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Hannele Heilä

SUICIDE AND SCHIZOPHRENIA.

A nationwide psychological autopsy study in Finland

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University of Helsinki
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ACADEMIC DISSERTATION

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II. Heilä H, Isometsä ET, Henriksson M, Heikkinen M, Marttunen M, Lönnqvist J. Antecedents of suicide among people with schizophrenia. British Journal of Psychiatry 173:330-333, 1998.

III. Heilä H, Heikkinen M, Isometsä E, Henriksson M, Marttunen M, Lönnqvist J: Life events and completed suicide in schizophrenia. A comparison of suicide victims with and without schizophrenia. Accepted for publication in the Schizophrenia Bulletin.

IV. Heilä H, Isometsä E, Henriksson M, Heikkinen M, Marttunen M, Lönnqvist J: Suicide victims with schizophrenia in different treatment phases and adequacy of antipsychotic medication. In press in the Journal of Clinical Psychiatry.

II. INTRODUCTION

1. SUICIDE

1.1 Definition of suicide

Committing suicide is a behavior; a mode or manner of death. As with all human behavior, it is complex and multifaceted in nature (Murphy 1994). Throughout recorded human history, inqueries into human suffering and suicide have taken place. During this century, suicide has been studied and defined in the contexts of all the human sciences. This study addresses suicide from the psychiatric perspective.

Although there is no single, unanimously accepted definition of suicide, definitions often include three components: the death occurs as a result of injury, which is both self-inflicted and intentionally inflicted. The least ambiguous factor is that the outcome of the injury is death. However, the retrospective evaluation of the victim´s mental intention to die at the time of suicide is usually problematic, unless obvious from the circumstances (Hirschfield & Davidson 1988, Rosenberg 1988, O´Carroll et al 1996). It has often been suggested that suicide intent may represent the varying degree of consciousness and determination to die in suicide (Stengel 1960, O´Carroll et al 1996), a view that has also been applied in defining suicide intention in attempted suicide by the World Health Organization (WHO) multicentre study on parasuicide (Bille-Brahe et al 1994).

Operational criteria for suicide are needed for the purposes of e.g. research. The legal classifications of causes of death are often used in psychiatric research. Most member nations of the WHO currently use the standardized International Classification of Diseases (ICD) to code mortality data, whereas some countries, like the United Kingdom and Canada, use the information provided by coroners and/ or medical examiners (Sakinofsky 1998). Comparisons of suicide rates and research findings between countries and time periods may be difficult when using data based solely on vital statistics: varying levels of evidence may be needed by medical and legal systems for classifying suicide as a cause of death, and there may also have been changes in the legal classifications of suicide over time within countries (Hirschfield & Davidson 1988, Garrison 1992, Neeleman et al 1997a). Underestimation of suicide rates may have various origins. First, suicidal deaths may be officially classified as accidental or undetermined, if the evidence for

suicidal intention has not been considered adequate (Lönnqvist 1977). Furthermore, the classification of suicide is likely to vary by the mode of death, overall rate of autopsies performed in the country , cultural concepts, age, and gender of the deceased (Sainsbury & Jenkins 1982, Litman 1989, Neeleman et al 1997a , Canetto and Sakinofsky 1998). Conversely, deaths preceded by mental illness or suicidal threats may lead to overcounting of suicide (Kleck 1988). Overall, the variation in official suicide rates is suggested to be affected less than 10% by biases of estimation. This may be of sufficiently minor consequence for national rates to allow meaningful comparisons of the rate between countries and over time (Lönnqvist 1977, Sainsbury & Jenkins 1982, Kleck 1988, Litman 1989, Mościcki 1997, Öhberg 1998).

In Finland, the classification of causes of death follows by the Official Classification of Causes of Death according to the current ICD-10 definition: suicide is a death resulting from an intentional self-inflicted self-harm. Finnish law requires a medicolegal investigation of the cause and manner of death when it is or is suspected to have been unnatural, or when it has been sudden and unexpected. The judgement of the mode of death is made by the medical examiner. Determination of causes of death is considered reliable in Finland due to the high overall autopsy and medicolegal autopsy rates compared to many other countries (Näyhä 1980, Öhberg 1998, WHO 1998).

1.2 Epidemiology of suicide

In industrialized countries suicide is among the ten causes of death constituting a major public health problem. Suicide rates differ by age, sex, race, living environment, and marital status (Monk 1987, Kreitman 1988, Mościcki 1997). In general, they tend to increase with age in most Western industrialized countries, particularly among men (Diekstra 1992, Garrison 1992). In Finland, however, rates peak at a somewhat younger age: among middle-aged and older working-age people (Härö 1995, Öhberg & Lönnqvist 1997). The marked increase in youthful suicides between the 1960s and 1990s has raised the question - still unanswered - of whether each age-cohort has its own susceptibility to and patterns of suicide, and whether a high rate of suicide persists constant throughout the cohort´s lifetime (Monk 1987, Klerman & Weissman 1989, Garrison 1992). Suicide rates are consistently found to be higher among men in industrialized countries (Canetto and Sakinofsky 1998, Garrison 1992, Mościcki 1997, Öhberg & Lönnqvist 1997).

