socially disruptive</td>
<td>1.7</td>
<td>0.4</td>
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<tr>
<td>Resists care</td>
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<td>1.0</td>
</tr>
<tr>
<td>Not at ease interacting with others</td>
<td>9.6</td>
<td>11.6</td>
</tr>
<tr>
<td>Cognition and physical functions, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPS 0</td>
<td>40.8</td>
<td>53.2</td>
</tr>
<tr>
<td>CPS 1-2</td>
<td>47.3</td>
<td>28.6</td>
</tr>
<tr>
<td>CPS 3-6</td>
<td>11.8</td>
<td>18.2</td>
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<tr>
<td>ADL</td>
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<td></td>
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<tr>
<td>ADL 0</td>
<td>77.5</td>
<td>69.6</td>
</tr>
<tr>
<td>ADL 1-2</td>
<td>13.5</td>
<td>10.8</td>
</tr>
<tr>
<td>ADL 3-6</td>
<td>9.0</td>
<td>19.6</td>
</tr>
<tr>
<td>Psychotropic medication, %</td>
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<tr>
<td>Antipsychotics</td>
<td>11.0</td>
<td>6.2</td>
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<tr>
<td>Antidepressants</td>
<td>24.3</td>
<td>14.9</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>12.7</td>
<td>11.1</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>44.2</td>
<td>19.7</td>
</tr>
</tbody>
</table>

§ DRS: Depression Rating Scale ≥3 indicates depression, # CPS: Cognitive Performance Scale: 0 no cognitive impairment, 1-2 mild cognitive impairment, 3-6 moderate to severe cognitive impairment, ## ADL: Activities of Daily Living Scale: 0 no dependence on assistance with daily living, 1-2 mild degree of dependence on assistance with daily living, 3-6 moderate to severe degree of dependence on assistance with daily living.
However, the use of conventional antipsychotics was only associated with any psychiatric diagnosis (OR 8.88, 95%CI 5.05-15.61) and age 85 and older (OR 0.65, 95%CI 0.44-0.98) (see Study IV Table 2).

Factors independently associated with the use of antipsychotics in nine European countries were: delusions (OR 3.09, 95%CI 1.66-5.76), any diagnosis of dementia (OR 2.57, 95%CI 1.70-3.87), youngest age group (65-74 years) (OR 2.37, 95%CI 1.53-3.66), and hallucinations (OR 2.28, 95%CI 1.17-4.45). Concomitant use of anxiolytics (OR 2.32, 95%CI 1.58-3.41), hypnotics (OR 2.08, 95%CI 1.44-3.03) and antidepressants (OR 2.06, 95%CI 1.41-3.00) likewise signs of depression (OR 1.78, 95%CI 1.24-2.56), moderate to severe cognitive impairment (OR 1.30, 95%CI 1.12-1.51), and residing in Finland (OR 2.52, 95%CI 1.21-5.24) or Italy (OR 2.15, 95%CI 1.10-4.19) were associated with the use of antipsychotics (see Study V Table 3).

4.3 Summary of the results

Statistically significant findings of the different studies are listed in Table 6.
Table 6. Summary of final statistically significant findings.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Three-year follow-up in long-term institutional care, (I)</th>
<th>Nonagenarian residents in long-term institutional care, (II)</th>
<th>Residents with schizophrenia in long-term institutional care, (III)¹</th>
<th>Home care in Finland (IV)</th>
<th>Home care in nine European countries (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group 65-74</td>
<td></td>
<td></td>
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<tr>
<td>Age group 85+</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td></td>
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<td><strong>Diagnosis</strong></td>
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<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Any psychiatric</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Dementia</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Psychiatric and behavioural symptoms</strong></td>
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<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Socially disruptive</td>
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<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Delusions</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hallucinations</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Wandering</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recurring anxious complaints</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recurring physical movements</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Unsettled relationships</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sense of initiative/involvements</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Not at ease interacting with others</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td><strong>Concomitant psychotropics</strong></td>
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<td>Anxiolytic</td>
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<td>Hypnotic</td>
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<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Cognitive and functional impairment</strong></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
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<tr>
<td>Moderate to severe cognitive impairment</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Severe degree of functional impairment</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Arrived from a psychiatric hospital</td>
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<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Impaired vision</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Underweight</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Finland</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

¹ = Association with the non-use of antipsychotics

+ = Positive association, - = Negative association
5 DISCUSSION

5.1 Main findings

The prevalence of the use of one or more antipsychotic medications in long-term institutional care in Finland was high, up to 42% (Study I). In the recent studies from various countries, the prevalence of use of antipsychotic medication among nursing home residents has varied between 15% (Liperoti et al. 2003) and 41% (Margallo-Lana et al. 2001). The findings of the present study are in accordance with an earlier Finnish study in which the prevalence of antipsychotic use among nursing home residents in Helsinki was 42.6% (Hosia-Randell and Pitkälä 2005). The prevalence of antipsychotic use in long-term institutional care decreased from 42% in 2001 to 39% in 2003. However, the overall confounder-adjusted decrease in antipsychotic use was not statistically significant.

In the present study the prevalence of antipsychotic use was constantly high and the caring patterns in 2001-2003 were quite stable. Adequate indications may not have been fulfilled in all cases. According to quality indicators based on the RAI the limit of good care in long-term institutional care has defined such that the prevalence of use of antipsychotics without any psychotic disorder or symptom should be below 13.4% (Zimmerman et al. 1995, Noro et al. 2005). The limit of excellent care is 5.4% among those residents without a psychotic disorder or psychotic symptoms. In high risk residents (impaired cognition and behavioural symptoms), the limit of good care is respectively 21.3% and excellent care 8.4% (Noro et al. 2005).

