

DRUG USE AMONG THE HOME-DWELLING ELDERLY

Trends, polypharmacy, and sedation

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Abstract

The elderly use drugs more commonly than younger persons. Many studies about drug use have concentrated on institutionalized elders. Knowledge of drug use by the oldest old, aged 85 years or over, is scant. Psychotropics are among the drugs most commonly used by the elderly. Psychotropics have many adverse effects, such as balance impairment, sedation, reduced cognition, depression, and extrapyramidal symptoms. We do not know the extent of sedative drug use, including psychotropics and drugs prescribed for somatic disorders that have sedative properties. Withdrawal of unnecessary drugs appears to be beneficial and to improve the functional capacities of the elderly.

The aim of this study was to describe the changes in prescription drug use, polypharmacy, and psychotropic use among home-dwelling elderly Finns in the 1990s by using two cross-sectional community surveys. The specific aim was to classify all drugs used in Finland into four groups based on their sedative properties.

Drug use, polypharmacy, and, to some extent, psychotropic use increased within a decade. The oldest old used prescription drugs most commonly. Polypharmacy was independently associated with higher age, and in 1998-99, with at least 3 chronic diseases, poor self-perceived health, and the use of home nursing services. Most psychotropic users were on regular medication. The use of hypnotics and antidepressants increased most. Persons with polypharmacy used significantly more commonly psychotropics compared to other people. Over 84-year-olds used psychotropics more commonly than younger persons.

Sedative use was common, as 40 % of drug users used them. Sedative use was significantly more common among persons with polypharmacy than others. According to logistic regression models, the use of many sedatives was independently associated with age 80 years or over, female gender, chronic morbidity, smoking, poor self-perceived health/life satisfaction, and the use of home nursing. Both polypharmacy and abundant sedative use were associated with impaired physical functional abilities.

Prescribers need to be aware of the increasing polypharmacy and abundant sedative use. Regular assessment of indications is needed to avoid overuse of drugs. Geriatric knowledge is needed to support health centers and specialized units in this demanding task.

Keywords: aged, community, drug therapy, elderly, hypnotics and sedatives, pharmacoepidemiology, polypharmacy, primary care, psychotropics, sedation

To my parents

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Abbreviations

ACE	Angiotensin-converting enzyme
ADL	Activities of daily living
ASA	Acetylsalicylic acid
ATC	Anatomical Therapeutic Chemical
CI	Confidence interval
CNS	Central nervous system
DDD	Defined daily dose
IADL	Instrumental activities of daily living
MCI	Mild Cognitive Impairment
MMSE	Mini-Mental State Examination
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
OTC	Over-the-counter
SD	Standard deviation
SSRI	Selective serotonin reuptake inhibitor
WHO	World Health Organization

List of original papers

The present thesis is based on the following original papers, referred to in the text by the Roman numerals I–IV. Some unpublished data are also presented.

- I Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivelä S & Isoaho R (2002) Use of medications and polypharmacy are increasing among the elderly. *Journal of Clinical Epidemiology* 55: 809–817.
- II Linjakumpu T, Hartikainen S, Klaukka T, Koponen H, Kivelä SL & Isoaho R (2002) Psychotropics among the home-dwelling elderly – increasing trends. *International Journal of Geriatric Psychiatry* 17: 874–883.
- III Linjakumpu T, Hartikainen S, Klaukka T, Koponen H, Kivelä SL & Isoaho R (2003) A model to classify the sedative load of drugs. *International Journal of Geriatric Psychiatry* 18: 542–544.
- IV Linjakumpu T, Hartikainen S, Klaukka T, Koponen H, Hakko H, Kivelä S-L & Isoaho R. Items connected with sedative drug use in the home-dwelling elderly. Submitted for publication.

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1 Introduction

The proportions of the elderly out of the total population are increasing in most western countries, including Finland (Statistics Finland 1998). People over 64 years old account for 15% of the Finnish population (Statistics Finland 1998), but their medication costs comprise 40% of the expenditure of the total population (Klaukka & Rajaniemi 1996, Klaukka 2002). This phenomenon has also been recognized in the other western countries (Mehl & Santell 2000). In 2010, the “baby boom generation” will be pensioners, which will cause increasing challenges and require rationing of the services provided by society and the health care system. In Finland, an estimated 26% of the citizens will be over 64 year old in 2030, but the proportion of over 80-year-olds will increase most, becoming over twofold by 2030 (Tilastokeskus 2002).

New drugs are being developed all the time, and they will be applied also in indications previously resistant to pharmacotherapy. Many diseases of the elderly, such as hypertension, are now treated more actively than before, and the threshold of starting medication has become lower (Joint National Committee 1997). With advancing age, a greater share of individuals become susceptible to chronic morbidity (Koskinen & Aromaa 2002), which requires long-term medical treatment and leads to the use of several medications.

The pharmacokinetic and pharmacodynamic changes secondary to age or illnesses require careful attention when prescribing medication to the elderly, because these changes make them particularly sensitive to the adverse effects of many drugs (Hughes 1998, Pollock 1998). Clinically significant drug interactions have been found in up to 15% of the elderly with polypharmacy (Barat *et al.* 2000).

There are many cross-sectional or longitudinal studies about drug use by the elderly in different countries (Chrischilles *et al.* 1992, Veehof *et al.* 2000). However, there is not much information available on the drug use, polypharmacy, and psychotropic use by the home-dwelling elderly or by the oldest old. Finnish follow-up studies on drug use by the elderly performed in the same location using an identical methodology are scanty. Knowledge of all sedative drug use, including drugs used for somatic disorders, has not been available before. This study concentrated on investigating these aspects of drug use by the elderly.

2 Review of the literature

2.1 Aging and health

2.1.1 Definition of aging

The simplest definition of age is a chronological count of calendar years (Jyrkämä 1995). Subjectively, many elderly persons do not feel themselves old even when retired or at the advanced age of 75. The elderly population has been divided into the young elderly aged 60–74 years and the very elderly over 74 years old (Devroey *et al.* 2002). With the increasing life expectancy, the terms “the oldest old” and “very elderly people” are currently used to refer to people 80 or 85 years of age or over (Haavisto & Mattila 1981, Päivärinta *et al.* 1999, Simiand-Erdociain *et al.* 2001).

In the literature, aging is defined most simply as a biological, psychological, and social phenomenon. Biological aging is associated with changes in the human organism and biological aging processes. (Jyrkämä 1995). Biological age is an attribute of body tissue relevant to pathogenesis (Last 1995). Pharmacokinetic and pharmacodynamic changes of drug efficacy are associated with the biological aging of the elderly (Pollock 1998). These changes are discussed in more detail below in section 2.1.4. of this thesis. The major organs affected by aging are the kidneys, the liver, and the cardiovascular (Pollock 1998) and central nervous systems (Koponen 2001). Aging may cause changes in the neurotransmission systems, and these changes may increase sensitivity to sedation by drugs (Pollock 1998, Koponen 2001).

Psychological aging takes place in the person’s psychic activities. Social aging is connected with the person as a member of society, and the term “the elderly” generally refers to people who have reached the socio-political age of 65 years. Social aging is more complicated to define than either biological or psychological aging, and the definitions partly overlap. Social aging is associated with changes that take place in the individual’s or social group’s relationship with their environment, and these changes may manifest at both individual and societal levels. (Koskinen 1994)

2.1.2 Aging and somatic morbidity

From the age of 75 years onward, chronic morbidity increases (Pitkälä & Strandberg 2003). It is important to differentiate changes associated with primary aging from those caused by illnesses, called secondary aging. Significant age-related changes take place in the body composition of the healthy elderly after the age of 59 years, as the body cell mass and the skeletal muscle mass decrease. (Kyle *et al.* 2001)

Physical disabilities are connected with advanced age, multiple diseases, particularly cardiovascular and musculoskeletal diseases (Stewart *et al.* 1989, Pitkälä & Strandberg 2003), depressive symptoms, and cognitive capacity (Laukkanen *et al.* 1994). Self-rated health is a useful indicator of physical health, but it may be sensitive to the cultural environment (Jylhä *et al.* 1998). Decline in vision and hearing also typically occurs in the course of aging (Lupsakko 2001, Bergman & Rosenhall 2001, Aromaa & Koskinen 2002), which may diminish the individual's capacity for normal physical functioning and medical self-care. Poor visual acuity is a risk factor for fracture-causing falls (Luukinen *et al.* 1997).

Good physical functioning and an optimistic attitude toward life increased and the need for assistance decreased in the older population over the 10 years from 1989 to 1999 (Pitkälä *et al.* 2001b). Physical functioning has also improved in the general Finnish population over the past 20 years, though chronic morbidity increases systematically from the young age groups toward the oldest elderly populations (Koskinen & Aromaa 2002). Based on the compression of morbidity hypothesis, healthy lifestyles may postpone and compress disability into a shorter period toward the end of life (Fries 1980). Thus, among the oldest persons, multiple chronic diseases may require long-term medical treatment and lead to the use of several medications. Most of the elderly suffer from chronic diseases. The prevalence of chronic morbidity grew among home-dwelling Finnish persons aged 75 years or over from 70% in 1964 to 79% in 1976 (Klaukka 1982) and to 90% in 1995–96 (Arinen *et al.* 1998). The prevalence was 86% in 75- to 84-year-olds and nearly 90% in over 84-year-olds in 2000–01 (Koskinen & Aromaa 2002).

2.1.3 Aging and mental disorders

In the general Finnish population, mental health has remained stable over the past 20 years (Aromaa & Koskinen 2002). The most prevalent mental disorders among the elderly are dementia, depression, and delirium (Johnson *et al.* 1994). Dementia with psychosis and depression with dementia or anxiety disorder are also common among them. Schizophrenia is not so common in the elderly.

The prevalence of dementia ranges globally from 6% to 14% among elderly persons (Juva *et al.* 1993, Koivisto 1995) or from 8% to 13% among the home-dwelling elderly (declined cognition, mostly dementia) (Lim *et al.* 2003). Moderate to severe dementia ranges from 9% to 12% in the Finnish elderly (Juva *et al.* 1993, Viramo 1994), increasing with advancing age (Juva *et al.* 1993, Viramo 1994, Koivisto 1995). Almost 27% of persons aged 85 years old had dementia (Juva *et al.* 1993), and every fourth to every third

(85+ years) had moderate to severe dementia according to some Finnish studies (Juva *et al.* 1993, Viramo 1994). Almost every third person aged 85 years or over had moderate to severe dementia in the elderly population (2000 consecutive patients) admitted to a medical department of a large university hospital (Erkinjuntti *et al.* 1986). It may be difficult to differentiate between a normal memory disorder and mild cognitive impairment (MCI) in an elderly person, because MCI is found in neurologically healthy individuals and may be a risk factor for dementia (Ylikoski *et al.* 1999).

Across Europe, the overall prevalence of depression in the elderly population is 12%, with women predominating (Copeland *et al.* 1999). Previous studies have shown 15–20% prevalences of depressive symptoms or depression in the elderly in community (Johnson *et al.* 1994, Pahkala *et al.* 1995, Manela *et al.* 1996), but as in the general population, 6% of the elderly suffer from major depression demanding drug treatment (Valvanne *et al.* 1996). Depression is associated with chronic morbidity, lowered physical functional capacity (Pahkala & Kivelä 1991, Penninx *et al.* 1996, Valvanne *et al.* 1996, Linjakumpu *et al.* 2001), and the use of cardiovascular, psychotropic, and analgesic drugs in the elderly (Pahkala & Kivelä 1991, Linjakumpu *et al.* 2001). Feelings of loneliness are typically experienced by the elderly, and they are associated with depression (Lindgren *et al.* 1994, Routasalo & Pitkälä 2003). Spousal bereavement is associated with increased morbidity and mortality (Charlton *et al.* 2001, Prigerson & Jacobs 2001).

Of the demented elderly admitted into a general hospital, 41% were delirious, and 25% of the delirious patients were demented (Erkinjuntti *et al.* 1986). Multiple acute illnesses, such as cardiovascular, neurological, endocrinological, metabolic, or infectious diseases, anticholinergic psychotropics, sedatives or cardiovascular drugs, intoxication, alcohol or sedative withdrawal, dementia, and psychosocial stress may precipitate delirium (Johnson *et al.* 1994).

Fifteen per cent of the home-dwelling elderly may suffer from anxiety (Manela *et al.* 1996), even though the prevalence of this disorder is lower among them than in younger adults (Aromaa *et al.* 1989, Flint 1994). Over one third of the home-dwelling elderly report sleeping disorders (Manela *et al.* 1996, Arinen *et al.* 1998). The incidence of psychoses increases with age (van Os *et al.* 1995, Targum & Abbott 1999), due to physical comorbidities, dementia, sensory deficits, social isolation, and polypharmacy (Targum & Abbott 1999). Panic symptoms are not so common in old age (Manela *et al.* 1996).

It has been concluded that the strong association between physical and mental health should be rigorously investigated (Berkman *et al.* 1986), and that the two aspects of health should not be considered separately. The social situation of the elderly should also be clarified. Mental disorders together with somatic diseases are common in the elderly. They therefore need drugs for the treatment of their diseases, and they use psychotropics more frequently than the general population (Blazer *et al.* 2000).

2.1.4 Pharmacokinetics and pharmacodynamics of drugs and aging

The pharmacokinetic and pharmacodynamic changes secondary to advanced age or various illnesses require careful attention, because these changes make the elderly particularly sensitive to adverse effects, toxic reactions, and interactions of many drugs. Pharmacokinetic alterations may be caused by changes in absorption, distribution, or elimination via metabolism in the liver and/or in excretion by the kidneys. (Hughes 1998, Pollock 1998, Paasonen & Tuomisto 2001). Renal function weakens clearly in advancing age because of decreased glomerular filtration rate in kidneys, whereas hepatic function is not reduced so much, provided there are no specific diseases in liver. E.g., digitalis which is excreted via kidneys mostly as unchanged drug may accumulate in patients with advanced age leading to intoxication. (Neuvonen 2001). Cardiac output and pulmonary action deteriorate and influence the pharmacokinetics of drugs.

Absorption is usually minimally changed in advancing age. The distribution of drugs is altered because of the increasing fat/muscle ratio, while the total body water decreases. Many drugs, including many psychotropics, are highly lipophilic, which means that their half-lives usually prolong and the drugs accumulate in the elderly. (Pollock 1998). In the elderly, the half-life of diazepam is up to 4- to 5-fold compared to younger persons, being 35 to 100 hours (Klotz *et al.* 1975, Sorock & Shimkin 1988). Individual differences in the half-lives of benzodiazepines increase upon aging, and even short-acting drugs have a prolonged effect in the body (Herings *et al.* 1995).

Psychotropics taken daily tend to accumulate in the central nervous system (CNS), even though the substance is adequately eliminated from the circulation (Tuomisto *et al.* 1984, Herings *et al.* 1995). For these reasons, the psychotropic doses of the elderly should be half or even one fourth of the doses prescribed for middle-aged patients (Koponen 2002).

In the elderly, hepatic metabolism is reduced because the liver mass and blood flow decrease (Pollock 1998). Drugs tend to accumulate if many drugs are used concomitantly resulting in an overload of the metabolic pathways (Casey 1997). If several drugs use the same cytochrome P450 enzyme pathways in hepatic metabolism, inhibition or induction of the enzyme may lead to remarkable adverse effects and drug-drug interactions. For example, fluoxetine inhibits the metoprolol-metabolizing enzyme, and the metoprolol concentration may consequently increase and cause bradycardia. (Pelkonen *et al.* 1998, Pollock 1998)

The pharmacodynamic changes induced by aging are less well characterized than the pharmacokinetic changes. Pharmacodynamics reflects an organ-specific response and a homeostatic counter-relation (e.g. postural hypotension), which changes along with aging. The sites of drug action include cell surface and intracellular receptors, enzymes, and membrane ion channels. (Cusack *et al.* 1997). Receptors control the quality of the drug's influence and its biological activity. Drugs may block receptors (antagonists) or activate them (agonists). Neurodegeneration upon aging or in diseases and many drugs, such as psychotropics, cause disorders in neurotransmission in the cholinergic (muscarinic and nicotinic receptors), dopaminergic, serotonergic, and noradrenergic systems, which are responsible for memory and learning. (Koponen 2001, Scheinin 2001, Ylinen *et al.* 2001)

Specific receptor and neurotransmitter changes associated with senescence include reductions in central cholinergic and dopaminergic activities and leading to greater sensitivity to medications acting on these systems (Pollock 1998). The cholinergic muscarinic receptor block decreases extrapyramidal symptoms, but causes anticholinergic adverse effects (e.g., reduced cognition, confusion, orthostatism, urinary retention, constipation, etc.). The dopaminergic receptor block decreases the positive symptoms of schizophrenia, but causes extrapyramidal adverse effects (parkinsonism – rigidity, tremor, bradykinesia, weakness, autonomic dysfunction, dementia, and tardive dyskinesia). (Pickar 1995, Koponen 1997)

Drugs that inhibit structural brain disorders or protect nervous cells from neurodegenerative disorders and apoptosis are being investigated actively. Cholinergic drugs are used in Alzheimer's disease and levodopa and dopaminergic receptor agonists in parkinsonism. (Cástreñ *et al.* 1998). Neurological adverse effects are less common in atypical antipsychotics than conventional ones (Pickar 1995, Casey 1997). New antidepressants (selective serotonin reuptake inhibitors = SSRIs) have fewer and less severe CNS and anticholinergic adverse effects than tricyclic antidepressants (Keller 2000).

2.2 Drug use in the elderly

2.2.1 History

Among home-dwellers aged 65 years or over, the use of prescription medications followed the same trend as in the general population and became more common in the 1960s, 1970s, 1980s, and up till 1996. The mean number of prescription drugs per elderly user increased systematically from 1968 to 1976 and further until 1987, most prominently among those aged 75 years or over, with women predominating. From 1976 to 1996, polypharmacy (≥ 5 prescription drugs) per user became more prevalent in the elderly. (Klaukka & Martikainen 1989, Klaukka & Rajaniemi 1998)

The number of prescriptions per inhabitant increased rapidly in the 1960s and 1970s, even in the general population, and continued to increase steadily as per inhabitant from 1979 till 1999. The increase of prescriptions in the 1960s and the 1970s was due to the development of the health care system and the increased use of health care services, the growing number of services available at pharmacies, the marked development of pharmaceutical industry, and the increasing drug research. The mortality of population has decreased, and the prolonged life expectancy has increased chronic morbidity and thereby drug use. The social insurance established in 1964 gave a financial opportunity for all persons to buy drugs. (Klaukka 1989, National Agency for Medicines and Social Insurance Institution 2001)

In a Finnish nationwide survey on the home-dwelling elderly, cardiovascular drugs were used most commonly from 1976 to 1987, with half of men and 61% of women using them in 1987. Cardiovascular drug use was most common in women aged 75 years

or over in 1987 (73%). From 1976 to 1987, the next most commonly used drugs among elderly home-dwellers were analgesics and antirheumatics, followed by psychotropics, which were used by 20% of men and 23% of women aged over 74 years in 1987, when they were the most common psychotropic users. The use of all psychotropics (anxiolytics, hypnotics, antipsychotics, antidepressants) by the elderly was more common in 1987 than in 1976, with the exception that antipsychotic use by the 65- to 74-year-old women and antidepressant use by the 75-year-old or older men decreased slightly in the 10-year period. (Klaukka & Martikainen 1989)

2.2.2 Drug use in general

World Health Organization (WHO) recommends a maximum use of 3 to 4 drugs by older persons (WHO 1987). This limit is commonly exceeded by the home-dwelling elderly according to clinical experience. Many studies show that the elderly are the largest per capita users of medications associated with both physical and mental abilities (Hanlon *et al.* 1996 & 1998).

