

**GENDER DIFFERENCES IN  
SCHIZOPHRENIA  
OBSERVATIONS FROM  
NORTHERN FINLAND**

**SAMI  
RÄSÄNEN**

Departments of Psychiatry and Public  
Health Science and General Practice

OULU 2000



*SAMI RÄSÄNEN*

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***To my sons Niko and Santtu***



## **Räsänen Sami, Gender differences in schizophrenia. Observations from Northern Finland**

Department of Psychiatry and Department of Public Health Science and General Practice, University of Oulu, FIN-90014 University of Oulu, Finland.

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### *Abstract*

Using three different schizophrenic populations from Northern Finland, gender differences in some sociodemographic variables, age at onset, incidence, treatment, outcome and deinstitutionalization of schizophrenia were examined. The first study population comprises the Northern Finland 1966 Birth Cohort, which is an unselected, general population birth cohort. We followed prospectively 11017 subjects from 16 to 28 years of age by means of the Finnish Hospital Discharge Register. From this study population gender differences at the age of onset and incidence of schizophrenia were calculated. The second study population was formed of 1525 patients who had their first treatment episodes at the closed therapeutic community ward situated at the Department of Psychiatry, University of Oulu during 1977 - 1993. Gender differences were assessed in relation to age at first admission, some sociodemographic variables, degree of active participation of the patients in individual, group, and milieu therapy and institutional outcome of the patients with schizophrenia. The third study population consisted of all the 253 long-stay psychiatric inpatients treated for at least six months without a break during 1992 in the Department of Psychiatry, Oulu University Hospital. From this study population gender differences at the age of onset and in relation to some sociodemographic and clinical variables were studied. The placements after the last discharge and at the end of the follow-up and factors predicting hospitalization after the follow-up were also monitored.

There were no statistically significant gender differences regarding age at onset in any of these three different study populations. The time lag between the first psychotic symptoms and the first psychiatric hospitalization was minimal. In the Northern Finland 1966 Birth Cohort study the annual incidence rate of DSM-III-R schizophrenia was relatively high, 7.9 per 10 000 in men and 4.4 in women by the age of 28. In men it was highest in the age group of the 20-24 year-olds while in women the peak occurred earlier in the age group of the 16-19 year-olds.

In the Therapeutic community study there were no statistically significant gender differences in the sociodemographic variables, in the length of stay and in the number of treatment episodes in this ward in any of the diagnostic groups. Differences with regard to male and female participation in individual, group and milieu therapy and the institutional outcome were minimal, some trends, however, favoring females.

In the long-stay patients study almost two-thirds of these patients were men. Very few gender differences were found in relation to sociodemographic and clinical characteristics or regarding the utilization of psychiatric hospital care.

About 70% of the long-stay patients were discharged during the four year follow-up period and only 15% were able to live without continuous support. Marital status (being not married), dwelling place (living in city), absence of negative symptoms and severity of the illness were associated with hospitalization at the end of the follow-up. Gender did not predict hospitalization at the end of the follow-up period.

The results of this study indicate that there are probably different subgroups of schizophrenia in which there are no gender differences regarding age at onset and in the clinical picture of the disturbance or there are regional differences in the manifestation of the illness. In Finland patients are hospitalized earlier after the onset of the first psychotic symptoms than in many other countries. According to the Northern Finland 1966 Birth Cohort study the incidence of schizophrenia is higher among young men than women and the total life-time incidence of schizophrenia may be smaller in women. The results from the Therapeutic community study suggest that therapeutic community treatment may level out the gender differences in the treatment process and outcome. The long-stay patient study showed that long-term patients are dependent on considerable support and that the most seriously ill patients are in fact in hospital. Alternative residential facilities have been a presupposition to the deinstitutionalization of the long-stay patients.

Keywords: age at onset, incidence, long-stay patients, deinstitutionalization





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Veturinmutka, Haukipudas, May 2000

Sami Räsänen

## **Abbreviations**

CGI	Clinical Global Impressions
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised
FHDR	The Finnish Hospital Discharge Register
GAS	Global Assessment Scale
ICD-9	Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, ninth revision
IRAOS	Interview for Retrospective Assessment of the Onset of Schizophrenia
PANSS	Positive and Negative Syndrome Scale for Schizophrenia
TC	Therapeutic community

## **List of original papers**

The present thesis is based on the following original papers, which will be referred to in the text by the Roman numerals I-V.

- I. Räsänen S, Pakaslahti A, Syvälahti E, Jones P & Isohanni M (2000) Sex differences in schizophrenia: A review. *Nordic Journal of Psychiatry* 54: 37-45.
- II. Räsänen S, Veijola J, Hakko H, Joukamaa M & Isohanni M (1999) Gender differences in incidence and age at onset of DSM-III-R schizophrenia. Preliminary results of the Northern Finland 1966 birth cohort study. *Schizophrenia Research* 37: 197-198.
- III. Räsänen S, Nieminen P & Isohanni M (1999) Gender Differences in Treatment and Outcome in a Therapeutic Community Ward, with Special Reference to Schizophrenic Patients. *Psychiatry Interpersonal and Biological Processes* 62: 235-249.
- IV. Räsänen S, Hakko H, Herva A, Isohanni M, Nieminen P & Moring J (1999) Gender Differences in Long-Stay Psychiatric Inpatients. Observations from Northern Finland. *International Journal of Mental Health* 28: 69-85.
- V. Räsänen S, Hakko H, Herva A, Isohanni M, Nieminen P & Moring J (2000) Community Placement of Long-Stay Psychiatric Patients in Northern Finland *Psychiatric Services* 51: 383-385.

# Contents

Abstract	
Acknowledgements	
Abbreviations	
List of original papers	
1. Introduction	15
2. Review of the literature	16
2.1. Definitions	16
2.1.1. Schizophrenia	16
2.1.2. Age at onset of schizophrenia	19
2.1.3. Incidence	20
2.1.4. Outcome of schizophrenia	20
2.1.5. Therapeutic community	21
2.1.6. Long-stay patients	21
2.1.7. Deinstitutionalization	22
2.2. Gender differences in the healthy population	22
2.3. Gender differences in schizophrenia	24
2.3.1. Gender difference in the age at onset of schizophrenia	24
2.3.2. Gender difference in incidence of schizophrenia	25
2.3.3. Gender differences in treatment and outcome of schizophrenia	26
2.3.4. Gender differences in long-stay patients	27
2.3.5. Gender differences in the deinstitutionalization process	28
3. Aims of the present study	29
4. Material and methods	30
4.1. Subjects	30
4.1.1. Subjects in the Northern Finland 1966 Birth Cohort study (II)	30
4.1.2. Subjects in the therapeutic community study (III)	31
4.1.3. Subjects in the long-stay patients study (IV, V)	32
4.2. Variables	33
4.2.1. Variables used in the Northern Finland 1966 Birth Cohort study (II)	33
4.2.2. Variables used in the therapeutic community study (III)	33
4.2.3. Variables used in the long-stay patients study (IV, V)	34
4.3. Statistical methods	37

4.3.1. Methods in the Northern Finland 1966 Birth Cohort study (II) .....	37
4.3.2. Methods in the therapeutic community study (III) .....	37
4.3.3. Methods in the long-stay patients study (IV, V) .....	37
5. Results .....	39
5.1. Age at onset of schizophrenia by gender (II,III, IV) .....	39
5.1.1. Age at onset in the Northern Finland 1966 Birth Cohort study (II) .....	39
5.1.2. Age at first treatment in the therapeutic community study (III) .....	39
5.1.3. Age at onset in the long-stay patients study (IV) .....	40
5.2. Incidence of schizophrenia by gender in the Northern Finland 1966 Birth Cohort (II) .....	41
5.3. Treatment and outcome of schizophrenia by gender in the therapeutic community study (III) .....	42
5.4. Gender differences of long-stay patients (IV) .....	43
5.5. Deinstitutionalization of long-stay patients by gender (V) .....	44
6. Discussion .....	50
6.1. Main findings of the study (I, II, III, IV, V) .....	50
6.2. Age at onset (II, III, IV) .....	51
6.3. Incidence (II) .....	52
6.4. Treatment and outcome (III) .....	54
6.5. Gender differences of long-stay patients (IV) .....	55
6.6. Deinstitutionalization (V) .....	56
6.7. Methodological concerns (I, II, III, IV, V) .....	60
6.7.1. Strengths and limitations of the Northern Finland 1966 Birth Cohort study (II) .....	60
6.7.2. Strengths and limitations of the therapeutic community study (III) .....	61
6.7.3. Strengths and limitations of the long-stay patients study (IV, V) .....	63
7. Conclusions .....	64
7.1. An evaluation of the study .....	64
7.2. Recommendations and clinical implications .....	65
7.3. Implications for future research .....	66
8. Summary .....	68
8.1. Background and aims of the study .....	68
8.2. Material and methods .....	68
8.3. Results and conclusions .....	69
9. References .....	71
Original articles	

## 1. Introduction

Schizophrenia is a severe mental disorder, characterized by a partial disorganization of personality functions, developmental regression, and a tendency to withdraw from interpersonal contacts into a subjective internal world of ideas, often colored by hallucinations or delusions (Alanen 1997). Schizophrenia is a significant public health problem and a great scientific mystery. It causes significant distress to the patients and their families. It affects about 1 percent of the world's population (Carpenter & Buchanan 1995). In Finland, the prevalence of schizophrenia may be even higher, 1.3% - 1.5% (Väisänen 1975, Lehtinen *et al.* 1990).

Schizophrenia may begin suddenly or gradually; it manifests itself usually in adolescence or in early adulthood and the pattern of course and outcome may be good, but it is often also chronic. This means that schizophrenia causes substantial costs to the patients themselves, their relatives and to the society. Patients may suffer from severe symptoms and may lose their productivity. The treatment of schizophrenia consumes a considerable portion of health care resources.

The causes of schizophrenia are still unknown. Despite the development of treatments of schizophrenia we are not able to treat schizophrenia satisfactorily. Therefore, further studies concentrating on the etiology and treatment of schizophrenia are needed. During the last decade schizophrenia research has emphasized the importance of gender differences especially in age at onset (Angermeyer and Kuhn 1988, Lieberman *et al.* 1993, Maurer & Häfner 1995) and outcome (Goldstein 1988, Angermeyer *et al.* 1990). Research on the gender differences in schizophrenia may provide answers to some very basic questions like what causes this disorder, and whether there are some kinds of gender specific protection mechanisms and what factors contribute to the more severe courses of the disease. Finding the answers to these questions may supply important information toward the etiology of schizophrenia, and may potentially give new ideas on how to develop efficient treatments of schizophrenia.

Homogenous patient groups have been suggested to represent important study populations with regard to future studies of gender differences in schizophrenia (Harding & Hall 1997). The purpose of the present study was to analyse gender differences in schizophrenia on the basis of some specific, clinically or epidemiologically homogenous patient groups.

## 2. Review of the literature

### 2.1. Definitions

#### 2.1.1. *Schizophrenia*

The concept of schizophrenia has had different definitions since 1898, when Kraepelin first presented it as a *dementia praecox* at the University Psychiatric Clinic in Heidelberg. In his historic lecture Kraepelin stressed the importance of distinguishing *dementia praecox* from manic-depressive disorder, because of the different prognosis in these two psychoses. Eugen Bleuler coined the term "schizophrenia" and presented schizophrenia as a group of illnesses. He also tried to identify specific fundamental or primary symptoms, caused by the etiological agent and accessory or secondary symptoms, which represented psychological reactions (Bleuler 1911). The primary symptoms can be summarized as the four As: associational disturbances, affective disturbances, autism and ambivalence. The secondary symptoms were hallucinations and delusions.

Although most of the basic characteristics of the concept of schizophrenia have remained the same, the diagnostic boundaries of the disorder have been under constant revision. For decades, clinical diagnoses of schizophrenia were based on medical textbooks and clinical experience, because systematic, operationalized, criteria-based diagnostic systems were not available.

Kurt Schneider (1959) attempted to define schizophrenia in symptomatological terms. He listed characteristic symptoms of schizophrenia defining "first-rank" and "second-rank" symptoms. First-rank symptoms were symptoms which were empirically of the greatest diagnostic importance. First-rank symptoms are: patient hearing his/her own thoughts spoken aloud, hearing voices talking to each other, voices that comment on the behaviour of the patient, feelings of influences on bodily functions, interference with thoughts, thought-stealing, communication of own thoughts to others and personal feelings being influenced from the outside with regard to emotions, drives and volition. Second-rank symptoms are hallucinations other than those mentioned, paranoid ideas, perplexity, depression or elation and feeling of loss of emotions. Feighner *et al.* (1972) determined diagnostic criteria for use in psychiatric research from which the "Research



Diagnostic Criteria” (RDC) were modified (Endicott *et al.* 1982). In 1980 the first symptom based diagnostic system Diagnostic and Statistical Manual of Mental Disorders (DSM-III) was published by the American Psychiatric Association (1980).

Diagnoses of schizophrenia have always been to some extent unreliable, because the etiology of schizophrenia has been unknown and there are no pathognomonic symptoms, which appear exclusively in schizophrenia. Thus, the development of descriptive diagnostic systems has been the only possibility to increase the reliability of the diagnosis of schizophrenia. Descriptive diagnostic systems like DSM-III-R, DSM-IV and ICD-10 (International Statistical Classification of Diseases and Related Health Problems) have made clinical diagnoses and research diagnoses more reliable and made it possible to compare different studies (American Psychiatric Association 1987, WHO 1992, American Psychiatric Association 1994). In this study schizophrenia has been defined according to the DSM-III-R criteria for the disorder (Table 1), because DSM-III-R criteria were officially used in Finland during the time when the diagnostic data for this study was collected.

Table 1. DSM-III-R diagnostic criteria for schizophrenia (American Psychiatric Association 1987).

Description
<p>A Characteristic psychotic symptoms of the active phase. Either (1), (2) or (3) for at least one week unless the symptoms are successfully treated:</p> <p>(1) two of the following:</p> <ul style="list-style-type: none"> <li>(a) delusions</li> <li>(b) prominent hallucinations</li> <li>(c) incoherence or marked loosening of associations</li> <li>(d) catatonic behaviour</li> <li>(e) flat or grossly inappropriate affect</li> </ul> <p>(2) bizarre delusions</p> <p>(3) prominent hallucinations of a voice with content having no apparent relation to depression or elation, or a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other</p>
<p>B During the course of the disturbance, functioning in such areas as work, social relations, and self-care markedly below the highest level achieved before onset of the disturbance.</p>
<p>C Schizoaffective Disorder and Mood Disorder with Psychotic Features have been ruled out.</p>
<p>D Continuous signs of disturbance for at least six months. The six month period must include an active phase during which there were psychotic symptoms characteristic for Schizophrenia, with or without a prodromal or residual phase, as defined below.</p> <p><i>Prodromal phase:</i> A clear deterioration in functioning before the active phase of the Disturbance that is not due to a disturbance in mood or to a Psychoactive Substance Use Disorder and involving at least two of a list of symptoms (not Reproduced here).</p> <p><i>Residual phase:</i> Following the active phase of the disturbance, persistence of at least two of the list symptoms (not reproduced here), these not being due to disturbance in mood or to a Psychoactive Substance Use Disorder.</p>
<p>E Not due to any Organic Mental Disorder</p>
<p>F If a history of Autistic Disorder, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present</p>

DSM-III-R classifies also the subtypes of schizophrenia, which are based on the clinical presentation of the disorder. They are paranoid, disorganized (formerly called hebephrenic), catatonic, undifferentiated and residual types. The paranoid subtype is characterized by the presence of delusions, the disorganized by a regression to primitive, unorganized behavior and the catatonic by disturbances in motor function. The undifferentiated type cannot be fitted into any of the three earlier mentioned subtypes.

The residual type is characterized by the presence of continuing evidence of the disturbance with negative symptoms like affective flattening and social withdrawal or attenuated positive symptoms (delusions and hallucinations).

### ***2.1.2. Age at onset of schizophrenia***

The definition of age at onset in schizophrenia is not unambiguous, because schizophrenia often begins with a long prodromal phase with negative or non-specific symptoms (Kaplan & Sadock 1998). It is difficult to determine whether the symptoms are "schizophrenic" before the positive symptoms of the disorder have started. The time criteria for a diagnosis of schizophrenia also vary in different diagnostic systems. According to DSM-III-R and DSM-IV, continuous signs of the disturbance for at least six months are needed (American Psychiatric Association 1987, American Psychiatric Association 1994), whilst in ICD-10 diagnostic guidelines this time is one month (WHO 1992). It is also possible that a patient suffers from schizophrenia for years before the first admission (Häfner *et al.* 1998). This means that assessments of illness data concerning the age of onset are retrospective.