Antipsychotic medication use among institutionalized nonagenarian residents was also very common, almost 30% (Study II). This finding concurs with that of Hosia-Randell and Pitkälä, who found that 31% of nonagenarian residents in nursing homes were taking antipsychotics (Hosia-Randell and Pitkälä 2005).
Although studies on antipsychotic medication use frequency in such very high age populations are rare, there are some earlier studies reporting 25-28% prevalence of antipsychotic medication use (Oborne et al. 2002, Briesacher et al. 2005). The residents in these earlier studies have been somewhat younger than the population in the present Study II. In any case, Lindesay et al. reported lower use (17%) of antipsychotics in nursing home residents aged >85 years (Lindesay et al. 2003). Accordingly, in Study II the antipsychotic use was three times more common than one earlier study from Sweden (Skoog et al. 1993).

The main finding of the study on older residents with schizophrenia in long-term institutional care was that approximately every fifth was not on any antipsychotic medication at all (Study III). Although the studies on antipsychotic medication use frequency in older residents with schizophrenia are sparse, this finding concurs with some earlier studies on older schizophrenic residents in nursing homes, where 15-19% were not receiving any antipsychotic medication (Bowie et al. 2001, Snowdon et al. 2005).

The main finding of the study of home care patients in Finland (Study IV) was more frequent use of antipsychotics (11.0%) than previously reported in home-dwelling elderly people in Finland and Sweden (3% to 9%) (Giron et al. 2001, Linjakumpu et al. 2002, Hartikainen et al. 2003a). Of home care patients in nine European countries 6.2% received antipsychotic medication (Study V), which was in line with earlier reports on home-dwelling elderly people (3% to 11%) (Giron et al. 2001, Linjakumpu et al. 2002, Hartikainen et al. 2003a, Linden et al. 2004, Rapoport et al. 2005). Frequency of use of one or more antipsychotic varied widely between study sites, ranging from 3.0% in Denmark to 12.4% in Finland. The mean consumption was somewhat higher than has been reported in the general population (from 1% to 1.4%) (Alonso et al. 2004, Percudani et al. 2005, Trifiro et al. 2005).
5.2 Specific findings

5.2.1 Long-term institutional care

There were several factors associated with the use of antipsychotics in a single study and some factors in more than one study.

5.2.1.1 Wandering and anxiolytics in institutionalized residents (I)

In 2001-2003 the use of antipsychotics decreased among residents who had wandering as a behavioural problem. However, the use of antipsychotics increased in those residents concurrently taking anxiolytics. There is surprisingly little published information about change in antipsychotic medications use and associated factors over time in nursing homes. In one earlier study in the UK Lindesay et al. have reported that the prescription rate of antipsychotics increased from 18% in 1990 to 22% in 1997 (Lindesay et al. 2003). In that report the only significant change in antipsychotic prescribing practice was an increase in the prescription rate in cognitively unimpaired residents in 1997, possibly related to mental hospital closures.

Wandering behaviour prevalence in the present Study I at 19% roughly matches the prevalence of 15-28% previously reported (Dawson and Reid 1987, Cooper et al. 1990, Cooper and Mungas 1993, Klein et al. 1999, Schonfeld et al. 2007) though as low rates as 6.5% (Sloane et al. 1998) and high as 63% (Hope et al. 1994) have also been reported. The different patient populations such as severity and type of dementia, as well as the different definitions of wandering may account for this variation. Although definitions vary, wandering refers to seemingly aimless or disoriented ambulation throughout a facility, often with observable patterns such as lapping, pacing or random ambulation (Algase et al. 2003). The MDS procedural manual describes wandering as “locomotion with no discernible, rational purpose” and differentiates wandering from purposeful movement.
Wandering behaviour and antipsychotic medication use have been associated in several earlier studies (Klein et al. 1999, Lövheim et al. 2006, Schonfeld et al. 2007). However, the prevalence of reported antipsychotic use associated with wandering behaviour has been 23% (Klein et al. 1999) compared to prevalences of 55% to 63% in Study I. The management of BPSD represents a significant part of the day-to-day workload of clinicians treating with dementia patients in institutional settings. Of all behavioural symptoms associated with dementia, wandering is among the most problematic from the perspective of resident management and safety. It has been reported that wandering, use of antipsychotics and also anxiolytics, were all correlated with falls (French et al. 2007b), causing e.g. hip fractures, especially in female patients (Cohen-Mansfield et al. 1991, Colon-Emeric et al. 2003).

Although the use of antipsychotics decreased between 2001 and 2003 among wandering residents, more than half of the wandering residents were still taking antipsychotic medication in 2003. Antipsychotics frequently have harmful adverse effects and show only modest efficacy in managing many behavioural problems in dementia (Ballard and O'Brien 1999, Howard et al. 2001). It is possible that in some cases antipsychotic adverse effects may be rated as wandering instead of akathisia (Wise and Tierney 1992), affective instability or general restlessness due to diverse neurological or psychiatric conditions.