The overall suicide rate in Finland has long been among the highest in the world (Lönnqvist et al 1988a, Diekstra 1992, Öhberg & Lönnqvist 1997); in 1996 1247 people (965 males and 282

females) killed themselves. The suicide rate was 24.3 / 100 000 inhabitants: 38.7/ 100 000 for men and 10.7/ 100 000 for women (Statistics Finland, 1996). During 1995, the age- and sex-standardized suicide rate for Finnish men was the seventh highest and for women the sixth highest in Finland compared to other WHO countries in Europe (WHO, 1998).

1.3 Psychiatric suicide research

1.3.1 Research methods

There has been a limited use of study designs in suicide research due to the low base rate of suicide, in addition, the risk factors have often been poorly delineated. Many of the studies have been retrospective in nature, because the ideal prospective study designs are extremely costly, time consuming, and inefficient (Pokorny 1983, Brent 1989). For these reasons, individual level studies have often been based on clinical samples at high-risk, or studies have been on the population level and thus correlational in nature (Pokorny 1983). Most studies have also been observational in nature. Applying experimental methods that use randomization, blinding and/or placebo techniques for testing determinants in the outcome of suicide would often be unethical and thus unfeasible, for example randomization of suicidal patients to different forms of treatment conditions (Mościcki 1997, Linehan 1997).

Ecologic studies reveal correlations between suicide rates and defined population groups (e.g. data for different geographic areas or time periods) without obtaining assessments on each individual subject (Garrison 1992, Zahner et al 1995). These studies are open to the possibility of cross-level bias or ecologic fallacy, which means an erroneous inference made about associations between measures on an individual level based on relationships observed on a group level. Analyzing time trends in suicide rates would involve taking complicated age, period, and cohort effects into account in order to obtain reliable information (Zahner et al 1995).

Follow-up studies of general or high-risk populations provide information about suicide rates within different groups of people. The variations in suicide mortality rates suggest hypotheses for risk factors for suicide. Findings from cross-sectional case studies can also be used to create hypotheses for high-risk groups within suicide populations (Klerman 1987, Monk 1987). Using cross-sectional, or ideally longitudinal, case-control designs allows examination of the relationships between risk factors, or exposures, and suicide, and these studies can also be used for quantifying

the strength of the risk. Ideally, these are prospective studies of persons with fixed markers for high suicide risk (Zahner et al 1995, Mościcki 1997, Kraemer et al 1997).

The most obvious problem in suicide research is the lack of self-reported data from suicide victims. Follow-up studies, either prospective or retrospective, are not usually able to collect data close to the time of death of the deceased, and knowledge of recent antecedents of suicide may be missed. The frequent use of patient record-based data is compromised by information biases concerning varying levels of information obtained, or information with varying levels of accuracy. In these studies, the quality of missing information on the suicide process is especially problematic: is the information truly absent, or just not noted. Studying risk factors for suicide requires large and representative populations in order to avoid selection biases, as the cases and/or controls should be representative of the population at risk (Brent 1989, Gould & Shaffer 1992, Zahner et al 1995).

1.3.2 Psychological autopsy method

The psychological autopsy study method, such as used in the present study, answers some of the problems caused by the use of retrospective chart data, being the only research method that makes feasible the study of recent life circumstances and psychological factors in the deceased prior to suicide (Gould & Shaffer 1992). The use of the psychological autopsy method originates from the late 1950´s in Los Angeles, USA, where it was first used as a method for determining the mode of death in equivocal cases of death. The suicidal process was reconstructed through interviews with informants important to the deceased (Litman et al 1963, Shneidman 1981). Since then, psychological autopsy has been used for suicide research purposes as a method of obtaining detailed information on the victim´s psychological state, behavior, health, interpersonal relations, and possible suicide motivation close to the time of suicide, as well as lifetime information on relevant aspects (Shneidman 1981). Other available data, such as hospital records, are also used for synthesizing and validating the information received (Shneidman 1981, Beskow et al 1990, Clark & Horton-Deutsch 1992).

The major methodological problems of psychological autopsy studies relate to information biases due to the interview-based information coming from others than the deceased. These biases may lead to under or over reporting of information (Brent 1989, Clark & Horton-Deutsch 1992, Kraemer et al 1997). However, using different sources and integrating all available data is likely to enhance the general level of information, and thus improve its validity (Brent 1989, Clark & Horton-Deutsch 1992)

Ethical issues that are involved in the use of the psychological autopsy method are concerned with the integrity of the victim, the integrity and health of the interviewees, and the psychological strain on the interviewer. Firstly, facts that the deceased had chosen to conceal from next-of-kin should not be revealed to them. Secondly, the interviewee should not be harmed in any way, and his/her distress should be anticipated. If necessary, the interviewee should be assisted in getting crisis help. Lastly, the interviewers should have appropriate psychiatric experience, training, and supervision, to manage the emotional strain that this kind of work demands (Brent 1989, Beskow et al 1990). When these issues have been adequately addressed, it seems that the interviewees have benefited from the psychological autopsy interview experience and are perhaps maybe experiencing also a better outcome of copying after suicide of a significant other (Runeson & Beskow 1991, Saarinen et al 1997).