This causes methodological problems in the analysis of the onset of this disorder. In different studies the age at onset has been defined in many ways. The onset has been defined, for example, as the time of: a) a first sign of mental disorder, b) a first psychotic symptom, c) index episode (leading to hospital admission) and d) first hospital admission for a diagnosis of schizophrenia (Häfner *et al.* 1993a).

Many studies of the course of schizophrenia have used first hospital admission as an indicator of the onset of schizophrenia because it is probably impossible to attain a representative sample using a prospective study design, because of the low annual incidence rate for schizophrenia (Maurer & Häfner 1995). There is a specially constructed standardized semistructured interview technique IRAOS (Interview for Retrospective Assessment of the Onset of Schizophrenia) for the retrospective assessment of the early course. Using this technique the time lag between the occurrence of the first sign of a mental disorder and first hospital admission with the diagnosis of schizophrenia has averaged 6.3 years and the first psychotic symptomatology has been found to appear on average two years prior to the first hospitalization with a diagnosis of schizophrenia (Häfner *et al.* 1993a).

There is also a mathematical model which integrates age-at-first-admission with estimates of the time lag between onset of symptoms and eventual contact with psychiatric services. With this model it is possible to transform register data and estimate the actual age-of-onset (Welham *et al.* 1996).

### 2.1.3. Incidence

Incidence can be defined as the number of new cases of illness in the study population over a period of time divided by the person time of risk (incidence rate) or the number of new cases of an illness over a period of time divided by the number of persons at risk at the beginning of the time period (incidence proportion) (Selvin 1996). The mathematical expression for the latter is:  $I = d/(n * t)$ , where I = incidence, d = number of new cases which became evident during the time interval, n = number of subjects at the beginning of the time interval, t = length of time interval in years, (n \* t) = person years at risk. Incidence rates are usually given as annual incidence rates per population of 10 000.

The proportion of patients developing the disease during a specified period of observation is called the cumulative incidence of the disease. It is calculated as the number of events occurring over a time interval divided by the size of the population at risk (Zahner *et al.* 1995).

Incidence rates of schizophrenia can be affected by the study sample, diagnostic procedures, design characteristics and methods of calculation (Kendell *et al.* 1993, Seeman 1995, Regier *et al.* 1998). For example in age cohorts the incidence rates will be high during the high risk years when the probability of getting ill is elevated. Respectively, the rates will be lower if stringent diagnostic criteria are used. Also there are many reasons why hospital first-admission rate may be an unreliable index of incidence. Some patients never come to medical attention or will be admitted to hospital, and not all patients with schizophrenia are so diagnosed at their first admission while some of the patients recorded as first admissions may actually be readmissions (Kendell *et al.* 1993).

The above mentioned methodological differences make it difficult to compare the incidences, reported in different studies, with each other. Comparisons of incidence rates between different studies are therefore easily misleading and consequently, it may be more reliable to compare male to female rate ratios in incidence rather than pure incidences, although it is possible that males and females are treated and diagnosed differently. Also comparisons of annual incidences within the same cohort are more reliable than comparisons between different studies.

### 2.1.4. Outcome of schizophrenia

There is no universal agreement on how the outcome of schizophrenia should be defined. In early studies outcome was defined in general terms like "recovered", "improved" or "unimproved" (Pakaslahti 1992). Hospitalization has widely been used as an outcome criterion, because it is easy and reliable to measure. However, in addition to the severity of the illness there are many other factors like health care policies, which have an effect on the number and duration of hospitalizations (Pakaslahti 1992). Other outcome criteria, which have been used include social relations, working ability and number and severity of symptoms. These can be assessed by using different validated structured interviews and scales like PANSS (Positive and Negative Syndrome Scale for Schizophrenia) in schizophrenic symptoms (Kay *et al.* 1988) and the Strauss-Carpenter scale in relation to

social functioning (Hawk *et al.* 1975). In many earlier studies, an array of self-developed, unvalidated outcome scales has also been used, but naturally the latter are not as reliable and comparable as the more widely used scales.

### ***2.1.5. Therapeutic community***

The concept of the therapeutic community (TC), developed mainly by Maxwell Jones in the 1950s (Jones 1953), can be defined as a unit that, on a professional organizational basis, involves the total treatment system, which by means of a human milieu, structured interaction and a planned treatment program, provides its participants with possibilities to undergo positive system changes in their intrapsychic, family and social situations (Isohanni 1983). In practice this means group activities, patient participation in decision making, peer help, co-operation with relatives and the surrounding society and active staff-resident interaction (Isohanni 1993). Milieu therapy is the use of the milieu itself as a mode of treatment (Clark 1977).

The aim of the TC treatment program is to encourage members towards a better understanding of their previous behavior and to enable them to improve their interpersonal functioning, first within the therapeutic community and ultimately in the wider, outside community. In the psychiatric ward, when the therapeutic community principles are used, the gender policy is a part of the therapeutic process. Intergender relations are an important part of the treatment structure and process. Especially the treatment culture of the ward aims at the development of a rich, healthy, multi-level co-operation and interaction between men and women; relations between males and females, for example, are one of the important focal points in group discussions.

In Finland the first experiments with therapeutic communities started in the early 1960s in some university clinics. Since the 1970s the therapeutic community practice has been widely accepted and used in many institutions. (Alanen 1975). Currently, many therapeutic community principles are applied in psychiatric treatment, but pure therapeutic community treatment is rare due to reduction of the hospital beds, shortening of treatment periods and economic problems in Finland (Isohanni 1993).

### ***2.1.6. Long-stay patients***

The focus of schizophrenia treatment lay in inpatient care until the 1950s, when the first neuroleptic medication and rehabilitative activities were developed (Alanen 1997). At that time a large number of patients spent years, often in fact the rest of their lives, after their first admission in psychiatric hospitals. The atmosphere of these large mental hospitals was stagnant and custodial (Isohanni 1983). During the 1950s the criticism against prolonged stays in large mental hospitals began to mount and more attention was paid to the patients who had been hospitalized for a long time. However, there is no uniform consensus about the definition of a "long-stay patient". Usually they have been

defined as patients who have been hospitalized continuously at least for six months (Leff *et al.* 1996, Rowlands *et al.* 1998, Tuori *et al.* 1998).

In studies concerning long-stay patients, the study populations have predominantly been people with schizophrenia, whose clinical symptoms have been severe and it has been problematic to place them somewhere else than in a hospital (Hobbs *et al.* 1992, Lamb 1993). Psychiatric inpatients have been found to be nowadays more severely disturbed than previously, before the deinstitutionalization process, possibly because of the deinstitutionalization process (Hobbs *et al.* 1992, Lamb 1993), allowing patients with milder clinical symptoms to be discharged or treated solely in outpatient care.

### ***2.1.7. Deinstitutionalization***

Deinstitutionalization can be defined as a process in which the preferred locus of psychiatric care is shifted to community care instead of mental hospitals and, at the same time, community-based services are developed (Bachrach 1978). Deinstitutionalization started in the early 1950s in the USA and the UK along with the development of antipsychotic medication (Baldessarini 1985), innovations in community care (Gruenberg & Huxley 1979, Wing and Morris 1981) and mounting criticism of the prolonged stays in mental hospitals (Thornicroft and Bebbington 1989). Prolonged hospitalization was thought to cause negative symptoms and a negative attitude towards discharge (Wing and Brown 1970).

The deinstitutionalization process has occurred years later in Finland (Raferty 1992, Korkeila 1998, Tuori *et al.* 1998), where new hospitals were still being built for chronic psychiatric patients in the 1960s. In Finland (population ca. 5.1 million in 1999) the transition from traditional custodial care to active rehabilitation practices has been the primary focus of psychiatric care since the 1980s. The total number of beds in psychiatric hospitals declined from the ca. 21000 at the end of the 1970s to the ca. 6600 beds in 1995 (Korkeila 1998). In the early 1980s there were 4 hospital beds designated for psychiatric treatment per 1000 residents. By the end of the decade this number had declined to 2 per 1000, and by the mid 1990s it had dropped to just over 1 per 1000 residents (Tuori *et al.* 1998). During the last decade, the deinstitutionalization process took also place in the catchment area of Oulu University Hospital (population ca. 350 000 in 1992). The total number of psychiatric beds decreased markedly. There were 962 beds in 1985; 594 in 1991; 425 in 1992; and 235 in 1996.

## **2.2. Gender differences in the healthy population**

Men and women are more similar than different, but it is obvious that men and women behave differently (Russo 1991). There is also evidence that gender affects the way a certain behavior is understood and how much attention is paid to it (Nadelson & Notman 1995). We don't have a clear understanding of the reasons that create the differences and thus gender studies are needed. But gender differences in a healthy population must be

taken into account in risk studies where the outcomes are analysed by gender. If these outcomes are different between males and females, it is important to know whether these differences are found also amongst the normal population.

Studies concentrating on gender differences in healthy populations have mostly been anthropological, psychological and biological. The biological factors are easier to study than the social, cultural or psychological factors. It is difficult to demonstrate sociological factors which affect a gender difference in behavior (Notman & Nadelson 1991). There are also many potential biases in gender research; for example, men and women are subject to different sex role expectations. Use of single-sex samples in research that is generalized to include all humans may lead to wrong conclusions. Observers may also rate individuals differently based on gender and sex role stereotypes (Russo 1991).

*Gender studies in psychiatry* have thus far generally concentrated on gender differences in different psychiatric disturbances. The meaning and significance of normal gender differences to these findings have not been widely discussed. However, it would be important to understand gender differences in the normal population to make interpretations of an association between gender and variables under study in the affected populations more reliable (Harding & Hall 1997). In other words, are the differences found in the affected population attributable to normal differences or to illness?

*Anthropological data* illustrate the social roles of men and women in different cultural settings. For example in traditional societies, men are more frequently assigned positions of power and authority, and they are generally more aggressive. Women have been found to take primarily care of the family and of their own offspring (LeVine 1991).

*Psychological data* show that a woman's life-cycle differs from that of a man. For example, women must make decisions about career, pregnancy and family in a way that differs from that of men (Nadelson & Notman 1995). Women are more involved in social activities, affiliate more, play in small groups, display more empathy and engage more frequently in nurturing behaviors (Block 1983). During normal social development females are also more susceptible to anxiety than men (Spence and Helmreich 1978). Men are more likely competitive, dominant, dominating and aggressive and they are more likely antisocial than women (Maccoby and Jacklin 1974). Men, on the whole, are also more active (Block and Block 1980) and impulsive (Eme 1979). In some neuropsychological tests men have been suggested to perform better than women in tests requiring imaginal rotation and women perform better in tests of perceptual speed (Kimura 1992). In the birth cohort study of Isohanni *et al.* (1998) school performance has been found to be better among girls than boys. The boys' means in school marks of all subjects were 0.6 units lower than those of the girls.

*Biological data* indicate that the female central nervous system matures earlier and is not as vulnerable as that of the males (Geschwind & Galaburda 1987, Notman & Nadelson 1991). This results in an earlier left hemisphere maturation and thus females speak earlier, they have more words and they are better readers (Kolb & Whishaw 1996). Many studies have demonstrated a greater lateralization of the hemispherical functions in males (McGlone 1980, Notman & Nadelson 1991). Differences in lateralization can explain the better verbal abilities of females and the better visual-spatial skills in males (Maccoby & Jacklin 1974). The male brain has also been found to be more plastic after a cortical injury - language function shifts more easily from left to right hemisphere in males (Strauss *et al.* 1983). However, reports also exist which claim just the opposite

(Notman & Nadelson 1991). Furthermore perinatal brain complications have been found to be more common in males than in females (Rantakallio *et al.* 1987) and they are known to increase the risk of schizophrenia (Jones *et al.* 1998)

Physiological and metabolic differences between men and women are well documented and men have frequently been found to be more physiologically stress-reactive (Polefrone & Manuck 1987). Hormonal effects were shown to explain some of the gender differences. Testosterone has an effect on the cerebral maturation process (Geschwind and Galaburda 1987); it initiates the masculinization of the brain and also masculinizes the reproductive system. It is believed that there are many features in the nervous system that are different in males and females as a result of this early action of testosterone (McEwen 1991). Additionally, testosterone has been known to contribute toward aggressive behavior and risk taking (Räsänen *et al.* 1999). In females estrogen probably exerts protective effects against schizophrenia (Häfner *et al.* 1993b, Seeman 1995).

## **2.3. Gender differences in schizophrenia**

### ***2.3.1. Gender difference in the age at onset of schizophrenia***

Emil Kraepelin reported nearly a century ago that women with schizophrenia are several years older at first admission than men (Kraepelin 1919/1987). The finding that men first manifest schizophrenia 3 - 4 years earlier than women has later been confirmed in numerous other studies (Angermeyer & Kuhn 1988, Lieberman *et al.* 1993, Maurer & Häfner 1995).

In the transnational ABC (Age of onset, Beginning and Course of Schizophrenia) Schizophrenia Study, which was based on Danish and the Mannheim (in Germany) national case registers, all 12- 59-year-old patients who were hospitalized for the first time with a diagnosis of schizophrenia or schizophrenia-like psychosis, formed the study population. There were 527 men and 642 women in the study population in Denmark in 1976 and 160 men and 176 women in Mannheim between 1978 and 1980. In this study there was a 4 - 5-year difference in age at first admission in spite of the broad or narrow diagnostic definitions used or the occupational status (Häfner *et al.* 1998). In the transnational World Health Organization ten-country study, 1431 15 - 54 year old first-contact patients with schizophrenia or a related disorder formed the study population. A total of 1192 subjects had a clinical diagnosis of schizophrenia. Age at onset was defined as the point in time when the first psychotic symptom could be identified. The mean difference in age between men and women at onset was 3.6 years (Jablensky & Cole 1997). The age of onset in first-episode schizophrenic patients has been found to be similar in the case of chronic patients (Szymanski *et al.* 1995).

It has also been reported that prodromal symptoms appear earlier among men and that a significant gender difference in age at onset exists even for non-specific symptoms at the very beginning of the psychosis, irrespective of the definition of onset applied (Angermeyer and Kuhn 1988, Häfner *et al.* 1993a, Faraone *et al.* 1994, Maurer and Häfner 1995). In one part of the ABC schizophrenia study in Germany from the



catchment area with a population of about 1.5 million, all 12 to 59 year old patients (n=276) with a clinical diagnosis of schizophrenia or a related disorder admitted for the first time during 1987-89 formed the study population. 232 of these patients had their first psychotic episode. All of these patients went through a careful retrospective assessment of the early course of the disorder (IRAOS). The means of the ages for men and women were compared in relation to five different definitions of onset from first sign to first admission, and once again the onset occurred 3 to 4 years earlier in men (Häfner *et al.* 1998).

The onset of schizophrenia is mostly in early adult life. Eaton *et al.* (1988) reviewed age at onset studies of schizophrenia and concluded that the peak of onset in men is between 15-24 years of age and in women 25-34 years of age throughout. According to the ABC study, men have a single, marked peak in their early twenties, while women have a second peak of onset between 45-54 years of age (Häfner *et al.* 1991). This finding has been confirmed also in other studies (Castle *et al.* 1993).

There are not many methodologically valid studies in which there is no gender difference at the age of onset in schizophrenia. In the Roscommon Family Study the age of onset in males was 1.5 years earlier than in females, but the difference was not statistically significant (Kendler & Walsh 1995). This study population was based on the case register and it is possible that it does not represent the whole spectrum of schizophrenia. Also, in the report the definition of age at onset was not clear. In the study of Salokangas (1993) there was no gender difference regarding the age of onset in DSM-III schizophrenia. This may be due to stringent diagnoses, because in the group of schizophreniform disorders, males were 3.6 years younger than females ( $p < 0.05$ ). An interesting question is how many of these patients might have developed schizophrenia later.

### ***2.3.2. Gender difference in incidence of schizophrenia***

The annual incidence of schizophrenia, compiled by Seeman (1995) from different studies and countries, ranges from approximately 0.5 to 2.0 per 10 000 population. It is conventionally believed that there is no gender difference in the total life-time risk of this illness (Castle & Murray 1991). However, gender differences in the incidence have been found in different age groups. The preponderance of females among later-onset schizophrenia patients compensates for the larger number of males among earlier-onset cases and results in an overall equal sex ratio of incidence rates (Castle *et al.* 1993). The World Health Organizations ten-country study, which is the largest cross-cultural study of schizophrenia, confirms these findings (Jablensky *et al.* 1992).