Most of the epidemiological studies on drug use by the elderly focus on a wide age range, mainly persons aged 65 years or over. There are some studies on the home-dwelling elderly that describe drug use patterns between defined time windows. In Florida, the total (prescribed and non-prescribed) number of drugs per home-dweller grew significantly from 3.2 to 3.9, and the prevalence of total drug use grew by 10% over the 10-year period from 1978 to 1988 in a cross-sectional study (Stewart *et al.* 1991a). In the longitudinal time frame of the same study, the mean number of drugs per person also increased significantly from 2.9 to 4.1 (Stewart *et al.* 1991b). In Finland, the prevalence of prescription and non-prescription drug users and the number of prescribed drugs per person increased in a longitudinal setting in the general elderly population (home-dwellers and institutionalized persons) from 1979 to 1989 (Jylhä 1994).

Among the elderly, cardiovascular and analgesic medications were the most common prescription and non-prescription drugs in the USA in the 1980s (Chrischilles *et al.* 1992). Cardiovascular drugs followed by central nervous system drugs are the most commonly used prescription drugs among the Danish and Swedish elderly (Rosholm *et al.* 1998, Barat *et al.* 2000, Jörgensen *et al.* 2001).

2.2.2.1 Prescribed drug use and the oldest home-dwelling elderly

Drug consumption patterns and drug assortments differ from country to country and between different areas within the same country, often without any specific reason. Any comparison of the results is difficult because of the different methods used.

Studies concerning particularly the home-dwelling oldest old are rare, and knowledge of their drug use is scant, since most studies are based on surveys carried out upon admission into a hospital or a nursing home (Kennerfalk *et al.* 2002). Table 1 shows the

trends in drug use with special reference to the oldest home-dwelling age groups, particularly those over 80, 85, or 90 years of age. In Finland, 84% of the people aged 85 years or over already had regular medication two decades ago (Haavisto & Mattila 1981). In the USA, average drug use decreased in the oldest age groups from 1978 to 1988 (Stewart *et al.* 1991b), but five years ago, in a national American survey recording annual visits to physicians, persons 80 years old and older were prescribed most frequently ≥ 4 different drugs (polypharmacy) during a single visit (Huang *et al.* 2002).

In the United Kingdom, the oldest old were the most prevalent drug users (79% to 100%) in the late 1980s, and the oldest old men had polypharmacy more commonly than women in the mid-1990s (Rumble & Morgan 1994, Kennerfalk *et al.* 2002). In the Nordic countries, drug use by the oldest old is also heterogeneous in the different countries and periods. In Finland, 81% of home-dwelling persons 100 years old or older used prescription drugs in the early 1990s (Louhija 1994). In France, centenarians used drugs less commonly than the other elderly in the late 1990s (Simiand-Erdociain *et al.* 2001).

Home-dwelling elderly Finns aged 100 years or over used less drugs commonly than younger elderly persons according to a recent study. Centenarians use old cheap drugs and many drugs for cardiovascular and musculoskeletal problems as well as psychotropics less frequently than 90- to 99-year-olds, which explains their lesser medication costs. Three out of four Finnish centenarians use cardiovascular drugs, while by every second of them use nervous system (mostly psychotropics) or antimicrobial drugs. (Klaukka *et al.* 2002)

Table 1. Prescription drug use by the home-dwelling elderly according to different studies with special reference to the oldest population.

Author(s)	Country/ population/ methodology	Age (years) of sample	Number of sample	Age (years) of targets (n)	Prescription drug use of targets (number or %)
Haavisto & Mattila 1981	Finland/ Tampere/ cross-sectional	85+	474	85+ (474)	84% regular medication (mainly prescribed)
Enlund <i>et al.</i> 1990	Finland/ 7 areas/ follow-up for 25 years	65–84 men	675	65–84 (675)	66 %
Stewart <i>et al.</i> 1991b	USA/ Florida/ longitudinal over 10 years	65+	924	80+ (55)	The mean increase in the number of drugs was highest (1.4) in the 80- to 84 -year-olds and 0.2 in the 85+-year-olds
Laukkanen <i>et al.</i> 1992	Finland/ Jyväskylä/ cross-sectional	65–84	1224	75–84 (589)	Men 70% and women 80%, mean number of drugs (3.4) highest in women aged 80–84 years
Louhija 1994	Finland/the whole country/ cross-sectional	100+	181	100+ home-dwelling (43)	81 %

Table 1. Continued.

Author(s)	Country/ population/ methodology	Age (years) of sample	Number of sample	Age (years) of targets (n)	Prescription drug use of targets (number or %)
Rumble & Morgan 1994	UK/Nottingham/ longitudinal 4 years	65+	662	89+ (24)	Most prevalent users, 79% (n = 28) in 1985 and 100% (n = 24) in 1989
Bjerrum <i>et al.</i> 1998	Denmark/Funen/ follow- up for 2 years	All inhabitants, 15+	466 567	90+ (n = not mentioned)	Prevalence of polypharmacy (2–4 or ≥ 5 drugs) was lower than among the other elderly
Rosholm <i>et al.</i> 1998	Denmark/Funen/ follow- up for 3 months	All inhabitants	466 567	70+ (54 427)	64%, under 70-year-olds 32%
Jørgensen <i>et al.</i> 2001	Sweden/Tierp/ retrospective over one year	65+	4642	85+ (651)	Men 72% and women 67%, most prevalent in the elderly aged 75–84 (84%)
Simiand- Erdociain <i>et al.</i> 2001	France/ Haute-Garonne/ retrospective over 7 months	50+	3026	80+ (1506) 100 (87)	Most prevalent in the 75- to 79-year-olds (86%), 45% in the 100-year- olds
Huang <i>et al.</i> 2002	USA/National sample, the National Ambulatory Medical Care Survey/ annual medical visit in 1997	65+ presenting all inhabitants in the US	191 million visits	80+ (50 million visits)	≥ 4 prescriptions per visit (polypharmacy) most frequently
Kennerfalk <i>et al.</i> 2002	UK/General Practice Research Database/cross- sectional at two different time points	65–90	5000	75–90 (2215)	≥ 5 drugs (polypharmacy) in men at maximum 10% or 20% and in women 17% or 24% at two different time points, polypharmacy most prevalent in 80- to 84 -year- old men and in 75- to 79-year- old women

n = number of targets. Targets are the oldest persons of the sample. For follow-up/longitudinal studies, the number of persons and the results of the latest population are given.

2.2.3 Polypharmacy

According to the literature, polypharmacy is usually defined in two ways, by simply counting the drugs or based on the administration of more drugs than are clinically indicated (Hanlon *et al.* 2001). There are numerous definitions for polypharmacy, and the criteria vary from study to study. Some researchers have defined polypharmacy as the long-term use of two or more medications or ≥ 4 prescriptions per medical visit, others as

the daily intake of 2 to 3, at least 3, or 4 to 5 drugs. In yet some other studies, the minimum limit for polypharmacy has been at least 5 drugs, more than 5 drugs, at least 7, or at least 10 drugs. (Ilfie *et al.* 1991, Chrischilles *et al.* 1992, Klaukka *et al.* 1993, Lee 1998, Barat *et al.* 2000, Flaherty *et al.* 2000, Veehof *et al.* 2000, Hanlon *et al.* 2001, Huang *et al.* 2002). Polypharmacy is sometimes characterized in more detail as minor (2 to 3 drugs), moderate (4 to 5 drugs), or major (> 5 drugs) polypharmacy (Veehof *et al.* 2000). WHO defines polypharmacy as concomitant use of ≥ 5 drugs (WHO 1985). Polypharmacy is usually regarded as an unwanted phenomenon but in certain situations, such as multiple cardiovascular pathology in the same subject, polypharmacy may be indicated (Strandberg *et al.* 2001).

In the home-dwelling elderly, the predictors of increasing polypharmacy are age, the use of many drugs, the use of drugs (especially hypnotics/sedatives) without a clear indication, cardiovascular diseases, diabetes, and abdominal symptoms. In over 4-year follow-up, almost 20% of the home-dwelling elderly developed polypharmacy. (Veehof *et al.* 2000). Forty per cent of the home-nursed elderly with polypharmacy had depressive symptoms and sleeping disorders, and polypharmacy was connected with impaired cognition (Lithovius *et al.* 1998).

Polypharmacy causes a risk of adverse effects, toxic reactions, and drug interactions (Tune *et al.* 1992, Barat *et al.* 2000, Mannesse *et al.* 2000). Polypharmacy is risk factor for falls (Tinetti *et al.* 1994), which may cause fractures and other injuries and constitute a risk for hospitalization. Studies have shown that the hospital admissions of 12% to 42% of elderly patients were due to adverse drug reactions (Colt & Shapiro 1989, Cunningham *et al.* 1997, Mannesse *et al.* 1997, Mannesse *et al.* 2000), and every fourth admitted person had a severe reaction related to drugs (Mannesse *et al.* 2000). Elderly patients with drug-induced illness had an average of 6.3 drugs compared to 3.8 drugs per elderly patient admitted for other reasons (Colt & Shapiro 1989). Clinically significant interactions have been found in up to 15% of the home-dwelling elderly with polypharmacy (Barat *et al.* 2000).

In 1995–96, every third (39%) Finnish drug user aged 75 years or over had polypharmacy (≥ 5 prescription drugs) (Klaukka & Rajaniemi 1998). Polypharmacy is also prevalent among the elderly elsewhere. In the United Kingdom, every third (30%) home-dwelling person over 74 years of age used three or more prescribed drugs (Ilfie *et al.* 1991). Their proportion in Denmark was 60% among 75-year-old persons, and 34% took 5 or more drugs (Barat *et al.* 2000).

2.2.4 Psychotropic use

Psychotropics are used for serious psychiatric diseases, such as schizophrenia, psychoses, or depression, and slighter problems, such as anxiety or insomnia. Psychotropics are usually divided into hypnotics/sedatives (anxiolytics and sleeping pills), antipsychotics (neuroleptics), and antidepressants (Aisen *et al.* 1992, Thapa *et al.* 1995, Ebly *et al.* 1997, Weiner *et al.* 1998, Leipzig *et al.* 1999a, Klaukka 2000a).

In previous studies, psychotropic use among the home-dwelling elderly has ranged from 10% to 38%, and hypnotics/sedatives (mostly benzodiazepines) have been the most commonly prescribed psychotropics, ranging from 6% to 31%. In previous studies, 1% to 4% of the home-dwelling elderly have been taking antipsychotics and 2% to 5% antidepressants. (Laukkanen *et al.* 1992, Skoog *et al.* 1993, Manela *et al.* 1996, Weiner *et al.* 1998, Kirby *et al.* 1999, Fourier *et al.* 2001)

The elderly use psychotropics more frequently than the general population in Finland and elsewhere (Cooperstock & Parnell 1982, Ohayon *et al.* 1998, Blazer *et al.* 2000, Hartikainen *et al.* 2000). A worldwide population-based review of psychotropic use more than 20 years ago pointed out the more common psychotropic use among the elderly, especially women, compared to any other age group (Cooperstock & Parnell 1982). According to Finnish national statistics, both men and women aged 75 years or over used anxiolytics, sleeping pills, antipsychotics, and antidepressants more commonly than the other age groups in the late 1990s (Klaukka 2000a).

Increasing trends of psychotropic use in the home-dwelling elderly have been described (Klaukka & Martikainen 1989). Opposite results have also been obtained during the past few decades. From 1986 to 1996, sedative/hypnotic/antianxiety medication use remained stable (13% vs 12%, respectively) in the home-dwelling elderly in the USA (Blazer *et al.* 2000). Antidepressant use was uncommon among the elderly until the 1990s in Finland. In the early 1990s, the symptoms of depressed elderly persons were more often treated with analgesics or hypnotics/sedatives than antidepressants (Linjakumpu *et al.* 2001). Antidepressant use increased, particularly among persons aged 75 years or older, in the 1990s, in which age group almost every fourth person bought antidepressants at least once in 1999 (Klaukka 2000a).

The prescriptions of psychotropics increase with age over 40 years, female gender, the prominence of psychologic complaints, the severity of mental disorders or social disability, low education, unemployment, and marital separation (Linden *et al.* 1999). The use of psychotropic medication without a specific indication is not uncommon. Of the home-dwelling elderly or other adults, 15% have been reported to take psychotropics or benzodiazepines with no diagnosed mental disorder (Joukamaa *et al.* 1995, Kirby *et al.* 1999), and 29% of the 85-year-olds may use psychotropics without a psychiatric diagnosis (Skoog *et al.* 1993).

The changes in the consumption of psychotropics in the Nordic countries have been documented in a comparable way for a long time in the general population. The changes in the 1990s are presented in Paper II, Fig. 1. The consumption of antidepressants increased in the Nordic countries and most other developed countries in the 1990s (McManus *et al.* 2000). In Australia, antidepressants were prescribed most commonly to working-aged people (McManus *et al.* 2000), which is opposite to the prescription practice in Finland, where the elderly predominate in this respect (Klaukka 2000a).

2.2.4.1 Psychotropic use and the oldest home-dwelling elderly

Table 2 shows the statistics of psychotropic and benzodiazepine use side by side, because benzodiazepines are the most extensively used psychotropics (Fourrier *et al.* 2001). In the USA, Ireland, and Sweden, psychotropic use did not correlate with higher age from about 25 years ago until the mid-1990s (Swartz *et al.* 1991, Isacson *et al.* 1992, Dealberto *et al.* 1997, Kirby *et al.* 1999, Blazer *et al.* 2000, Jørgensen *et al.* 2001). In the USA, national annual data in 1995 provided even opposite evidence about psychotropic prescriptions to the oldest old. The frequency of visits at which psychotropics were prescribed was greater among patients aged over 84 years. (Aparasu *et al.* 1998). In Finland, too, psychotropic use concentrated to the older age groups in the late 1980s (Laukkanen *et al.* 1992, Joukamaa *et al.* 1995). Every second old client of primary health care used psychotropics, and every third used benzodiazepines (Joukamaa *et al.* 1995). However, over two decades ago, only every ninth Finn aged 85 years or over used psychotropics regularly and every fifth when needed (Haavisto & Mattila 1981).

A quarter of a century ago, benzodiazepine use was equally common in the oldest old as in the younger elderly in Sweden (Isacson 1997). About 20 years ago, among the 18- to 84-year-olds, the oldest group used psychotropics most commonly (Isacson & Haglund 1988). In Finland, psychotropic use was twice as common among elderly women than among men (Laukkanen *et al.* 1992), as it was in Sweden among the 85-year-olds in the latter half of the 1980s (Skoog *et al.* 1993). In large population studies conducted in Denmark and Italy, psychotropic or antidepressant use was most common among the oldest old, though antidepressant use in Italy decreased toward centenarians in 2000 (Rosholm *et al.* 1994, Pietraru *et al.* 2001). In Finland, too, only 9% of the home-dwelling people aged 100 years or over used hypnotics/sedatives over ten years ago (Louhija 1994).

Table 2. Prescription psychotropic use by the home-dwelling elderly according to different studies with special reference to the oldest population.

Author(s)	Country/population/ methodology	Age (years) of sample	Number of sample	Age (years) of targets (n)	Prescription psychotropic use of targets (number or %)
Haavisto & Mattila 1981	Finland/Tampere/cross -sectional	85+	474	85+ (474)	11% regularly, 20% when needed
Cooperstock & Parnell 1982	USA, Europe, Canada, Australia/total populations ^a	All ages	Millions	Older adults ^b	Psychotropic use more prevalent than in the middle- aged population or in children
Isacson & Haglund 1988	Sweden/Tierp/ prescriptions data from pharmacies to individuals in 1981	18-84	15 915	75-84 (1595)	Psychotropics 34%, most prevalently of all age groups
Morgan <i>et al.</i> 1988	UK/the Nottinghamshire Family Practitioner Committee's records/ cross-sectional	65+	1020	75+ (about 500)	Hypnotics 20% sometimes, in 65- to 74-year-olds 13%
Swartz <i>et al.</i> 1991	USA/North Carolina/ retrospective over one year	18-75+	3798	55-74 (1414) 75+ (425)	Benzodiazepines 14% and 14 %
Isacson <i>et al.</i> 1992	Sweden/Tierp/ prescription data from pharmacies to individuals in 1976	0-85+	19 926	75-84 (1435) 85+ (303)	Benzodiazepines 26% and 23% . After 8 years, mostly 75- to 84-year-olds (45%) were continuous users
Laukkanen <i>et al.</i> 1992	Finland/Jyväskylä/ cross-sectional	65-84	1224	65-74 (635) 75-84 (589)	Psychotropics 8% of men and 14% of women Psychotropics 13% of men and 23% of women
Skoog <i>et al.</i> 1993	Sweden/Gothenburg/ cross-sectional	85	417	85 (417)	Psychotropics 37%, men 24% and women 42%
Louhija 1994	Finland/the whole country/cross-sectional	100+	181	100+ home- dwelling (43)	Hypnotics/sedatives 9%
Rosholm <i>et al.</i> 1994	Denmark/Odense/ follow-up for 2 years, persons purchasing psychotropics	All ages	210 000	90+ (n = not mentioned)	Psychotropics 18% (hypnotics/anxiolytics excluded), most prevalently of all age groups
Joukamaa <i>et al.</i> 1995	Finland/Turku/ primary health care, follow-up for 3 years	18-89	1000	75-89 (56 psychotropic users)	Psychotropics 49%, benzodiazepines 37% - most prevalently of all age groups

Table 2. Continued.

Author(s)	Country/population/ methodology	Age (years) of sample	Number of sample	Age (years) of targets (n)	Prescription psychotropic use of targets (number or %)
Dealberto <i>et al.</i> 1997	USA/New Haven/from 1982 to 1988 follow-up	65+	2589 in 1982	75+ (n = not mentioned)	Psychotropic use did not correlate with higher age
Isacson 1997	Sweden/Tierp/ at least one prescription in 1976	15+	19 926	85+ (303)	Benzodiazepines 23%, most prevalently (26%) in 75–84- year-olds
Aparasu <i>et al.</i> 1998	USA/National sample, National Center for Health Statistics/ annual physician visits	65+	36 857	85+ (n = not mentioned)	Most prevalently visits to physicians, when psychotropic drugs were prescribed
Kirby <i>et al.</i> 1999	Ireland/Dublin/ cross- sectional	65+	1701	65–74 (981) 75+ (720)	Benzodiazepines 17% and 18 %
Blazer <i>et al.</i> 2000	USA/7 areas throughout the US/ follow-up 10 years	65–105	4162 at baseline	65–74 (2580) 75+ (1582)	No difference at baseline between the age groups in sedative/hypnotic/antianxiety drug use, in 65+-year-olds 13% in 1986 and 12% in 1996
Jørgensen <i>et al.</i> 2001	Sweden/Tierp/ retrospective over one year	65+	4642	85+ (651)	Nervous system drugs, men 36%, women 44% (75- to 84 year-olds almost the same)
Pietraru <i>et al.</i> 2001	Italy/Chivasso/ follow- up for 6 months	All ages Antidepress ant users	197 592 3751	75+ (766 antidepressant users)	Antidepressant use in 85- year-old men ^c and 80/90-year- old women ^d was most prevalent, after this their use decreased

^a All inhabitants, ^b varied by country. ^c Rate 35/1000 inhabitants, ^d rate 62/1000 inhabitants. In follow-up/longitudinal studies, the number of persons and the results of the latest population are expressed. n = number of targets. Targets are the oldest persons of the sample.