1.4 Risk factors for suicide

Despite the substantial research into factors relating to suicide, its causal factors for suicide (by definition: manipulation of the factor changes the outcome) have yet to be identified (Kraemer et al 1997). The prospective risk factor should at least have been shown to precede the corresponding outcome, which is not always the case in cross-sectional, retrospective study designs. The risk factors of greatest interest in the search for causality, and that would reach specificity in suicide prevention, would also show time-varying features. For example, marriage is a risk factor for suicide among teenage girls, and a protective factor among adult women. However, in cross-sectional studies many of the identified risk factors associating with suicide are often fixed markers (i.e. fixed, non-varying over life-time, or "trait"-like) (Kraemer et al 1997). Moreover, the complex nature of suicide implies that risk factors are likely to have interaction effects; for example, lack of social support could be a strong predictor of suicide in the absence of persecutory delusions, but a weak indicator if such delusions are present. In suicidology the strategy of examining interactions among risk factors is little used (Young et al 1994).

1.4.1 Sociodemographic factors and health behavior

At the population level suicide is strongly associated with sociodemographic characteristics. In Western countries male sex and older age have been found to increase suicide risk (Garrison 1992, Öhberg 1988, Canetto & Sakinofsky 1998). Unemployment and occupational stress appear to be factors that correlate with high suicide rates, as also found in cross-sectional studies at the

individual level (Platt 1984, Wasserman 1992, Gunnel et al 1995). Marriage, particularly among men (Stack 1992), parenthood, particularly among women (Høyer & Lund 1993), and some religious affiliation (Neeleman et al 1997b) have correlated with low suicide rates. Cigarette smoking and suicide have a positive association (Harris & Barraclough 1997), as do alcohol consumption and suicidal acts (Romanov et al 1994), whereas caffeine consumption and risk of suicide showed a strong inverse association in a prospective study among female nurses (Kawachi et al 1996). The interpretation of sociodemographic factors and health behavior as risk factors or markers for suicide risk is complicated by their interaction with and similarities to psychiatric disorders and their possible etiological factors and consequences (Wasserman 1992, Heikkinen et al 1995, Isometsä et al 1996, Lindeman et al 1997, Harris & Barraclough 1997).

1.4.2 Mental disorders

Mental disorders have been confirmed as risk factors for suicide in both short-term and long-term follow-up studies of general populations (Babigian & Odoroff 1969, Rorsman 1974, Tsuang & Woolson 1978, Pokorny 1983, Black et al 1985, Neeleman et al 1998) and in parasuicidal patients (Suokas & Lönnqvist 1991, Nordentoft et al 1993, de Moore & Robertson 1996). The magnitude of the suicide risk among patients who have previously received any kind of treatment for psychiatric disorder is estimated to be 11 times (range 6-27) greater than expected (Harris & Barraclough 1997). In the general population the life time prevalence of mental disorders is estimated to be 22% to 49% (Regier et al 1988, Kessler et al 1994), the 12-month prevalence to be approximately 28 % (Regier et al 1993, Kessler et al 1994), and the one-month prevalence or point prevalence to be 16% to 32% (Lehtinen et al 1990 (a), Lehtinen et al 1991, Regier et al 1993), implying that a considerable number of people are at potentially high risk of suicide at the population level.

Psychological autopsy studies of general population suicides have estimated the prevalence of current mental disorders at the time of suicide to be as high as 81% to 98% (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Hagnell et al 1979, Chynoweth et al 1980, Mitterauer 1981, Rich et al 1986, Arato et al 1988, Henriksson et al 1993, Cheng 1995, Conwell et al 1996, Foster et al 1997). The most prevalent DSM-III or DSM-III-R mental disorders in general population suicides have been depressive disorders, alcohol abuse and dependence, and schizophrenia (35%-90%, 17%-54%, and 3%-7%, respectively) (Rich et al 1986, Henriksson et al 1993, Cheng 1995, Foster et al 1997). In mood disorders, the current illness episode has been reported to increase the suicide risk more than a life-time diagnosis (Brent et al 1994).