However, it has been suggested that the incidence of schizophrenia may be higher in men than in women. In a population-based study of Iacono and Beiser (1992), the annual incidence of schizophrenia in males was two to three times higher according to five different diagnostic systems. The two authors provided figures of 0.7 per 10 000 for men and 0.2 per 10 000 for women. The study included all first-episode cases of psychosis from a catchment area of 480 000 persons. Cooper *et al.* (1987) also reported higher annual incidence rates of DSM-III-schizophrenia among men in Nottingham: 1.7 per 10

000 for men and 0.7 per 10 000 for women. Higher rates in schizophrenic males have also been reported in other centres participating in the WHO collaborative study (Sartorius *et al.* 1986). One reason for these differences may be that late-onset cases were not included in most of these studies.

It has frequently been discussed that the incidence of schizophrenia may have changed over time. A decrease in first admissions with schizophrenia has been demonstrated in Scotland, England, Wales, Denmark, and New Zealand (Munk-Jørgensen 1986, Geddes *et al.* 1993, Kendell *et al.* 1993) and also according to a recent study in Finland (Suvisaari *et al.* 1999). Earlier there have been only few studies examining incidence of schizophrenia in Finland. Also methodological differences have made it difficult to compare the incidence rates of schizophrenia between different studies (Regier *et al.* 1998). Therefore, irrespective of the increasing evidence of the lower incidence rates of schizophrenia from different countries, it is still too early to conclude that schizophrenia is really decreasing (Kendell *et al.* 1993).

### ***2.3.3. Gender differences in treatment and outcome of schizophrenia***

Most of the literature on gender and treatment of different psychiatric disorders comes from the area of psychotherapy (Nadelson & Notman 1995). There is little research on the gender differences and their impact on the treatment of schizophrenia. Women with schizophrenia are generally more inclined to seek psychiatric help than men (Seeman 1986). Furthermore, women with schizophrenia are overall more committed to their treatment, their treatment periods tend to be shorter (Goldstein & Kreisman 1988, Angermeyer *et al.* 1989, Angermeyer *et al.* 1990) and their compliance is usually better than that of men (Lewis 1992). Women have also been found to exhibit better inpatient treatment responses to treatment than men in a study where treatment of the schizophrenic patients had a standardized medication regimen and there were no differences between men and women in the plasma drug levels (Szymanski *et al.* 1995).

In the study of Salokangas and Stengård (1990) 227 first-contact schizophrenic patients and their treatment were followed-up over a period of 2 years. Psychotherapeutic treatment methods were more commonly recommended to schizophrenic women, who also used them more actively and to which women were more committed than men. Some studies, however, have found no differences between men and women with schizophrenia in the use of psychotherapy and in attitudes towards hospital treatment (Kuusi 1986, McCarrick *et al.* 1988). Gender may influence the patient's choice of the therapist, an attitude that is often based on stereotyped expectations about men or women (Nadelson & Notman 1995). There are gender issues also in group therapy, and some data suggests that group behavior between group members and with the leader is affected by gender. For example in female-led groups men may experience a sense of loss of control, because they may feel that their ability to function as "males" is hampered (Nadelson & Notman 1995). Schizophrenic women, on the other hand, seem to respond better to family interventions than men (Spencer *et al.* 1988, Haas *et al.* 1990).

The doses of neuroleptic medication of women have been found to be smaller than those of men (Andia *et al.* 1995, Baldessarini *et al.* 1995) and women with schizophrenia

are more responsive to the neuroleptic medication (Hogarty *et al.* 1974a, 1974b, Seeman 1986, Lewis 1992, Szymanski *et al.* 1995). This difference becomes even more attenuated in older age groups; postmenopausal women seem to require higher doses of neuroleptic medications than premenopausal women (Seeman 1983).

The number of studies finding a better course of the disorder in female schizophrenics clearly exceeds that of studies reporting a better outcome in men. Angermeyer *et al.* (1990) reviewed studies reporting on the effects of gender regarding the course of schizophrenia. In spite of methodological limitations of the reviewed studies, for example a lack of controlling for confounding factors such as age or marital status of patients, the survey of this literature suggests that women more often experience a favorable course of schizophrenia. Women have more clinical remissions (Navarro *et al.* 1996) than men who more commonly suffer from chronic and the more severe forms of schizophrenia (Salokangas 1983, Seeman 1986, Goldstein 1988). The course of schizophrenia has been found to be more moderate among women and also their long-term prognoses have been found to be better, although sex differences regarding outcome may become more attenuated at longer term follow-ups (Harding *et al.* 1987, Childers & Harding 1990, McGlashan & Bardenstein 1990, Mortensen & Eaton 1994, Harding & Hall 1997).

In the World Health Organizations "ten country outcome study of first admission schizophrenic patients" involving many different cultures, being male was one of the predictors of poor outcome and there was an over-representation of females in the group of patients with the most favorable pattern of the course of the condition (Jablensky *et al.* 1992). Lewis (1992) reviewed the effects of gender on the course of schizophrenia and concluded, that there was a consensus, that the outcome of schizophrenia was generally better in women.

#### ***2.3.4. Gender differences in long-stay patients***

In the studies concerning psychiatric long-stay patients, the study populations have predominantly been schizophrenia patients (Lamb 1993). The studies have mainly been outcome studies and other gender differences in this patient group have received only minor attention. There are some well-documented gender differences in the outcome of schizophrenia: Women experience fewer and shorter hospitalizations and they survive longer in the community than schizophrenic men (Angermeyer *et al.* 1989). Also, the long-term outcome tends to be better in women (Harding & Hall 1997). As far as we know, there are no studies concentrating purely on gender differences in long-stay psychiatric inpatients. Thus, conclusions on gender differences of this population have been derived from the gender studies concerning the whole schizophrenia spectrum, including first admission patients.

### ***2.3.5. Gender differences in the deinstitutionalization process***

The development of alternative residential facilities has made the deinstitutionalization of long-term psychiatric patients possible (Carlsson *et al.* 1996). Only the most seriously ill patients have remained in hospital care and especially the patients with aggressive behavior have been found to be difficult to place in alternative units (Bigelow *et al.* 1988, Trieman & Leff 1996).

In the Vermont 32-year Longitudinal Study at the end of the 10-year follow-up, about 70% of the 269 severely mentally ill patients remained out of hospital, and being female was an important predictor of good functioning. After a 20- to 25-year follow-up there were only five patients in the hospital and all were men (Harding *et al.* 1987). In the TAPS (Team for the Assessment of Psychiatric Services) Project, 65% of 72 long-stay patients who were considered patients "difficult to place" by the hospital staff (too problematic to live in ordinary group homes) were men (Trieman & Leff 1996).

In many other studies, men have been shown to use more hospital services than women (Angermeyer *et al.* 1989, Borgå *et al.* 1991). This observation can be accounted for by the better outcome in schizophrenic women (Goldstein 1988, Angermeyer *et al.* 1990) and the men's poorer social functioning (Seeman 1986, Salokangas & Stengard 1990, Häfner *et al.* 1993b, Andia *et al.* 1995, Salokangas 1997).

### **3. Aims of the present study**

The purpose of the present study was to investigate gender differences with regard to some sociodemographic variables, age at onset, incidence, treatment, outcome and deinstitutionalization of schizophrenia patients using three different schizophrenic populations from Northern Finland. The numbers I-V hereafter refer to the original publications. The aims of the present studies were:

1) To review gender differences in schizophrenia (I), which is a very extensive field including practically all schizophrenia research areas.

2) To explore gender differences with regard to the age at onset of schizophrenia in Northern Finland using the large epidemiological Northern Finland 1966 Birth Cohort with thoroughly validated diagnoses (II) and two selected patient groups from a psychiatric hospital: the schizophrenia patients in a closed therapeutic community ward (III) and a group of long-stay psychiatric patients (IV).

3) To explore gender difference in the incidence of schizophrenia using the Northern Finland 1966 Birth Cohort (II).

4) To examine gender differences in the schizophrenia patients' sociodemographic, treatment, and outcome factors at the closed therapeutic community ward (III).

5) To examine whether there are gender differences in a variety of sociodemographic and clinical variables of the long-stay psychiatric inpatients (IV), who have been treated continuously for at least six months in the Department of Psychiatry, Oulu University Hospital.

6) To determine where the long-stay psychiatric inpatients have been placed as a consequence of the rapid deinstitutionalization process in Finland (V). In addition, clinical and sociodemographic factors predictive of hospitalization were studied, and gender differences were explored (V).

## 4. Material and methods

### 4.1. Subjects

#### *4.1.1. Subjects in the Northern Finland 1966 Birth Cohort study (II)*

The Northern Finland 1966 Birth Cohort was originally assembled by Professor (emerita) Paula Rantakallio to investigate the social and biological characteristics of mothers whose babies had low birth weight, were premature or had suffered perinatal death. The Northern Finland 1966 Birth Cohort Study is an unselected, general population birth cohort based upon 12068 pregnant women in the provinces of Lapland and Oulu with an expected delivery date during 1966. Their 12058 live-born children represent 96.3% of all births in the region (Rantakallio 1988).

The first information on the mothers and children was collected from the routine antenatal and post natal clinic visits. The first follow-up was performed at one year of age, at the routine children welfare clinic. The second follow-up was performed at the end of 1980 and in early 1981. Data has also been collected using the Finnish Hospital Discharge Register (hereafter FHDR), the cause of death register and the criminal records maintained by the Ministry of Justice of Finland (Rantakallio 1995).

The current investigation of psychiatric morbidity arising in adult life concerned the 11017 individuals (males 5636, 51.2% and females 5381, 48.8%) alive and living in Finland at the age of 16. From 1041 lost cases, 273 had died and 768 emigrated, mainly to Sweden. Firstly, all study members appearing on the FHDR until the end of 1994 for any mental disorder (i.e. DSM-III-R diagnoses 290-319) were identified. FHDR covers all mental and general hospitals, as well as bed wards of local health centers, military and prison hospitals nation-wide. The FHDR contains the personal and hospital identification code and data on age and gender, length of stay, and primary diagnosis at discharge, together with maximally 3 subsidiary diagnoses. We also requested all psychiatric organizations in Finland to identify all their psychotic outpatients who were born in Northern Finland in 1966. Two additional outpatient schizophrenia cases were traced (Isohanni *et al.* 1997).

A total of 387 (265 males, 122 females) subjects received at least one psychiatric hospital diagnosis during 1982-1994. The DSM-III-R diagnoses of these patients were ensured by using a three phase diagnostic validation process (Isohanni *et al.* 1997). All case records of the patients were scrutinized. Clinical information was extracted according to the Operational Criteria Checklist for Psychotic Illness (McGuffin *et al.* 1991), and processed by the associated OPCRIT program, which generates DSM-III-R diagnoses (Mäkikyrö 1998). In addition, clinical information was also entered onto the checklist for DSM-III-R diagnoses as used by the Finnish Adoption Study (Tienari *et al.* 1993). All clinical material was then considered by senior clinicians in order to reach a consensus DSM-III-R diagnosis. Cases of schizophrenia were defined as any individual who at any time met the DSM-III-R schizophrenia criteria. Interrater reliability for diagnosis was ensured in many phases, having good kappa values from 0.6 to 0.9 (Isohanni *et al.* 1997).

After the validation process there were 89 DSM-III-R schizophrenia cases (295.1, 295.3, 295.9) of which 58 were men (65.2%) and 31 women (34.8%).

#### ***4.1.2. Subjects in the therapeutic community study (III)***

This study is a part of action research performed between 1977 - 1993 involving the closed mixed ward situated at the Department of Psychiatry, University of Oulu (Isohanni 1983, Nieminen 1996). The goal was to determine whether modified therapeutic community principles can be applied to the institutional care of mainly acute and subacute psychoses and severe non-psychotic disturbances. The catchment area of the psychiatric hospital included 353 713 people on 31.12.1992 and in practice one quarter of the acute psychotic patients of this area were treated at this unit.

The ward was originally a 42-bed unit and in 1993 a 21-bed unit. The whole staff of the ward comprised a total of 25 employees with different professions, and posts usually equally divided between men and women.

A total of 30-50% of the patients were admitted in acute situations during the evening or the night shift. Inclusion criteria for admission were: acute psychosis or severe nonpsychotic disorders, need of hospitalization at the closed ward and earlier benefit from the therapeutic community treatment. Good motivation to treatment was to be hoped for, but not obligatory. Exclusion criteria were: very chronic disorder, violent behavior and severe disorganization (Isohanni 1983). 1525 patients who had their first treatment episodes at the ward during 1. Jan., 1977 to 2. July 1993 formed the main study population: 51 % (n = 784) males, 49 % (n = 741) females.

The diagnostic classification was based on ICD-8 until the end of 1986, and from Jan 1, 1987 on the Finnish version of the ICD-9 (WHO 1977) based on the DSM-III-R criteria (American Psychiatric Association 1987, Kuoppasalmi *et al.* 1989), officially used in Finland at that time. The diagnoses were mainly determined by a psychiatrist (Matti Isohanni) with extensive work experience (1972 - 1989) in the ward. He tested his diagnostic reliability using 40 case summaries from the Finnish Adoptive Family Study (Tienari *et al.* in press). The kappa between Matti Isohanni and the reference diagnosis

(the opinion of the majority of the cross-national expert team, consisting of two Americans and eight Finns) for this approach was good, 0.78 (Isohanni *et al.* 1997).

The sample was divided into five diagnostic subcategories:

- 1. schizophrenia (ICD-9 codes: 295.1, 295.2, 295.3, 295.6, 295.9): 85 males, 64 females
- 2. schizophreniform/schizoaffective (295.4, 295.7) psychoses: 112 males, 90 females
- 3. other psychotic disorders (297.1, 298.8, 298.9): 178 males, 208 females
- 4. mood disorders (296.2, 296.3, 296.4, 296.5, 296.6, 296.7, 300.4, 311.0): 161 males, 183 females
- 5. non-psychotic disorders (other 300, 301, other non-psychotic disorders; mostly borderline personality disorders): 248 males, 196 females.

#### ***4.1.3. Subjects in the long-stay patients study (IV,V)***

This study is based on the four year follow-up (1992-1995) research of 253 long-stay psychiatric inpatients (157 males, 96 females) treated for at least six months without a break during 1.1.1992 to 31.12.1992 (index hospitalization) at the Department of Psychiatry, Oulu University Hospital. The department provides both inpatient and outpatient service to the catchment area, which had a total population of approximately 270 000 during the study period.

Patients for the study were identified from the computerized patient register, which is also a basis for the Finnish Hospital Discharge Register. Sociodemographic and clinical data were collected retrospectively from this register, from case records and from personnel of the last inpatient ward, where the patient had been at the end of the index hospitalization in 1992. The follow-up began at the end of the index hospitalization and ended on 31.12.1995 or the date of death. If the patients' treatment period continued after the end of the year 1992, the follow-up began in 31.12.1992. If the patient deceased during the index hospitalization, s/he did not have a follow-up at all.

The diagnostic classification was based on the Finnish version of the ICD-9 based on criteria from the DSM-III-R, which was officially used in Finland 1987-1995 (Kuoppasalmi *et al.* 1989). Diagnoses were clinically set by the specialists of psychiatry in the wards.

Five diagnostic categories were used:

- 1. schizophrenia (ICD-9 codes: 295.1, 295.2, 295.3, 295.6, 295.9): 129 males, 74 females
- 2. other functional psychosis (295.7, 297.1, 298.9): 5 males, 8 females
- 3. personality disorders (301.6, 301.8, organic personality disorder excluded): 3 males, 3 females
- 4. mood disorders (296.1, 296.3, 296.8): 2 males, 5 females
- 5. organic disorders and organic psychoses (291.4, 293.8, 294.1, 294.8, 310.1, 317.0, 318.0, 330.8, 331.8, 334.3, 345.2, 389.7, 907.0): 18 males, 6 females.



Overall diagnostic distribution of the study sample was: 80.2% schizophrenia, 5.1% other functional psychoses, 9.5% organic disorders, 2.4% personality disorders and 2.8% mood disorders. Patients were analyzed as a single group with regard to the diagnosis. To ensure comparability with the previous studies concerning schizophrenic patients, all analyses were repeated in the group of schizophrenic patients (n=203).