2.2.5 Polypharmacy of psychotropics

Concomitant use of CNS-active medications has been defined in a variety ways in the scientific literature. Polypharmacy of psychotropics may be defined as, for example, the simultaneous purchasing of two different major psychotropics (neuroleptics, antidepressants, or lithium). About a decade ago, polypharmacy with psychotropics was most prevalent in outpatients aged 70 years or over in Denmark. (Rosholm *et al.* 1994). Polypharmacy with psychotropics may also be defined as concurrent use of three or more drugs, at least two drugs from the same therapeutic class, or three or more drugs

concurrently which may cause confusion, and polypharmacy with psychotropics correlates with behavioral problems (Schmidt & Svarstad 2002).

According to another definition, polypharmacy consists of simultaneous use of benzodiazepines, other hypnotics/sedatives, tricyclic antidepressants, neuroleptics, or opioids. The use of two or more of these drugs concomitantly is related to an increased risk of accidents compared to the use of one CNS-active drug alone. (Weiner *et al.* 1998). Two benzodiazepines used simultaneously increased the risk of falls 15-fold in over 84-year-olds (Caramel *et al.* 1998). Concomitant use of antidepressant and benzodiazepine is a well-established policy in the elderly, and it is also quite common, occurring in more than half of the cases (van Dijk *et al.* 2002). With respect to the different groups of antidepressants, no differences in psychomotor reaction performance were observed in polydrug treatment in persons who were mainly middle-aged, but also included some elderly persons (Grabe *et al.* 1998).

2.2.6 Sedation

Psychotropics (hypnotics/sedatives, antipsychotics, antidepressants) are conventional sedating drugs. Other sedatives include opioids, anticonvulsants, and antihistamines. (Bowen & Larson 1993, Ebly *et al.* 1997, Weiner *et al.* 1998, Slater *et al.* 1999, Maletta *et al.* 2000, Blokland *et al.* 2001). Sedation is sometimes intentional, as in the treatment of acute psychiatric diseases or insomnia (Thompson *et al.* 1983, Batty *et al.* 2000), but often injurious in elderly and frail persons, as it may cause drowsiness (Pelkonen 1998) and falls (Weiner *et al.* 1998). While sedation may initially be beneficial, it impairs the person's functioning (Casey 1997).

Part of the sensitivity to drug-induced sedation, motion disturbances, and falls is associated with the aging processes (Koponen 2001). Sedation may result from multiple mechanisms, such as antagonism of the histaminergic receptors (conventional low-potency neuroleptics, some tricyclic antidepressants) (Koponen 1997) or agonism of the opioid receptors (potent analgesics) (Pharmaceutical Information Centre 2000), or be related to the anticholinergic effect of the compound (diminished arousal) (Bowen & Larson 1993, Tune & Bylsma 1991, Tune *et al.* 1992). Benzodiazepines influence the central nervous system by acting on specific benzodiazepine receptors. Only very large amounts deprive the circulatory or ventilation systems.

2.2.7 Adverse effects of drugs

Most of the data on the effects of a new drug have been obtained from young or middle-aged persons, which means that unexpected adverse effects are not infrequent in the old (Pollock 1998). Adverse effects affecting younger persons are assumed also to affect the elderly. Life-threatening adverse drug effects are more likely to be reported to the

authorities than less serious ones. If an adverse effect is seen in < 1% of cases, it may or may not be reported to the authorities. (Himberg & Kuitunen 2002)

Adverse effects associated with drugs were collected from Pharmaca Fennica (Pharmaceutical Information Centre 2000), a textbook of Clinical Pharmacology and Drug Treatment (Himberg & Kuitunen 2002), and various other sources, and they are shown in Appendix table 1. The summaries of the product characteristics of drugs are accepted into Pharmaca Fennica by the relevant authority (National Agency for Medicines in Finland) at the time when the drug receives a sales licence or when the drug information is updated.

The examples of drugs in the Appendix table 1 show that the drugs most commonly used by the elderly, such as cardiovascular or CNS (psychotropic) drugs (Rosholm *et al.* 1998, Barat *et al.* 2000, Jørgensen *et al.* 2001), may cause adverse effects. On the other hand, many drugs may cause different cardiovascular and nervous system adverse effects. Both phenomena have been pointed out before. (Gerety *et al.* 1993). All psychotropics are associated with balance disorders (Aisen *et al.* 1992, Malmivaara *et al.* 1993, Ruthazer & Lipsitz 1993, Cumming 1998, Wang *et al.* 2001) and may thus result in fractures and other injuries. They may cause balance disorders, acting on both the central (delayed actions and reflexes, delirium) and the peripheral (muscle relaxation) nervous systems (Sorock & Shimkin 1988, Ray *et al.* 1989, Cumming *et al.* 1991, Ryynänen *et al.* 1993). In the Appendix table 1, other psychotropic adverse effects include orthostatism, cardiac arrhythmias, anticholinergic effects, tardive dyskinesia/ extrapyramidal symptoms, sedation, cognitive decline, delirium, and depression.

Anticholinergic drugs are numerous (Appendix table 1), and the anticholinergic effects of many drugs and their metabolites are unknown. Elderly persons with polypharmacy may develop an anticholinergic intoxication syndrome when their total anticholinergic load rises, due to some or all of their drugs having moderate anticholinergic effects. (Tune & Bylsma 1991, Tune *et al.* 1992). The acute symptoms of the anticholinergic syndrome include tachycardia, dry mouth, mydriasis, hot skin, atonic bladder, delirium, hallucinations, agitation, memory disturbances, paralysis, convulsions, somnolence, and even death. These symptoms may be due to central or peripheral cholinergic blocking. Chronic anticholinergic syndrome may be present simultaneously with other symptoms, such as confusion or memory problems due to psychiatric illnesses (Moreau *et al.* 1986). Withdrawal of tricyclic antidepressants may result in a rebound syndrome, probably caused by increased cholinergic flux after cessation of treatment with an anticholinergic effect. The symptoms are gastro-intestinal, sleep disturbances, mood fluctuations, or movement disorders. (Wolfe 1997, Ali & Milev 2003). Even in healthy older adults, the use of anticholinergic medications is considered potentially inappropriate (Beers 1997, McLeod *et al.* 1997). Partly inappropriate medications of the elderly (e.g., anticholinergic amitriptyline, doxepin, or hydroxyzine) also cause sedation (Tune & Bylsma 1991, Tune *et al.* 1992, Bowen & Larson 1993, Beers 1997).

It could be mentioned as an example that high-dose non-steroidal anti-inflammatory drugs cause a risk for cognitive decline (Karplus & Saag 1998), but chronic use may have beneficial effects on cognition (Rozzini *et al.* 1996, Karplus & Saag 1998).

2.2.8 Physical functional abilities connected with medications

Drug use connected with physical functional abilities has not been studied widely in Finland or elsewhere. The possibilities of elderly persons to live alone and to continue living at home depends on their ability to manage the activities of daily living (ADL), mobility, and instrumental activities of daily living (IADL), provided they have appropriate medication and no injurious sedative medication.

The influence of drugs may be positive and improve the patient's abilities, but an excessive sedative influence on the central nervous system impairs the physical functional status (Ried *et al.* 1998) and may expose a person to falls, for example (Aisen *et al.* 1992, Malmivaara *et al.* 1993, Ruthazer & Lipsitz 1993, Rynnänen *et al.* 1993 & 1994, Tinetti *et al.* 1994, Herings *et al.* 1995, Lord *et al.* 1995, Ebly *et al.* 1997, Cumming 1998, Thapa *et al.* 1995 & 1998, Leipzig *et al.* 1999a, Wang *et al.* 2001). Frequent fear of falling is also a risk factor for fracture-causing falls (Luukinen *et al.* 1997). Injurious accidents may lead to hospitalization because of fractures, brain commotions and contusions, or even death (Malmivaara *et al.* 1993).

Physical functional abilities connected with sedative drugs have traditionally been studied concerning psychotropic drug use (Ried *et al.* 1998, Blazer *et al.* 2000, Ridout & Hindmarch 2001). As shown by previous studies, a single sedative (zolpidem) is sufficient to increase the risks of falls (Wang *et al.* 2001) and may expose the person to hospitalization and mortality (Malmivaara *et al.* 1993). Impaired physical function, use of health services, and poor self-rated health have been found to correlate with the use of sedatives, hypnotics, and antianxiety drugs among the home-dwelling elderly (Blazer *et al.* 2000). Benzodiazepines have also been found to be associated with poor physical functioning (Ried *et al.* 1998, Gray *et al.* 2002). Ahto *et al.* (1998) found an association in the elderly between dependence or difficulties in ADL and antipsychotics as well as between dependence in mobility or IADL and hypnotics. Difficulties or dependence in physical activities were associated independently with cardiovascular drug use, particularly diuretic use.

Home nursing is a challenge for health care professionals because extremely fragile elderly persons often live alone. Home nursing patients use plenty of drugs (Lithovius *et al.* 1998). A high number of drugs is associated with poor physical functioning (Rozzini *et al.* 1993) and hypotension (Cohen *et al.* 1998).

3 Aims of the study

The purpose of the present study was to investigate drug use in two cross-sectional elderly home-dwelling populations in southwestern Finland in the 1990s. The aims of the present study were:

1. to describe drug use and polypharmacy in the early and late 1990s
2. to describe and analyze sociodemographic, clinical, and physical functional items connected with polypharmacy
3. to describe psychotropic use in the early and late 1990s
4. to create a classification of drugs by their sedative properties and to describe the extent of sedative drug use
5. to describe and analyze sociodemographic, clinical, and physical functional items connected with sedative drug use

4 Materials and methods

4.1 Study design and populations

This study is part of a larger epidemiological study of subjects aged 64 years or over in the community of Lieto, Finland. Two consecutive cross-sectional surveys comprising an interview followed by a health examination were conducted. The purpose of the Lieto study was to investigate general illnesses among the elderly, with particular reference to cardiovascular and pulmonary diseases.

The first survey was carried out between October 1990 and December 1991 and the second between March 1998 and September 1999. Persons born in 1926 or before who had been Lieto residents according to Population Register Center on 23.3.1990 ($n = 1360$) were invited to attend the first study. The invitation to attend the second study was sent to the persons born in 1933 or before who had been Lieto residents according to Population Register Center on 16.2.1998 ($n = 1596$). The study populations are presented in Fig. 1. The participants were invited to come to the Lieto Health Center in a random order. In 1990–91, 77 subjects died before they could be examined, 68 declined (4 because of relatives), 5 had moved elsewhere, 12 could not be traced, 1 was hospitalized before the study, and 1 failed to turn up. In 1998–99, 63 died before they could be examined, 200 declined, 4 had moved elsewhere, 59 did not respond, and 10 could not be traced. No information was available on those who did not participate (Isoaho 1995, Wendelin-Saarenhovi 2002).

The only exclusion criterion of the present study was living in a long-term institution. The home-dwelling elderly were selected from the population to evaluate their drug use, with the hypothesis that drug use would be more prevalent if institutionalized persons had been included.

In 1990–91, altogether 1196 persons (93% of those eligible) participated, and 1131 (469 men and 662 women) of them were living at home. In 1998–99, altogether 1260 persons participated (82% of those eligible), and 1197 (518 men and 679 women) of them were living at home. The ages of the home-dwelling participants ranged from 64 to 96 years in 1990–91 and from 64 to 97 years in 1998–99. Their mean age was the same in both surveys, 72 years for men (SD 6.3 in 1990–91 and SD 6.2 in 1998–99) and 73 years

for women (SD 6.6 in both surveys). The use of psychotropics by the young elderly aged 64–71 years in 1990–91 ($n = 573$, 46% men) and 1998–99 ($n = 583$, 46% men) was studied separately, because they were different persons in both surveys.

Lieto is a semi-rural southwestern municipality near the City of Turku in Finland. The living conditions of this population are typical of those prevailing in southern Finland. Previously mainly an agricultural area, Lieto has been transformed since the Second World War into a commuter and partly industrialized community with a growing population. Its population was 12255 in 1990 and 13845 in 1999, with about 10% and 12% of the people aged 65 years or over, respectively, compared to 13% in 1990 and 15% in 1999 in Finland (Central Statistical Office of Finland 1991, Statistics Finland 1998, Statistics Finland 2000). The age distributions of these Lieto elderly populations were similar to those of the whole nation in both surveys. Today, residents of Lieto work in the social service sector, industry, and agriculture in the same proportions as Finns in general (Statistics Finland 2001), but in the late 1980's, working-aged persons in Lieto held industrial jobs more prevalently than Finns in general (Tilastokeskus 1991).

The municipal Health Center in Lieto provides primary health care for the population. The number of people in institutional long-term care remained stable from the early to the late 1990s. In Lieto, as elsewhere in Finland, most of the physicians working in health centers are general practitioners, and there was no staff turnover between 1990 and 1998–99, with the exception of a couple of new physicians.

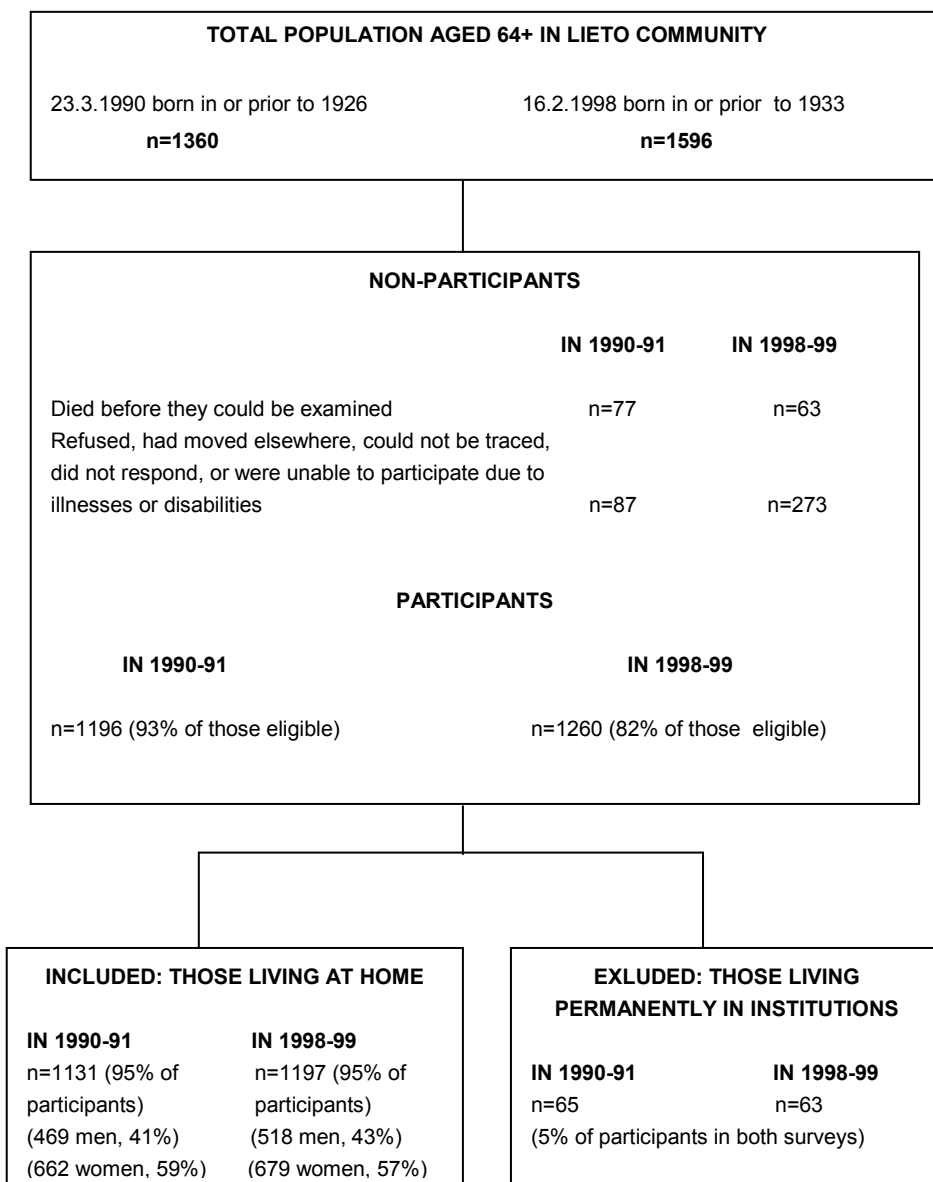


Fig. 1. Structure of the study populations in 1990–91 and 1998–99.

4.1.1 Background data of participants

Background data of the participants are presented in Table 3a–c. In section 5.1.1, results concerning the use of different amounts of drugs vs sociodemographic and other factors will be presented in more detail.

4.2 Study protocol

In addition to the question of prescription drug use during one week prior to the interview, the questionnaires included items asked or measured by one of two trained nurses on

1. sociodemographic and other background data
2. physical, psychic, and social functional abilities
3. smoking, alcohol consumption (the latter in 1998–99)
4. tests and measurements: several laboratory examinations, x-rays, physical/physiological measurements
5. quality of life (in 1998–99 self-perceived health and life satisfaction), home nursing services
6. two health center physicians who belonged to the research team conducted the clinical examinations of the participants

The connections of depression and dementia with drug use were not analyzed in this study. Both diseases are multifactorial, and their connections with drug use would warrant another study. Nor were the associations of single diagnoses with drug use analyzed, because the basic approach of this study was pharmacoepidemiological rather than clinical. Instead, in the latter survey, the diseases recorded by Social Insurance Institution as entitling the patient to a special refund of medication costs were counted.

4.2.1 Ethics

The study was conducted according to the guidelines of the Declaration of Helsinki, and the Ethics Committee of Turku University and Turku University Central Hospital. All subjects gave written informed consent.

Table 3a. Sociodemographic and other characteristics of the home-dwelling elderly by the number of drugs used in community in 1990–91 and 1998–99.

Characteristics of persons	Number of drugs								Significance ^c	
	0		1–5		> 5		Total		1990–91	1998–99
	1990– 91	1998– 99	1990– 91	1998– 99	1990– 91	1998– 99	1990– 91	1998– 99		
	n = 252	n = 141	n = 659	n = 756	n = 220	n = 300	n = 1131	n = 1197		
	%	%	%	%	%	%	%	%		
Age in years									< 0.0001	< 0.0001
64–74	80	82	64	69	48	51	65	66		
75–84	19	16	30	27	46	36	31	23		
> 84	2	1	6	5	6	13	5	7		
Mean age in years ^a	70	70	73	73	75	75	73	73	< 0.0001	< 0.0001
Gender									< 0.05	< 0.05
Men	49	65	42	42	32	35	41	43		
Women	51	35	58	58	68	65	59	57		
Marital status									< 0.001	< 0.01
Married/ cohabiting	68	72	58	61	45	55	58	61		
Widowed	20	13	32	28	47	38	32	29		
Other	9	11	10	11	8	7	8	7		
Living alone	23	18	34	31	40	35	33	31	ns	ns
Poor self- perceived health status ^b	–	2	–	10	–	31	–	14	–	< 0.0001
Poor life satisfaction ^b	–	1	–	3	–	6	–	3	–	< 0.01
Home nursing services	0	0	3	4	16	13	5	6	< 0.0001	< 0.0001

^aAll the results are presented as percentages except mean age. ^bThese items were asked only in 1998–99.