There is a suggestion that the severity of the current psychiatric morbidity increases the magnitude of the suicide risk in the general population, as well as in depressed and suicidal patient populations. This is a reflected by the high prevalence of comorbidity or co-occurence of mental, addictive and physical disorders in suicides (55-88%; Shafii et al 1988, Marttunen et al 1991, Henriksson et al 1993, Brent et al 1993a, Lesage 1994, Brent et al 1994, Shaffer et al 1996, Foster et al 1997). Comorbidity increases the potency of the suicide risk compared with the risk of non-comorbid mental disorders (Cheng 1995). The most common comorbidity pattern has been substance use disorder with major depression, found among 28% - 58% of suicide victims (Fawcett et al 1990, Henriksson et al 1993, Cheng 1995, Conwell et al 1996). In the US general population, the overall 1-year comorbidity prevalence in psychiaric disorders was found to be as high as 59%; and in contrast to suicide populations, the most commonly observed comorbidity patterns were anxiety disorders co-occuring with major depressive disorder (Kessler et al 1994, Kessler et al 1996). The substantial high prevalence of comorbidity in living general populations may be explained by more sensitive diagnostic screening methods achieved by direct interview that may yield higher prevalence of psychiatric disorders in the general population, compared to the indirect diagnostic methods used in suicide populations (Henriksson et al 1993, Regier et al 1998).

Knowledge of the role of severity and specific quality of the current mental disorder and its symptoms in increasing the potency of suicide risk comes mainly from studies among depressed persons. A greater severity of current depressive symptoms tends to be found more often in suicides than non-suicides among depressed patients (Barraclough et al 1974), as well as in suicide attempters (Michel 1987). These studies also suggested that some accompanying symptoms in depression, such as insomnia, anhedonia, self-neglect and impaired memory, may differentiate suicide victims from living subjects. Somewhat similarly, a follow-up study has suggested that the short-term risk for suicide (within one year) in depressed patients was associated with symptoms of insomnia, anhedonia, diminished concentration, and anxiety (Fawcett et al 1990). Concerning the effect of the duration of the current depressive episode, or of episode recurrence on suicide risk, the findings have been somewhat inconsistent. Some studies (Barraclough & Pallis 1975, Chynoweth et al 1980), but not all (Cheng 1995), have found an association of longer duration of current depressive episode with suicide among depressed patients. A recurrent major depressive episode has suggested to carry a higher suicide risk compared to a current single episode in the general population (Cheng 1995). However, in patients with major affective disorders, the risk of suicide was reportedly higher among those with fewer previous episodes, indicating high risk early in the course of illness (Fawcett et al 1987). These somewhat contraversial findings may be due to the observation that the risk of suicide remained high throughout the first decade of

long-term follow-up (Tsuang & Woolson 1978), and probably increased at each relapse during the illness course.

The risk of suicide may also vary with age and sex among people suffering from mental disorders as it does in the general population. A comparison of depressive suicides and non-suicides found older female depressed patients and male patients at all ages to be at the highest risk of suicide (Barraclough & Pallis 1975).

1.4.3 Previous suicidality

In the general population one-year prevalences of suicidal ideation of 2% - 7 % have been reported (Paykel et al 1974, Hintikka et al 1998). In psychological autopsy studies communication of suicidal intent has occurred in 43% - 83% of suicide cases (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Rich et al 1986, Cheng 1995). Suicidal ideation is associated with increased risk of suicide in follow-up, but the association seems to result from the combination of mental illness and high suicide intent in people with suicidal ideation (Harris & Barraclough 1997). In addition, a family history of suicidal ideation as a risk factor for suicide has been explained by the presence of mental illness among family members, and not by the suicidal ideation itself (Brent et al 1996).

The one year prevalence of suicidal behavior in the general population has varied between 0.3% - 1.1% (Mościcki et al 1988, Hintikka et al 1998). Follow-up studies of hospital-referred suicide attempters show that 1% - 3% complete suicide within one year of the attempt (Hawton & Fagg 1988, Nordström 1995a), while among drug-overdosers and patients with affective disorders the suicide risk has been highest within the first few years of an attempted suicide (Nordentoft et al 1993, Nordström et al 1995b). In a follow-up of over ten years the suicide risk was as high as 10-15% (Maris 1992).

A history of previous suicide attempt/s is a proven risk factor for suicide in the general population (Hagnell & Rorsman 1980, Cheng 1995) as well as in psychiatric patients (Fawcett et al 1990, Nordström et al 1995b). The number of previous attempts has been found to increase the suicide risk (Goldstein et al 1991). Psychological autopsies report a history of previous suicide attempts among suicide victims ranging between 21% - 44% (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Rich et al 1986, Arato et al 1988, Cheng 1995, Isometsä & Lönnqvist 1998). The magnitude of the suicide risk is estimated to be 38 times (range 0-77) the expected rate

in people with a history of suicide attempts (Harris & Barraclough 1997).

Parasuicide rates vary with age and sex. They are generally higher for women than men, and for younger than older (Mościcki 1988), although in Finland the parasuicide rate has been higher among men (Schmidtke et al 1996, Hintikka et al 1998). In follow-ups after attempted suicide males are at higher risk for suicide than females, and older persons than younger (Suokas & Lönnqvist 1991, Nordström et al 1995b). When both age and sex are taken into account, older and younger men as well as older women are at higher risk for suicide compared to younger women (Nordström et al 1995b).