The overall high use of antipsychotics among the present residents with wandering-related behaviour (55-63%) suggests a need to review the indications themselves. However, not all wandering should be deemed problematic in the sense that the resident keeps active (Cohen-Mansfield and Werner 1998, Yao and Algase 2006). Within institutions, a variety of environmental manipulations are often introduced to decrease the behaviours (Robinson et al. 2007). Fossey and co-workers have demonstrated that antipsychotic therapy was reduced by 19% following the introduction of a training and support intervention that focused on alternatives to drug use for the management of agitated behaviour (Fossey et al. 2006). Key elements in that programme involved initial skill training, behavioural management techniques, and ongoing training and support.
There was a positive association between the change in the use of antipsychotics and concomitant use of anxiolytics in the present residents. During the follow-up period this use increased in those residents who concomitantly used anxiolytics. Approximately every third resident was taking anxiolytics and more than half of them received concomitant antipsychotics. In 1990-1991 among the home-dwelling elderly in Finland, the prevalence of a combination of hypnotic/sedative and antipsychotic medications was only 3% (Linjakumpu et al. 2002). However, the institution residents in the present Study I were ten years older than those in the study by Linjakumpu et al.

5.2.1.2 Negative attitudes to others in nonagenarians (II)

In this study, factors associated with the use of antipsychotics among nonagenarian residents were investigated. The most interesting finding was an increasing risk of antipsychotic use among querulous residents and decreasing risk among those with good social skills. The behavioural items independently associated with the use of antipsychotics among nonagenarian residents were socially inappropriate or disruptive behavioural symptoms, recurring anxious complaints, recurring physical movements and unsettled relationships, all of which are inappropriate indications for antipsychotic use. However, these findings concur with those of Briesacher and coworkers, who stated that nonaggressive behavioural problems, such as restlessness (51.7%), unsociability (34.2%), uncooperativeness (30.4%) and indifference to their surroundings (25.1%), were common among residents receiving inappropriately prescribed antipsychotics (Briesacher et al. 2005). Individuals who have a good sense of initiative or involvement were less likely to receive antipsychotic medication. They could interact easily with others and were involved in group activities and responded positively to new activities. However, there were no associations between any psychiatric diagnoses or symptoms and the use of antipsychotics among nonagenarian residents. Furthermore, there was no association between diagnosis of dementia or cognitive impairment and the use of antipsychotics.
Clearly defined indications for antipsychotic use among nonagenarian residents in the present study may not be fulfilled in many cases. In a recent study a large discrepancy has been reported between mental health diagnoses and the use of antipsychotics (French et al. 2007). However, the frequent use of antipsychotics among the present residents does not necessarily indicate misuse of these drugs, but there is a considerable gap between the recommendations for antipsychotic medication and clinical practice (Alanen et al. 2006). According to some recommendations, 18% to 19% would be appropriate use of antipsychotic medications (Oborne et al. 2002, Briesacher et al. 2005). In a recent Canadian study one out of six residents in nursing homes received antipsychotics without appropriate clinical indication (Rochon et al. 2007). Rather, the decision to prescribe an antipsychotic medication appeared to be related to the nursing home environments, with some environment being more permissive than others regarding antipsychotic use. Prescribing decisions in practice was usually based on clinical information provided by the nursing home staff. Sorensen et al. have reported that staff perceptions of psychiatric morbidity and norms may have a greater impact on the prescription of antipsychotics than standardised clinical criteria (Sorensen et al. 2001).

The risk of inappropriate use of antipsychotics might be especially high in those nonagenarian residents who were querulous or were involved in staff-resident friction. However, it may possible to make a reliable distinction of these attitudes from behavioural symptoms. In a recent Swedish study, Lövheim and co-workers suggested that antipsychotic treatment among dementia patients in geriatric care is determined not only by the resident’s symptoms but also by factors related more closely to the caregiver and the caring situations (Lövheim et al. 2006).

There is concern that once antipsychotic medication has started it is rarely discontinued despite adverse effects. The average length of time that residents in long-term care facilities in Canada had been receiving antipsychotic medications was 0.87 years (Hagen et al. 2005). In that study only 16% of all antipsychotic prescriptions demonstrated evidence of dose reduction within six months of the
prescription being written. However, it has been recommended that when antipsychotics are administered to patients with dementia, long-term treatment should be avoided if at all possible and that treatments should be reviewed regularly, preferably with trial discontinuation at 3-6 monthly intervals (Alexopoulos et al. 2004, Ballard and Howard 2006, Pirttilä et al. 2006). It has suggested that approximately 25% of patients on antipsychotic therapy in the nursing home could have their antipsychotics safely discontinued (Courtney 1994). Three recent placebo-controlled withdrawal studies among patients with dementia reported that in many cases there is no deterioration of behaviour when antipsychotic medications were discontinued (Bridges-Parlet et al. 1997, Cohen-Mansfield et al. 1999, Ballard et al. 2004). In the present Study III the portion of nonagenarian residents whose antipsychotic medication had been experimentally discontinued was unknown.

5.2.1.3 Dependence and functional impairment in residents with schizophrenia (III)

The proportion of nursing home residents with schizophrenia has varied from 6% to 7% in the US and Australia, whereas according to this study it was 4.8% in Finland (Gurland and Cross 1982, McAlpine and Mechanic 2000, Snowdon et al. 2005). Interestingly, the present proportion of those residents with schizophrenia without any antipsychotic medication (19%) concurs with earlier studies (15-19%) (Bowie et al. 2001, Snowdon et al. 2005). The results suggested that residents with schizophrenia in later life without any antipsychotic medication were those with greater dependence and impaired functional capacity. Any diagnosis of dementia, severe underweight and severely impaired vision was associated with non-use of antipsychotics among these residents.