^cStatistical tests were made only between persons with 1 to 5 and > 5 drugs separately in 1990–91 and 1998–99. Categorical variables were tested with Chi-square test, and continuous variables with Student's t-test. ns = no statistical significance.

Table 3b. Sociodemographic and other characteristics of home-dwelling elderly men by the number of drugs used in community in 1990–91 and 1998–99.

Characteristics of persons	Number of drugs								Significance ^c	
	0		1–5		> 5		Total		1990–91	1998–99
	1990–	1998–	1990–	1998–	1990–	1998–	1990–	1998–		
	91	99	91	99	91	99	91	99		
n = 123	n = 92	n = 275	n = 321	n = 71	n = 105	n = 469	n = 518			
%	%	%	%	%	%	%	%			
Age in years									< 0.05	< 0.01
64–74	81	82	65	72	58	55	68	70		
75–84	18	17	30	23	42	36	29	25		
> 84	1	1	5	5	0	9	3	5		
Mean age in years ^a	70	70	72	72	74	75	72	72	ns	< 0.001
Marital status									ns	ns
Married/ cohabiting	83	77	77	79	70	75	78	78		
Widowed	9	8	15	14	24	14	15	13		
Other	8	15	8	7	6	10	8	9		
Living alone	13	14	22	19	20	17	19	18	ns	ns
Poor self- perceived health status ^b	–	3	–	12	–	34	–	15	–	< 0.0001
Poor life satisfaction ^b	–	1	–	2	–	7	–	3	–	< 0.05
Home nursing services	0	0	4	3	17	9	5	3	< 0.0001	< 0.01

^aAll the results are presented as percentages except mean age. ^bThese items were asked only in 1998–99.

^cStatistical tests were made only between persons with 1 to 5 and > 5 drugs separately in 1990–91 and 1998–99. Categorical variables were tested with Chi-square test, and continuous variables with Student's t-test. ns = no statistical significance.

Table 3c. Sociodemographic and other characteristics of home-dwelling elderly women by the number of drugs used in community in 1990–91 and 1998–99.

Characteristics of persons	Number of drugs								Significance ^c	
	0		1–5		> 5		Total		1990–91	1998–99
	1990–1991	1998–99	1990–91	1998–99	1990–91	1998–99	1990–91	1998–99		
	n = 129	n = 49	n = 384	n = 435	n = 149	n = 195	n = 662	n = 679		
	%	%	%	%	%	%	%	%		
Age in years									< 0.0001	< 0.0001
64–74	78	84	64	66	43	48	62	62		
75–84	19	14	29	29	48	36	32	30		
> 84	2	2	7	5	9	16	6	8		
Mean age in years ^a	70	71	73	73	76	76	73	73	< 0.0001	< 0.0001
Marital status									< 0.05	< 0.01
Married/cohabiting	53	61	45	48	33	44	44	48		
Widowed	30	24	44	39	58	50	45	41		
Other	16	14	11	14	9	6	11	11		
Living alone	32	27	43	40	49	45	42	41	ns	ns
Poor self-perceived health status ^b										
Poor life satisfaction ^b	–	2	–	3	–	6	–	4	–	ns
Home nursing services	0	0	3	6	15	15	5	8	< 0.0001	< 0.001

^aAll the results are presented as percentages except mean age. ^bThese items were asked only in 1998–99.

^cStatistical tests were made only between persons with 1 to 5 and > 5 drugs separately in 1990–91 and 1998–99. Categorical variables were tested with Chi-square test, and continuous variables with Student's t-test. ns = no statistical significance.

4.3 Data collection and the Anatomical Therapeutic Chemical (ATC) classification system

The personal interviews were made by two trained nurses in Härkätie Health Center, Lieto. The subjects had been asked to take their prescriptions and drugs along to show the medication that they were currently taking. The nurses also confirmed the respondents' medication use with a close relative or a care-giver or from home nursing and the medical records of the health center, if the person was unable to answer questions, had dementia, or was not in a good condition. If the subject was unable to visit the health center, a

trained nurse made a home visit to check the medications in use. Two health center physicians who belonged to the research team also reviewed the information on medications and collected the participants' diagnoses from the medical records.

The brand names of all prescription drugs (both regular and irregular medication) taken by the interviewee during seven days prior to the interview were recorded and categorized during both study periods by the ATC classification system of National Agency for Medicines (2000): Classification of Medicines (ATC) and Defined Daily Doses (DDD) 2000. Because the ATC codes of some drugs had changed between 1990–91 and 1998–99, they were re-coded according to the classification of the year 2000 to attain comparable recording. The ATC system was created by the Nordic Council on Medicines, version 1996 (Nordic Council on Medicines 1996, National Agency for Medicines 2000), and has been recommended by WHO (1995). In the ATC system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, therapeutic, and pharmacological properties (National Agency for Medicines and Social Insurance Institution 2001). The drugs are classified into 14 main groups at 5 different levels. For example, furosemide is coded as C03CA01 (C = cardiovascular, C03 = diuretics, C03C = high-ceiling diuretics, C03CA = sulphonamides, C03CA01 = chemical substance furosemide) and diazepam as N05BA01 (N = nervous system, N05 = psycholeptics, N05B = anxiolytics, N05BA = benzodiazepines, N05BA01 = chemical substance diazepam).

4.4 Use of official registers

National prescription data from Social Insurance Institution were utilized to compare the use of psychotropics in the late 1990s by all Finnish home-dwelling elderly and by the elderly in Lieto. The national data revealed the proportions of the elderly per 1000 persons who purchased psychotropic drugs at least once during the year 1999.

The national health insurance scheme refunds part the cost of medicines prescribed by a physician for the treatment of an illness. The coverage of the prescription register is, in practice, nearly 100% of all reimbursed medications. (Social Insurance Institution 2000)

4.5 Definitions

Age and sex. As far as age was concerned, the population was either considered as a whole, i.e. including all persons aged 64 year old or over, or stratified into groups aged 64–74 and 75+ years, 64–74, 75–84, and 85+ years, or 64–69, 70–74, 75–79, 80–84, and 85+ years. The young elderly were defined to consist of 64- to 71-year-old persons, who were different persons in the two cross-sectional assessments.

Marital status and living alone. Marital status was divided as follows: married/cohabiting, widowed, unmarried, and other or married/cohabiting, widowed, and other. Persons living alone were differentiated from those living with someone.

Basic education. Basic education was defined as under basic compulsory, basic compulsory, and over basic compulsory.

Previous occupation. Previous occupations were in service, industry, agriculture, or family.

Chronic morbidity. The diseases recorded by Social Insurance Institution as entitling the patients to special refunds of medication costs were counted as chronic morbidity (ranging from 0 to 5 diseases) in 1998–99.

A single question about self-perceived health and life satisfaction. The persons with poor self-perceived health or poor life satisfaction had chosen the alternatives “quite or very poor situation” compared to those reporting a “good situation” (alternatives “moderate, quite or very good”) in 1998–99.

Smoking and alcohol consumption. Smoking history was asked, and the subjects were classified as non-smokers, ex-smokers, or current smokers. If a person had smoked at least one cigarette per day (or one cigar per week or 28 g of tobacco per month) for at least a year and had not smoked for the previous 6 months or more, he/she was defined as an ex-smoker. In 1998–99, the frequency of alcohol consumption (beer, wine, or spirit) per month as 0, 1–4, or > 5 times was recorded.

Home nursing. The persons receiving supervised home nursing services were counted and included into the studies.

Drug use and polypharmacy. Both regular and irregular prescription drug use during seven days prior to the interview were defined as use of medication. Medication was defined as regular if it was taken daily or at regular intervals, e.g., once a week or month, as is the case with, for instance, vitamin B12 or long-acting antipsychotics injected intramuscularly once a month or at other regular intervals. If the person used a drug once a month or at other regular intervals, but had not had an intramuscular injection, for example, during the previous week, his/her drug use was recorded as regular use. Irregular medication was taken when needed. Polypharmacy was defined as concomitant use of more than five prescription medications. WHO defines polypharmacy as the concomitant use of five or more drugs (WHO 1985), and Finnish studies follow the same principle (Klaukka *et al.* 1993, Klaukka & Rajaniemi 1998).

Psychotropics. Psychotropics had ATC codes of N05-6. Psychotropics were divided into hypnotics/sedatives (N05B-C), including anxiolytics (e.g., diazepam, alprazolam, chlordiazepoxide) (N05B) and hypnotics (e.g., temazepam, nitrazepam, zopiclone, zolpidem) (N05C), as well as antipsychotics, including lithium (N05A), antidepressants (N06A), and antidepressants, including other psychotropics (benzodiazepines or antipsychotics) (N06C). Antidepressants and combination preparations were mostly included in the same category (N06A, N06C) in this study. Neuroleptics are called antipsychotics in the ATC system. None of the study subjects used anti-dementia drugs (N06D) in 1990–91, and only three persons used them in 1998–99. Hypnotics/sedatives

were divided into short-acting benzodiazepines, such as midazolam and triazolam, medium-acting ones, such as lorazepam, oxazepam, and temazepam, and long-acting ones, such as diazepam, flunitrazepam, chlordiazepoxide, chlorazepate, medazepam, nitrazepam, and alprazolam (Pelkonen 1998), and non-benzodiazepine sleeping pills, such as zopiclone and zolpidem. In clinical practice, many benzodiazepines are used either as anxiolytics or hypnotics, including oxazepam. They were therefore mostly analyzed together as hypnotics/sedatives for the purposes of this thesis. Any use of two or more psychotropics was defined as concomitant use.

Classification of drugs by their sedative properties. Summaries of the product characteristics of the drugs approved for prescription in Finland in 1998–2001 were checked for the key words “sedating, sedative, drowsiness, sleepiness, lassitude, exhaustion, tiresome and fatigability”. The source of information was *Pharmaca Fennica*, the Finnish drug compendium. In addition, updated online product information was reviewed in autumn 2001, when nearly 900 different compounds were available in Finland. A psychogeriatrician, a geriatrician, and a physician specialized in drug epidemiology provided expert knowledge about the categorization of drugs, particularly concerning the elderly. Mainly the official summaries of the product characteristics of drugs were used, but in uncertain cases, if for example, a synonymous preparation containing the same ingredients had a sedative effect, leading manuals, textbooks, and the Medline database were consulted. The drug was classified into the group with least sedation if its sedative quality was uncertain or undocumented.

The drugs were divided into 4 groups based on the ATC system: 1. primary sedatives with the aim to sedate (conventional psychotropics), 2. drugs with sedation as a prominent side/adverse effect or preparations with a sedating component, 3. drugs with sedation as a potential adverse effect, and 4. drugs with no known sedative effect (Paper III, Table 1). Drugs injurious in traffic were placed into group 1 or 2, which included all known sedative drugs (proper sedatives). Almost all drugs in group 2 were said to be “injurious in traffic”, but other sedating drugs prescribed to the elderly, such as metoclopramide (Wynne *et al.* 1993) and second-generation psychotropics, were also included. Group 2 drugs further included psychotropics in combinations indicated for somatic disorders. Drugs of the groups 3 and 4 were not reported to be injurious in traffic.

Sedation may be a desirable side effect (strong analgesic) or an undesirable adverse effect (old antihistamines in the daytime). The effect may be expected and connected with the pharmacological properties of the drugs, or it may be unexpected. If the effect is not associated with pharmacological properties, it may be a partly subjective feeling (drugs in group 3) or mixed with symptoms of diseases or their other treatments.

Sedation score, sedation sum score, and polysedation. In this study, proper sedatives were rated numerically to calculate the sedative drug load per drug user. Each drug in group 1 was rated as having a sedation score of 2, and each drug in group 2 was rated as having a sedation score of 1. The sedation scores were added up, and this sum score ranged within 0–9 in the study series. A total sedation sum score of 3 or more was defined as polysedation, and to have polysedation, one was to have at least two proper sedatives.

Physical functional abilities. The questions about physical functional abilities included four items about ADL (getting in and out of bed, using the lavatory, dressing and undressing, washing and bathing), four items about mobility (walking between rooms, using stairs, moving outdoors, walking at least 400m), and four (1990–91) (light housekeeping tasks, heavy housekeeping tasks, carrying a heavy load, cutting one's toe nails) or eight (1998–99) (light housekeeping tasks, heavy housekeeping tasks, carrying a heavy load, cutting one's toe nails, handling finances, use of public transportation, taking care of one's medication, ability to use the phone) items about IADL. The following reply alternatives were available in most cases: 1. cannot do the activity in question, 2. can do the activity if someone helps, 3. can do the activity with difficulties, but without help, 4. can do the activity without difficulties and without help. For the purposes of this study, all items were dichotomized, with the values 1–3 indicating “difficulties or dependence” in the activity.

4.6 Statistical methods

Statistical analyses were performed using the SAS statistical software package (SAS Institute Inc. 1990), release 6.1 to 8.2. The results on categorical variables were presented as cross-tabulations in the papers I–IV. Chi-square tests were used to compare the categorical variables between groups of persons. Fisher's two-sided probability test was used when the Chi-square test was not valid. Student's t-test was used for continuous variables. The statistical significance of the results was presented as p-values, and p-values of less than 0.05 were considered as statistically significant.

Paper I. Drug use (%) was first cross-tabulated with age and sex. The mean number of drugs per study person and per drug user was counted. The prevalence of the use of each medication category was calculated among all study persons, in the different age and sex groups and among the persons with polypharmacy. The persons with polypharmacy were compared to those with 1 to 5 drugs in use, and the odds ratios (95% confidence interval - CI) were calculated to assess the probability of polypharmacy among the drug users by comparing the prevalences of the persons with polypharmacy by sex in 1998–99 to those in 1990–91 as a function of time (Table 4a-b) and women to men in 1990–91 and separately in 1998–99 (Table 5a-b). All comparisons were made in the different age groups.

The drug users with 0 to 5 drugs were compared with the persons with polypharmacy in terms of the sociodemographic factors using the Chi-square test. After that, a multivariate model was created by means of stepwise logistic regression analysis in order to assess the probability of polypharmacy using the following explanatory variables: age, sex, marital status, basic education, previous occupation, living alone, smoking, and uses of home nursing services in both surveys and, in 1998–99, additionally chronic morbidity, self-perceived health, life satisfaction, and frequency of alcohol consumption.

Drug users with 0, 1–5, and > 5 drugs (polypharmacy) were first cross-tabulated with the different items of ADL, mobility, or IADL, to find out the prevalence of persons with difficulties or dependency in activities. In covariance analysis, the mean number of drugs

was calculated after adjustment for age and sex among the persons with difficulties or dependence and without difficulties or dependence in activities, in order to find out if a greater adjusted mean number of drugs (95% CI) was independently associated with poorer physical functional abilities after controlling for age and sex.

Paper II. The prevalences of different psychotropic use patterns in community were compared with the national prescription data provided by Social Insurance Institution by age and sex. Psychotropic use (any use and regular use) (%) was cross-tabulated with age and sex in community. Concomitant (≥ 2 , ≥ 3 , or ≥ 4) psychotropic use was calculated (%), as was also the use of different psychotropics (%) among the young elderly (64–71 years old), who were different persons in 1990–91 and 1998–99.

Paper III. The classification of drugs by their sedative properties was applied only in 1998–99 to a cross-sectional survey of the home-dwelling elderly subjects in Lieto, because the classification was made around that time. It was not correct to make a similar classification in the early 1990s, because some drugs used at that time were from decades ago. The sales licences of some drugs had expired by that time, e.g., the sales licence of a respiratory drug consisting of diprophyllinum and amobarbital (Cardiofyllin comp®, sedative drug) had expired in 1990 (Source: National Agency for Medicines). The purpose was to make as current a classification as possible, which could be updated and utilized in the future years.

Paper IV. Persons with no sedative drugs (no drug users and drug users), with some sedative drugs (sedation sum score 1–2), and with polysedation (sedation sum score ≥ 3) were compared for sociodemographic factors. The groups (mainly with no sedatives and polysedation) were compared in cross-tabulation using the Chi-square test. After that, a multivariate model was created by means of stepwise logistic regression analysis in order to assess the probability of polysedation by using as explanatory variables age, sex, marital status, basic education, previous occupation, living alone, smoking, use of home nursing services, chronic morbidity, self-perceived health, life satisfaction, and frequency of alcohol consumption.

The physical functional abilities (ADL, mobility, or IADL) of the persons were first cross-tabulated with the sedation sum scores (0, 1, 2, 3, 4, ≥ 5) to show the trend of possible difficulties or dependence in abilities versus sedative drug use. Covariance analysis, after adjustment for age and sex, was used to compare the adjusted mean sedation sum scores (95% CI) between persons with or without difficulties or dependence in activities (ADL, mobility, or IADL).

5 Results

5.1 Drug use and polypharmacy (I)

5.1.1 Medication use in general

The elderly persons taking 1 to 5 drugs (without polypharmacy) were relatively similar to the total study populations based on the sociodemographic and other characteristics in both surveys (Table 3a). The persons with polypharmacy (> 5 drugs) were older than the other drug users, and two thirds of them were women. The proportions of widowed persons and users of home nursing services were greater in the group with polypharmacy than among the other drug users. Every third person with polypharmacy had poor self-perceived health, and 6% of them had poor life satisfaction. Living alone was the only variable that did not differ significantly between the drug users with or without polypharmacy.

The elderly men with polypharmacy were relatively typically married or cohabiting, though the difference was not statistically significant between the surveys (Table 3b), but the women with polypharmacy were mostly widowed (Table 3c). Among the women with polypharmacy, a greater part were aged 85 years or over compared to men. Poor self-perceived health/life satisfaction was almost equally common in men as in women with polypharmacy.

Prescription drug use increased significantly among the home-dwelling elderly in the 1990s (from 78% to 88%) ($p = 0.001$) in both sexes and in all age groups (Paper I, Fig. 1). A greater share of women than men used medications in both surveys. The figure for women in 1990–91 was 81% and that for men 74% ($p = 0.007$), and the respective figures in 1998–99 were 93% and 82% ($p < 0.0001$). The proportion of drug users grew most in the age group of 64–74 years, from 72% to 85% ($p = 0.001$), and quite notably among those aged 75–84, from 86% to 93% ($p = 0.004$). Almost every oldest old (over 84 years old) person used at least one drug in both surveys. The figures were 93% and 97%,

respectively, and the prevalences did not reach statistical significance between the surveys.

The mean number of all medications per person increased markedly, from 3.1 (SD 2.8) to 3.8 (SD 3.1), between the surveys ($p = 0.0001$). The mean number of regular medications per person also grew markedly, from 2.4 (SD 2.4) to 3.0 (SD 2.6) per person, between the surveys ($p = 0.0001$). The number of medications per user grew most rapidly in the oldest women between the surveys (Fig. 2). In this age group, women used most medications, the average being 6.8 (SD 3.5) drugs in 1998–99, which was clearly above the limit of polypharmacy.

Cardiovascular drugs were used most commonly (over 50%) in both surveys (Paper I, Fig. 3), particularly by the oldest (85 years or over) women: 85% in 1998–99 (Paper I, Table 2). Central nervous system (CNS) drugs ranked second in frequency in both study periods, and their use grew significantly, being almost 40% in the late 1990s. Most CNS drug users used psychotropics (N05-6). The medications most commonly used by men in the oldest age group in 1998–99 were CNS drugs (74%) followed by cardiovascular drugs (56%).