Mental disorders are in general considered almost necessary for suicide, although not sufficient for the final tragic outcome (Murphy 1983). This idea is reflected in the DSM-classifications that cross-refer suicidal behavior as a possible complication, symptom, or consequence of major depressive disorder or borderline personality disorder (APA 1987, APA 1994). However, it has also been suggested, that there might be a phenotype of suicidal behavior independent of mental disorders, transmitted by a familial mechanism distinct from familial transmission of psychiatric disorders (Brent et al 1996). In line with this, there is also a suggestion that a "suicidality syndrome" could be distinguished from major psychiatric disorders by a common phenomenology of symptoms. This is hypothesized to be trait-like, in latent form without symptoms, but possibly clinically important if triggered by life stressors (Ahrens & Linden 1996).

1.4.4 Psychological factors

The most widely studied psychological factor found to relate to psychiatric disorders and suicidality is hopelessness (a state of negative expectations) (Weishaar & Beck 1992). This has been shown to be a risk factor for suicide in follow-up, but it may be related to selected characteristics of psychiatric morbidity. Three prospective follow-up studies in depressed patients, hospitalized suicidal ideators and psychiatric outpatients with mixed diagnoses showed baseline hopelessness to be a risk factor for long-term suicide risk (Beck et al 1985, Beck et al 1990, Fawcett et al 1990), and a retrospective controlled study of schizophrenic inpatients showed those who subsequently committed suicides within varying time periods to differ from non-suicides in base-line hopelessness (Drake & Cotton 1986). Among subjects with alcoholism the findings of hopelessness as a predictor of suicide have not been consistent (Beck & Steer 1989, Young et al 1994).

1.4.5 Adverse life events

Adverse life events are reported to associate with a variety of illness outcomes, including the onset or relapse of psychiatric disorders (Paykel et al 1969, Paykel & Dowlatshahi 1988). They are also an established risk factor for suicide among persons in the general population (MacMahon & Pugh 1965, Bunch 1972, Hagnell & Rorsman 1980, Shafii et al 1985, Kaprio et al 1987, Brent et al 1993b), as well as among psychiatric patients (Bolin et al 1968, Humphrey 1977, Pokorny & Kaplan 1976, Fernando & Storm 1984). They are suggested to function as precipitating factors in the suicide process by interacting with other risk factors for suicide, while social support may modify the impact of life stresses by functioning as a protective factor (Paykel et al 1969, Heikkinen et al 1993).

1.4.6 Familial factors

Suicidal behavior tends to cluster in families. A prospective follow-up study of psychiatric patients, which included also a group of suicide victims, showed an increased risk of suicide among the first-degree relatives of both groups compared to the control patients´ relatives (Tsuang 1983). Retrospective studies with age-matched general population controls have also shown that family history of completed suicide or suicide attempt and/or affective disorder is a marker for high risk of suicide in the proband (Brent et al 1994, Cheng 1995, Gould et al 1996, Brent et al 1996). In youth this has applied even after adjusting for differences in the rates of familial and proband DSM-axis I and II disorders (Brent et al 1996).

For non-genetic familial transmission mechanisms among young people, negative family environment and decreased and less satisfying communication with parents are suggested to explain the increased risk of suicide in families with psychiatric histories (Gould et al 1996). The suggestion of genetic transmission comes from adoption studies, and twin studies have suggested monozygotic twins to have a greater concordance for suicidal behavior than dizygotic twins (Roy et al 1997). Molecular genetic studies of polymorphisms of the tryptophan hydroxylase gene which controls serotonin metabolism have also shown an association with suicidal behavior (Nielsen et al 1994, Mann et al 1997). Although there is a suggestion of a genetic susceptibility to suicide, the transmission mechanisms and subject of transmission (e.g. genetic predisposition for psychiatric disorder or suicide) for the phenotype of suicidal behavior remain unclear (Brent 1996, Roy et al 1997).

1.4.7 Biological markers for suicidal behavior

The two main strategies used to study the neurobiology of suicide are neuroendocrine challenges (e.g. HPA-[hypothalamic-pituitary-adrenal] axis) and neurotransmitters (e.g. serotonin measures). The majority of the studies have concentrated on the serotonin (5-HT) system. In suicide attempters reduced amounts of a 5-HT -metabolite, 5-hydroxyindoleacetic acid (5-HIAA), have been found consistently in the cerebrospinal fluid (CSF). The most lethal suicide attempts have been associated with the lowest levels of 5-HIAA. Lowered 5-HIAA levels in CSF have been found in suicide attempters with personality disorders, major depression, alcoholism and schizophrenia (Åsberg 1997, Mann 1998). Further evidence comes from several studies of psychiatric patients, in which low CSF 5-HIAA was a marker for high suicide risk in suicide attempters (Åsberg 1997). Aggression dyscontrol may partly explain the association of low serotonin with suicidal behavior (Linnoila &Virkkunen 1992). Nonhuman primate studies indicate that factors related to genetics, rearing, cholesterol, and stress can lower CSF 5-HIAA (Arango et al 1997). Altered HPA activation is also reported in suicidal behavior. It may be linked by elevated CRH (corticotrophin-releasing factor) to clinical severe anxiety and agitation. It has yet to be determined, whether and how these are different from the neurochemical changes associated with the psychopathology of psychiatric disorder that may have generated the suicidal ideation in the first place (Arango et al 1997).