Harvey et al. found that nursing home residence was associated with more severe negative and cognitive, as well as greater functional impairment than among community dwellers and psychiatric inpatients (Harvey et al. 1999). In the present study approximately two out of three residents with schizophrenia had a severe degree of cognitive and functional impairment. Among the nonusers of antipsychotics this prevalence was even higher, 76% and 80% respectively. It
has also been reported that the severity of negative symptoms correlated inversely with functional status in older schizophrenic residents (Palmer et al. 2002). In the present study population, however, negative symptoms may be difficult to identify because of confounding effects such as cognitive impairment, depression and institutionalization.

Malnutrition is a common problem among older people living in nursing homes (Suominen et al. 2005, Wojszel 2006). According to an earlier Finnish study one third of nursing home residents were suffering from malnutrition (Suominen et al. 2005). Accordingly, 42% of the nonusers of antipsychotics in the present study were severely underweight (body mass index <20) compared to 19% of users of antipsychotics. It has been reported that risk factors for being underweight are cognitive and functional decline, eating dependencies and swallowing difficulties (Suominen et al. 2005, Wojszel 2006). Nutrition in geriatric psychiatry has been stated to be a neglected field (Bhat et al. 2005), although undernutrition appears to be an independent risk factor for morbidity and mortality (Pirlich and Lochs 2001, Guigoz et al. 2002). Research on Alzheimer’s disease suggests that weight loss precedes the clinical onset of the dementia in Alzheimer’s disease (Barrett-Connor et al. 1996). However, present residents with schizophrenia who were not receiving any antipsychotics often also had dementia and a severe degree of functional impairment and may have had swallowing difficulties. Some of the non-users may have needed to be fed.

The reason for the association between impaired vision and non-use of antipsychotics in the present study is unknown, because of the lack of documentation of medical history. Conventional antipsychotics such as phenothiatzines may cause retinopathies, which may be severe and irreversible (Fornaro et al. 2002). This severe progressive visual loss may occur several years after the cessation of chronic thioridazine treatment for example (Chaudhry et al. 2006). In some of the present non-users of antipsychotics, medication may have been discontinued due to vision problems.
5.2.2 Home care

5.2.2.1 Problems in social functioning in home care patients (IV)

Several predictive factors such as psychiatric diagnosis, delusions and cognitive impairment were associated with the use of antipsychotics whereas there was a negative association between age and the use of antipsychotics. Of the home care patients in Study IV, one in ten had problems in social functioning indicated by “not at ease interacting with others” (e.g. patients did not like to spend time with others) and 29% of them were taking antipsychotics. Antipsychotics might be used in many cases to relieve symptoms associated with lack of social contacts or poor life satisfaction. In Study IV two thirds of the patients were living alone. However, this was not independently associated with the use of antipsychotic medication.

Antipsychotic medication use among home care patients in Finland with any psychiatric diagnosis was decidedly high 40% (Study IV). The use of antipsychotics in this group was associated both with conventional and to a lesser extent with atypical antipsychotics. However, the psychiatric diagnoses subsumed under this criterion were heterogeneous, and included diagnoses such as schizophrenia, delusional disorder on the one hand mood and anxiety disorder on the other. In addition, these patients may or may not have had a concomitant diagnosis of dementia.

The prevalence of parkinsonism was 2.1% in the Study IV population and every fourth patient with parkinsonism was on antipsychotic medication. Psychosis is a frequent complication of Parkinson’s disease (PD) affecting 15 to 40% of patients (Aarsland et al. 1999, Fenelon et al. 2000). On the other hand, a recent study has shown that the use of antipsychotic medications, age and disability were strong predictors of developing PD (Noyes et al. 2006). It has been demonstrated that only in a small proportion of elderly patients with PD receiving antipsychotics had their antipsychotic medication been discontinued before starting antiparkinsonian medications (Simon et al. 2005).
In addition to Parkinson’s disease, parkinsonism may complicate many brain
disorders such as Alzheimer’s disease and Lewy body dementia (LBD). Postmortem findings suggest that LBD may account for as many as 20% to 34%
of all dementia cases and is often underdiagnosed (Luis et al. 1999). It is estimated that 75% of LBD patients will develop parkinsonian features during
the course of their illness (McKeith et al. 1999). LBD is important because of the
difficult clinical management issues caused by the high frequency of psychiatric
symptoms (Baskys 2004) and the risk of severe antipsychotic sensivity reactions
(Ballard et al. 1998). Visual hallucinations and delusions are more common in
LBD than in AD (McShane et al. 1995, Ballard et al. 2001b).

In Study IV one in two of those patients on antipsychotic treatment were on
conventional antipsychotics, whereas in some earlier reports this proportion has
been less than 40% (Snowdon et al. 2005, Wang et al. 2005). Conventional
antipsychotics especially may cause movement disorders and other motor side
effects. However, drug-induced parkinsonism has also been described with a
great diversity of other compounds such as antiemetics, drugs used for the
treatment of vertigo and antiepileptics (Mena and de Yebenes 2006). At least
10% of patients with drug-induced parkinsonism develop persistent and
progressive parkinsonism in spite of the discontinuation of the causative drug
(Mena and de Yebenes 2006). Friedman et al. reported that parkinsonism was a
very common and underdiagnosed condition among elderly residents taking
antipsychotics in nursing homes (Friedman et al. 2004). In Study IV, however,
the causal relationship between parkinsonism and antipsychotics was obscure in
the elderly receiving home care services. In patients requiring antipsychotic
medication, adequate monitoring is needed for early parkinsonian symptoms and
rapid discontinuation if these occur. Although the antipsychotic medication
doses of both atypical and conventional antipsychotics were low in Study IV
(overall mean dose in chlorpromazine equivalents 75.8 mg/day), there is a
possibility that a greatly increased total proportions of patients treated with
(atypical) antipsychotics in a growing population might paradoxically even lead
to increased total numbers of patients with EPS and TD (Lohr et al. 2004).
Patients with severe mood disorders may be especially at risk also when using atypical antipsychotics (Kane 1999).