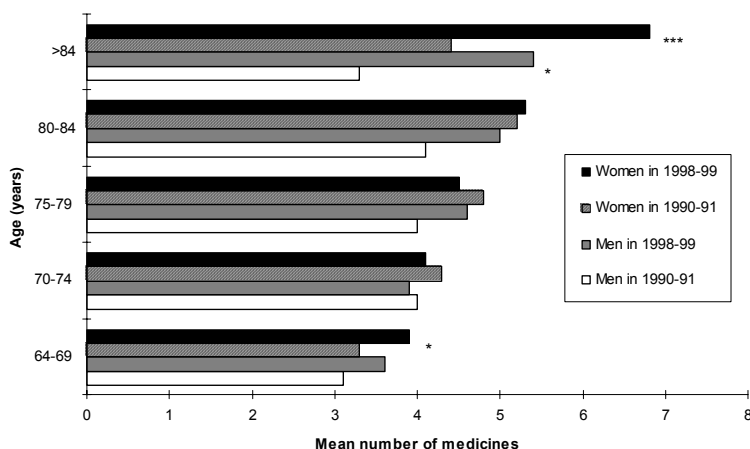


Fig. 2. Mean number of prescription drugs used during seven days prior to the interview by medicine-using home-dwellers aged 64 years or over in community in 1990–91 and 1998–99 by age and sex. The p-values are based on Student's t-test. p-values * ≤ 0.05 , *** ≤ 0.001 .

5.1.2 Polypharmacy

Polypharmacy was significantly more common in the second survey (25%) than in the first (19%) ($p = 0.006$). It increased from 15% to 20% ($p = 0.015$) among men, and from 23% to 29% ($p = 0.107$) among women.

Polypharmacy increased most in the oldest age group (≥ 85 years): from 23% to 51% ($p = 0.001$), and especially among the oldest women. The oldest women were three times more likely to have polypharmacy in 1998–99 than in 1990–99 (Table 4a-b). The oldest women were also three times more likely to have polypharmacy compared to men of the same age in 1998–99 (Table 5a-b). The proportion of the elderly who used ten or more medications doubled from 3% to 6% between the surveys ($p = 0.057$).

The elderly with polypharmacy commonly used the same main categories of medications as all participants. In both surveys, 90% of the elderly with polypharmacy used cardiovascular medications. In 1990–91, the elderly with polypharmacy used drugs for the alimentary tract/metabolic system second most commonly (67%), while in 1998–99, CNS medications ranked second (63%).

The use of medications for circulatory/blood-forming organs (42% to 56%) and the genito-urinary system (10% to 29%) increased significantly ($p = 0.001$) among the persons with polypharmacy between the surveys. Among those persons, the use of systemic anti-infectives and medications for the alimentary tract/metabolic system decreased significantly, the respective figures being 18% to 8% ($p = 0.001$) and 67% to 58% ($p = 0.041$).

Among the drug-using elderly, the use of medicines (Paper I, Table 3) increased between the surveys similarly in those with and without polypharmacy. Persons with polypharmacy used nearly all drugs statistically significantly more commonly than those without polypharmacy, and they used psychotropics, diuretics, and nitrates most commonly in both surveys. Persons with polypharmacy used psychotropics significantly more commonly in 1998–99 (53%) than those without polypharmacy (18%) ($p < 0.0001$). The results were in accordance with those obtained in 1990–91. In 1998–99, persons with polypharmacy used almost three times more prevalently (67% vs 24%) proper sedatives (groups 1–2) than those without polypharmacy ($p < 0.0001$), and the differences were statistically significant in all age groups (64–74, 75–84 and ≥ 85 years).

Table 4a. Distribution of male home-dwelling elderly prescription drug users in 1990–91 and 1998–99 by age and number of medicines with special reference to the risk (OR) to have polypharmacy (> 5 drugs) as a function of time.

Number of drugs	1990–91	1998–99	(64–74)	p-value ^a	1990–91	1998–99	(75–84)	p-value ^a	1990–91	1998–99	(85+)	p-value ^a
	n = 219	n = 288	OR		n = 113	n = 112	OR		n = 14	n = 26	OR	
	%	%	(95% CI)		%	%	(95% CI)		%	%	(95% CI)	
			1.1	0.690			1.4	0.228			^b	0.016
			(0.7–1.7)				(0.8–2.5)					
1–5	81	80			73	66			100	65		
> 5	19	20			27	34			0	35		

^a p-values are based on Chi-square test or Fisher's two-sided test. ^b Not estimable. OR = Odds ratio.

CI = confidence interval.

Table 4b. Distribution of female home-dwelling elderly prescription drug users in 1990–91 and 1998–99 by age and number of medicines with special reference to the risk (OR) to have polypharmacy (> 5 drugs) as a function of time.

Number of drugs	1990–91			p-value ^a	1998–99			p-value ^a	1990–99			p-value ^a
	n = 310	n = 382	OR (95% CI)		n = 185	n = 197	OR (95% CI)		n = 38	n = 51	OR (95% CI)	
	%	%			%	%			%	%		
			1.3 (0.9–1.8)	0.217			0.9 (0.6–1.3)	0.494			3.0 (1.2–7.1)	0.013
1–5	79	75			61	64			66	39		
> 5	21	25			39	36			34	61		

^a p-values are based on Chi-square test or Fisher's two-sided test. OR = Odds ratio. CI = confidence interval.

Table 5a. Distribution of home-dwelling elderly prescription drug users in 1990–91 by age and number of medicines with special reference to the risk (OR) of polypharmacy (> 5 drugs) among women compared to men.

Number of drugs	64–74				75–84				85+			
	Men	Women	OR (95% CI)	p-value ^a	Men	Women	OR (95% CI)	p-value ^a	Men	Women	OR (95% CI)	p-value ^a
	n = 219	n = 310			n = 113	n = 185			n = 14	n = 38		
	%	%			%	%			%	%		
			1.1 (0.7–1.7)	0.585			1.8 (1.1–2.9)	0.029			^b	0.011
1–5	81	79			73	61			100	66		
> 5	19	21			27	39			0	34		

^a p-values are based on Chi-square test or Fisher's two-sided test. ^b Not estimable. OR = Odds ratio. CI = confidence interval.

Table 5b. Distribution of home-dwelling elderly prescription drug users in 1998–99 by age and number of medicines with special reference to the risk (OR) of polypharmacy (> 5 drugs) among women compared to men.

Number of drugs	64–74				75–84				85+			
	Men	Women	OR (95% CI)	p-value ^a	Men	Women	OR (95% CI)	p-value ^a	Men	Women	OR (95% CI)	p-value ^a
	n = 288	n = 382			n = 112	n = 197			n = 26	n = 51		
	%	%			%	%			%	%		
			1.3 (0.9–1.9)	0.172			1.1 (0.7–1.7)	0.776			2.9 (1.1–7.8)	0.030
1–5	80	75			66	64			65	39		
> 5	20	25			34	36			35	61		

^a p-values are based on Chi-square test or Fisher's two-sided test. OR = Odds ratio. CI = confidence interval.

5.1.2.1 *Factors associated with polypharmacy*

According to logistic regression models, polypharmacy was independently associated with advancing age in both surveys (Table 6). In the first survey, polypharmacy was also independently associated with female gender, widowed status, ex-smoking, and especially the use of home nursing services. In the latter survey, having at least 3 chronic diseases was the most prominent factor associated with polypharmacy, followed by poor self-perceived health and use of home nursing services. In both surveys, living alone, basic education, and previous occupation were not independently associated with polypharmacy. In 1998–99, gender, marital status, smoking, frequency of alcohol consumption, and poor life satisfaction were not associated independently with polypharmacy.

In both surveys, the proportions of persons with difficulties or dependence in the activities of daily living (ADL), mobility, or instrumental activities of daily living (IADL) were associated significantly ($p < 0.0001$) with the increasing number of drugs (Appendix table 2). Difficulties or dependence were found most frequently among those with polypharmacy. After adjustment for sex and age, the persons with difficulties or dependence in activities had a significantly ($p < 0.0001$) greater mean number of drugs (many near or above the limit of polypharmacy) compared to those without difficulties or dependency in activities (Fig. 3).

Table 6. The most essential variables, adjusted odds ratios (OR), and 95% confidence intervals (CI) predicting the probability of polypharmacy among the home-dwelling elderly in 1990–91 and 1998–99.

Variable	1990–91		1998–99	
	OR (95% CI) ^a	p-value	OR (95% CI) ^a	p-value
Age (years)		0.0001		0.006
64–69	1		1	
70–74	2.2 (1.4–3.4)		1.2 (0.7–1.8)	
75–79	2.8 (1.7–4.4)		1.8 (1.1–3.0)	
80–84	3.1 (1.9–5.3)		2.0 (1.1–3.7)	
85–89	2.1 (1.0–4.6)		2.7 (1.3–5.9)	
≥ 90	^b		6.3 (1.8–22.4)	
Gender		0.002		0.075
Men	1		1	
Women	2.1 (1.3–3.4)		1.4 (1.0–2.0)	
Marital status		0.013		0.097
Married/cohabiting	1		1	
Widowed	2.0 (1.2–3.2)		1.1 (0.7–1.6)	
Other	1.2 (0.6–2.2)		0.5 (0.3–1.0)	
Smoking		0.007	^c	
Non-smoker	1			
Ex-smoker	2.1 (1.3–3.4)			
Current smoker	1.0 (0.5–2.2)			
Chronic morbidity ^d		^e		< 0.0001
< 3 diseases			1	
≥ 3 diseases			13.2 (7.2–24.2)	
Self-perceived health		^e		< 0.0001
Good			1	
Poor			4.2 (2.7–6.5)	
Home nursing services		< 0.0001		0.023
No	1		1	
Yes	5.6 (3.1–10.2)		2.2 (1.1–4.3)	

^a Multivariate stepwise logistic regression analysis. ^b No result, because no person of this age had polypharmacy. ^c Smoking did not remain in the model in 1998–99. ^d Diseases recorded by Social Insurance Institution as entitling the patients to special refund of medication costs. ^e Chronic morbidity and self-perceived health were only inquired from the participants in 1998–99.

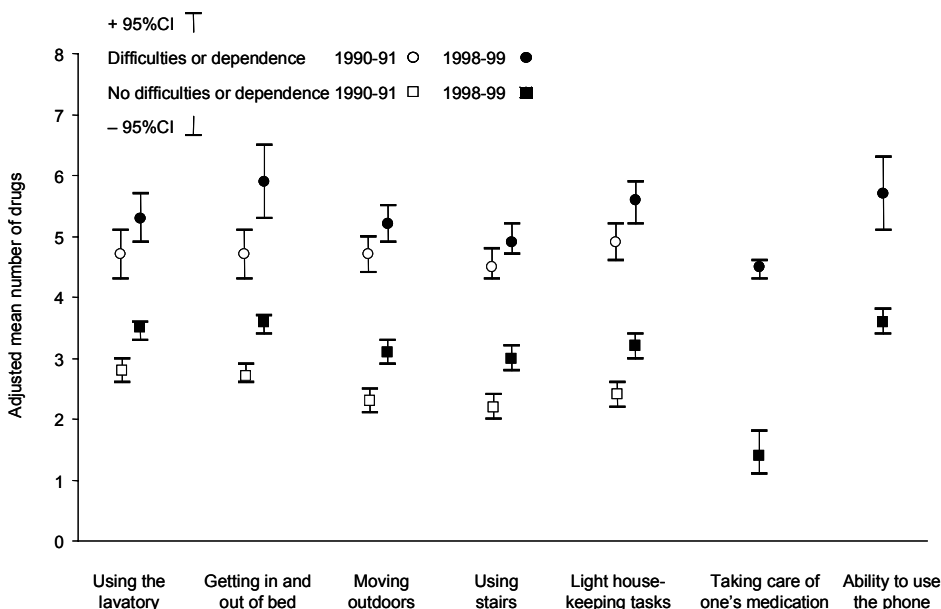


Fig. 3. After adjustment for sex and age, the mean number of drugs (95% confidence intervals) used by the elderly with or without difficulties or dependence in ADL, mobility, or IADL.

5.2 Psychotropic use (II)

5.2.1 Comparison of national and community prescription data

National data from the prescription register maintained by Social Insurance Institution and data from community showed that the use of all types of psychotropics increased systematically along with increasing age among the home-dwelling elderly in the late 1990s (Paper II, Table 1a–b). The elderly used psychotropics more commonly than middle-aged adults, and elderly women used them more commonly than men. The register showed that the use of psychotropics among the elderly in Lieto in the late 1990s was similar to that elsewhere in southwestern Finland (the hospital district where Lieto is situated) and the whole country. The use of anxiolytics and hypnotics predominated over the use of antipsychotics and antidepressants in every part of the country. In Lieto, antipsychotics and hypnotics were used less commonly and anxiolytics and antidepressants more commonly than in the whole country.

5.2.2 Psychotropic use in general

Every fourth elderly person used psychotropics in both surveys, and the use appeared to be slightly increasing (3%) (Paper II, Table 2). The mean number of psychotropics per user was 1.4 in both surveys (SD 0.63 in 1990–91 and SD 0.66 in 1998–99). Most persons took psychotropics regularly.

The use of psychotropics became more common only in the oldest old in the 1990s (Table 7). Regular use of any psychotropics or hypnotic/sedatives decreased significantly in the oldest old toward the late 1990s. This means that their use as needed increased. The gender differences in neither psychotropic use nor hypnotic/sedative, antipsychotic, or antidepressant use among the oldest old were not statistically significant.

Every fifth elderly person used hypnotics/sedatives in both study periods, and their use seemed to be slightly increasing (3%). The use of hypnotics/sedatives became markedly more common only among the oldest old between the surveys.

Antipsychotic use dropped to a half of the previous level in the 1990s among all study persons. Only one person used an atypical antipsychotic (risperidone) in 1998–99 in Lieto, and many used conventional ones at low doses. A few of the oldest men and women used antipsychotics. The use of antidepressants doubled among all study persons. Selective serotonin reuptake inhibitor use increased most drastically. The oldest old used relatively more commonly antidepressants in 1998–99 compared to the other age groups, though their use increased significantly only in the younger age groups between the surveys.

The use of anxiolytics (e.g., diazepam, chlordiazepoxide) (N05B) was equally common, i.e. about 10%, in both surveys. The use of hypnotics (e.g., temazepam, zopiclone) (N05C) increased from 11% to 15% ($p \leq 0.001$) between the surveys. The use of short-acting benzodiazepines (midazolam, triazolam) decreased from 7% to 2% ($p \leq 0.001$), while the use of non-benzodiazepine sleeping pills (e.g., zopiclone, zolpidem) increased from 1% to 9% ($p \leq 0.001$). The use of medium- and long-acting benzodiazepines remained stable. Mostly medium-acting benzodiazepines were used by 40% of psychotropic users in both study periods.

Table 7. Proportions (%) of home-dwelling elderly psychotropic users and regular use by them in 1990–91 and 1998–99 by age.

Medication	Age (years)											
	64–74				75–84				> 84			
	1990–91 (n = 730)		1998–98 (n = 786)		1990–91 (n = 345)		1998–98 (n = 332)		1990–91 (n = 56)		1998–98 (n = 79)	
	All users	Regular use	All users	Regular use	All users	Regular use	All users	Regular use	All users	Regular use	All users	Regular use
	%	%	%	%	%	%	%	%	%	%	%	%
Any psychotropic drug (1)	19	71	22	73	31	78	33	81	32	100	52*	80*
Hypnotics/ sedatives (2)	15	68	18	64	27	79	28	77	25	100	43*	71*
Antipsychotics (3)	4	78	3	91	8	67	5	67	9	100	5	100
Antidepressants (4)	3	86	6**	89	4	93	9*	97	5	100	15	92

Medication use during seven days prior to the interview was recorded. ATC codes of medications: (1) N05-6, (2) N05B-C, (3) N05A, (4) N06A, N06C. p-values are based on Chi-square test. p-values * ≤ 0.05 , ** ≤ 0.01 .

5.2.3 Concomitant use of psychotropics

The proportion of people using two or more psychotropics increased significantly from 7% to 10% ($p < 0.05$) between the surveys. In 1990–91, most users had a combination of hypnotic/sedative and antipsychotic medication (3%), while in 1998–99, the most common combination was one of a hypnotic/sedative and an antidepressant (5%). About one third of all psychotropic users were taking at least two psychotropics concomitantly, and the proportions of users of three or more psychotropics were also equal in both surveys, being 6% and 8%, respectively. Of all psychotropic users, 1% were taking four or more psychotropics concomitantly in both surveys.

5.2.4 Psychotropic use and the young elderly

Among the young elderly aged 64–71 years, women used psychotropics nearly twice as commonly (23%) as men (14%) in the first survey ($p < 0.01$). In 1998–99, the respective figures were 25% and 12% ($p < 0.001$). Young elderly men used hypnotics equally often in both surveys, but their use by women increased from 9% to 14% ($p < 0.05$). Young elderly women doubled (3% to 8%) their use of antidepressants ($p < 0.01$), while the use of antidepressants among men remained stable. The use of antipsychotics decreased significantly among young elderly men from 3% to 0.4% ($p < 0.05$), but not among women. In the second survey, the young elderly used long-acting benzodiazepines and

cyclic antidepressants equally commonly as in the first. None of the young elderly used atypical antipsychotics in 1998–99.

5.3 Classification of drugs by their sedative properties (III)

Paper III, Table 1 shows a classification of the drugs used in Finland in 1998–2001 by their sedative properties into three groups. Group 4 drugs accounted for the rest of the drugs used. Primary sedatives (about 40 drugs in Finland) included only psychotropics, particularly hypnotics/sedatives, conventional antipsychotics, and cyclic antidepressants. Group 2 (about 80 drugs in Finland) included mainly drugs for somatic disorders. Psychotropics were found in almost all major medical classes in group 2. Group 2 included opioids, some NSAIDs (non-steroidal anti-inflammatory drugs), indomethacin, old antihistamines, and combination preparations with a sedating component for the treatment of somatic symptoms or diseases. Group 3 (about 220 drugs in Finland) included the 12 major medicinal categories (ATC) and only drugs for somatic disorders. The only medicines lacking a sedative effect were those for circulatory/blood-forming organs or dermatological conditions.

Group 4 included all the other medicines, e.g., drugs for the circulatory/blood-forming organs (acetylsalicylic acid, dipyridamole) and dermatological preparations (creams). Alimentary (laxatives, vitamins, mineral supplements), cardiovascular (digoxin, pentoxifylline, antihemorrhoidals for topical use), genito-urinary drugs (sildenafil, finasteride), systemic hormones (corticosteroids, thyroid therapy), systemic anti-infective drugs (doxycycline, penicillin), antineoplastic/immunomodulating agents (interferons), musculoskeletal (gold preparations, NSAIDs for topical use), CNS drugs (moclobemide), antiprotozoals (chloroquine), respiratory drugs (inhalation anti-asthmatics), ophthalmologicals/otologicals (local anti-infectives), and miscellaneous drugs (food preparations) belonged to this group. Intravenous drugs, vaccines, or other disposable drugs were also classified into group 4.

5.3.1 *Application of the classification in community*

Altogether 88% (n = 1056) of the home-dwelling elderly had medication, and 40% of them took proper sedatives (groups 1–2). Women used proper sedatives more commonly than men (45% vs 33%, $p < 0.0001$), and persons aged over 84 more commonly than the younger elderly (65% vs 38%, $p < 0.0001$). Most drug users (79%) took group 3 drugs. Group 4 drugs were used by 14% of drug users.