1.5 Suicide prevention in mental disorders

Suicide is an outcome of a process involving a complex interaction of sociodemographic, psychiatric, familial, biological and situational factors. There is large body of research devoted to these risk factors. However, the knowledge deficit about specific causal risk factors and protective factors in suicide inevitably creates a lack of potency in suicide prevention. Structuring effective prevention programs requires a focus on causal risk factors rather than more unspecific risk factors (Kraemer et al 1997). Thus the need to identify and specify the characteristics of persons at high risk of suicide remains crucial. On the basis of the findings about risk factors or markers for suicide, hypotheses for psychiatric suicide prevention interventions have been formulated both at the individual and population level (Hawton 1987, Jenkins 1994, Gunnel & Frankel 1994, Lewis et al 1997).

Most of the knowledge about suicide risk factors is based on long-term studies producing information on predisposing factors for suicide. These are likely to differ from short-term risk factors that may also function as precipitating or triggering factors (Hawton 1987, Fawcett et al 1990, Jenkins 1994). In an individual (as opposed to population), most practical opportunities for suicide prevention are related to clinical and short-term suicide risk factors. Clinical risk factors include the presence and severity of only psychiatric disorder, the intensity of suicidality, and the degree of hopelessness. Since the primary prevention of factors relating to suicide risk is not feasible, the suggested preventive strategies have aimed at better treatment and cure, or better coping, among high-risk individuals (Appleby 1992, Jenkins 1994, Linehan 1997).

The evidence for the efficacy of suggested suicide prevention interventions is still limited and suggestive (Gunnel & Frankel 1994, Linehan 1997, Goldney 1998). Adequately controlled, randomised prospective studies would be required to examine the impact of these treatments on suicide, but these are generally not feasible. However, this does not imply that such interventions cannot reduce the rate of suicidal deaths. Among the factors that could be influenced by suicide prevention interventions, are psychiatric treatments of mental disorders or suicidal behavior (Gunnel & Frankel 1994, Jenkins 1994).

1.5.1 Individual level

1.5.1.1 Factors relating to treatment of mental disorders

This strategy assumes that suicidal behavior is a symptom or complication of a mental disorder, whose effective treatment leads to a reduction in suicidality (Linehan 1997). The importance of psychiatric assessment of suicidal people was suggested by a naturalistic study of hospital referred suicide attempters with high intent in follow-up, those with psychiatric assessment showed a lower risk of suicide than those without (Suokas & Lönnqvist 1991).

Inadequate antidepressant treatment among depressed suicide victims has been a consistent finding in cross-sectional clinical and psychological autopsy studies in general population. A high suicide rate in major depression has been suggested to be due to non-diagnosis of the disorder (Modestin 1985, Rihmer et al 1990), inadequate dosages of antidepressants (Barraclough et al 1974, Modestin 1985, Rihmer et al 1990, Isacsson et al 1994, Isometsä et al 1994a, Cheng 1995), medication non-compliance (Barraclough et al 1974, Isacsson et al 1994, Cheng 1995), or inadequate treatment supervision (Isometsä et al 1994a, Cheng 1995). In a high-risk group of discharged psychiatric

patients, a lower proportion of suicide victims received pharmacotherapy and lithium than non-suicide cases (Modestin & Schwarzenbach 1992). Findings relating to inefficient treatment of depression have also applied among living depressed people (Keller et al 1986).

Possibly due to the relative rarity of suicidal behavior, there is no evidence from follow-up studies for the effect of antidepressive medication in reducing suicide attempts or suicide in depressed people (Beasley et al 1991), whereas there is evidence for its effectiveness in reducing suicidal ideation among the depressed compared to placebo (Beasley et al 1991, Tollefson et al 1993, Malone 1997). However, among suicidal patients without current major depressive disorders or psychosis, evidence for decreased suicidal behavior in short-term follow-up has been reported in a double-blind placebo-controlled study of SSRI (selective serotonin reuptake inhibitor) antidepressant treatment (Verkes et al 1998). In patients with personality disorders, too, neuroleptic flupenthixol injection was reported to decrease suicidality compared to placebo during six months of treatment (Montgomery & Montgomery 1982).

1.5.1.2 Factors relating to coping among high-risk persons

These strategies hypothesize that offering better coping strategies or support systems to suicidal patients can lead to a reduced incidence of suicide. However, no data are yet available from controlled studies. Recent reviews of controlled randomized trials of various psychosocial treatments for suicidal patients have suggested weak evidence for reduceds rates of repeated parasuicide in some treatment groups, although uncertainty remains about which forms of treatments are effective (Linehan 1997, Hawton et al 1998). Dialectic behavioral therapy, which resembles cognitive therapy, as well as problem solving therapy have shown some signs of efficacy (Hawton et al 1998).