5.2.2.2 Antipsychotic use in home care patients in Finland and Italy (V)

Antipsychotic use among home care patients in nine European countries varied widely (3.0% to 12.4%). This wide variation may primarily be attributable to the differences in health care systems and in care practices, or to different attitudes to antipsychotic therapy in different countries. In Finland (12.4%) and Italy (11.2%) antipsychotic use was more than twice as common as in Denmark (3.0%) when adjusted for confounders. In accordance with these results, a high prevalence of antipsychotic medication use in the elderly has also been previously reported in institutional care in Finland as well as in Italy (Hughes et al. 2000, Hosia-Randell and Pitkälä 2005). The high level of use of antipsychotics both in home and long-term institutional care may reflect the overall prescribing tradition pertaining to the use of antipsychotic medications for elderly people in Finland and Italy.

Around 3% of the patients in Study V had hallucinations, which matches the prevalence of hallucinatory symptoms 4% previously reported among dementia sufferers living in resident care environments in the UK (Margallo-Lana et al. 2001). However, the rate of hallucinations in the present study was substantially lower than reported in the review of 55 studies of AD patients where the median prevalence of hallucinations was 18% (Ropacki and Jeste 2005). Interestingly, only one fourth of subjects with hallucinations in the present study were on antipsychotic treatment, which concurs with one earlier report (Östling and Skoog 2002). However, hallucinations may lead to subjective distress on the part of the patients and have adverse effects on caregivers. The early recognition of hallucinations and interpretation of underlying etiologies coupled with the initiation of appropriate treatment interventions will reduce morbidity and improve the quality of life for these patients.

Depression in the present patients was also associated with the use of antipsychotics this concurs with several earlier studies (Giron et al. 2001,
Lövheim et al. 2006). Altogether 12% of the present patients with depression symptoms were taking antipsychotics. In one report from nine European centres, depressive psychosis prevalence ranged from 2% to 11% (Copeland et al. 1999). However, the exact proportion of psychotically depressed patients in the present study is unknown. Concomitant use of antipsychotics and other psychotropics was common in the present population, which concurs with earlier studies (Hughes et al. 2000, Hartikainen et al. 2003a, Hartikainen et al. 2003b, Holmquist et al. 2005, Kim and Whall 2006). In a Finnish study on the home-dwelling elderly the proportion of psychotropic combinations was 10% among elderly people without dementia and as high as 26% among those with dementia (Hartikainen et al. 2003b).

5.2.3 Other important factors and antipsychotic use

5.2.3.1 Younger age in elderly people and antipsychotic use (IV, V)

Based on the results of home care Studies IV and V the likelihood of receiving antipsychotic treatment was more common in the youngest age group (65-74 years). In Study IV, the patients 85 years and older in home care in Finland were significantly less likely to be taking antipsychotics. This may conflict with some earlier studies in which the likelihood for the use of antipsychotics increased with age (Hartikainen et al. 2003a, Percudani et al. 2005, Trifiro et al. 2005). However, the results of the present study agree with some other studies in which the frequency of antipsychotic use was lower among the oldest age groups in nursing homes (Liperoti et al. 2003, Hosia-Randell and Pitkälä 2005). Differences in the study populations may explain this discrepancy and one explanation for the more common antipsychotic use in the youngest age group may be the more frequently troublesome disruptive behaviour in this age group. Medications may thus have been given for purposes of social control. Another explanation for the lower use in the oldest age group may be that these medications are considered especially harmful to the oldest patients. Indeed,
these individuals are the most sensitive to antipsychotic medication adverse effects and the relevant indications should be more carefully evaluated.

5.2.3.2 Dementia and antipsychotic use (III, IV, V)

Severe degree of cognitive impairment was associated with use of antipsychotics in Studies IV and V. Diagnosis of dementia was associated with antipsychotic use among home care patients in nine European countries (Study V) and with non-use of antipsychotics among residents with schizophrenia in long-term institutional care (Study III).

The prevalence of Alzheimer’s disease in community living elderly patients with chronic schizophrenia has ranged from 2% to 9% (Dwork et al. 1998, Murphy et al. 1998, Purohit et al. 1998, Jellinger and Gabriel 1999). In the present study this prevalence in generally was higher, up to 20%. However, this was even higher among those residents with schizophrenia who did not take any antipsychotics (44%). The schizophrenia residents without antipsychotics were relatively old, more commonly demented and had a high level of dependence on assistance with daily living.