Of the drug preparations used by the study population, every drug in group 1 belonged to the CNS category. In group 2, over half (55%) of the drugs belonged to the CNS category, and 43% of them were psychotropics and 39% opioids. In group 2, every fourth (23%) drug belonged to the musculoskeletal category. In group 3, 55% of the drugs belonged to the cardiovascular and 22% to the musculoskeletal category, with analgesics

predominating, and 10% of the drugs were used for the alimentary system. Every fifth drug in group 4 had been prescribed for the circulatory blood-forming organs, mainly aspirin under 300 mg per day, and every fifth drug belonged to the cardiovascular and 14% to the alimentary category.

5.4 Items connected with sedative drug use (IV)

Every third person with polysedation was old, aged 80 years or older (Paper IV, Table 1). The persons with polysedation were older in mean age than the other persons. Polysedation was significantly associated with female gender, widowed status, low basic education or poor self-perceived health/life satisfaction, living alone, having home nursing, and having many diseases. The persons with polysedation used very many drugs, and two thirds of them had polypharmacy.

According to logistic regression models, after controlling for confounding factors, high age, female gender, having at least 3 chronic diseases, smoking, having poor self-perceived health/poor life satisfaction, and, marginally, use of home nursing services remained in the final model and were associated with polysedation (Table 8). Marital status, basic education, previous occupation, living alone, and frequency of alcohol consumption did not remain in the final model.

The proportion of persons with difficulties or dependence in daily activities (ADL, IADL) or mobility was associated significantly with the rising sedation sum score, i.e. the increasing amount of sedative drugs (Paper IV, Fig. 1). After adjustments for sex and age, the mean sedation sum scores of drugs were significantly ($p < 0.0001$) higher for the persons with difficulties or dependence compared to those without difficulties or dependence in physical abilities (Fig. 4), which means that a larger number of sedative drugs was associated with poor physical ability.

Table 8. The most essential variables, adjusted odds ratios (OR), and 95% confidence intervals (CI) predicting the probability of polyseidation among the home-dwelling elderly.

Variable	OR (95% CI) ^a	p-value
Age (years)		< 0.0001
64–69	1	
70–74	2.84 (1.57 – 5.12)	
75–79	1.74 (0.87 – 3.50)	
≥ 80	4.62 (2.37 – 9.00)	
Gender		< 0.001
Men	1	
Women	2.81 (1.60 – 4.92)	
Chronic morbidity ^b		0.014
< 3 diseases	1	
≥ 3 diseases	2.32 (1.17 – 4.61)	
Smoking		< 0.001
Non-smoker	1	
Ex-smoker	1.04 (0.54 – 2.01)	
Current smoker	3.71 (1.80 – 7.64)	
Self-perceived health status		< 0.0001
Good	1	
Poor	4.13 (2.37 – 7.19)	
Life satisfaction		0.002
Good	1	
Poor	5.03 (1.82 – 13.9)	
Home nursing services		0.054
No	1	
Yes	2.19 (0.97 – 4.94)	

^a Multivariate stepwise logistic regression analysis. ^b Diseases recorded by Social Insurance Institution as entitling the patients to special refunds of medicine costs.

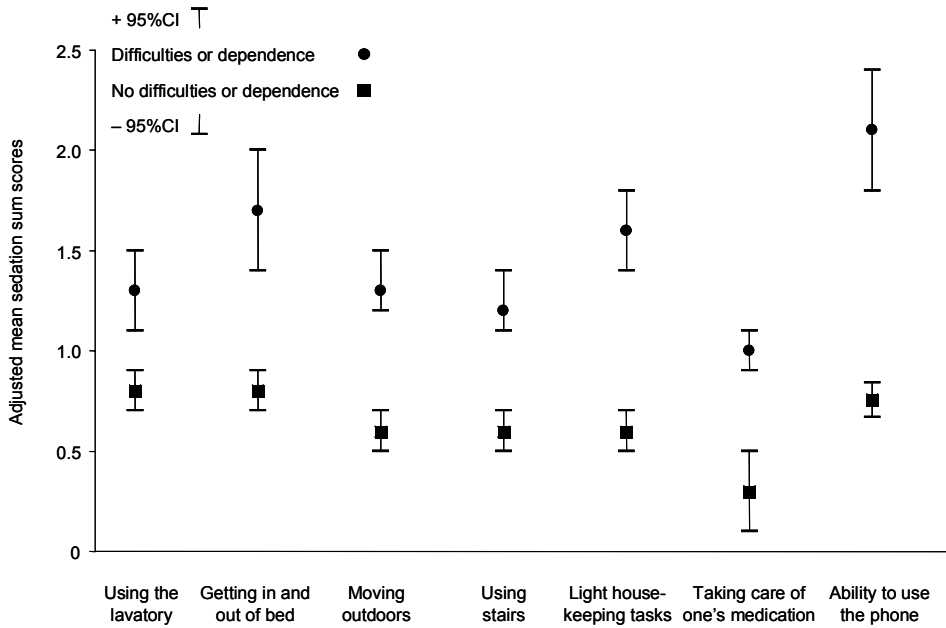


Fig. 4. After adjustment for sex and age, the mean sedation sum scores (95% confidence intervals) of the elderly with or without difficulties or dependence in ADL, mobility, or IADL.

6 Discussion

6.1 Study population, strengths and limitations of the study

The populations are representative samples of elderly persons living in southern Finland in the early and late 1990s (response rates 93% and 82%, respectively). The living conditions of the Lieto population are typical of those in southwestern Finland. The age distributions were similar in both surveys, and comparable to those of the general population (Central Statistical Office of Finland 1991, Statistics Finland 1998). Of the persons invited in a random order to attend the Lieto surveys, only permanently institutionalized persons were excluded.

The main reason for non-participation in the studies was refusal. Non-participants (those who declined) were more prevalent in Lieto in 1998–99 than in 1990–91, partly due to the fact that participation was more demanding due to the study arrangements at the latter time point than at the first. In the early 1990s, two visits to the health center were enough, but on the latter occasion, three to five or even more visits were needed for the interviews, measurements and medical checkup. In the 1990–91 population, some persons were diagnosed for new diseases during the study, and they were treated and appropriately controlled. The number of these patients is not known, but their interest in participating in the second study was not high and they preferred non-participation. Data on drug use, sociodemographic background and other characteristics of the non-participants were not available. Hence, the data of the participants and non-participants were not mutually comparable, and this study did not indicate if that affected the results significantly.

There are two main strengths in this study: firstly, the relatively large population size and its natural location in a single municipality and the reporting of the actual use of prescription medications by the home-dwelling elderly, and secondly, the possibility to compare the use of psychotropic drug use in Lieto with that in the whole country based on the national reimbursement data obtainable from the Social Insurance Institution of Finland.

The results on the prevalences of drug use are not directly representative of the whole country, but illustrate the trend of drug use in the past decade. The use, consumption, and

assortments of drugs vary from country to country and regionally, often without any specific reason (Aromaa *et al.* 1989, National Agency for Medicines and Social Insurance Institution 2001). Prescription practices also differ between doctors (Bjerrum *et al.* 1998). Regional variations must be considered in evaluating the results of this study. Any comparison with the results of different studies is difficult because of methodological issues, including the reasons for compiling information on drug use, differences in the drugs selected for study, and categorization of drugs. The present results can be used in the future to assess regional variations and trends over time in drug use by the home-dwelling elderly in Finland.

An example of regional drug policies is provided by the East-West study started in Finland in 1959 (among men aged 40–59 years). In its follow-up studies in 1984 and 1989, the participating men were 65 years or over. Men in the East used prescription drugs in larger quantities and more prevalently than men in the West. (Enlund *et al.* 1990b, Martikainen 1995)

The limitations of this study are the lack of data on the indications of the prescriptions and the dosage and duration of drug use by each elderly person, the latter because of the cross-sectional study design. The indications for prescriptions at the population level may be difficult to find out, because they are not included in all prescriptions or medical records. The strengths and limitations of the classification of drugs by their sedative properties are pointed out in the discussion on paper III. The strengths and limitations of the studies I–IV are discussed in each paper.

Combination preparations including two or more ingredients were not counted separately, even though this would have given extra substances and added to polypharmacy. Manesse *et al.* (2000) counted the different pharmacologically active ingredients of combined preparations separately, but their study population was much smaller ($n = 158$) than the present population. Cardiovascular combination preparations commonly contained three to five (Stakes 1993) pharmacologically active ingredients in 1990–91 and mostly two in 1998–99 (Pharmaceutical Information Centre 2000). Analgesic drug combinations were also common both in 1990–91 and in 1998–99, not to mention many other medications.

Only prescription drugs were included in the analysis, but non-prescription drugs (Over-the-counter = OTC drugs) would also have given extra information of drug use. It can be suggested that OTC drugs (many analgesics, etc.) would have increased the average number and prevalence of drug use. Non-pharmacological natural drugs, homeopathic or antroposophic preparations, which may have adverse effects or interactions with medical drugs, were not included in this study (Enkovaara 1999).

Reported drug use one week, two weeks, one month, etc., previously does not indicate real use and doses of drugs, because drugs prescribed to be taken as needed, such as hypnotics, are taken irregularly or regularly, and the patient's compliance with drug use may be different from that prescribed by the physician. Up to 39% of the elderly may underuse the drugs prescribed to them. (Enlund *et al.* 1990a). As many as one fifth of psychotic patients were non-compliant with their medications in a Finnish study (Kampman *et al.* 2002).

Conventional statistical methods were used, and the statistical approach was suitable to this work. No new statistical methods were created. The correlations between drug use, polypharmacy, polysedation, and various other items may be considered representative,

though the cross-sectional multivariate analyses only covered the associations between the factors and drug use and not the causes and effects in their mutual relationships.

6.2 Data and data collection

The data collection methods were similar in both Lieto surveys (Isoaho 1995, Wendelin-Saarenhovi *et al.* 2002). The questionnaires and health examination procedures were similar in both surveys, and the results may hence be considered comparable with each other. Medication use was recorded by a trained nurse. She also checked the respondents' medication use with a close relative or a care-giver or from the home nursing and medical records of the local health center. Two general practitioners, who belonged to the research team, also reviewed the medications and medical records. Thus, the data on medications can be considered reliable. This point prevalence approach is recommended in studies concerning medication use (Mantel-Teeuwisse *et al.* 2001).

Longitudinal or follow-up study designs would have yielded information about the same persons over a long period. In a cross-sectional survey, regularly used medications are likely to be recorded more reliably than those used temporarily. Cardiovascular medications are typically used daily for a long period, while the use of, analgesics and antibiotics, for example, is shorter in duration. Interviewees may also over-report particularly cardiovascular drug use or under-report the use of sedatives (Ryynänen *et al.* 1993). The high prevalence of cardiovascular drug use in this study may be due to the cross-sectional study design and the facts that cardiovascular drugs are used for long periods. Even though sleeping pills may have only been prescribed for a short period, regular use of hypnotics/sedatives was prevalent among the elderly (every three of four user).

6.3 Definitions

Similar definitions of smoking habits as in this study have been used before (Medical Research Council 1986, Isoaho 1995, Wendelin-Saarenhovi 2002). In 1998–99, the frequency of alcohol consumption (beer, wine, or spirit) was recorded as 0, 1–4, or ≥ 5 times per month, which cannot be a very detailed measurement. It gave the trend about the person's alcohol consumption, but did not indicate the amount of pure alcohol consumed. Similar rough estimations of alcohol consumption (liters per day or week) have been used in other epidemiological studies (Thomas *et al.* 1999, Fourrier *et al.* 2001).

Polypharmacy was defined as the concomitant use of more than five prescription medications. WHO defines polypharmacy as the concomitant use of five or more drugs (WHO 1985), similarly to many Finnish studies (Klaukka *et al.* 1993, Klaukka & Rajaniemi 1998). In the first survey of the present study, concomitant use of over five drugs was considered as polypharmacy, which it is close to the previous definitions. It

should be taken into account that even drugs taken as needed were included in this study. In the second survey, the same definition of polypharmacy had to be used to retain comparability. There are various definitions of polypharmacy, but major polypharmacy has been defined as the use of > 5 drugs (Veehof *et al.* 2000). According to a review of the literature, polypharmacy is usually defined in two ways, by a simple count of medications or by the administration of more medications than are clinically indicated (Hanlon *et al.* 2001). The first alternative was used in this study, and it is widely accepted.

The purpose was to make as current a classification of sedatives as possible, which could be updated and utilized in the future. When Pharmaca Fennica from 1998 to 2001 (Pharmaceutical Information Centre 1997 & 2000) was reviewed systematically to classify drugs by their sedative properties, the head words varied between the brand names of the drugs, even when exactly the same substances were involved. By a systematic drug-by-drug review of brand names, all head words for each substance were found. Because, in autumn 2001, updated online information of the head words was reviewed, the classification may be considered reliable.

Sedation score, sedation sum score, and polysedation were created particularly for this study. In Sweden, Schmidt and Svarstad (2002) scored polymedicine (concurrent use of three or more psychotropics), therapeutic duplication (two drugs from the same therapeutic class), and the use of three or more drugs concurrently, which may cause confusion according to certain guidelines. A score of 0 or 1 was assigned for each criterion, with 1 indicating deviation from the recommended drug practice.

Partly similar questions about physical functional abilities (ADL, mobility, IADL) as were used in this study have been used before (Jylhä *et al.* 1998), including ADL (Katz *et al.* 1963, Katz 1983) and mobility or IADL (Lawton & Brody 1969), the latter of which authors, namely Katz, Lawton & Brody, are legendary developers of measurements in this field. The measurements of physical functional abilities in this study were modified from previous measurements. In the early 1990s, questions were gathered about ADL, mobility, and IADL, which were also used in the late 1998s. Some new IADL questions (handling finances, use of public transportation, taking care of one's medication, ability to use the phone) were added to the interview in 1998–99. Eating and cooking were asked about on both occasions, but these items were excluded from this study, because even the persons in a poor condition were mostly able to eat, although they may have been totally dependent on others in other physical functional abilities. Cooking was excluded, because many Finnish elderly men traditionally do not cook. ADL, mobility, and IADL measures help to identify problems that require treatment or care. Such evaluation produces useful information about the prognosis and is important in monitoring the health and illnesses of elderly people. Difficulties in these functions usually mean definite impairment of physical functional abilities. (Katz 1983)

6.4 Drug use (I)

According to this study, the prevalence of prescription drug use among home-dwelling elderly men and women was high and increased further during the 10-year follow-up period. The mean number of drugs in use grew during the study period. Similar results on an increased prevalence of prescription drug use or an increased mean number have been reported among the elderly in Finland and elsewhere (Klaukka & Martikainen 1989, Klaukka *et al.* 1990, Stewart *et al.* 1991a & 1991b, Jylhä 1994, Rumble & Morgan 1994). The prevalence of prescription drug use increased among home-dwellers of all ages from the early 1960s to the late 1980s (Klaukka *et al.* 1990). This study showed the increasing trend of drug use to have continued in the 1990s.

Almost all of the oldest persons, aged 85 years or over, used prescription drugs in both surveys. It may be that even the oldest old, similarly to the younger elderly, are nowadays treated more actively than before. Over 20 years ago, the oldest old used drugs less commonly than nowadays (Haavisto & Mattila 1981). In the late 1980s, people aged 80 years or over used prescription drugs (Enlund 1988) equally commonly as in this study. In England, the oldest home-dwellers used drugs more prevalently than the other elderly population (79% in 1985 and 100% in 1989) (Rumble & Morgan 1994), as did also the oldest old in this study. Contradictory results have also been reported. In Sweden and the USA, the home-dwelling oldest old used less drugs than the younger elderly (Stewart *et al.* 1991b, Jørgensen *et al.* 2001). Toward 100 years of age or over, drug use decreases again in Finland (Klaukka *et al.* 2002), as also in France (Simiand-Erdociain *et al.* 2001), suggesting that only the healthiest persons survive up till that age.

Cardiovascular drugs were most commonly used in this study, as they were in the previous studies among the elderly (Chrischilles *et al.* 1992, Rosholm *et al.* 1998, Barat *et al.* 2000, Jørgensen *et al.* 2001, Klaukka *et al.* 2002). These drugs also constitute the biggest group in the sales of pharmaceutical products to pharmacies (National Agency for Medicines and Social Insurance Institution 2001), which suggests that the elderly do not differ from the total population in their use of the main drug categories. The incidence of coronary heart disease has been postponed toward older age groups (Arinen *et al.* 1998), which might explain the common cardiovascular drug use.

Particularly the oldest women used cardiovascular drugs. Nitrates and diuretics have been used for decades, and they explained most of the cardiovascular drug use by the elderly in this study. In the USA, only 40% of home-dwellers over 85 years old used cardiovascular drugs daily (Krach *et al.* 1996), but in the present study, short-acting nitrates taken when needed might explain part of high prevalence of these drugs.

6.5 Polypharmacy (I)

Polypharmacy became more common during the study period. Polypharmacy might have been even more common if non-prescription drugs had been included or combination preparations had been counted separately. In an earlier Finnish nationwide series of home-dwelling surveys, polypharmacy (≥ 5 prescription drugs) increased from 14% to

22% among men aged over 64 and from 22% to 29% among women from 1976 to 1987 already. Polypharmacy was most common (37%) in women aged 75 years or over in 1987. (Klaukka & Martikainen 1989). Polypharmacy increased most in drug users aged 75 years or over: from 21% in 1976 to 39% in 1995–96 (Klaukka & Rajaniemi 1998). This study showed that the increasing trend in polypharmacy continued toward the end of the 1990s.

Drug users with polypharmacy used most commonly cardiac and gastrointestinal (1990–91) or CNS drugs (psychotropics) (1998–99). This finding is in concordance with the earlier Finnish study where the home-dwelling elderly with polypharmacy used most commonly cardiovascular drugs and second most commonly analgesics followed by psychotropics or gastrointestinal drugs (Klaukka *et al.* 1993). In other countries, cardiovascular drugs (Bjerrum *et al.* 1998, Thomas *et al.* 1999) and analgesics (Bjerrum *et al.* 1998) or CNS drugs (Thomas *et al.* 1999) have also been part of the most common drug regimens of the elderly with polypharmacy.

There are many explanations for polypharmacy. The absolute and relative proportions of the elderly have been growing and will continue to grow in the future, which may increase drug use among the older populations compared to the other age groups (Statistics Finland 1998, Tilastokeskus 2002). Polypharmacy may accumulate, because treatment guidelines are generally defined for specific diseases. Guidelines and evidence-based medicine are important, but they do not recognize the risk for polypharmacy in case of multiple morbidity among elderly persons. The development of medication was rapid in the 1990s, including the treatment of cardiovascular diseases, but pharmaceutical trials have rarely included persons older than 75 (Barat *et al.* 2000, Strandberg *et al.* 2001).

On the other hand, underuse of beneficial drug therapy by the elderly has been associated with increased morbidity, mortality, and impaired quality of life. Beta blockers after myocardial infarction, antihypertensive treatment and other evidence-based medications (lipid-lowering drugs, acetylsalicylic acid) for cardiovascular diseases belong to these medications (Rochon & Gurwitz 1999, Strandberg *et al.* 2001). Suboptimal use of other medications, such as iron supplements for anemia, calcium supplements for osteoporosis, drugs for asthma or chronic obstructive pulmonary disease, or opioids for cancer pain are also common (Lipton *et al.* 1992, Rochon & Gurwitz 1999, Hanlon *et al.* 2001).