## **4.2. Variables**

### ***4.2.1. Variables used in the Northern Finland 1966 Birth Cohort study (II)***

Age at onset of schizophrenia was determined at two time points as recorded in the case notes: (a) the age when psychotic symptoms first became evident and (b) the age at first hospitalization due to any psychiatric disorder (DSM-III-R codes 290-319). The schizophrenic patients were divided into three age groups according to the onset age at first psychotic symptoms (16-19 years, 20-24 years and 25-28 years). There was only one male patient who was documented to have the age at onset before the age of 16 years. In statistical analyses, this patient with an onset age of 14 years was included in the group of 16-19 year-olds except in the calculations of the mean values. Means of the latency periods between first psychotic symptoms to first psychiatric hospital admission (age at the first psychotic symptoms subtracted from the age at the first hospitalization) were also calculated.

The cumulative incidence (%) was calculated and presented graphically for schizophrenic men and women separately. Annual incidence rates per 10 000 population were given for men and women separately and male to female rate ratios with 95% confidence limits (Breslow and Day, 1980) were calculated for three time intervals (1982-1985 = 4 years, 1986-1990 = 5 years, 1991-1994 = 4 years). The number of deceased subjects (n males =117, n females = 27 ) was not taken into account in the calculations of person years at risk. However, had they been included, the effect would have been minimal and conclusions unchanged.

### ***4.2.2. Variables used in the therapeutic community study (III)***

The following sociodemographic variables were used: age (mean and dichotomized over/under 23) - the cutting point of 23 years was based on earlier findings from this study population (Isohanni 1983, Nieminen 1996), education (no professional education/lower professional education/higher professional education), dwelling place (urban, town with population over 10 000/rural, with population under 10 000 ), status of admission (voluntary/involuntary). The age at the first treatment period in the therapeutic community ward was used as indicative for the age at onset of the disorder.

The degree of active of participation of the patients in individual, group, and milieu therapy or therapeutic community was assessed at the time of discharge by 3-5 team members, who always included the personal doctor and nurse. The activity was divided into three categories: 1) Very active (the patient participated regularly as planned and these meetings were working well, as assessed by the therapists). 2) Moderately active (the patient maintained a moderately functional interaction). 3) Passive (therapy was planned and agreed on, but the patient participated minimally or refused to take part in this therapy).

The institutional outcome was divided into the following categories: positive, conflicting and negative. The assessment of the outcome was based on the assessed clinical status of the patient at the end of the episode by the treatment team and on the attainment of treatment goals, which had been agreed on and corrected in treatment planning sessions. The outcome was positive when the goals were met, conflicting when there were limitations in goal attainment and negative when the clinical status had worsened during the hospital treatment (Isohanni 1983, Nieminen 1996).

The reliability of ratings of the participation in psychosocial therapies and outcome classification were tested so that the assessment team was divided into two groups, which independently rated 105 (45 male and 60 female) consecutive patients during 1989 using the classifications described above. The interrater reliability of activity in individual, group, and milieu therapy and regarding institutional outcome was calculated separately in males and females. The classifications were satisfactory (in males agreement 53 - 76%, kappa 0.25 - 0.55, in females 65-92%, 0.46 - 0.67).

The patients were divided into quartiles according to the length of hospitalization: 1 - 16 days, 17 - 36 days, 37 - 72 days and over 72 days. The mean, median and maximum of the length of stay and of the number of treatment episodes at this ward were also evaluated. The length of stay was individually determined in the treatment planning sessions by consensus with the patient and his close relatives.

#### ***4.2.3. Variables used in the long-stay patients study (IV, V)***

The following sociodemographic variables were gathered at the end of the index hospitalization: gender (male/female), age (years) mean/median and age categorized as follows ( $\leq 33$  / 34 - 43 / 44 - 53 /  $\geq 54$ ), dwelling place (City of Oulu, ca. 117 000 inhabitants / other, maximum 20 000 inhabitants), marital status (study IV: married or common-law marriage / single / divorced / widowed), (study V: married/not married), children (no / yes), and education (basic compulsory education or less / professional education), social class (I-III = highest social class to skilled workers / IV = unskilled workers) (Sosiaaliryhmitys 1954), accommodation before the index hospitalization (study IV: alone / with primary family / with secondary family / in psychiatric hospital / in other institution) and (study V: alone / with family / institution / psychiatric hospital). The proportion of patients on disability pension, on sick-leave and those who stayed in a psychiatric hospital until the end of the follow-up was also calculated.

Data related to the onset (year) of the psychiatric disturbance were examined at five different time points: 1) first sign of the psychiatric symptoms (includes all non psychotic

symptoms), 2) manifestation of first psychotic symptoms, 3) first contact with the health care system for psychiatric reasons, 4) first contact with psychiatric care system, 5) first psychiatric hospital admission. Time lag in years from the first sign of the psychiatric disorder and from the manifestation of the first psychotic symptoms to the first psychiatric hospital admission was also calculated.

CGI (Clinical Global Impressions) (Bech *et al.* 1993) and GAS (Global Assessment Scale) (Endicott *et al.* 1976) were used to assess the severity of the psychopathology of the patients at the end of the index hospitalization. The seven classes of CGI were combined and analyzed in three classes in study IV: (not at all ill, borderline ill or mildly ill / moderately or markedly ill / severely or extremely ill). GAS ratings were combined into four classes in study IV: (0-20, many symptoms and severely dysfunctional / 21 - 40 / 41 - 60, / 61 - 100, minimal symptoms or mild functional difficulties) and in three classes in study V: ( $\leq 30$  / 31-40 /  $\geq 41$ ). The categorizations of CGI and GAS ratings were based on the clinical experience of the researchers. Extreme psychopathological groups, identified with CGI or GAS, needed to be separated.

The level of social functioning was measured on a 9-item Strauss-Carpenter scale (Hawk *et al.* 1975). Each item was rated between 0 (low) to 4 (high). The total sum of these nine items formed the social functioning score (the higher the score, the better the functioning). The mean social functioning score measured with the Strauss-Carpenter scale was categorized as follows in study V: ( $\geq 1$  /  $< 1$ ).

Eight clinically important items selected from the DSM-III-R criteria of schizophrenia and two items of depression (American Psychiatric Association 1987) were used to quantify the psychopathology of each patient. These items included four items for positive symptoms (delusions, hallucinations, incoherence and inappropriate or uncontrolled anger), four items for negative symptoms (flat affect, poverty in amount of speech, constricted affect, rarely expressing strong emotions) and two items for depressive symptoms (depressed mood, feelings of worthlessness or guilt). Each symptom was considered to exist if the criteria for the symptom were definitely or probably met. Alternatively, if the criteria of the symptom were possibly or definitely not met, the symptom was considered to be absent. Symptoms were summed up to form the total positive, negative and depressive symptom score. In study V, the symptoms were dichotomized (absent/present) describing the absence or presence of the symptoms (present = one or more symptoms).

The interrater reliability for symptoms and the outcome ratings were tested between researchers with 30 randomly selected patients. This was satisfactorily measured with the Kendall rank-order correlation (Siegel & Castellan 1988): CGI 0.75, GAS 0.66, DSM-III-R symptoms 0.65 (range 0.39-1.0) and Strauss-Carpenter scale 0.75 (range 0.52-1.0).

The patients' daily doses of any antipsychotic medication were calculated as equivalents of chlorpromazine (Baldessarini 1985) at the end of the index hospitalization, and categorized as follows in study IV: (0 / 1mg - 150mg / 151mg - 300mg / 301mg - 600mg / 601mg - 1200mg / 1200mg - 2000mg /  $> 2000$ mg) and in study V: ( $\leq 300$ mg / 301-600mg /  $\geq 601$ mg).

Utilization of inpatient care before index hospitalization was examined by calculating the number of hospitalizations and the proportion of days in inpatient care between the first psychiatric admission and at the beginning of index hospitalization and, also between the end of the index hospitalization and the end of the follow-up period. Data on

hospitalizations and treatment days during the follow-up were missing from 11 patients (4 %).

The placements after the last discharge and at the end of the follow-up were identified from the computerized patient register or case records or obtained directly from the personnel of the last inpatient ward known. The last discharge is defined as the latest discharge during the follow-up; following that there were no admissions to the psychiatric hospital until the end of the follow-up.

In the literature there is no uniform international practice for the terminology of the different types of residential facilities. Thus, short descriptions of the placements after the last discharge are presented in Table 2.

*Table 2. Descriptions of the placements of the long-stay patients after the last discharge in the long-stay patient study.*

Placement	Description
1. Psychiatric hospital ward	Psychiatric hospital. The staff are on duty at all hours
2. Rehabilitation home	Rehabilitation units of psychiatric services in the community with treatment programs. The aims of the treatment programs are for the patients to progress in their rehabilitation process. In most of these places the staff are on duty only during daytime, but in some of them at all hours.
3. Supported home	Mostly private units which represent supported housing with rehabilitative activities. Usually no treatment programs and goals. Patients use outpatient services when needed. The staff are on duty during daytime, but only occasionally at all hours.
4. Supported lodging	Supported housing organized by health care authorities, no staff, patients use outpatient services or home-visit services.
5. Somatic hospital ward	Temporary treatment unit for the patients with severe somatic problems. The staff are on duty at all hours.
6. Old people's home	Housing for elderly people. The staff are on duty at all hours
7. Unit for mentally handicapped	Supported residential or institutional care for mentally handicapped.
8. Unit for alcoholics	Temporary residential setting for alcoholics. The staff are on duty at all hours.
9. Home	Living in own apartment or with parents. Patients use open care services when needed.
10. Deceased patients	Died before the end of the follow-up

In the analyses of the original paper V, the placements were combined into five categories on the basis of similarity of services or support they offer as follows: Psychiatric hospital, residential facility (rehabilitation and supported homes), other institution (somatic hospital, old people's home, units for mentally handicapped and alcoholics), home (supported lodging and home), dead.

### **4.3. Statistical methods**

#### ***4.3.1. Methods in the Northern Finland 1966 Birth Cohort study (II)***

Gender differences with regard to continuous and normally distributed variables were assessed with Student's t-test (Altman 1991). The ordinary chi-square test was chosen to test for the statistical significance of differences in frequency distributions in case of categorical variables. Finally, male to female rate ratios with 95% confidence limits were calculated for each age group (Ingelfinger *et al.* 1994). The statistical software used was SPSS for Windows version 6.1 (Norusis 1994).

#### ***4.3.2. Methods in the therapeutic community study (III)***

The readmission period (the number of days from discharge following the first admission to rehospitalization) was evaluated in all diagnostic groups. The groups of schizophrenia, schizophreniform and schizoaffective were combined, and the readmission period of this combined group was presented graphically.

The data were analyzed using the SPSS for Windows software. Cross-tabulation was used as the main tool for data presentation and analysis. The statistical significance of factors associated with gender was evaluated using the Chi-square test and the Mann-Whitney U-test. The gender differences were evaluated by diagnostic groups.

The Kaplan-Meier method, as operationalized in the Kaplan-Meier survival analysis procedure of the SPSS for Windows software (Norusis 1994), was used to obtain the estimated time to readmission of patients. These curves (III: Figure 1) represent the proportion of readmitted patients at a certain time point after discharge and are expressions of the time elapsed before rehospitalization. The curves were approximations for male and female patients in different diagnostic groups. The statistical significance of the differences between gender groups was determined by log-rank statistic.

#### ***4.3.3. Methods in the long-stay patients study (IV, V)***

In the original paper IV, the Chi-square and Fisher's exact test were used to test statistical significances of differences in frequency distribution between genders. For continuous variables, statistical significance of gender differences were assessed with Student's t-test or the non-parametric Mann-Whitney U-test if the variables were not normally distributed. A two-group discriminant function analysis was performed to determine the most essential variables that discriminated male and female long-stay psychiatric patients.

In the original paper V, cross-tabulation was used as the main tool for data presentation. Statistical significance of differences between two independent groups were assessed with the Chi-square test, Fisher's exact test or Student's t-test, whichever appropriate. The logistic regression analysis was used to assess the probability of

hospitalization at the end of the follow-up after the most essential clinical and sociodemographic variables were adjusted.

In the original papers IV and V the primary software used to analyze the data were SPSS and SAS for Windows (Norusis 1994). The level of significance was set at  $P \leq 0.05$  in all statistical analyses.

## **5. Results**

### **5.1. Age at onset of schizophrenia by gender (II, III, IV)**

#### ***5.1.1. Age at onset in the Northern Finland 1966 Birth Cohort study (II)***

There were 89 DSM-III-R schizophrenia cases (58 men = 65.2% and 31 women = 34.8%) of which one man and one woman were traced through outpatient search. Mean age at onset (first psychotic symptoms) in men was 21.4 (SD 3.4) and in women 21.2 (SD 3.5) (Student's t-test with equal variances  $p = 0.756$ ).

The peak of onset in men lay in the 20-24 year age group whereas in women it occurred in the 16-19 year age group. There were no statistically significant gender difference in age at onset. Table 1 in the original paper II presents the distributions of age at onset (first psychotic symptoms) in male and female schizophrenia patients in three age groups.

The mean age at first hospitalization due to any psychiatric disorder in men ( $n=57$ ) was 21.5 (SD 4.0) and in women ( $n=30$ ) 21.4 (SD 3.9) (Student's t-test  $p=0.874$ ). The first psychotic symptoms appeared slightly earlier than the first hospitalization. The mean time difference between first psychotic symptoms and first psychiatric hospital admission was 0.05 years (SD 2.4) for men and 0.20 (1.5) for women (Student's t-test  $p=0.757$ ).

#### ***5.1.2. Age at first treatment in the therapeutic community study (III)***

The mean age for males at the time of their first treatment episode in this ward was 30.4 years (SD 10.4) and for females it was 31.2 (SD 10.6). The mean age of patients with schizophrenia was lower, being 27.4 years in men (SD 7.4) and 27.8 in women (SD 7.5) and in patients with diagnoses of schizophreniform/schizoaffective disorders 26.5 years in men (SD 7.2) and 27.4 in women (SD 7.7). Of the men with schizophrenia 34 %, and of the women 31%, were under 23 years of age at the onset of the illness. In the group of men with schizophreniform/schizoaffective disorders 38% and in the women 37% were

under 23 years old. There were no statistically significant differences between men and women in age distribution in the groups of schizophrenia and schizophreniform/schizo-affective disorders.

### 5.1.3. Age at onset in the long-stay patients study (IV)

The mean and median ages as well as standard deviations of long-stay patients at five different points in time are presented in Table 3. There were no statistically significant differences between men and women in any of these age variables.

*Table 3. Mean and median ages as well as standard deviations of long-stay patients at five different points in time .*

Definition of age at onset	Males			Females			All		
	mean	median	SD	mean	median	SD	mean	median	SD
First sign of the psychiatric symptoms	22.2	20.0	10.1	24.3	21.0	11.8	23.0	20.0	10.8
Manifestation of the first psychotic symptoms	24.0	21.0	9.7	25.4	22.0	11.8	24.5	21.0	10.5
First contact with health care for the psychiatric reasons	23.5	21.0	10.2	24.7	21.0	11.4	24.0	21.0	10.6
First contact with specialist care	23.9	21.0	10.4	25.3	22.0	11.9	24.4	21.0	11.0
First psychiatric hospital admission	24.6	21.9	10.0	26.5	22.3	13.0	25.3	22.1	11.3

Mean/median time lag in years between the first sign of psychiatric symptoms and the first psychiatric hospitalization was 2.5/1.0 (SD 5.1) overall, 2.6/1.0 (SD 4.4) for males and 2.2/1.0 (SD 6.0) for females. Statistically significant gender differences were not found. Mean/median time lag in years between the first psychotic symptoms and the first psychiatric hospitalization was 0.06/0.0 (SD 3.5) overall, 0.04/0.0 (SD 3.3 ) in males and 0.09/0.0 (SD 3.7) in females. Again, no statistically significant differences were observed. There were 32 patients (13.2% in all, of which 20=13.1% were male and 12=13.5% were female) whose first psychotic symptoms appeared after the first hospitalization.



## 5.2. Incidence of schizophrenia by gender in the Northern Finland 1966 Birth Cohort (II)

The cumulative incidence was two times as high among men as among women until the age of 28. Fig. 1 displays the cumulative incidence (%) of DSM-III-R schizophrenia in males and females.



**Fig. 1. The cumulative incidence (%) of DSM-III-R schizophrenia by gender up to the age of 28 in the Northern Finland 1966 Birth Cohort.**

The annual incidence in men was highest in the age group of the 20-24 year-olds while in women the peak occurred in the age group of the 16-19 year-olds (II: Table 1). Until the end of the follow-up period (at the age of 28) there was a decreasing trend in the incidence rates for women. Male to female rate ratios differed statistically significantly only in the age group of the 20-24 year-olds.