The patients with moderate to severe cognitive impairment (CPS 3-6) took antipsychotics twice as commonly (22.3%) as cognitively intact (CPS 0) patients (8.4%) in home care in Finland (Study IV). However, in the study of nine European countries (V) the subjects with moderate to severe cognitive impairment took antipsychotics as much as four times more often than the cognitively sound patients (13.4% vs. 3.4%). In some earlier reports, the use of antipsychotics has been 6-times more frequent among individuals with dementia than among those without dementia (Giron et al. 2001, Hartikainen et al. 2003b). Although one out of two patients in the European Study (V) and at least 60% of home care patients in Finland (Study IV) were assessed to have some degree of cognitive impairment, only 12% to 18% respectively were recorded as having a diagnosis of dementia. This discrepancy may be due to the fact that the cause of cognitive impairment among home care patients is only seldom ascertained. This may imply insufficient diagnostic procedures as to neurodegenerative disease, or
that cognitive impairment was caused by stroke or depression. Another explanation may be that not all diagnoses of dementia have been adequately recorded in the files. As other recent research has reported that less than half of the patients with dementia had their diagnosis documented in primary care medical records (Löppönen et al. 2003).

Recently, serious concerns have been raised regarding the use of antipsychotics in people with dementia, particularly the increased mortality rates, the increased risk of stroke and other cardiovascular adverse events, as well as the increase in parkinsonian symptoms and drowsiness. The main reason for the widespread prescription of antipsychotics in this group could be the limited evidence for alternative treatment approaches (Hermans et al. 2007, Robinson et al. 2007).

In clinical studies, typical antipsychotics have been effective against BPSD, but they were also characterised by their range of adverse effects (Schneider et al. 1990). There have been several randomised, placebo-controlled trials of atypical antipsychotics olanzapine (Street et al. 2000, Clark et al. 2001, De Deyn et al. 2004), risperidone (De Deyn et al. 1999, Tune 2001, Brodaty et al. 2003, Brodaty et al. 2005), quetiapine (Tariot and Ismail 2002, Zhong et al. 2007) and aripiprazole (De Deyn et al. 2005), showing variable efficacy against BPSD. Meta-analysis of atypical antipsychotics has found evidence for the effectiveness of olanzapine and risperidone in dementia (Schneider et al. 2006). Schneider and his colleagues analysed the mortality rates in 15 clinical trials in which aripiprazole, olanzapine, quetiapine or risperidone were compared to placebo (Schneider et al. 2005). Overall, in the trials studied, people taking atypical antipsychotics were 1.5 times more likely to die than those taking a placebo.

Cholinesterase inhibitors (ChEIs) are the primary treatment for cognitive symptoms of AD. In a recent Canadian population-based study Herrmann et al. reported that elderly patients with dementia are treated for lengthy periods of time with ChEIs in the community and in long-term care facilities (Herrmann et al. 2007). However, the recent systematic reviews and meta-analysis of the efficacy of ChEIs in the treatment of neuropsychiatric symptoms and functional
impairment in AD have demonstrated only a low or modest beneficial effect on behavioural symptoms and functional abilities (Sink et al. 2001, Trinh et al. 2003, Wild et al. 2003, Grimmer and Kurz 2006). There is only one head-to-head study that compared an atypical antipsychotic (quetiapine) with a ChEI (rivastigmine) and placebo in patients with probable AD found no differences in efficacy between the three treatments (Ballard et al. 2005). However, in a recent report it has been suggested that nursing home residents with AD treated with ChEI have a reduced risk from therapy with antipsychotics compared with these residents without ChEIs (Narayanan et al. 2006). In the present study the data of ChEIs were not available in studies in institutional care and in Study IV the subgroup with that data was too small (n=49) for statistical purposes.

Over the past 4 years, also regulatory authorities in Europe (EMEA) and the US (FDA) have also raised concerns about an apparent increase in cerebrovascular events and deaths associated with atypical antipsychotics. These regulatory authorities warning to physicians and patients stated that off-label use of all atypical antipsychotics could be dangerous to elderly patients with dementia. In contrast to this, several observational studies have found no increase in the risk of cerebrovascular events in patients suffering from different kinds of dementia receiving either atypical or typical antipsychotics (Herrmann et al. 2004, Gill et al. 2005, Layton et al. 2005). There are no head-to-head comparisons of atypical and typical antipsychotics in patients with dementia. However, meta-analysis by Wang and colleagues suggests that typical antipsychotic medications are at least as likely as atypical agents to increase the risk of death among elderly patients, and that typical medications should not be used to replace atypical agents discontinued in response to the FDA warning (Wang et al. 2005). In addition, Raivio et al. found that neither atypical nor conventional antipsychotics increase mortality among elderly patients with dementia (Raivio et al. 2007), but the use of restraints doubled this risk. In recent studies on elderly patients with and without dementia, the risk of death associated with typical antipsychotic medications is comparable or possibly greater than the risk of death associated with atypical antipsychotics (Gill et al. 2007, Schneeweiss et al. 2007). However, the recent study in community living
patients with AD suggests that the adverse effects of atypical antipsychotics may offset advantages in the efficacy for the treatment of psychosis, aggression or agitation (Schneider et al. 2006).

It has been recommended that atypical antipsychotics should be used as a first-line management strategy only when severe and distressing symptoms of dementia are occurring that cannot be easily contained, and when the individual affected or others are at risk (Ballard and Howard 2006). A careful decision needs to be made on the basis of the distress to the patients and their caregivers as to whether the potential benefits of an atypical antipsychotic might outweigh the risk of adverse effects.

5.2.3.3 Delusions and antipsychotic use (IV, V)

Delusions were associated with antipsychotic use in Studies IV and V.