Most of the elderly suffer from chronic diseases. The prevalence of chronic morbidity grew in home-dwelling Finns aged 75 years or over from 70% in 1964 to 90% in 1995–96 (Klaukka 1982, Arinen *et al.* 1998). On the other hand, development of polypharmacy is not necessarily related to an increase in the number of diseases (Veehof *et al.* 2000). Increasing use of health services (Klaukka 1989) may also be one reason for the increase of polypharmacy.

The assortment of medications is wide, and new drugs are being developed all the time. Pharmaceutical industry is international business predominated by major financial interests. An elderly person without drugs is becoming a rarity, and the elderly have partly accepted the patient's role. (Lumme-Sandt *et al.* 2000). Medicalization has moved the line from sick persons toward healthier ones. For example, almost every elderly man has a hyperplastic prostate, but new effective treatments have made this a disease that should be treated, at least with drugs, in all cases with even minor symptoms.

Some of the increasing trends and changes in treatment patterns can be explained partly by more extensive marketing and partly by better therapeutic efficacy. For instance, proton pump inhibitors have replaced H₂ antagonists and antacids, and their use in the eradication of *Helicobacter pylori* has increased. Statins and antidepressants have been marketed heavily and are used commonly by the elderly. Many diseases of the elderly, such as hypertension, are now treated more actively than before, and the threshold to start medication has become lower (Joint National Committee 1997). More sophisticated diagnostic tools are available, and they enhance the chances to make specific diagnoses and to start treatments.

This study cannot reveal whether the increased drug use is iatrogenic. The clinical diagnostic problems associated with diseases are more complicated in the elderly than in other adults. It may be difficult for the doctor to estimate which symptoms are physical and psychic, or whether they are just part of normal aging. (Kyle *et al.* 2001). It is difficult to know if the new symptom of an elderly person is caused by drug withdrawal. Drug withdrawal causes many symptoms, such as hallucinations and seizures, which may need to be treated with new drugs (Gerety *et al.* 1993). This tends to increase polypharmacy. To avoid adverse effects of withdrawal, the longer the drug has been in use, the more slowly should its use be discontinued. The doses should be reduced first to half or to two thirds. After some weeks or months, a new halving or reduction by one third is needed. Withdrawal should be continued in this way, until the dose is so small that the drug can be left off. Long-acting drugs, such as benzodiazepines, that have been used for many years, require very slow withdrawal over six months to one or more years. (Hartikainen 2002). Because the risk of adverse drug reactions increases with the number of drugs taken, it is important to discontinue any treatment that is not efficacious (Cusack *et al.* 1997).

No interventions to reduce polypharmacy were made in this study. In an earlier Finnish study, an attempt to reduce polypharmacy permanently failed. The number of drugs used by home care patients returned to its earlier level (to polypharmacy) after some months (following the first 2-month intervention). When prescription drug use decreased during follow-up, the elderly compensated for it by increasing their use of non-prescription drugs. (Pitkälä *et al.* 2001a)

Polypharmacy grew most in the oldest persons aged 85 years or over between the study periods. In the USA, a similar trend was seen in a study of the oldest old and their prescription policy toward polypharmacy (Huang *et al.* 2002). Contradictory studies also exist. Danish home-dwellers aged 90 years or over had polypharmacy less commonly than the younger elderly (Bjerrum *et al.* 1998). Kennerfalk *et al.* (2002) found in England that the younger elderly had polypharmacy more prevalently than 90-year-olds.

6.6 Factors associated with polypharmacy

In the late 1990s, person with polypharmacy was typically 85 years or older, had many diseases, had poor self-perceived health, and used home nursing services. In a cross-

sectional, nationally representative Finnish home-dwelling survey, polypharmacy was associated with age and chronic morbidity, but not with gender (Klaukka *et al.* 1993), as in this study in 1998–99. Polypharmacy increases with advanced age, as also shown by earlier studies (Chrischilles *et al.* 1992, Laukkanen *et al.* 1992, Klaukka *et al.* 1993, Bjerrum *et al.* 1998, Thomas *et al.* 1999, Bardel *et al.* 2000, Veehof *et al.* 2000). Gender differences were more distinct in the early 1990s. The oldest women, aged 85 years or over, showed the greatest increase in the mean number of drugs per user in the 1990s and had a threefold risk for polypharmacy. Marital status did not influence the probability of polypharmacy in 1998–99. Similar results on some sociodemographic variables' associations with drug use have been reported before. (Chrischilles *et al.* 1992)

Poor self-rated health correlated with polypharmacy in this study. Self-rated health is a useful summary of physical health, and it is associated with the regular use of 3 or more drugs (Jylhä *et al.* 1998). It also correlates with advancing age and predicts mortality (Jylhä *et al.* 1992). Relations between drug use or polypharmacy and lower self-rated health (Chrischilles *et al.* 1992, Thomas *et al.* 1999) and home nursing (Lithovius *et al.* 1998, Linjakumpu *et al.* 2001) were also seen in some previous studies. The elderly incur a disproportionate share of the health care costs, i.e. up to one third or half of total health care expenditure (Roberts 1999), including the cost of drugs and home nursing during the past few decades (Eddy 1994). This gives rise to increasing challenges and requires the rationing of services in society and the health care system.

Poorer physical functioning (ADL, mobility, IADL) was associated with an increasing number of drugs and polypharmacy. Similar results in connection with physical functioning and drug use or the high number of drugs have been reported before (Chrischilles *et al.* 1992, Rozzini *et al.* 1993). Difficulties or dependence in physical activities were associated with cardiovascular drug use, particularly diuretics (Ahto *et al.* 1998). Persons with polypharmacy typically used cardiac drugs, including diuretics, in this study. In addition to chronic morbidity, aging processes and disabilities caused by inactivity should be considered in the search for ways to reduced ADL performance (Laukkanen *et al.* 1994). Physical disabilities are connected with advanced age and multiple diseases, particularly cardiovascular, musculoskeletal, and mental diseases (Stewart *et al.* 1989, Laukkanen *et al.* 1994, Pitkälä & Strandberg 2003). Drugs seem to be one important factor related to the physical functioning of the elderly.

Multifactorial risk assessment with targeted management, including reduction of polypharmacy and high-risk drugs (psychotropics, anticonvulsants, cardiovascular drugs), balance and gait training, strengthening exercise, and reduction of home hazards are recommended and have turned out effective in randomized clinical trials aiming to improve functioning and to reduce falls by elderly persons (Tinetti 2003). More detailed discussion of the prevention of falls is beyond the scope of this study.

More education in geriatrics, psychogeriatrics and clinical pharmacology is needed in medical schools, and more medical specialists in geriatrics are needed. Geriatricians and physicians specialized in pharmacology are needed to train physicians and other health care personnel in primary health care and specialized hospitals concerning appropriate drug use.

6.7 Psychotropic use (II)

CNS drugs (psychotropics) ranked second in the frequency of use after cardiovascular drugs in this study. The elderly use all psychotropics more commonly compared to other adults nationwide in Finland. It is interesting that in the Mini-Finland Health Survey conducted 20 years ago, self-rated mental health problems were already most prevalent among 40- to 64-year-olds, but the elderly used psychotropics more commonly. (Aromaa *et al.* 1989)

In previous studies, psychotropic use among the home-dwelling elderly has ranged from 10% to 38%, and hypnotics/sedatives (mostly benzodiazepines) have been the most commonly prescribed psychotropics, ranging from 6% to 31%. In previous studies, 1% to 4% of the home-dwelling elderly have been taking antipsychotics and 2% to 5% antidepressants. In this study, the use of psychotropics was in the middle of the range established by other studies, the use of antipsychotics was very much as in previous studies, and antidepressants were used more often in the late 1990s. (Laukkanen *et al.* 1992, Skoog *et al.* 1993, Manela *et al.* 1996, Weiner *et al.* 1998, Kirby *et al.* 1999, Fourrier *et al.* 2001). Of the European countries, France ranks close to the top of on the list of benzodiazepine use (Fourrier *et al.* 2001).

Psychotropic use was slightly increasing in the 1990s in Lieto. Increasing trends of psychotropic use in the Finnish home-dwelling elderly have been described since 1976 (Klaukka & Martikainen 1989). The use of hypnotics/sedatives was also slightly increasing. The biggest increase in this study was seen in hypnotics and antidepressants. The same trend is visible in the use of these drugs in the total population of Finland and in the other Nordic countries, with the exception of Denmark and Norway, where hypnotic use was decreasing in the 1990s (Source: Statistics on medicines in Nordic countries from different sources). The Finnish prescription practice according to this study is contrary to the guidelines on temporary use of hypnotics (Klaukka 2000b), because most hypnotic/sedative users were on regular medication. Regular use may result in habit, dependence and a loss of the drug's efficacy. Sleepy patients should be first diagnosed for possible somatic and psychiatric diseases, and non-medical treatments should be tried first. The elderly have more sleeping problems than before (Arinen *et al.* 1998).

Among the oldest old, on the other hand, any regular psychotropic or regular hypnotic/sedative use, which data were gathered from prescriptions or medical records, decreased in this study. This trend is beneficial if it decreases adverse effects. Also, the elderly may control drug use more freely by symptoms and feelings, which may result in uncontrollable hypnotic/sedative use.

The consumption of antidepressants increased in most western countries in the 1990s (McManus *et al.* 2000) as the use in this study. Antidepressants are being actively marketed, and depressions are diagnosed more commonly. Not all melancholic or depressive elders need drugs, however, but might rather benefit from psychic support. Studies show 11–20% prevalences of depressive symptoms or depression in the elderly overall in Europe (Copeland *et al.* 1999) or in the community (Johnson *et al.* 1994, Manela *et al.* 1996, Kirby *et al.* 1999, Linjakumpu *et al.* 2001). Major depression, which requires drug therapy, is diagnosable in 6% of the elderly (Valvanne *et al.* 1996), but this

study does not give an answer to the question of whether the right patients received antidepressants. Still, selective serotonin reuptake inhibitor prescribing, for example, increased in the 1990s in Finland (National Agency for Medicines and Social Insurance Institution 2001), as in Lieto, anxiolytic use did not diminish in this study in the 1990s.

Antipsychotic use dropped to a half in the 1990s in this study, though their consumption in the total population was only slightly decreasing (Source: Statistics on medicines in Nordic countries from different sources). Decreased antipsychotic use by the elderly may be due to their decreased use as sleeping pills, of which non-benzodiazepine sleeping pill (eg. zopiclone) use increased significantly in Lieto. This trend may be considered good because of the harmful adverse effects of antipsychotics (Appendix table 1). Antipsychotics are used increasingly by the working-aged population, though their use is still most prevalent in the older populations (Klaukka 2000a).

In the Lieto community, the use of hypnotics and antipsychotics was less common among the elderly aged 75 years or older than in Kuopio, a city in eastern Finland (Hartikainen *et al.* 2003), or in the whole country (Source: Social Insurance Institution) at the end of the 1990s. Of the different benzodiazepine hypnotics, medium-acting ones, which are recommended to the elderly if benzodiazepines must be chosen, were most commonly used both in Lieto and in Kuopio.

The use of antidepressants was equal in the two districts (Lieto and Kuopio) (Hartikainen *et al.* 2003). These results are opposite to the findings of the East-West study several years ago, where elderly men in the East used all kinds of prescription drugs more commonly than men in the West (Enlund *et al.* 1990, Martikainen 1995). Previous results suggest that drug use varies at different times in the same areas and between countries, possibly without any specific reason. Study designs vary, which must be taken into account when evaluating the study results. The health care system has impacts on drug utilization and prescription, and the findings may thus not be applicable from one to other areas or countries. In a recent study, among millions of elderly home-dwelling people aged 65 or older in the USA, 19% used psychotropics (Aparasu *et al.* 2003), which figure is close to that obtained in the present study. They used hypnotics/sedatives much less (5%) than our subjects, but used antidepressants slightly more commonly (9%) than in this study. National differences have been reported in many studies. Hypnotics/sedatives seem to be over-prescribed and over-used by the home-dwelling elderly in Finland.

Concomitant use of two psychotropics increased in the 1990s, being quite similar in the southwestern Lieto community and in the eastern City of Kuopio (Hartikainen *et al.* 2003). A combination of hypnotic/sedative and antidepressant medication was most prevalent in both areas. A nationwide survey suggests concomitant use of psychotropics to be common among the Finnish home-dwelling elderly (Klaukka 2000a). Concomitant use of CNS drugs is associated with an enhanced risk of falls more often than the use of one CNS-active drug alone (Caramel *et al.* 1998, Weiner *et al.* 1998, Leipzig *et al.* 1999a). Polypharmacy of psychotropics may cause confusion or behavioral problems (Schmidt & Svarstad 2002). On the other hand, there are indications for concomitant psychotropic use even among the elderly in primary health care, including depressed patients (Mulsant *et al.* 2001), and particularly in psychotic depression. Much of the

management of dementia and depression in the elderly is undertaken by primary care physicians rather than psychiatrists (Johnson *et al.* 1994).

The visions concerning the psychotropic use of particularly the younger (64–71 years) female elderly did not seem optimistic in the present research. Their psychotropic use seemed to be slightly increasing rather than decreasing. Hypnotic and antidepressant use became more prevalent among the younger elderly women in the 1990s. Atypical antipsychotics were not used at all by the southwestern younger elderly or by the older elderly in eastern Finland (Hartikainen *et al.* 2003). Neurological adverse effects are less common due to atypical than conventional antipsychotics (Pickar 1995, Casey 1997). Long-acting benzodiazepines and cyclic antidepressants still remained in the drug assortment of the young elderly in the late 1990s, even though these drugs impair cognition (Foy *et al.* 1995) and memory, cause drowsiness in the morning and tiredness in the daytime (Pelkonen 1998), and may cause paradoxical anxiety (Pharmaceutical Information Centre 1997). Cyclic antidepressants have anticholinergic adverse effects (Appendix table 1). Hypotension, dry mouth, tachycardia, urinary retention, constipation, and blurring of vision are common in users. (Bazire 1999, Pollock 1998)

Young elderly persons feel better, but physicians prescribe to women psychotropics more than ever. According to a Finnish study, 65- to 69-year-olds had a similar prevalence of mental disorders in 1988 and 1996. Tiredness, sleepiness, depression, and lack of strength had decreased in both genders during a 10-year period. (Laukkanen *et al.* 1999). In a Finnish nationwide study, especially 55- to 64-year-old working women experienced exhaustion because of work relatively more prevalently than men of the same age (Pirkola *et al.* 2002). This may lead to more prevalent polypharmacy and psychotropic use by the young elderly women, if they already start medication before the pensionable age for many symptoms, such as insomnia and anxiety. This means that the load of drugs already begins to increase before the pensionable age in women. Thus, primary care physicians need knowledge to rationalize their psychotropic prescription policies, which do not seem optimistic in view of the future.

Psychotropic use became most common in the oldest persons, aged 85 years or over, in the 1990s in this study. In Kuopio, every second oldest home-dwelling person also used psychotropics (Hartikainen *et al.* 2003). Similarly in Turku, in southwestern Finland, ten years ago every second 75- to 89-year-old primary health care client used psychotropics (Joukamaa *et al.* 1995). In Denmark, persons aged 90 years or over used psychotropics more commonly than younger persons (Rosholm *et al.* 1994), as in this study. In the USA, the trend toward increasing psychotropic use was evident among 85-year-olds and older persons (Aparasu *et al.* 1998). In Italy, 80- to 90-year-olds used antidepressants more than the younger elderly (Pietraru *et al.* 2001). In Finland, 90- to 99-year-olds used antidepressants more prevalently than persons aged 100 years or older, and in Sweden, antidepressant use increased toward the age group of 80 years or over (Klaukka *et al.* 2002, Svensk läkemedelstatistik 2001), which is in accordance with the present results. Toward centenarians, antidepressant use also decreases in Italy (Pietraru *et al.* 2001).

On the other hand, in most Finnish and international studies (USA, Sweden, and Ireland) of older or the oldest old persons, psychotropic use is equally or less common compared to use by the younger elderly (Haavisto & Mattila 1981, Swartz *et al.* 1991, Isacson *et al.* 1992, Laukkanen *et al.* 1992, Louhija 1994, Dealberto *et al.* 1997, Isacson

1997, Kirby *et al.* 1999, Blazer *et al.* 2000, Jørgensen *et al.* 2001). Over 81-year-old women received reimbursement for antipsychotics more often than men in 1999 in Finland (Martikainen 2001). In Lieto, antipsychotics were used equally by men and women over 74 years old. According to the nationwide prescription register of Social Insurance Institution, the use of antidepressants increases systematically toward the age group of over 84 years, especially among women (Klaukka *et al.* 2002). These results are in concordance with the results obtained in Lieto. Toward centenarians, psychotropic use decreases in Finland (Louhija 1994).

Many things may explain the increasing trends of psychotropic use. The situation is alarming in several respects. The high frequency of use and the great number of medications increase the possibility of adverse effects and interactions, and the risk is further increased by pharmacokinetic and pharmacodynamic changes taking place secondary to high age or illnesses (Hughes 1998, Pollock 1998).

6.8 Classification of drugs by their sedative properties (III)

Development and updating of the classification will be the major challenge in the future after local elaboration of the national drug assortments. The updated method can be utilized in the future to estimate load and dosage of sedative drugs prescribed to elderly persons in practice, provided the method is easily available in an electronic format at workplaces and in prescription registers.

The strength of the present study is that it gives a method to estimate the load of sedation of elderly individuals. Another strength is that drugs whose sedative properties were uncertain or undocumented were not taken into account. The method used in this study also identified drugs prescribed for somatic disorders, which are not traditionally considered sedatives.

The limitation is that the method may underestimate the person's sedative load because some drugs are placed into the lowest group of sedation. Pharmacologically, drugs including psychotropics for somatic disorders in group 2 could have been placed in group 1, but this was not done to avoid exaggerating the sedative property of the drug. Also, doses were not calculated, but that will warrant further research. It would be useful to develop the concepts of sedation score, sedation sum score, and polysedation further by counting DDD/1000 inhabitants/day or by dividing the four groups into subgroups. Equipotent doses have already been calculated for antipsychotics. The duration of sedative drug use by each elderly person was not followed up over a longer period because of the cross-sectional study design. The lack of data on the indications for prescription, the severity or duration of sedation, the frequency of reported sedation by each drug, and co-morbidity will require further study.

All conventional antipsychotics were placed into group 1, though there are differences between them. Haloperidol (conventional) is not so sedative at low doses, but clozapine (atypical) is highly sedative even at therapeutic doses. There are also differences in sedative properties between antidepressants of the new generation. For example, low-dose mirtazapine makes the person sleepy in the evening, but when compared with

tricyclic antidepressants, SSRIs only seldom cause sedation. Thus the classification presented in this study is supposed to be rough estimation of sedative load of drugs in the elderly.

Psychotropics (hypnotics/sedatives, antipsychotics, antidepressants) were conventional sedative drugs in group 1 (primary sedatives) in this study. Other sedatives, e.g., opioids, anticonvulsants, and old antihistamines, belonged to group 2 (Bowen & Larson 1993), and histamine (H₂)-receptor antagonists (ranitidine, etc.), cardiovascular drugs, anti-infectives, antineoplastic agents, most important anti-parkinsonian drugs, major NSAIDs, second-generation antihistamines, pulmonary drugs, etc. (Bowen & Larson 1993, Slater *et al.* 1999, Blokland *et al.* 2001) belonged to the category of drugs with a potential sedative property. Bowen & Larson (1993) found many previous drugs also to cause delirium in the elderly. Many previous drugs also have anticholinergic effects, which predict the clinical severity of delirium symptoms (Han *et al.* 2001).