### 5.3. Treatment and outcome of schizophrenia by gender in the therapeutic community study (III)

There were no statistically significant ( $p < 0.05$ ) differences between men and women regarding age distribution, education, dwelling place and way of admission of any diagnostic group. In the group with schizophrenia, however, the general trend was that the men's educational levels were lower than those of the women and that most of the men were living in small localities (under 10 000 inhabitants). Distribution of some first episode (at the ward under study) patient variables in the therapeutic community ward are presented in the original paper III: Table 1.

Women participated more actively than men in individual therapy of the diagnostic group of mood disorders (very active males 60.2% and females 72.7%,  $p = 0.033$ ), as well as in group therapy in the patient group of schizophreniform/schizoaffective disorders (very active males 34.8% and females 46.7%,  $p = 0.037$ ).

There were no statistically significant differences regarding the participation in milieu therapy of any diagnostic group. In the groups of schizophrenia and psychosis generally, there was a trend towards women participating more actively in milieu therapy than men.

A difference in the institutional outcome was established between men and women in the group of schizophreniform/schizoaffective disorders ( $p = 0.038$ ). A positive outcome was more common among women and a negative outcome among men. A conflicting outcome (limitations in goal attainment) was equally common in both gender groups. A similar trend was observed also in the group with schizophrenia, but not in other diagnostic groups. Data on the distributions of men and women in the participation of psychosocial therapies, length of stay and outcome according to the five diagnostic groups are presented in the original paper III: Table 2.

No statistically significant gender differences were found with regard to the length of stay in the different diagnostic groups when assessed as quartiles or when evaluating the means, medians and maxima (III: Table 3). In the groups with schizophrenia, the lowest number of patients who had a short length of stay were encountered. Correspondingly, in those same groups there were the largest number of patients with very long lengths of stay when compared with other diagnostic groups.

There were no significant gender differences in the number of treatment episodes at the ward under study in any of the diagnostic groups. The number of episodes was highest in the group of schizophrenia. Original paper III: Table 3 presents also the means, medians and maxima of the number of episodes at the ward in all diagnostic groups.

The rate of readmission was evaluated in all diagnostic groups. There were no significant gender differences in any of these groups. Among the combined group of schizophrenia, schizophreniform and schizoaffective patients, no gender differences were detected at the time to readmission (III: Fig. 1).

In the diagnostic groups of schizophrenia, the proportion of male and female patients did not change during the second and third treatment periods, but the gender differences diminished. During the second treatment period, the gender difference came out as a more negative outcome among males with schizophreniform/schizoaffective disorders: positive outcome male 32 / female 34 (61.5 % / 85.0 %), controversial 12/6 (23.1 % / 15.0 %), negative 8/0 (15.4 % / 0.0 %) ( $p=0.013$ ). During the third treatment period, there was a gender difference with regard to the activity in milieu therapy in the group of

schizophreniform/schizoaffective disorders, women being more active than men: very active male 6 / female 12 (23.1 % / 57.1 %), moderately active 12/4 (46.2 % / 19.0 %), passive 8/5 (30.8 % / 23.8 %) ( $p=0.044$ ).

#### 5.4. Gender differences of long-stay patients (IV)

About 62% of the patients were males and 38% females. The mean/median age (standard deviation) of all subjects at the end of the index hospitalization was 47.0/46.0 (15.5). The age of the men was 45.6/45.0 (14.4) and that of the women 49.4/47.5 (16.9), resulting in a statistically marginal difference between men and women with regard to age ( $P=0.069$ ).

Compared to women, men were living more commonly outside the City of Oulu. Men were also more commonly single, had fewer children, and lived more commonly in a primary family than did women. In original paper IV: Table 1 presents the sociodemographic characteristics of the patients by gender before the index hospitalization.

Of the patients 97% were on disability pension at the end of the index hospitalization. Three of the patients were so young (under 16 years) that they did not have the right to collect a disability pension.

About 40% of the patients had most of the time ( $\geq 75\%$ ) been in inpatient care since their first admission to the psychiatric hospital. There were no statistically significant gender differences in the number of admissions, in the number of involuntary hospitalizations and in the proportion of treatment days under psychiatric hospital care before the index hospitalization (IV: Table 2).

The diagnostic distribution did not differ significantly between genders. There was a trend that women had more other functional psychoses and mood disorders than men and men had more organic disorders than women. There were no significant gender differences in CGI- and GAS-scores. Men had more DSM-III-R negative symptoms than women. The mean of the total Strauss-Carpenter score in men was lower (10.3, sd 4.7) than in women (11.6, sd 5.0) ( $t$ -test,  $P=0.039$ ). There was no statistically significant gender difference in the doses of the antipsychotic medication as determined by analyses in the seven categories and in the mean/median quantities of equivalents of chlorpromazine (men 755/460, women 723/500) (IV: Table 3).

A total of 51 patients had depot-injection medication; 39 of them were men (24.8% of all men) and 12 of them were women (12.5% of the women) ( $P=0.018$ ).

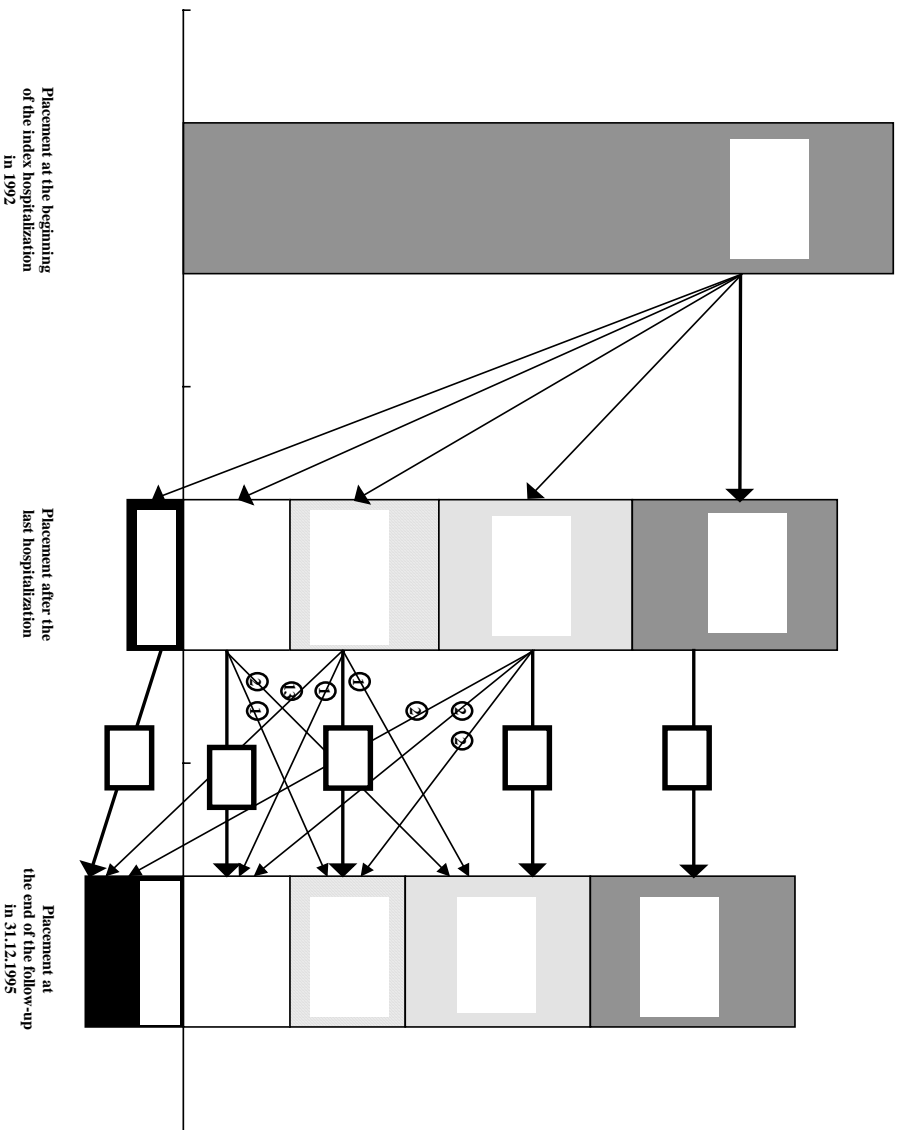
A discriminant analysis between male and female long-stay psychiatric patients revealed that a higher number of children ( $F=17.619$ ,  $P<0.001$ ), fewer negative symptoms ( $F=5.402$ ,  $P=0.021$ ) and being married ( $F=6.305$ ,  $P=0.013$ ) were more typical for females and served as the only significant factors for discriminating the genders.

The patients were homogeneous with regard to diagnoses. To ensure the comparability with the previous studies concerning schizophrenia patients, all analyses were repeated in the group of schizophrenic patients ( $n=203$ ). The results, however, remained unchanged.

### **5.5. Deinstitutionalization of long-stay patients by gender (V)**

During the follow-up, about 90 % of all patients had had at least one hospitalization. About one third of both men and women were less than 25% of the follow-up period in hospital care and one third over 75% of the time. There was no difference between men and women in the utilization of hospital care.

The placements after the last discharge and at the end of the follow-up as well as the change of the placements between the last discharge and at the end of the follow-up are presented graphically in Fig. 2. During the follow-up there were only minor changes in the placements of the patients. About 90% of the patients placed in residential facilities or at home did not change the placement. If the patients were discharged to other institutions, 72% of them stayed there and 25% of the patients died



**Fig. 2. Placements of the long-stay psychiatric patients after their last discharge and at the end of the four year follow-up in the long-stay patient study. Placement changes between last discharge and end of the follow-up are indicated with arrows.**

The placements and the distributions of the placements after the last discharge and at the end of the follow-up are presented in V: Table 1. After the last discharge, men (31.2%) were placed in residential facilities (rehabilitation or supported homes) more commonly than women (20.8%), whilst women (27.1%) were placed more commonly than men (17.2%) in other institutions (somatic hospital, old people's home, unit for mentally handicapped or alcoholics). Men (13.4%) were discharged to live at home or at supported lodgings as commonly as women (17.7%). The number of deceased men (9.6%) was slightly higher than that of women (5.2%).

At the end of the follow-up, the distribution of placements remained essentially unchanged. The number of deceased patients increased from 20 to 35 during the follow-up. There were no statistically significant gender differences in the distributions of the placements after the last discharge and at the end of the follow-up period.

Table 4 presents sociodemographic and clinical factors of the patients who were hospitalized or non-hospitalized at the end of the follow-up. Married patients were less commonly hospitalized than unmarried ones. Hospitalized patients had lower GAS-scores, more involuntary hospitalizations and higher doses of neuroleptic medication at the end of the index hospitalization than non-hospitalized patients. Hospitalized patients had spent more time in inpatient care before the index-hospitalization. There were no statistically significant differences in the remainder of the variables. The gender distribution was similar for hospitalized and non-hospitalized patients.

Table 4. Non-hospitalized and hospitalized long-stay patients at the end of the follow-up and their sociodemographic and clinical characteristics <sup>a</sup>

Variable	Non-hospitalized (n=145)		Hospitalized (n=73)		Total (n=218)		Chi-square test and significance	
	n	%	n	%	N	%	$\chi^2$	p-value
Gender <sup>b</sup>							0.001	0.970
Females	56	38.6	28	38.4	84	38.5		
Males	89	61.4	45	61.6	134	61.5		
Marital status <sup>b</sup>							5.303	0.021
Not married	129	90.2	72	98.6	201	93.1		
Married	14	9.8	1	1.4	15	6.9		
Children <sup>b</sup>							0.169	0.681
No	115	79.9	60	82.2	175	80.6		
Yes	29	20.1	13	17.8	42	19.4		
Dwelling place <sup>b</sup>							2.210	0.137
City of Oulu	64	55.9	40	54.8	104	52.3		
Other	81	44.1	33	45.2	114	47.7		
Living <sup>b</sup>							1.418	0.701
Alone	22	15.5	8	11.0	30	14.0		
With family	40	28.2	24	32.9	64	29.8		
Institution	14	9.9	9	12.3	23	10.7		
Psychiatric hospital	66	46.5	32	43.8	98	45.6		
Age (years) <sup>c</sup>							2.605	0.457
≤33	31	21.4	22	30.1	53	24.3		
34-43	36	24.8	19	26.0	55	25.2		
44-53	34	23.4	15	20.5	49	22.5		
≥54	44	30.3	17	23.3	61	28.0		
Negative symptoms <sup>c</sup>							1.542	0.214
Absent	74	51.4	44	60.3	118	54.4		
Present	70	48.6	29	39.7	99	45.6		
Positive symptoms <sup>c</sup>							2.115	0.146
Absent	27	18.6	8	11.0	35	16.1		
Present	118	81.4	65	89.0	183	83.9		
Depressive symptoms <sup>c</sup>							0.467	0.494
Absent	98	69.5	54	74.0	152	71.0		
Present	43	30.5	19	26.0	62	29.0		

Table 4. continued

Variable	Non-hospitalized (n=145)		Hospitalized (n=73)		Total (n=218)		Chi-square test and significance	
	n	%	n	%	N	%	$\chi^2$	p-value
GAS <sup>c</sup>							5.595	0.061
> 40	60	41.4	21	28.8	81	37.2		
31-40	58	40.0	29	39.7	87	39.9		
≤ 30	27	18.6	23	31.5	50	22.9		
Strauss-Carpenter scale (mean score) <sup>c</sup>							0.001	0.975
≥1	101	69.7	51	69.9	152	69.7		
<1	44	30.3	22	30.1	66	30.3		
Neuroleptic medication <sup>c</sup>							6.275	0.043
≤ 300	53	36.6	15	20.5	68	31.2		
301-600	40	27.6	22	30.1	62	28.4		
> 600	52	35.9	36	49.3	88	40.4		
Involuntary hospitalizations <sup>c</sup>							4.658	0.031
≤6	77	53.5	26	37.7	103	48.4		
>6	67	46.5	43	62.3	110	51.6		
Number of hospitalizations <sup>b</sup>							0.195	0.659
1-10	84	57.9	40	54.8	124	56.9		
> 10	61	42.1	33	45.2	94	43.1		
Proportion (%) of treatment days <sup>d</sup>							95.668	<0.001
0 < 25	71	49.0	4	5.5	75	34.4		
25-50	40	27.6	6	8.2	46	21.1		
50-75	19	13.1	10	13.7	29	13.3		
≥75	15	10.3	53	72.6	68	31.2		

<sup>a</sup> Total n on which percents are based varies because of missing data for some subjects

<sup>b</sup> Before index hospitalization

<sup>c</sup> At the end of index hospitalization

<sup>d</sup> Proportion of days in inpatient care between the first psychiatric hospitalization and the beginning of index hospitalization

The probability of hospitalization at the end of the follow-up was examined with a logistic regression analysis after controlling for clinical and sociodemographic variables presented in Table 4. Table 5 presents only those variables, which reached statistical significance in the logistic regression analysis. The results showed that being not married,



living in the city of Oulu, absence of negative symptoms, low GAS-scores, high doses of neuroleptic medication and time spent in inpatient care prior to the index-hospitalization were associated statistically significantly with the probability of hospitalization.

*Table 5. Most essential variables, adjusted Odds ratios (OR) and 95% confidence intervals (CI) predicting the probability of hospitalization of the long-stay patients at the end of the follow-up.*

Variable	OR	95% CI	p-value
Dwelling place <sup>a</sup>			0.014
Other	1.0		
City of Oulu	2.6	1.2 - 5.5	
Marital status <sup>a</sup>			0.037
Married	1.0		
Not married	14.2	1.2 - 170.5	
Negative symptoms <sup>b</sup>			0.033
Present	1.0		
Absent	2.5	1.1 - 5.8	
GAS <sup>b</sup>			0.012
> 40	1.0		
31-40	1.1	0.4 - 2.5	
≤ 30	4.6	1.5 - 14.5	
Neuroleptic medication <sup>b</sup>			0.045
≤ 300	1.0		
301-600	2.6	1.0 - 6.8	
> 600	3.4	1.2 - 9.2	
Proportion (%) of treatment days <sup>c</sup>			0.049
< 25	1.0		
25-50	6.8	1.7 - 27.7	
50-75	5.2	1.1 - 24.9	
≥75	7.3	1.6 - 33.6	

<sup>a</sup> Before index hospitalization

<sup>b</sup> At the end of index hospitalization

<sup>c</sup> Proportion of days in inpatient care between the first psychiatric hospitalization and the beginning of index hospitalization

All other variables (gender, number of children, way of living, age, positive and depressive symptoms, social functioning measured with the Strauss-Carpenter scale, number of involuntary hospitalizations, number of psychiatric hospitalization) remained non-significant.