Around 6% of the patients in home care in Finland (Study IV) and 2% of the patients in the European Study V had delusions which match the point prevalence of psychotic symptoms of 5.7% previously reported in Australian community living elderly (Henderson et al. 1998). However, the rates of delusions in Studies IV and V were substantially lower than those reported in studies among residents with delusions in nursing homes (16-56%) (Brodaty et al. 2001, Margallo-Lana et al. 2001). Risk factors for delusions have been older age (Bassiony et al. 2000) and AD diagnosis (Lyketsos et al. 2000). However, in the recent study hallucinations but not delusions were related to an increased risk of subsequent development of dementia (Östling et al. 2007).

In Study IV 45% of patients with delusions received antipsychotics and 32% in Study V. Delusions as well as hallucinations are well-established indications for antipsychotic treatment and according to earlier studies mortality rate may be double in individuals over 70 with these psychotic symptoms (Henderson and Kay 1997). However, psychotic symptoms have been linked to cognitive and
functional decline (Chui et al. 1994, Lopez et al. 1999) and earlier institutionalization (Gonzalez-Salvador et al. 1999, Lopez et al. 1999). Interestingly, the proportion of delusional patients taking no antipsychotics was more than half in Studies IV and V. This concurs with a study in which more than half of nursing home residents with delusions were not on antipsychotics (Brodaty et al. 2001, Margallo-Lana et al. 2001). In addition, Forsell et al. have reported that elderly people with paranoid symptoms often took psychotropic medications, although only 10% took antipsychotics (Forsell and Henderson 1998).

It is also unknown whether the onsets of delusions in the present patients have occurred de novo or are associated with pre-existing psychiatric or medical disorders. Delusions may not be severe or persistent enough and may not result in disruption or distress (Studies IV, V). It has also been reported that in more than half of the patients with delusion associated dementia the symptoms do resolve over the year of follow-up independent of pharmacological treatment (Ballard et al. 2001).

5.2.3.4 Anxiolytics and antipsychotic use (I, II, V)

The use of antipsychotics was significantly associated with concomitant use of anxiolytics in Studies I, II and V.

Antipsychotic use among residents in long-term institutional care with concomitant use of anxiolytics was decidedly high. Among the long-term care residents up to 56% used antipsychotic medication concomitantly with anxiolytics (Studies I, II). The use of anxiolytics concomitantly with antipsychotics in home care patients in Europe was 14% (Study V). These percentages seem to be higher or equal to some previously reported (3-13%) (Giron et al. 2001, Gobert and D'hoore 2005). In a population-based Swedish study on very old people with and without dementia one of the most frequent psychotropic combination was antipsychotics and anxiolytics (Giron et al. 2001). Hartikainen et al. have reported that in home-dwelling elderly two out of three nondemented users of antipsychotics were taking at least one other psychotropic
drug (Hartikainen et al. 2003b). In that report the most common combination was hypnotics and antipsychotics among the demented subjects. A population-based study from Finland has reported that half of non-demented people aged 75 and older even used hypnotics or antipsychotics and one out of three used these medications concomitantly (Hartikainen et al. 2005). However, in that study the use of different types of psychotropics or several antipsychotics was a risk factor for death in demented patients.

However, as a general principle it has been recommended that polypharmacy of psychotropics should be avoided among elderly people (Howard et al. 2001). As the possible impact of the growing use of these may include the increased risks of neurological and other adverse effects (Centorrino et al. 2002).

5.3 Limitations and strengths of the study

The major limitations of this study include mostly the limitations in register database. Because of the cross-sectional nature of these studies it was not possible to establish the chronological order of any associations.

5.3.1 Limitations of the MDS

The MDS is a multidimensional assessment tool originally created for both clinical work and for research. This duality leads to compression of all data collection to the minimum necessary to reveal the main problem areas, not to assess these areas fully.

The limitations of the ability of the MDS to reveal the lack of individual indications for the use, doses (except Study IV), duration and discontinuation of antipsychotics are not available. Moreover, generic names of antipsychotics were not available in long-term institutional care studies (I-III), thus, distinguishing between atypical and typical antipsychotics was not possible. Lack of documentation of indications makes it impossible to know whether these drugs were being used for the appropriate reasons. Even though adherence to
medications was checked in home care as a routine part of the MDS questionnaire and home care nurses delivered the medications, some uncertainty about the actual consumption cannot be totally excluded (Study IV-V).

Although the MDS is a standardized, comprehensive assessment instrument, the recording of psychiatric symptoms was not its main focus. Psychiatric symptoms were assessed by nursing staff (including the attending physician), and the potential for over- and underestimation remains. In addition the data collected do not include any severity or frequency assessment of psychiatric or behavioural symptoms.

Although the MDS items have demonstrated good to excellent general reliability, it is uncertain how appropriate the MDS is in the nursing home assessment of the oldest old or people with chronic mental illness. In addition, the MDS, however, has not been validated specifically for nursing home residents with schizophrenia. Little is known about the ability of nursing home personnel to accurately recognize the symptoms of schizophrenia. Bowie et al. suggest that symptoms such as thought disorder and hallucinations go almost completely unnoticed by nursing staff when they were asked to give a present-absent rating (Bowie et al. 2001).

Other limitations include uncertainty that not all psychiatric and dementia diagnoses have been adequately recorded in the files. The concern in Study III was the reliability of the database diagnosis of schizophrenia. Earlier studies indicate that Finnish psychiatrists tend to apply a narrow definition of schizophrenia in their clinical practice and that the diagnosis of schizophrenia can be considered reasonably reliable (Salokangas 1993, Isohanni et al. 1997, Kampman et al. 2004).