As far as inappropriate medication (Beers 1997) and drug interactions are concerned, there are many well known recommendations (McLeod 1997, Hanlon *et al.* 2001), but this topic requires further research. Partly inappropriate medications, e.g., the anticholinergic muscle relaxant orphenadrine, belong to our category of sedative drugs. Even for healthy older adults, the use of anticholinergic medications is considered potentially inappropriate. Inappropriate drugs also include many psychotropics (e.g., amitriptyline, diazepam, meprobamate), dipyridamole, or cardiovascular drugs, such as digoxin at more than 0.125 mg daily, disopyramide, or the urinary antispasmodic oxybutynin (Beers 1997, McLeod 1997), which are included in our classification of drugs by their sedative properties.

Persons with polypharmacy used proper sedatives significantly more commonly than those without polypharmacy. In an earlier study, one predictor of polypharmacy was the use of especially hypnotics/sedatives without a clear indication (Veehof *et al.* 2000). Polypharmacy partly hides sedative drug use, which has not been widely studied before this study. The persons with polypharmacy or many sedative drugs were the oldest and sickest ones in this study, and they were not feeling good. Their quality of life is not assumed to be at a high level, and institutionalization is a threat for them. Hence, they need careful consideration in primary health care.

6.9 Items connected with sedative drug use (IV)

The home-dwelling elderly use drugs, particularly sedative drugs, commonly. The most frail persons aged 80 years or over, women, those with many diseases, smokers, those with poor self-perceived health/poor life satisfaction, and those having home nursing are most likely to have polysedation.

Part of the sensitivity to drug-induced sedation, motion disturbances and falls, are associated with aging processes (Koponen 2001). Sedation is sometimes a subjective experience and its influence varies from person to person. Hence, reliable objective measurements of sedation are difficult to develop, and they would require laboratory conditions. In this study, no objective measurements were used. Reaction times,

sensorimotor functions, and balance control have been measured as indicators of sedation (Lord *et al.* 1995, Ridout & Hindmarch 2001).

The home-dwelling elderly used sedative drugs commonly. Up to 40% of drug users took proper sedatives. The elderly with polysedation also used a lot of other medicines with sedative properties, i.e. analgesics (Hoppmann *et al.* 1991), antihistamines (Slater *et al.* 1999), and drugs with possible sedative properties, such as cardiovascular drugs (Pharmaceutical Information Centre 2000). Insidious extra sedation may be caused by drugs in the large and variable group 3, to which the above-mentioned drugs mainly belong. We do not know the whole sedative load of individual elderly persons, but it is anticipated to be much higher than that reported in this study. A potential sedative combination of drugs may result from complicated medication regimens involving medications, some or all of which have modest sedative effects.

Polysedation was associated with impaired physical functioning. In other words, a large number of sedative drugs cause physical functional disabilities in the elderly. Sedation is sometimes intentional, as in the treatment of acute psychiatric diseases or insomnia (Thompson *et al.* 1983, Batty *et al.* 2000). While sedation may initially be beneficial, it impairs the person's functioning (Casey 1997). Impaired physical functioning and poor self-rated health have been found to correlate with the use of sedatives by the home-dwelling elderly (Ried *et al.* 1998, Blazer *et al.* 2000), not to mention the risk of falls (Aisen *et al.* 1992, Rynänen *et al.* 1993, Rynänen *et al.* 1994, Tinetti *et al.* 1994, Thapa *et al.* 1995, Ebly *et al.* 1997, Cumming 1998, Leipzig *et al.* 1999a), which risk is increased by a single sedative (zolpidem) alone (Wang *et al.* 2001). The risks of falls and other accidents should be explored in the future by taking into account the total sedative load of drugs. This study also identified drugs prescribed for the treatment of somatic disorders, which are not traditionally considered sedatives.

In this study, the persons with polysedation used more commonly home nursing services than the other elderly. Home nursing is a challenge for health care professionals because extremely frail elderly persons often live alone. They commonly have physical and mental disorders, polypharmacy, and psychotropic medication (Lithovius *et al.* 1998), and they are thus at a high risk of institutionalization. On the other hand, polypharmacy in itself is associated with poor physical abilities (Rozzini *et al.* 1993) and hypotension (Cohen *et al.* 1998), which also expose the person to balance disorders and mobility problems.

We may be able to improve these persons' health by withdrawing the injurious extra sedative load of drugs. The use of many sedatives is a risk for functional independence and may cause physical disabilities. The load of sedative drugs may thus increase the need for health and social care and the consequent costs.

7 Conclusions

In Finland, there are not many studies concerning drug use, polypharmacy, and sedative use among the home-dwelling elderly and the oldest old between two time windows. In other countries, such studies have been carried out, but most of them also include institutionalized persons. This study aimed to illustrate the drug use policy in Finland from 1990–91 to 1998–99.

According to the findings and in view of the literature, the following conclusions and clinical implications can be made:

1. The use of prescription drugs and polypharmacy among home-dwelling elderly people in a Finnish municipality became more prevalent over a period of a decade. The mean number of drugs per user grew during the study period, most markedly in the oldest women. In this study cardiovascular and CNS drugs were used most commonly by the general elderly population and also by the persons with polypharmacy. The oldest old, aged over 84 years, used drugs most commonly, and polypharmacy grew most among them.

Overall assessments of medication should be made regularly, and the main target in the reduction of polypharmacy should be elderly women and the oldest old. Physicians should have a possibility to consult a geriatrician when necessary.

2. The persons with polypharmacy were typically the oldest ones and had many diseases and poor self-perceived health and used home nursing services. Difficulties or dependence in daily activities or mobility were typical of persons with polypharmacy.

Quality of life should be improved among persons with polypharmacy. Training of nurses to check medication use and to identify the adverse effects of drugs should be available for all patients in home care/nursing.

Persons with polypharmacy should be trained to diminish physical functional disabilities. The importance of a critical and conservative approach toward drug therapy in elderly patients cannot be overemphasized.

3. Psychotropic use showed a slightly increasing trend. The oldest old, who are supposed to be at the highest risk of adverse drug reactions, use psychotropics most commonly.

Most psychotropic users were on regular medication. Hypnotic and antidepressant use grew most significantly. Anxiolytic use remained stable. Regular use of hypnotics/sedatives is against the recommendations. Treatment of depression may have improved among the elderly, though this study was unable to demonstrate whether or not the right persons, i.e. the persons with major depression, receive antidepressants. The prevalence of antipsychotic use dropped to a half, and they are probably not used so much in sleeping pills any longer. New atypical antipsychotics were not used.

Concomitant use of psychotropics should be avoided without proper indications. The young elderly women have not diminished their psychotropic use, and they should be assessed very carefully, in order to avoid increasing their psychotropic use in the course of life.

4. Sedative drug use is very common, and the classification of drugs by their sedative properties was helpful. Development and updating of the classification will be the major challenge in the future after local elaboration of the national drug assortments. The pharmacokinetics and pharmacodynamics of drugs in the elderly should be presented in more detail in medical schools, to avoid polypharmacy and sedation, and the information should be easily available from Pharmaca Fennica.
5. The most frail persons aged 80 years or over, women, those with many diseases, smokers, those with poor self-perceived health/poor life satisfaction, and those with home nursing are most likely to have abundant sedative drug use. They should be assessed with particular care by physicians.

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Appendix tables 1-2

Table 1. Examples of adverse effects and symptoms associated with medications prescribed for the elderly.

Organ/ symptoms	Adverse effects	Examples of medications	References
Cardiovascular system	Orthostatism	Diuretics, beta blockers, nitrates, vasodilators	Cohen <i>et al.</i> 1998
		ACE inhibitors	Beers 1997
		Dipyridamole	Glassman <i>et al.</i> 1979
		Cyclic antidepressants	Casey 1997,
		Antipsychotics	Bazire 1999
		Anticholinergics ^a (list in nervous system section)	
	Arrhythmia/ prolongation of QT interval	Antiarrhythmics (quinidine, sotalol, amiodarone), vasodilators, diuretics, antidepressants (cyclic antidepressants), antipsychotics (chlorpromazine, thioridazine, haloperidol), antimicrobials (erythromycin, trimethoprim/sulfa), corticosteroids	O'Brien <i>et al.</i> 1999
		Atypical antipsychotics	
		Terfenadine, astemizole	Campbell <i>et al.</i> 1999
		Anticholinergics ^a (list in nervous system section)	Slater <i>et al.</i> 1999
	Bradycardia	Beta blockers, digoxin	b, c
	Heart failure/insufficiency	Diopyramide, beta blockers, calcium channel blockers, NSAIDs	, b, c
Nervous system	Dry mouth, constipation, urinary retention, orthostatism, tachycardia, blurring of vision, glaucoma, cognitive decline	Examples of drugs with anticholinergic properties ^a : - nitrate, nifedipine, furosemide, captopril, nortriptyline, hydroxyzine, diphenhydramine, ranitidine, cimetidine, warfarin, dipyridamole, theophylline, prednisolone, codeine	Tune & Bylsma 1991 ^a , Tune <i>et al.</i> 1992 ^a
		- antipsychotics, cyclic antidepressants	Roe <i>et al.</i> 2002, ^b
		- disopyramide, imipramine, amitriptyline, doxepin, olanzapine, atropine, antihistamines, oxybutynin, orphenadrine, antiemetics, antiparkinsonian drugs, scopolamine	Roe <i>et al.</i> 2002

Table 1. Continued.

Organ/ symptoms	Adverse effects	Examples of medications	References
Sedation		Antipsychotics, hypnotics/sedatives, most antidepressants, opioids	^b
		Old antihistamines	Slater <i>et al.</i> 1999
Cognitive decline or delirium		Some new antihistamines (cetirizin)	Blokland <i>et al.</i> 2001
		Anticholinergics ^a	Bowen & Larson 1993
Depression		Antihypertensives, antiarrhythmics, digoxin, hypnotics/sedatives, cyclic antidepressants, conventional antipsychotics, anticonvulsants, antiparkinsonian drugs, NSAIDs, paracetamol overdose, opioids, histamine H ₂ - receptor antagonists, insulin, antibiotics, aminophylline, corticosteroids, antineoplastic agents	Beers 1997
		Hydroxyzine, disopyramide, oxybutynin	Rawson & Rawson 1999
		Benzodiazepines	Goodwin & Regan 1982,
		NSAIDs	Hoppman <i>et al.</i> 1991, Karplus & Saag 1998
		Scopolamine	Miller <i>et al.</i> 1988
		Benzodiazepines	Hall & Joffe 1972, Rawson & Rawson 1999
		Antipsychotics	Weinstein 1980
		Opioids	Weissman <i>et al.</i> 1976,
		Levodopa	^b
		Ibuprofen, aspirin	Blechman <i>et al.</i> 1975
Depression/ paranoia	Neuropathias	Beta blockers, corticosteroids	^b
		NSAIDs	Browning 1996
Myopathias	Psychosis, aseptic meningitis	Gold preparations, nitrofurantoin, antineoplastic agents, tricyclic antidepressants	^c
		Statins	Weimer 2003
Psychosis, aseptic meningitis		Statins	^b
		NSAIDs	Hoppman <i>et al.</i> 1991

Table 1. Continued.

Organ/ symptoms	Adverse effects	Examples of medications	References
Extrapyramidal symptoms		Neuroleptics	Campbell <i>et al.</i> 1999
		Metoclopramide	^b
- tardive dyskinesia/tremor		Neuroleptics	Rapoport <i>et al.</i> 1998, Jeste <i>et al.</i> 1999
		Neuroleptics	^b
Malignant neuroleptic syndrome		Neuroleptics	
		SSRIs	^b
Serotonin syndrome		Anticholinergics ^a , metronidazole, diltiazem, nifedipine	^c
Changes in taste		NSAIDs	O'Brien 1986, ^c
Gastrointestinal system	Gastrointestinal ulcer, gastritis	Glucocorticoids	^b
	Constipation	Anticholinergics ^a , calcium channel blockers, opioids, sucralfate	^b
		Aluminium/calcium containing antacids	^c
		Antipsychotics, cyclic antidepressants	Bazire 1999
Diarrhoea		Antibiotics, magnesium-containing antacids	^c
Incontinence		Hypnotics/sedatives, lithium	^b
Nausea		Erythromycin, opioids, digoxin, iron preparations	^c
		Anti-dementia drugs	^b
		SSRIs	Edwards & Anderson 1999
		Benzodiazepines	Rawson & Rawson 1999
Liver effects			
	- hepatitis	ASA, phenytoin, paracetamol	^c
- other liver adverse Effects		Statins	^b
		NSAIDs	Nuki 1990
		Glucocorticoids, valproic acid, estrogens, oral blood glucose-lowering drugs, conventional antipsychotics	^c
Hyperplastic gingiva		Phenytoin, nifedipine	^c
Pharyngeal fungus		Inhaled glucocorticoids	^c

Table 1. Continued.

Organ/ symptoms	Adverse effects	Examples of medications	References	
Urinary system	Urinary retention	Anticholinergics ^a , hypnotics/sedatives, opioids, diuretics	^b	
	Urinary incontinence	Antipsychotics, cyclic antidepressants	Bazire 1999	
	Kidney insufficiency	Hypnotics/sedatives, lithium, diuretics	^b	
		NSAIDs	O'Brien 1986, Nuki 1990	
	Visual	Eye lens damage	NSAIDs, paracetamol, antibiotics, allopurinol, diuretics, ACE inhibitors, phenytoin, gold preparations	^c
			Glucocorticoids	^c
		Blurring of vision	Anticholinergics ^a	^c
			Ototoxic	Salicylates, furosemide
		Coughing	ACE inhibitors	^c
			Obstruction	Beta blockers, opioids, ASA, cephalosporins, penicillin
Respiratory insufficiency		Benzodiazepines, opioids	Rawson & Rawson 1999, ^c	
Mucus in respiratory organs		Anticholinergics ^a	^c	
Immunologic reactions		Nitrofurantoin	^c	
Blood system		Fibrosis in pulmonum	Antineoplastic agents	^c
	Vasculitis	Gold preparations, nitrofurantoin, phenytoin	^c	
	Bleeding	Warfarin, ASA, NSAIDs	^c	
	Blood cell damage	Antibiotics, gold preparations, antineoplastic agents, NSAIDs, diuretics, quinidine	^c	
			Clozapine, mianserin, conventional antipsychotics	^b
	Skin		Amoxicillin, cephalosporins, trimethoprim/sulfa, carbamazepine	^c

Table 1. Continued.

Organ/ symptoms	Adverse effects	Examples of medications	References
Miscellaneous organs/symptoms			
Headache		Nitrates	b
Electrolyte disturbances	Hyponatremia	Diuretics, carbamazepine, oxcarbazepine	b
	(delirium, arrhythmia, tiredness, weakness)	SSRIs	Pradalier <i>et al.</i> 1998, Odeh <i>et al.</i> 1999, Wilkinson <i>et al.</i> 1999
	Hypomagnesemia,	Diuretics	b
	Hypokalemia (weakness)	Diuretics	b
	Hypocalcemia (convulsiones)	Herbal drugs	Enkovaara 1999
Allergy			
Metabolic disturbances	Glucose balance changes		
	- hyperglycosemia	Diuretics, corticosteroids, antipsychotics	b
	- hypoglycosemia	Sulphonamides, insulin, other blood glucose-lowering drugs	b
	Body weight gain	Second-generation histamine H1 receptor antagonists	Slater <i>et al.</i> 1999
		Antipsychotics, mirtazapine	b
	Hyperlipidemia	Antipsychotics	Koro <i>et al.</i> 2002

Table 1. Continued.

Organ/ symptoms	Adverse effects	Examples of medications	References
Falls	Contusions, fractures	Diazepam, diltiazem, diuretics, laxatives Vasodilators, diuretics Neuroleptics, benzodiazepines Anxiolytics, antipsychotics Antidepressants Benzodiazepines, analgesics, digoxin	Cumming 1991 Myers <i>et al.</i> 1991 Aisen <i>et al.</i> 1992 Malmivaara <i>et al.</i> 1993 Ruthazer & Lipsitz 1993 Ryyänänen <i>et al.</i> 1993, Ryyänänen <i>et al.</i> 1994 Tinetti <i>et al.</i> 1994 Sorock & Shimkin 1988, Herings <i>et al.</i> 1995 Lord <i>et al.</i> 1995 Ebly <i>et al.</i> 1997 Cumming 1998
		Sedatives Benzodiazepines	Liu <i>et al.</i> 1998 Weiner <i>et al.</i> 1998
		Long-acting benzodiazepines, antidepressants Antidepressants	Thapa <i>et al.</i> 1998, Leipzig <i>et al.</i> 1999a & 1999b Wang <i>et al.</i> 2001
		Diuretics, antihypertensives, digoxin, vasodilators, analgesics (NSAIDs), psychotropics (antidepressants) SSRIs	
		Psychotropic-opioid combinations	
		Diuretics, type I antiarrhythmics, digoxin, SSRI, tricyclic antidepressants, neuroleptics, benzodiazepines, anticonvulsants	
		All psychotropics, including non-benzodiazepine hypnotics	

^a Anticholinergic effects of many drugs and their metabolites are unknown. Thus, this list of drugs with these effects may be far away from the real clinical situation.

^bPharmaca Fennica 2001, ^c Himberg & Kuitunen 2002. ACE = angiotensin-converting enzyme, SSRI = selective serotonin reuptake inhibitor, NSAID = nonsteroidal anti-inflammatory drug, ASA = acetylsalicylic acid.

Table 2. Division of the home-dwelling elderly in community in 1998-99 (the corresponding results in 1990-91 are given in parenthesis) by the number of drugs in use and by difficulties or dependence in ADL, mobility, or IADL.

Difficulties or dependence in activities	Number of drugs						p-value*
	0		1-5		> 5		
	%	(%)	%	(%)	%	(%)	
Number of drug users	141	(252)	756	(659)	300	(220)	
Difficulties or dependence in ADL:							*
Getting in and out of bed	2	(2)	5	(15)	19	(36)	
Using the lavatory	4	(2)	14	(12)	31	(30)	
Dressing and undressing	2	(3)	7	(14)	24	(31)	
Washing and bathing	2	(3)	9	(17)	27	(37)	
Difficulties or dependence in mobility:							*
Walking between rooms	3	(6)	13	(22)	32	(49)	
Using stairs	9	(10)	35	(36)	62	(72)	
Moving outdoors	8	(8)	29	(31)	57	(66)	
Walking at least 400 m	8	(8)	27	(32)	57	(69)	
Difficulties or dependence in IADL:							*
Light housekeeping tasks	5	(5)	19	(24)	46	(57)	
Heavy housekeeping tasks	16	(12)	41	(42)	73	(84)	
Carrying a heavy load	11	(12)	36	(35)	67	(75)	
Cutting one's toe nails	12	(9)	32	(33)	56	(68)	
Handling finances ^a	5		15		36		
Use of public transportation ^a	6		16		43		
Taking care of one's medication ^a	14		82		96		
Ability to use the phone ^a	2		5		16		

* p-values are based on Chi-square test, $p < 0.0001$. ^a Asked from participants only in 1998-99.