## **6. Discussion**

### **6.1. Main findings of the study (I, II, III, IV, V)**

The main findings in a review of gender differences in schizophrenia (I) were that most studies have accepted that the lifetime risk of schizophrenia has been equally common in both sexes, with men developing schizophrenia 3 - 4 years earlier than women and women having more often a favorable course of the disease than men. Males with schizophrenia furthermore tend to have more central nervous system abnormalities than females. However, there were also opposite findings, and thus the final conclusions at this point in time, are difficult to formulate.

In the Northern Finland 1966 Birth Cohort study (II) there were no significant gender differences in age at the onset of schizophrenia. However, the peak of onset occurred earlier in females than in males. The incidence rates of schizophrenia were relatively high compared to earlier incidence studies and incidence among men was about two times higher than in women. In the Therapeutic Community Study (III) only minimal gender differences were observed in the sociodemographic variables, with regard to participation in psychosocial therapies (individual, group and milieu therapy) and in the institutional outcome of the schizophrenia patients. In the long-stay patients study (IV,V) almost two-thirds of the long-stay patients were men. Some gender differences were found in sociodemographic and clinical characteristics or in the utilization of psychiatric hospital care. Long-term patients were dependent on considerable support, but only the most seriously ill patients were left in hospital at the end of the follow-up. Most of the patients were placed in alternative residential facilities. Gender was not associated with hospitalization at the end of the follow-up period.

## 6.2. Age at onset (II,III,IV)

The Northern Finland 1966 Birth Cohort study and the Therapeutic Community study did not detect any gender difference with regard to age at onset of schizophrenia, which was contradictory to findings in the numerous earlier studies (Angermeyer & Kuhn 1988, Goldstein *et al.* 1989, Evenson *et al.* 1993, Häfner *et al.* 1993, Susser & Wanderling 1994, Maurer & Häfner 1995). In the long-stay patient study, the mean age at the onset of the illness, using five different criteria, was between 22.2-24.0 years in men and 24.3-25.4 years in women. The results remained practically the same when only the schizophrenia group was analysed. Age at onset in men was lower than that of women, but the difference was about two years smaller than that found in earlier studies on schizophrenia patients. This can be explained by the selected study sample. Our study population represented the most chronic schizophrenia patient group, which is probably more homogeneous with regard to the course of the illness than the schizophrenia patient group in the broader hospital population.

In the Northern Finland 1966 Birth Cohort study, the probands were 28 years old at the end of the present follow-up. This means that if there are more females in new schizophrenia cases of the older age groups (Angermeyer *et al.* 1989, Goldstein *et al.* 1989, Jablensky 1993) and a second peak of onset in women appears, as reported earlier (Häfner *et al.* 1991, Castle *et al.* 1993), the gender difference with regard to age at onset will probably appear in the future. Naturally, the extent of the possible age difference will depend on the number of men and women in the new schizophrenia cases of the older age groups.

In the Therapeutic Community study, the same age of males and females at their first admissions to the ward can be explained by the selected study sample. It is also possible that men and women were selected in different ways. Most of the patients were selected for therapeutic community treatment by personal interview or by discussing a patient's medical records in a team before the patient's admission to the ward. For example, extensive age gaps and gender disproportions were avoided, if possible, although different adult age groups were admitted. Also, it was considered in the selection of the patients that the patients benefit from the therapeutic community treatment (Isohanni 1983). In this study group there were also some patients who were not real first timers in the psychiatric hospital, although the treatment period under study was their first at this particular therapeutic community ward. Thus, the findings of this study may not be generalisable and applicable to other schizophrenic populations.

In the Northern Finland 1966 Birth Cohort study the schizophrenia patients were divided into three age groups according to the onset age at the first psychotic symptoms (16-19 years, 20-24 years and 25-28 years). This kind of grouping facilitated comparisons with earlier studies. In our study a remarkable proportion (42%) of the female schizophrenia patients had become schizophrenic before the age of 20. This finding challenges earlier studies in which the peak of onset in women has been reported to occur after 25 years of age (Eaton *et al.* 1988, Goldstein *et al.* 1989, Häfner *et al.* 1991). The finding may even indicate that the main peak of onset could be earlier in women than in men. The peak of onset in men occurred in the age group of the under 24 year-olds, which concurs with earlier studies (Eaton *et al.* 1988, Goldstein *et al.* 1989). Naturally, this finding may be a chance phenomenon and requires replication.

The onset age of schizophrenia has been defined in several ways - from the first sign of mental disorder to the first hospital admission with a diagnosis of schizophrenia (Häfner *et al.* 1993). In spite of the different definitions, a significant gender difference in age at onset has been found to exist (Häfner *et al.* 1993, Maurer and Häfner 1995). In the Northern Finland 1966 Birth Cohort study, the age at onset was defined in two ways and in the long-stay patient study in five different ways.

In the Northern Finland 1966 Birth Cohort study and in the long-stay patient study, there was practically no time lag between the age at which the first psychotic symptoms appeared according to the patients' case notes and the age at first hospitalization due to any psychiatric disorder. It was much smaller than in some other studies where the first psychotic symptomatology had been found to appear on average two years prior to the first hospitalization with a diagnosis of schizophrenia (Häfner *et al.* 1993a, McGorry *et al.* 1996). The small difference noticed in this study may be due to incomplete information, because our data for symptoms were collected from case records retrospectively and some information may have been missing from the case notes. In addition, the first psychiatric hospitalization may not necessarily have been critical for the diagnosis of schizophrenia. It is also possible that in Finland the patients are hospitalized earlier than in many other countries after the manifestation of the first psychotic symptoms. In Finland good social security and relatively small localities (people know each other) have led to the well-developed practice of taking care of the patients and, therefore, this time lag may be smaller than in many other countries.

### 6.3. Incidence (II)

In the Northern Finland 1966 Birth Cohort study, the incidence of schizophrenia was higher in men than in women. The male to female rate ratio ranged from 1.3 to 2.3 in three different age groups. These ratios were similar to ratios observed in previous studies and thus supported the findings that incidence among young men was higher than in young women (Sartorius *et al.* 1986, McCovern & Cope 1987, Goldstein *et al.* 1989, Castle *et al.* 1993). Opposite to our hypothesis and also to earlier studies, the male to female rate ratio remained relatively high in the oldest age group, that of the 25-28 year-olds. There was also a trend that, regarding women, the number of new schizophrenia cases decreased with age. Based on earlier studies we expected a smaller difference of the ratios as well as an increase in the incidence of schizophrenia in women over time, because women have been found to exhibit a peak of onset after an age of 25 and men before the age of 24 (Eaton *et al.* 1988, Goldstein *et al.* 1989, Häfner *et al.* 1991). This study does not cover the incidence of schizophrenia in age groups older than 28 years of age and therefore a final conclusion of the total life-time incidence can not yet be formulated. However, the results of this study suggest that the number of female schizophrenia cases may not reach the number of male cases. Such a conclusion would support the finding of a higher prevalence of schizophrenia in males (2.4%) than in females (1.8%) in Northern Finland, reported in the Mini-Finland Health Survey (Lehtinen *et al.* 1991). The same life-time incidence in men and women of this study population would require a remarkable second peak of onset

in women. Such a big second peak does not seem to be probable, because until the age of 28 only 35% of all schizophrenia cases involved women.

As far as we know, prospective age cohort studies like this study of the incidence of schizophrenia have not previously been performed and a comparison of the incidence rates of this study with earlier studies may be difficult. Sampling differences may lead to misleading conclusions concerning the differences in incidence rates between different studies. For example, hospital first-admission rates, which have been used in many earlier incidence studies may be unreliable, because not all patients with schizophrenia are so diagnosed at the time of their first hospital admission and some patients recorded as first admissions can be re-admissions. Diagnostic procedures and methods of calculation of incidence statistics may also vary between studies. For example, diagnostic criteria may have been changed during the study period or different diagnostic criteria were used in different studies. (Kendell *et al.* 1993). The diagnostic criteria used have been found to be related to the incidence rates and to the apparent gender differences in incidence (Regier *et al.* 1998). It has been suggested that the more stringent the diagnostic criteria for schizophrenia are, the more females are excluded (Lewine *et al.* 1984, Lewis 1992, Castle *et al.* 1993, Navarro *et al.* 1996, Haas & Castle 1997). Especially the age criteria are important, because late onset cases are more common in women. In this study, diagnoses were based on DSM-III-R schizophrenia criteria, which are rather stringent, but not as stringent as, for example, DSM-III criteria used in some earlier reports. Furthermore, there is a tendency to diagnose women with schizophrenia at a later age than men (Bardenstein & McGlashan 1990), but in this study the careful validation process has led to a reduction of this potential bias.

However, compared with many other incidence studies, the annual incidence rates of DSM-III-R schizophrenia in this study over the whole 13 year follow-up period were relatively high (7.9 per 10 000 in men and 4.4 in women). Cooper *et al.* (1987) reported incidence rates of DSM-III schizophrenia in men of 1.7 per 10 000 and in women of 0.7 per 10 000, while Iacono and Beiser (1992) provided respective figures of 0.7 and 0.2. In the study of Nicole *et al.* (1992), the incidence of DSM-III-R schizophrenia was 4 per 10 000 in men and 2.2 per 10 000 in women. The main reason for the rather high incidence rates of schizophrenia observed in the present study may be the young age of the study population. Thus far, the cohort has been followed through the high risk years for the morbidity to schizophrenia. Presumably the annual incidence rates will decrease as time goes on and the follow-up continues. One explanation for the high rates may also be the earlier finding of a higher prevalence of schizophrenia in Northern Finland rather than in other parts of Finland (Lehtinen *et al.* 1990, Hovatta *et al.* 1997).

A sizeable reduction of first admissions with schizophrenia has been demonstrated in Scotland, England, Wales, Denmark, and New Zealand (Geddes *et al.* 1993, Kendell *et al.* 1993) and it has been discussed whether the incidence of schizophrenia has, indeed, been decreasing (Kendell *et al.* 1993). The incidence of schizophrenia has also been reported to decline in Finland (Suvisaari *et al.* 1999). In Finland there are only few studies reporting incidence rates of schizophrenia and methodological discrepancies make it difficult to compare the incidence rates of different studies with each other (Kendell *et al.* 1993). However, in spite of the major differences between the studies, the high annual incidence rates in our study compared with earlier DSM-III schizophrenia findings of incidences in Finland (1.6-2.8 per 10 000 population) (National Board of Health in Finland 1988;

Pakaslahti 1992) and all psychotic disorders (20 per 10 000) (Lehtinen 1996) do not support the view that the incidence of schizophrenia is actually decreasing in Finland.

#### **6.4. Treatment and outcome (III)**

In the therapeutic community study, there were no statistically significant differences between men and women regarding the sociodemographic factors (age, education, dwelling place). However, in the schizophrenia group the educational level of men was somewhat lower than that of women. A higher proportion of the men with a diagnosis of schizophrenia and schizophreniform/schizoaffective disorders were living in sparsely inhabited localities, compared with the women. These two trends may indicate a poorer social functioning of male patients. Men with a psychiatric illness are commonly staying in their home districts with their parents.

Involuntary admissions into a mental hospital were equally common for both genders. A similar finding has been described earlier in another Finnish sample (Kaltiala-Heino 1995), but it does not support the expectation often presented that women would be more inclined to apply for psychiatric help than men (Seeman 1986). The same rates of involuntary admission in men and women into this acute, closed, therapeutic community ward can be explained by the selected study sample. Besides, there were equal proportions of male and female nurses amongst the staff, which in practice made it impossible to treat the violent male patients who were difficult to treat. During the day shift, three out of five staff members were women and two were men. The hospital attendants and the ward secretary were all women. During the night shift there were two nurses, one of them was always a man.

There were no major gender differences among patients with a diagnosis of schizophrenia regarding participation in psychosocial therapies. This group of patients had the most severe clinical profile; their clinical pictures were very uniform and they participated in their treatments in the same way. The women in the group of schizophreniform/schizoaffective disorders participated significantly more actively in group therapy and, to some extent, also in milieu therapy. On the other hand, there were no statistically significant differences in the level of activity in individual therapy between men and women in any other diagnostic group apart from mood disorders. However, this shows that women are more actively involved in their treatment than men.

Statistically significant gender differences regarding the length of stay, number of episodes and readmission rates were not found in this study. These findings are at odds with various other studies suggesting that female patients with schizophrenia have shorter and fewer hospital treatment stays than men (Salokangas 1983, Seeman 1986). The finding of this study can be explained by the selection of the patients, a process that probably homogenized the study population. It was also very clearly shown that the more severe the diagnosed disorder which the patient had (non psychotic vs. psychotic), the longer was the stay in hospital. The same result has also been obtained previously in a study on the same sample (Nieminen *et al.* 1994).

The women with schizophreniform/schizoaffective disorders had better institutional outcomes than the men, but this was not seen in the case of schizophrenia or in the other

diagnostic groups. Previous studies have shown that there are gender differences in outcome especially among the patients with schizophrenic disorders (Bardenstein & McGlashan 1990, McGlashan & Bardenstein 1990, Mueser *et al.* 1990). At least in part, the better outcome of women may be due to women having more remissions and their psychosocial functioning being better than that of men (Pakaslahti 1992). The better outcome in the diagnostic group of schizophreniform/schizoaffective disorders can also be partly explained by the finding that women were more seriously committed to their treatment in this diagnostic group than men. However, the minor gender differences are indicative of the realization of the treatment goals of a milieu-therapy-oriented ward in the treatment of severe disorders.

The gender differences of the patients in this study sample were found to be very minor also during the second and third treatment periods. This is due to the even more stringent selection of the patients at the beginning of the second and third treatment periods than at the first. The patients who had responded positively to the therapeutic community treatment during their first treatment period were admitted to the same ward at re-hospitalization and the patients who did not respond at all were more probably admitted to another ward. On the other hand, the clinical picture of the patients with several treatment periods was probably more severe. Thus, the patients with several treatment periods formed the more homogenous group of the patients with a severe clinical picture.

## **6.5. Gender differences of long-stay patients (IV)**

In the long-stay patient study, women were more commonly married, more likely to have had children and lived alone or with a secondary family than men. All these factors are indicators of the women's better ability to cope socially even when suffering from schizophrenia; this has also been shown in earlier studies (Salokangas 1996). Women lived more commonly in the city of Oulu, which reflects better social functioning in Northern Finland, because many people have to move to the city because of work, study or spouse. On the other hand, there was no gender difference in relation to social class or education. The difference between men and women regarding social functioning seemed to remain stable at the end of the index hospitalization, as measured by the Strauss-Carpenter scale. It seems that in our study population the better social functioning of women did not protect them from long-stay hospitalization.

Men exhibited significantly more negative symptoms than women, which is compatible with other studies (Salokangas & Stengård 1990, Gur *et al.* 1996, Salokangas *et al.* 1997). There were no significant gender differences with regard to positive symptoms.

There were also no gender differences in the number of hospitalizations, proportion of treatment days and number of involuntary hospitalizations after the first admission to the psychiatric hospital. There were, however, differences between men and women in CGI- and GAS-scores at the end of the index hospitalization. All these variables provide a good measure of the severity of the illness. Almost all patients had had more than one hospitalization and at least one involuntary hospitalization before the index hospitalization. Over half of the patients had spent at least 50% of the days between the first psychiatric admission and the index hospitalization in inpatient care. In practice this

has meant years of hospitalization because the difference between mean/median age of first contact for psychiatric care as marked on the patients' case notes and mean age at index hospitalization of all subjects was 22.6 years.

The patients' psychopathological state, assessed by CGI scores, was rated as at least moderately ill in almost every patient and severely or extremely ill in over half of the patients. The low GAS scores confirmed these results. Almost every patient displayed a remarkable deficiency in social functioning according to measurements on the Strauss-Carpenter-scale. Almost all were on a disability pension. Collectively, all these results indicated that the long-stay patients were seriously ill.