A review by Lester (1997) of the effectiveness of suicide prevention centers on suicide rates found a small, but inconsistent preventative effect. However, these studies were ecological in nature, providing only correlational information rather than any cause-effect conclusions (Lester 1997). In an early study, a trend towards reduced rates of suicide was reported after simply sending nondemanding letters and making brief phone calls to persons at high suicide risk who had refused treatment (Motto 1976).

1.5.2 Public health level

1.5.2.1 Primary care of mental disorders

The biggest task for suicide prevention at the public health level is dealing with high rates of depressive disorders, which have also been assessed as creating the greatest burden for public health generally among the psychiatric disorders (Murray & Lopez 1997). A population level approach to suicide prevention has been suggested with the aim of reducing the rate of depression in the general population, but the effectiveness of the programmes involved would depend on the degree of causality between depression and suicide (Appleby 1992).

It has been shown that a minority of persons suffering from non-psychotic mental disorders have had a contact with health care systems in cross sectional studies (Lehtinen et al 1990b, Regier et al 1993, Kessler et al 1994). Most lifetime treatment contact has been reported delayed, the median delay time between 6 and 14 years (Kessler et al 1998). Among depressed persons themselves, the perceived need for seeking treatment for depression maybe rather low (Lehtinen et al 1990b, Isometsä et al 1997, Greenfield et al 1997). The ability of general practitioners to detect mental disorders in primary health care also varies greatly (Joukamaa et al 1995). Voluntary community-based screening for depression may be a promising method for bringing certain untreated depressed individuals to treatment (Greenfield et al 1997).

About 40% of people who later commit suicide have sought help from primary or specialist health care during their last month, and two-thirds of these have suffered from depression (Isometsä et al 1995a). Up to 20% of suicide victims have visited primary health care services during their last week (Pirkis & Burgess 1998). However, according to prescription databases and toxicologic screenings at the population level, the proportion of suicide victims who have been receiving and/or taking antidepressant medication has been very low (Marzuk et al 1995, Isacsson et al 1997, Öhberg 1998). There is some evidence for the efficacy of post-graduate education of primary health care clinicians in early detection, diagnosing and better treatment of depression, reflected in diminished suicide mortality. The effect of one educational intervention seemed to be of short duration, and thus should be repeated at intervals (Rutz et al 1989, Rutz et al 1992, Rihmer et al 1995). Further, improved prescription of antidepressants as a means of reducing suicide mortality among depressed people has been suggested in ecological studies by low rates for suicide among treated compared to non-treated depressed people (Isacsson et al 1996), and by reduced suicide rates coinciding with increased antidepressant sales in Nordic countries and Hungary during 1990´s (Isacsson & Bergman 1998).

1.5.2.2 Psychiatric care

In Finland, less than half of suicide victims with major depressive disorder have been in contact with psychiatric care at the time of suicide (Isometsä et al 1994a). There is some evidence that special clinics in psychiatric care for high risk populationsmay be able to decrease suicide rates. In high risk groups of patients with major affective disorders good monitoring and maintenance of lithium care in special clinics has associated with a lower suicide mortality risk than expected (Müller-Oerlinghausen et al 1992, Müller-Oerlinghausen et al 1996, Tondo et al 1998). This may be explained by many mechanisms: reduced recurrences of illness, compliant patient population, better suicide prevention in special clinics, and the effects of lithium on suicidal behavior (Ahrens et al 1993). It has been suggested that better referral to psychiatric care among high suicide-risk individuals would explain the recent 20% drop in suicide rate in the Netherlands correlating positively with a concurrent increase in psychiatric hospital suicides . A high ratio of treated to non-treated patients at high-risk of suicide may be a good indicator at the population level of improved suicide prevention (Kerkhof & Clark 1998).

The postdischarge period after psychiatric inpatient careis known to be a period of high suicide risk for these patients. Thus increased monitoring and care around the time of discharge may be beneficial in suicide prevention. Predictive risk factors in the discharged population at the individual level need to be further studied to identify high-risk subgroups (Goldacre et al 1993, Isometsä et al 1993, Gunnel & Frankel 1994, Dennehy et al 1996).

1.5.2.3 Restriction of suicide methods

Due to the overall small sizes of identified high risk populations, such as recently discharged psychiatric patients or parasuicidal people, it has been suggested that restricting the general availability of suicide methods may have the greatest potential to reduce suicide rates (Gunnel & Frankel 1994). The restriction of suicide methods as a means of suicide prevention is based on the idea that suicidal intention may vary over time within individuals (Murphy 1994). There is evidence that restricting the availability of methods for suicide can prevent some suicides. For example, barriers at commonly used high jumping sites (O´Carroll et al 1994), and more restrictive gun ownership laws have been found to decrease suicides by these methods (Marzuk et al 1992). However, such interventions may only be effictive temporarily as other methods are utilized instead (Marzuk et al 1992, Gunnel & Frankel 1994, Öhberg et al 1995, Isometsä & Lönnqvist 1998).