5.3.2 Reliability

The characteristics, diagnoses and symptoms of residents, residential care systems and clinical practices vary widely between countries making international comparisons and reliability in other populations complex. Despite
the common use of the term “nursing home”, there are no generally accepted definitions for the different types of long-term care services. There will be differences in the types of patients who are admitted to these facilities and the ways in which they are diagnosed and treated. Additionally, the more standardized way of assessing residents in long-term institutional and home care might also influence care practice with antipsychotics. Furthermore, the samples in Studies IV and V consisted solely of users of home care services, especially home care patients and the results cannot be generalized to all community-dwelling elderly people. No direct comparison of antipsychotic use between home care patients and community-dwelling individuals is available.

5.3.3 Unstudied factors

These studies did not include antipsychotic medications prescribed “as required”. However, some “as required” medications may actually be used quite regularly. Thus, the actual prevalences of antipsychotic medication use may have been higher than is reported here.

There may be an association between facility characteristics and the use of antipsychotics (Hughes et al. 2000) suggesting that the high prevalence of antipsychotic use may be related to low staffing rates in Finnish nursing homes. The mean actual staffing level during the past 5 years in nursing homes in Finland has been 0.43 nurses per resident on weekdays (Noro A et al. 2005). The National Framework for High-Quality Care and Services for Older People suggest an appropriate staffing level of 0.8 nurses per resident. However, there are no comparisons of staffing rates between different countries. In the present study it was impossible to evaluate the influence of staffing rate on the use of antipsychotics. It may be possible that low staffing rates and pressure of work life have affected assessments of patients. Other possible predictors of antipsychotic use such as costs and prescription procedures are beyond of the present thesis.
5.3.4 Strengths of the study

The only exclusion criteria were aged <65 years and assisted living. Every resident in every participating institution and every patient in only home nursing, and common patients for home nursing and home care units were included. In addition, total population sizes were relatively large in all levels studied. The total units comprised approximately 17% of long-term institutional care for the elderly in 2001 in Finland. All types of institutional settings in Finland took part: small and large, from cities and from rural areas, nursing homes and hospital-based beds. These study populations can be considered to be representative of older populations in long-term care in Finland. Thus, the spectrum of cognitive and physical impairment together with essential psychiatric disorders and symptoms prevalent was likely to be captured.

5.4 Implications for future research

More studies on elderly people are needed in order to identify the factors that associated with the type and doses of antipsychotics in long-term care settings. This study also points to the importance of studying the longitudinal changes in prescribing patterns of antipsychotics for elderly people both in long-term institutional and home care. More attention should be paid to the appropriate use of antipsychotics and especially staff training including intervention studies for the care of the elderly. More studies are also needed on antipsychotic use based on prospective long-term follow-up design to ascertain the factors associated with such use. Future research should also address the question of whether there are predictors to differentiate the older patients with schizophrenia who will not relapse with discontinuation of antipsychotics.
6 SUMMARY

The prevalences of antipsychotic use were high in all the studies.

The present study focused on five specific questions as follows.

1. *Is there any change of the prevalence of antipsychotic use during the study period and which factors would explain the change? (Study I)*
   Findings: The prevalence of antipsychotic use in long-term institutional care decreased from 42% in 2001 to 39% in 2003. The overall confounder-adjusted decrease in antipsychotic use was not statistically significant. During the study period the use of antipsychotics decreased among residents with wandering as a behavioural problem. On the other hand, the use of antipsychotics increased in those residents concurrently receiving anxiolytics.

2. *What is the prevalence of antipsychotic use among nonagenarian institution residents and which factors associate with such use? (Study II)*
   Findings: Antipsychotic medication use among nonagenarians in long-term institutional care was common (30%) and seemed in many cases to be associated with residents’ negative attitudes to others. Thus, there was an increasing risk of antipsychotic use among querulous residents and decreasing risk among those with good social skills.

3. *What is the prevalence of older residents with schizophrenia not having any antipsychotics at the time of the data gathering and which factors associate with non-use of antipsychotics? (Study III)*
   Findings: Approximately 19% of the older residents with schizophrenia in long-term institutional care were not on antipsychotic medication. Any diagnosis of dementia, severe underweight and severely impaired vision was associated with non-use of antipsychotics among these residents.
4. What is the prevalence of antipsychotic use among home care patients in Finland and which factors are associated with such use? (Study IV)

Findings: Antipsychotic use among home care patients in Finland was lower (11.0%) than that in long-term institutional care. Several factors such as psychiatric diagnosis, delusions and cognitive impairment were associated with the use of antipsychotics whereas there was a negative association between age and the use of antipsychotics.

5. Is there any variation of antipsychotic use among home care patients in nine European countries and which factors contribute to such variation? (Study V)

Findings: Of home care patients in nine European countries 6.2% were taking antipsychotic medication. The frequency of the use of one or more antipsychotic varied widely between study sites, ranging from 3.0% in Denmark to 12.4% in Finland. Certain factors such as delusions, hallucinations, depression, dementia and cognitive impairment as well as youngest age group and concomitant use of other psychotropics explained the use of antipsychotics. Residing in Finland and Italy was also a risk indicator.

The use of antipsychotic medications in long-term institutional and home care in Finland was among the highest in the world.
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