Mean daily doses of antipsychotic medication were relatively high in the long-stay patient study group, also being a reflection of the severity of the illness in these patients. Doses were surprisingly high in females and, therefore, no differences between men and women were noticed. The finding is contradictory to many earlier studies in which the doses of antipsychotic medication have been reported to be lower in females (Andia *et al.* 1995, Baldessarini *et al.* 1995). On the other hand, the gender difference in medication has been found to become smaller in older patient groups and especially following menopause (Seeman 1983). In this study, the mean age of the women was close to menopause, which might explain the similarity of medication in male and female patients. Men had significantly more neuroleptic depot-injections than women, which could be a consequence of the men's poorer ability to take care of their medication and their greater lack of compliance (Lewis 1992).

Our study population represented a selected group of the most severely ill, long-stay psychiatric patients, of whom 80% were diagnosed as schizophrenic. About 10 % of our sample were patients with organic disorders, which demonstrates that these patients along with the schizophrenia patients in this catchment area are also most frequently included in the long-stay patient group (Lamb 1993). Only a few patients could be assigned to the diagnostic groups of personality disorders, mood disorders or other functional psychoses. The lack of gender differences within the various diagnoses, may be a reflection of the homogeneity of the long-stay patient group. The hospital diagnoses used can be regarded as reliable, because every patient had been in the ward for at least six months and in addition a great majority of the patients had already experienced years of earlier hospitalizations. The possibility of false positive diagnoses is very unlikely (Pakaslahti 1986, Isohanni *et al.* 1997).

## 6.6. Deinstitutionalization (V)

In the long-stay patients study, at the end of the follow-up privately supported homes were by far the most commonly employed units in which to place the patients. This use of alternative types of residential psychiatric care has also been the finding of earlier studies (Borgå *et al.* 1991, Carlsson *et al.* 1996). Only 15% of the patients were living on their own or with their families which indicates a high level of need of support among this patient group. As a consequence of this tendency, long-term patients use a considerable proportion of the health care resources. In Western countries, the cost of treatment of mental illnesses has been estimated to be 1-2% of the national income (Gundersen &



Mosher 1975, McGuire 1991). In Finland, schizophrenia accounts for about one-third of the costs of all mental disorders (Vinni and Sintonen 1989).

Other institutions (somatic hospital, old people's home, units for mentally handicapped and alcoholics) were the second-most commonly used placements. This indicates that these long-term psychiatric patients had high rates of comorbidity with physical disorders and that they needed primarily somatic treatment.

It is evident that the utilization of psychiatric hospital care has diminished concurrently with the development of alternative types of residential psychiatric care (Carlsson *et al.* 1996). The development has been very rapid in Finland during the last decade (Korkeila 1998), because of financial factors, changing attitudes, and a new treatment culture. In Finland, the change in legislation of state subsidies for municipalities in 1993 and a major economic recession in the early 1990s have had major effects on municipality health care budgets. It was no longer economically reasonable for municipalities to hospitalize psychiatric patients. Consequently, municipalities have been developing programs for outpatients, funding positions for health care professionals and increasing cooperation with related specialists. Earlier studies support the positive aspects of this kind of change: open-care has proved to be cheaper, more humane and even more effective than inpatient care (Hoult *et al.* 1984, Bums & Raftery 1991, Wiersma *et al.* 1991, Anderson *et al.* 1993, Lamb 1993). Numerous length-of-stay studies have demonstrated that there is no advantage for chronic schizophrenia patients to be treated for long periods in psychiatric hospitals (Talbot & Glick 1986). It has also been a consistent finding that patients and their relatives prefer community to hospital care (Marks 1992).

Changes in the treatment culture of psychiatric care have been emphasized as a new effort in the rehabilitation of long-term patients, but in spite of this only few patients in our study were placed in rehabilitation homes. This can be partly explained by the select patient group who after years of treatment and rehabilitation efforts needed, in the first place, staff-supported housing.

Men were placed in supported and rehabilitation homes more commonly than women. In earlier studies men have been found to need more social support (Salokangas & Stengård 1990, Andia *et al.* 1995, Salokangas 1997). In this study, however, there were equal proportions of men and women living independently on their own or with family. However, this group of patients was too small to draw any robust conclusions.

Proportionately more women than men were placed in somatic hospitals and in old people's homes. This may be related to the older age and greater longevity of the women, generally. It is, however, also possible that the staff in these places cope better with female patients, for example in the case of aggressive or severe, overt psychotic behavior.

Every discharged patient had an address. Thus, the discharge of these long-term patients did not cause homelessness. This is in agreement with earlier studies (Leff 1993). Moreover, it indicates that in this respect the deinstitutionalization process has been successful in Finland. On the other hand, homelessness has been found to be a minor problem in Finland thanks to the good social security system. Due to the long and cold winters in Finland, it is very difficult to survive without a permanent place of residence. This, as well as a long tradition of mutual care, has led to well-developed practices of taking care of the patients even outside the hospital. The finding that every discharged patient had a place of residence, can probably be generalized and extended to Finland as a

whole and to some extent also to other Nordic countries, since social, economic and other living conditions are very similar in these countries.

The placements remained very much the same after the last discharge till the end of the follow-up period (Fig. 2). The changes were most notable in the group of other institutions (somatic hospital, old people's home, units for mentally handicapped and alcoholics), where 13 patients deceased during the follow-up. The oldest patients, who probably had the most severe somatic problems, were accommodated directly in somatic hospitals. Only two patients moved forward from residential facilities to the rehabilitation program. The reason for this may be that this group included mostly patients who were placed in private staff-supported homes where the rehabilitation of the patients was not the primary goal. Minimal changes in placements indicate again that the deinstitutionalization process has been successful and that the choices and selections of the placements have been realistic. However, the times between the last discharge and the end of the follow-up may vary markedly and final conclusions of the success of deinstitutionalization are impossible to draw at this stage. For example, it is too early to conclude anything about the progress of the patients in their rehabilitation process.

Of the total study population (253), 35 (13.8%) patients died during the whole study period. The number of deceased men (23) was higher than that of women. The mortality of psychiatric male patients has been found to be higher than that of females (Sohlman & Lehtinen 1999). The relatively high number of deceased patients indicates that the patients probably had some important somatic diseases, which is in line with earlier findings of physical disorders among psychiatric patients (Mäkikyö *et al.* 1998, Sohlman & Lehtinen 1999). It is also possible that the treatment of physical diseases in this patient group was unsatisfactory especially during the psychiatric hospital treatment, because most of the deceased patients (20) died in psychiatric hospitals. However, it is not possible to draw any conclusions without further analyses concerning the causes of the deaths.

Living in the city of Oulu (capital of Oulu province, about 117 000 inhabitants in 1999, the only "big" city in the catchment area) was an independent predictor for hospitalization at the end of the follow-up. This finding highlights the importance of the development of alternative types of residential psychiatric care in the deinstitutionalization process. Instead of organizing alternative treatment places, the city of Oulu tried to cut down the expenses since 1994 by funding its own organization for the whole psychiatric care, including the psychiatric hospital. Many of the patients of this study population, registered as inhabitants of Oulu, moved into the hospital of the city of Oulu during the follow-up. Also, the more traditional treatment policy of this hospital may partly explain the slower deinstitutionalization process of these patients than those of the University Central Hospital of Oulu.

For the small municipalities around the city of Oulu, to organize alternative treatment facilities was the only possibility to cut down the expenses of the psychiatric care of long-term patients. For the smallest municipalities (the smallest one contains about 700 inhabitants) even a single long-term patient in the psychiatric hospital may have a remarkable effect on the health care budget. For example, the costs for the county of one patient in psychiatric hospital care in the catchment area in 1999 was about 160-240 USD per day while in the supported home it was only about 40-50 USD. Furthermore, in small counties it is easier to organize the patients' living conditions to meet their personal

requirements, because these patients are personally known to health care organizations as well as to the social services personnel.

The low GAS scores and high doses of antipsychotic medication, both indicating severe symptomatology, were associated with the probability of being hospitalized at the end of the follow-up period. Thus, the most seriously ill patients were left in the hospital. This agrees with the finding that the patients who were in hospital care after the follow-up had significantly more involuntary hospitalizations before the index hospitalization (Table 4). It is known from earlier studies that especially aggressive behavior has been found to cause difficulties in placing the patients in alternative units (Bigelow *et al.* 1988, Trieman & Leff 1996).

Duration of hospital care before the follow-up was also an independent predictor of hospitalization after the follow-up, reflecting indirectly the severity of the disorder. This is in full agreement with previous studies where earlier use of hospital care predicted future hospitalizations (Strauss & Carpenter 1977, Appleby *et al.* 1993). Also, absence of negative symptoms predicted hospitalization, perhaps because patients who exhibit mostly negative symptoms are easier to be treated in units with few staff.

Good social functioning of the patients has been found to predict longer survival in the community. In this study, marital status (being not married) was one independent predictor for hospitalization after the follow-up. This highlights the importance of the patients' social functioning and also the meaning of the social support the patients can obtain from their family. In earlier schizophrenia studies, women were found to use fewer hospital services than men (Angermeyer *et al.* 1989, Borgå *et al.* 1991) and the men's poorer social functioning (Seeman 1986, Häfner *et al.* 1993b) has been used to explain this (Salokangas & Stengård 1990). The total number of men in this sample was higher, but gender itself did not predict hospitalization at the end of the follow-up period. The higher number of men can be accounted for by the better outcome in schizophrenic women reported earlier (Goldstein 1988, Angermeyer *et al.* 1990) or the lower incidence of schizophrenia in Northern Finland in women than in men.

According to this study, the patients left in hospital are the most severely ill patients. In the process of deinstitutionalization, a too rapid reduction of the availability of hospital beds may lead to repeated hospitalizations, problems in living and social isolation (Caton & Goldstein 1984, Leff 1992, Nordentoft *et al.* 1992, Lamb 1993). Thus, if the continuation of deinstitutionalization is the aim of psychiatric care, it requires the development of new kinds of treatment units with more and better educated staff than what is found in rehabilitation units and in residential facilities at the moment. This could possibly be more expensive than hospital care (Häfner & an der Heiden 1989, Goldberg 1991, Häfner & an der Heiden 1991), but one should keep in mind that assessing the overall costs of schizophrenia must take into account the costs to the patient and the costs to the family including suffering and loss of productivity (Andreasen 1991). The ongoing changes and developments in psychiatric care must not be dependent on financial factors alone, although the latter certainly seem to add speed to them.

## **6.7. Methodological concerns (I, II, III, IV, V)**

This thesis is based on three different study populations, which enabled analyses of gender differences in patients representing either different phases of the illness or different subgroups of patients with the same diagnosis. To study clinically homogenous samples has been suggested to be important in future gender research (Harding & Hall 1997). This study allows comparisons of the results from selected study populations with the results from earlier studies representing the whole spectrum of schizophrenia. There are, however, no earlier studies of gender differences in schizophrenia from the therapeutic community and, considering everyday clinical problems, the studies from the therapeutic community ward and the long-stay patients are clinically important.

In a review article of gender differences in schizophrenia (I), mostly studies involving the whole schizophrenic population are reviewed. To include this article as a separate part of this thesis was legitimate because the theme of gender differences in schizophrenia is very extensive and covers practically everything under the topic of schizophrenia. This practice provided better possibilities to focus in the summary of this study on gender differences that were examined in the other original papers (II-V) and also gave a wider perspective to the differences in schizophrenia between men and women.

### ***6.7.1. Strengths and limitations of the Northern Finland 1966 Birth Cohort study (II)***

The major strength of the Northern Finland 1966 Birth Cohort is the large study population - over 12 000 individuals. The study population is an unselected epidemiologically intact general population sample, representing 96% of all births in the region in one year and thus the results can be generalized to the population in Northern Finland.

The second strength is that psychiatric diagnoses in this study can be regarded as reliable (Isohanni *et al.* 1997). Diagnostic codes appeared to transfer reliably from case records (Keskimäki & Aro 1991, Mähönen 1993) into the FHDR and therefore probably only few, if any, of the psychiatric hospital treated cases were lost (Isohanni *et al.* 1997). In this study all psychotic outpatients of the age group were identified to diminish any bias. All psychiatric diagnoses were also validated carefully using the criteria of DSM-III-R, which allows comparison of the results with the results from other methodologically valid epidemiological studies. The third strength of this study is the very reliable information of the age at first hospitalization.

The first limitation of this study is that the information of the time point when the first psychotic symptoms appeared was collected from the case notes. Although it is the basic data that a physician and other staff should gather through psychiatric interviews and report them in the case notes, it is possible that in some cases this information is inexact. The amount of the documented information may vary between different physicians, hospitals and years. However, the information from the case notes may even be more reliable or at least as reliable as more retrospective interviews. The number of recalled events decreases steadily over time, which is called the "fall-off" effect (Maurer & Häfner

1995). Also, several studies have reported a lower number of positive findings in the retest situation, which is called "retest artefact" (Maurer & Häfner 1995). In the study of Maurer and Häfner (1995), different sources of information of age at onset of schizophrenic disorders were compared. There were no differences in age at onset defined as first positive symptom, age at first treatment or first admission for schizophrenia between the ratings of a research psychiatrist on the basis of medical case records and the results of structured interviews of the patients or close relatives.

The second limitation is the possibility, that some schizophrenic cases have not yet or may never come to medical attention. This bias, however, can not be significant, because almost all the schizophrenic patients in Finland and also in many other developed countries will be admitted to a mental hospital at a relatively early phase of a disturbance (Häfner *et al.* 1993, Maurer & Häfner 1995, Isohanni *et al.* 1997).

The third limitation of this study is the fact that the first psychiatric hospitalization could have been due to any psychiatric disorder prior to manifestation of schizophrenia. The fourth limitation of this study is the relatively young age of the study population. The probands were 28 years old at the end of the follow-up, thus representing only the high-risk years for the morbidity to schizophrenia and not the whole spectrum of schizophrenia. Late-onset cases for schizophrenia are still lacking from the study population (Castle *et al.* 1995, Häfner *et al.* 1998). However, there are no other birth cohorts than the Northern Finland 1966 Birth Cohort, in which the morbidity to schizophrenia has been followed for this long.

The fifth limitation of this study is the possibility that prospective cohort studies may be inapt when rare diseases are studied. Because of the low annual incidence rate it is difficult to gather enough subjects to identify the true differences, because of limited statistical power. Also, when interpreting and generalizing the results of this study one should keep in mind that the prevalence of schizophrenia may be higher in Northern Finland than in other parts of Finland (Lehtinen *et al.* 1990, Lehtinen *et al.* 1991, Hovatta *et al.* 1997).

### ***6.7.2. Strengths and limitations of the therapeutic community study (III)***

The principal strength of the Therapeutic community study is the high number of subjects, 1525 patients, representing all first treatment episodes during 17 years at the therapeutic community ward. The second strength of this study is the fact that the median length of hospitalization was relatively long, 39 days in all patients and 62 days in schizophrenia patients (Nieminen *et al.* 1994). Long treatment periods give sufficient time to observe the patients and consider the diagnoses, the degree of active participation and the outcome properly.

The third strength of this study is that the degree of active participation and the institutional outcome were assessed at the time of discharge by 3-5 team members, always including the personal doctor as well as the nurse. Also the interrater reliability of the classifications was tested and it was shown to be satisfactory (Nieminen 1996).

The first limitation of this study population from the therapeutic community ward is that it does not represent a random hospital population. Most of the patients in the therapeutic community unit were selected by personal interview or by discussing a patient's medical records in the team before a patient's admission to the ward. However, different adult age groups were admitted and at a rough estimate a total of 30-50% of the patients were admitted in emergency situations during the evening or night shift, and many of them involuntarily. This diminished to a certain degree the selectivity of the study population (Nieminen 1996).

The second limitation of this study is that the diagnoses of this study were not validated. They were clinical and determined by the psychiatrists working at the ward. However, they were probably more reliable than clinical diagnoses generally, because they were mainly based on the decision made by a psychiatrist (Matti Isohanni) with long work experience (1972 - 1989) in the ward. Furthermore, he has later tested his diagnostic reliability and it was found to be very satisfactory (Tienari *et al.* in press, Isohanni *et al.* 1997). There have also been changes in the diagnostic practice during the study period. For example, at the beginning of the study period, the diagnoses were not based on the criteria-based diagnostic classification and in uncertain cases giving the diagnosis of schizophrenia was avoided. Thus, false positive schizophrenia diagnoses were not likely.

### **6.7.3. Strengths and limitations of the long-stay patients study (IV,V)**

The first strength of this study is that the study population represents all long-stay psychiatric patients (n=253) in the region in 1992, because at that time there were no other psychiatric hospitals in the catchment area. Thus the study population can be considered as representative regarding similar patient groups in general.

The second strength of this study is that the case records included detailed information on the patients, because the patients had been for such a long time in the ward. Also the majority of them had had several admissions, which meant practically years of hospitalization and copious written case notes. Thus, the collected data and the clinical hospital diagnoses used in this study can be regarded as reliable although the diagnoses of this study were not validated. False positive schizophrenia diagnoses are not likely, because in earlier diagnostic studies in Finland, only false negative diagnoses of schizophrenia have been found to be remarkable (Pakaslahti 1986, Isohanni *et al.* 1997).

The third strength of this study is that the interrater reliability regarding assessments of CGI, GAS, DSM-III-R symptoms and Strauss-Carpenter scale was satisfactory between researchers.

The fourth strength is that we were able to complete the data concerning the placements of the patients after the last discharge by interviewing the personnel of the last inpatient ward.

The first limitation of this study is that the data of the long-stay patients, including symptoms, were collected retrospectively from case records. Due to this procedure, some information may be lacking. However, the data collection from the case records diminish the "fall-off" effect and "retest artefact" (Maurer & Häfner 1995) compared to more retrospective interviews. These phenomena are described and discussed in more detail earlier in chapter 6.7.1.

The second limitation in this study is that the time between the last discharge and the end of the follow-up may differ in theory from one day to three years. This means that further follow-ups are needed to draw final conclusions about the success of the deinstitutionalization at this area. However, one third of the patients were less than 25% and two thirds of the patients were less than 75% of the follow-up period in hospital care.

## **7. Conclusions**

### **7.1. An evaluation of the study**

A gender difference in age at onset of schizophrenia was not revealed in any of the three study populations (II, III,IV); this finding contradicts many earlier findings (Angermeyer and Kuhn 1988, Lieberman *et al.* 1993, Maurer & Häfner 1995). One explanation may be that these study populations (Northern Finland 1966 Birth Cohort, therapeutic community study, long-stay patients study) do not represent the entire schizophrenic population, although they complement each other, representing three different subgroups in schizophrenia. The result, however, challenges earlier findings by indicating that there are probably different subgroups of schizophrenia patients in which there are no gender differences with regard to age at onset or there are regional differences in the manifestation of the illness.

Minimal time lag between the first psychotic symptoms and the first psychiatric hospitalization in the 1966 Birth Cohort (II) and in the long-stay patients study (IV) indicates that in Finland the patients are probably hospitalized earlier than in many other countries after a manifestation of the first psychotic symptoms.

The higher incidence of schizophrenia among young men when compared with women (II) is in agreement with current incidence studies (Jablensky *et al.* 1992, Castle *et al.* 1993). However, the highest frequency of schizophrenia in women was found in the age at onset group of the 16-19 year-olds, which is several years earlier than usually reported. The peak in men was concurrent with earlier studies being in the 20-24 year age group (Eaton *et al.* 1988). The results suggest that the peak of onset of schizophrenia is earlier in females than in males, and the total life-time incidence of schizophrenia may be smaller among women than among men, because only 35% of schizophrenia cases in this study were women. This supports the finding of a higher prevalence of schizophrenia in males than in females in Northern Finland, reported in the Mini-Finland Health Survey (Lehtinen *et al.* 1991). There was also a trend that the number of new female schizophrenia cases diminished with age. Future follow-up studies on the Northern Finland 1966 Birth Cohort are expected to add further valuable information about the incidence of schizophrenia. As far as we know, earlier incidence studies have not analyzed similar large-scaled, genetically homogenous birth cohort study populations like the one used in this study.



The lack of gender differences of schizophrenic patients in relation to participation at psychosocial therapies and in the outcome in the Therapeutic community study (III) is contradictory to various earlier studies, which suggest that women are more committed to their treatment (Goldstein & Kreisman 1988) and that their outcome (Angermeyer *et al.* 1990) is better than that of the men. The finding may be due to the selection of the study population, but it is possible that the therapeutic community treatment model levels out the gender differences in the treatment process and outcome. The therapeutic community model used in the ward and its staff with an equal gender distribution could possibly help mentally frail male patients better than the traditional treatment.

According to the long-stay patients study, the long-stay psychiatric patients in the 1990s were seriously ill and needed considerable inpatient care after their first psychiatric hospitalization (IV). Nearly all the patients were suffering from schizophrenia. The serious picture of the illness of these patients describes the rational use of psychiatric hospitals in Northern Finland.

The whole long-stay patient group was more homogeneous with regard to gender differences than schizophrenia patients in general (IV). However, there were more men than women among these patients, probably because of the generally worse outcome of the disorder for men in general. The observed similarity in different sociodemographic variables and in the severity of the psychopathology between male and female patients could be a result of the severe nature of the illness in the patient group. Both men and women have had to pass through several filters from the community through health care contacts before they reach this most intense part of the health services. At each filter, clinical characteristics will become constrained and thus differences between the sexes will be attenuated. It is also possible that a clinically severe, chronic form of schizophrenia is in itself more homogeneous than broadly defined schizophrenia. On the other hand, this homogeneity can also be partly iatrogenic - caused by the traditional custodial care in a hospital environment and by high doses of medication.

It can be stated that the long-term psychiatric patients still left in the hospital after rapid deinstitutionalization during the 1990s represent the most seriously ill patients (V). The patients who were discharged, needed also a high degree of support (V). Thus, the development of alternative residential facilities during the 1990s in Finland has been a precondition to the deinstitutionalization process of long-term patients. Minimal changes in placements of the long-stay patients after the last discharge indicate that the deinstitutionalization process in the study area has been successful and that the choices of the placements have been realistic. However, the continuation of deinstitutionalization in its present form is questionable, unless new kinds of alternative treatment units with better resources will be established.

## **7.2. Recommendations and clinical implications**

There seems to be a significant period of time difference between the first sign of psychiatric symptoms and the first psychiatric hospitalization of schizophrenia patients. It would be important to shorten this time lag, because early detection and intervention may offer a possibility to prevent the continuation of the illness to its manifest form

(McGlashan & Johannesen 1996). This is expressly important for males, because of their overall poorer treatment results and prognoses.

High incidence rates of schizophrenia emphasize the need of providing direct resources to the psychiatric care of patients with psychotic disorders in Northern Finland. Because of the two times higher incidence rates of schizophrenia in men than in women, it would seem to be of the utmost importance to pay more attention to the early detection of the disorder particularly in men.

In spite of the decreasing number of mental hospital beds and the increased use of outpatient services there are still groups of patients needing psychiatric hospitalization (Saarento 1996). This indicates, together with requirements of modern psychiatric care, that more attention should be paid to the development of the content of the hospital care. Gender issues and differences are one of the main topics which should be taken more into consideration in the treatment of the patients and in structuring and developing adequate treatment methods (Test *et al.* 1990). Special attention should particularly be paid to the development of the treatment programs of the schizophrenic male patients because they are the ones known to have poorer treatment outcome. According to this study, the therapeutic community treatment approach may be one possibility to enhance the success in the treatment of schizophrenia.

Among the long-stay patients, the number of men was higher, men had poorer social functioning and more DSM-III-R negative symptoms than women. This indicates that any special attention should focus on the development of the treatment and rehabilitation programs especially of the long-stay schizophrenic male patients. In particular the treatment of the negative symptoms needs more attention, and in this approach the new antipsychotic agents may have an important role to play.

The long-stay hospitalized patient population represents the most severely ill psychiatric patients. However, also the discharged patients are in need of considerable support. Because of that, it is extremely important to take care that alternative treatment places really can offer adequate treatment instead of simply custodial care for seriously ill patients. Also, if the continuation of deinstitutionalization is the declared aim of the psychiatric service system, it requires the development of new kinds of treatment units with more and better educated staff than what is found in rehabilitation units and residential facilities at the moment.

### **7.3. Implications for future research**

Schizophrenia is a diverse multi-faceted illness. It may begin suddenly or gradually, it may have early or late onset and its prognosis may be good or poor. Because of this diversity, some information may be lost if the whole schizophrenia spectrum is represented as a single study population. More studies with clinically homogenous samples are needed. In addition to studying long-term patients it would be important to study gender differences from a group of schizophrenia patients with good prognoses. It would be especially important to study the determinants of the different prognoses.

More studies concerning the gender difference regarding the time lag between the first sign of psychiatric symptoms and the first psychiatric hospitalization or the starting point

of the treatment due to schizophrenia are needed. It would be important to follow up what happens to the time-lag as consciousness of the meaning of the early detection and the intervention in the treatment of schizophrenia sinks in and deepens understanding.

Methodology in epidemiological studies has improved and become gradually more uniform. Especially the diagnoses of mental disorders have nowadays become more reliable. This allows more believable comparisons between different studies in different countries than earlier. On the other hand, a continuous monitoring of the prevalence and incidences of different illnesses are needed, since treatments and society change constantly and changes of the illnesses themselves are also possible. It would furthermore be important to analyze if there is a decline in the incidence of schizophrenia and whether there are gender differences possibly linked to changes in incidence. Observations of this kind might offer important information on possibilities to influence the course of schizophrenia and even provide a better understanding of the etiology of schizophrenia. It would also be important to study further the underlying factors for the gender differences in age at onset and incidence of schizophrenia.

Gender differences with regard to the different treatment methods and practices from different subgroups of schizophrenia should be studied to increase data based on evidence as to how best to focus treatment on different patients or patient groups. In other words - are there some subgroups of patients who benefit from some specific treatments? For example, gender differences regarding the efficacy of new antipsychotic agents in the treatment of negative symptoms in long-term patients would be an important area of study.

In Finland the deinstitutionalization process has proceeded strongly during the last decade. More information on the benefits and disadvantages of alternative treatment places are needed - the kinds of places, for example, which contribute best to the progress of the rehabilitation process in schizophrenic patients need to be identified

## **8. Summary**

### **8.1. Background and aims of the study**

During the last decade schizophrenia research has emphasized the importance of gender differences. The purpose of the present study was to analyze gender differences with regard to some important sociodemographic variables, age at onset, incidence, treatment, outcome and deinstitutionalization in three different, mainly schizophrenic populations from Northern Finland.

### **8.2. Material and methods**

The first study population was the Northern Finland 1966 Birth Cohort, an unselected, general population birth cohort based upon 12068 pregnant women in the provinces of Lapland and Oulu with an expected delivery date during 1966. Their 12058 live-born children represent 96.3% of all births in the region. We followed prospectively 11017 subjects (males: 5636 = 51.2%; females: 5381 = 48.8%) from the age of 16 up to the age of 28 by means of the Finnish Hospital Discharge Register. All the case notes of the 387 subjects hospitalized due to the psychiatric disorder were obtained. The diagnoses were validated for the DSM-III-R criteria resulting in 89 (males: 58 = 65.2%; females: 31 = 34.8%) DSM-III-R schizophrenia cases. From this study population gender differences with regard to age at onset and incidence of schizophrenia were calculated.

The second study population was derived from the closed therapeutic community ward situated at the Department of Psychiatry, University of Oulu. A total of 1525 patients who had their first treatment episodes at the ward between 1. Jan., 1977 and 2. July 1993 formed the study population. Of them, 51 % (n = 784) were males and 49 % (n = 741) females. 85 males and 64 females had been diagnosed as schizophrenics, 112 males and 90 females had been diagnosed to suffer from schizophreniform or schizoaffective psychoses. Age at first admission, the degree of active participation of the patients in individual, group, and milieu therapy and the institutional outcome of these patients were assessed.

The third study population was formed of 253 long-stay psychiatric inpatients treated for at least six months without a break during 1992 (index hospitalization) in the Department of Psychiatry, Oulu University Hospital. The patients were identified from the computerized patient register and data were collected from this register and from case records at the end of the index hospitalization and at the end of the four year follow-up (1992-1995). About 80% of the patients had a diagnosis of schizophrenia and because of the homogeneity of the patients, they were analyzed as a single group with regard to the diagnosis. From this study population gender differences regarding age at onset and other sociodemographic and clinical variables were studied. Also the placement after the last discharge and at the end of the follow-up as well as factors predicting hospitalization after the follow-up were studied.

### **8.3. Results and conclusions**

In the Northern Finland 1966 Birth Cohort study the mean age at onset of schizophrenia using two different criteria was between 21.4-21.5 in men and 21.2-21.4 in women. The peak of onset in men lay in the 20-24 year age group whereas in women it occurred in the 16-19 year age group. The time difference between first psychotic symptoms and first psychiatric hospital admission was minimal for men and women. In the therapeutic community study the mean age of the patients with schizophrenia at their first admission to this ward was 27.4 years in men (SD 7.4) and 27.8 in women (SD 7.5) and patients with the diagnoses of schizophreniform/schizoaffective disorders 26.5 years in men (SD 7.2) and 27.4 in women (SD 7.7). In the long-stay patients study, mean age at onset of illness using five different criteria was between 22.2-24.0 years in men and 24.3-25.4 years in women. Mean/median time lag in years between the first sign of psychiatric symptoms and the first psychiatric hospitalization was 2.5/1.0 (SD 5.1) overall, 2.6/1.0 (SD 4.4) for males and 2.2/1.0 (SD 6.0) for females. Mean/median time lag in years between the first psychotic symptoms and the first psychiatric hospitalization was minimal in both males and females. There were no gender differences regarding age at onset in any of these three different studies. However, the peak of onset of females was lower than that of men. These results are contradictory to numerous earlier clinical studies of age at onset and indicate that there is no gender difference with regard to age at onset. The cohort studied is presently about halfway through the period of risk for schizophrenia and the other study populations did not represent random hospital populations. This suggests the possibility that within the schizophrenic patient group there are homogeneous subgroups with regard to the onset of illness. The minimal time lag between the first psychotic symptoms and the first psychiatric hospitalization indicates that in Finland the patients are hospitalized earlier than in many other countries after the manifestation of their first psychotic symptoms.

In the Northern Finland 1966 Birth Cohort study the annual incidence rate of DSM-III-R schizophrenia was high: 7.9 out of 10 000 in men and 4.4 in women by the age of 28 years. In men it was highest in the age group of the 20-24 year-olds while in women the peak occurred in the age group of the 16-19 year-olds. There was a decreasing trend in the incidence rates for women of the older age groups. The higher incidence rates in men

support the findings of earlier studies that incidence among young men is higher than in women. The high annual incidence rates of DSM-III-R schizophrenia in this study over the whole 13 year follow-up period may be due to the fact that the cohort has been followed through the high risk years for the morbidity to schizophrenia and a final conclusion of the total life-time incidence can not yet be formulated. However, the high rates do not support the view that the incidence of schizophrenia is decreasing in Finland. Incidence among men was almost two times higher than that in women. It suggests that the number of female schizophrenia cases will never reach the number of male cases, because an identical life-time incidence in this study population of men and women would require a remarkable second peak of onset in the women.

In the Therapeutic community study there were no gender differences regarding the sociodemographic variables, the length of stay and the number of treatment episodes in this ward in any diagnostic group. Differences in the degree to which males and females participated in the psychosocial therapies (individual, group and milieu therapy) and differences with regard to the institutional outcome were minimal, some trend favoring females. These minimal gender differences indicate the achievement of the treatment goals, or achieving intergender equality and balance. These goals are especially important for schizophrenic males because of their more severe clinical profile and poorer prognoses. The therapeutic community model may help psychotic male patients in approaching their age- and gender-specific life span challenges.

In the long-stay patients study almost two-thirds of the long-stay patients were men. Very few gender differences were found in sociodemographic and clinical characteristics or in the utilization of psychiatric hospital care. The female patients had a better ability to adjust socially. It would seem that men are overrepresented amongst long-stay inpatients because of their poorer outcome. The observed similarity between male and female patients could be a result of the severe nature of the illness in the patient group. Patients have had to pass through several filters through health care contacts before they reach this most intensive of the health services. At each filter, clinical characteristics will become constrained and thus differences between the sexes will be attenuated. The homogeneity of men and women can also be partly iatrogenic - caused by the traditional custodial care and by the high doses of medication.

About 70% of the long-stay patients were discharged during the four year follow-up and only 15% were able to live without continuous support. The discharge did not cause homelessness. Marital status, dwelling place, absence of negative symptoms and severity of the illness were associated with hospitalization at the end of the follow-up. Gender was not associated with hospitalization at the end of the follow-up period. Our study showed that long-term patients are dependent on considerable support and that the most seriously ill patients are, in fact, in hospitals. Alternative residential facilities have to be regarded as pre-requisites for the deinstitutionalization process of the long-stay patients to be successful.

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