In psychiatric hospitals restricting available suicide methods in the ward environment may reduce suicides when treating patients (Goh et al 1989). Furthermore, the prescription of psychiatric medication should be carefully planned and monitored when treating high-risk groups: taking both the efficacy and toxicity of the specific agent must be taken into account, as well as limiting the quantities of toxic agents prescribed at one time (Gunnel & Frankel 1994, Jick et al 1995, Henry et al 1995, Isacsson et al 1997, Öhberg 1998).

2. SCHIZOPHRENIA

2.1 Concept of schizophrenia

The diseases of brain and mind have preoccupied humanity throughout history. Syndromes that can be recognized as forms of psychosis already appear in the writings of Hippocrates. Attempts to classify severe mental disorders, and later schizophrenia, have always attracted controversy about their nature. At the turn of this century Emil Kraepelin (1919) introduced the first widely accepted delineation for "dementia praecox" later to become schizophrenia. He introduced a dichotomy between conditions characterized by mental deterioration, and those with more periodic forms of mania and melancholia. In the beginning of this century Eugen Bleuler (1950) enlargened and deepened the ideas of Kraepelin by retaining the separation from manic depressive psychosis, while pointing out that affective symptoms could coexist during the disorder. He renamed the disorder as schizophrenia to highlight the primary symptomatology of severe fragmentation of thinking and personality (Andreasen 1995a, Wing 1995, Andreasen 1997).

Currently, schizophrenia is considered as a heterogeneous clinical syndrome with diverse disorders of perception, inferential thinking, goal-directed behavior, and emotional expression. None of the clinical features is pathognomonic of schizophrenia, and all known biological and psychological tests lack some sensitivity and specificity in the diagnosis. At the present, schizophrenia is a diagnosis of exclusion that also requires a combination of psychotic symptoms. The first step toward the diagnosis is to exclude psychoses with known organic causes. The second is to differentiate psychoses associated with affective disorders from that associated with schizophrenia.

The duration and relationship of mood symptoms to psychotic symptoms are considered to be distinguishable between affective and schizophrenic disorders. In schizophrenia, affective symptoms, if they occur, are considered to be of shorter duration than psychotic symptoms during the illness course (Carpenter & Buchanan 1994, Andreasen 1995a).

2.1.1 Current diagnostic classifications of schizophrenia

The concerns regarding inconsistency in reliability and validity of schizophrenia prompted the World Health Organization (WHO) and the American Psychiatric Association (APA) to produce criterion-based systems for diagnosing schizophrenia. The evolving concept of schizophrenia has been reflected in the changes in the different editions of these classification systems. For example, since the introduction of DSM-III in the 1980´s (APA 1980), followed by its further editions DSM-III-R (APA 1987) and DSM-IV (APA 1994), schizophrenia has been classified in narrower terms emphazing in its chronic course (Carpenter & Buchanan 1994, Andreasen 1997). The diagnostic system introduced by Feighner 1972, which was further elaborated into the Research Diagnostic Criteria (RDC; Spitzer et al 1977) also employs restrictive criteria, and has been widely used in research (Andreasen 1997).

The most recent versions of the currently used diagnostic classification systems are ICD-10 (WHO 1992) and DSM-IV (APA 1994). These diagnostic criteria have been widely accepted for the purposes of case identification and treatment. The symptoms and their mode of selection for schizophrenia diagnosis are similar in DSM-III-R, DSM-IV and ICD-10. For the diagnosis of schizophrenia, a combination of two symptoms of positive or negative type is required, but only one symptom if it is considered to be "typically" schizophrenic in the active phase of illness (APA 1987, WHO 1992, APA 1994). DSM-IV criteria require an increased duration of active-phase symptoms from DSM-III-R´s one week to one month. This change was suggested to reduce false positive diagnoses (in approximately 10%) due to substance-induced psychoses, and to increase compatibility with ICD-10 diagnostic criteria for research (WHO 1993). New course specifiers have also been adapted from ICD-10 to DSM-IV. The introduction of DSM-IV, however, has not been found to improve the agreement between DSM-III-R and ICD-10 (APA 1994, APA 1998). The main differences between the two systems are the requirement of an illness duration of six months in DSM-IV, compared to only one month in ICD-10, and of deterioration in functioning in DSM that is not mentioned in ICD. The DSM-classification of schizophrenia is thus narrower than that of ICD (Carpenter & Buchanan 1994, Andreasen 1995a, APA 1998).

2.2 Incidence and prevalence of schizophrenia

Different definitions of schizophrenia as well as varying methods of ascertainment between studies internationally make interpretations about the epidemiology of schizophrenia difficult. It is estimated using restrictive criteria for schizophrenia that the incidence of or morbidity risk for schizophrenia is 0.1/ 1000 population per year (range 0.07-0.14) (Häfner & an der Heiden 1997). Regional incidence rates appear to be stable over time. The main age range with the highest risk of schizophrenia is 20 to 35 years. Prevalence is a combination of both incidence and length of illness. Length of illness may vary due to differences in mortality rates and treatment, making prevalence comparisons difficult (Häfner & an der Heiden 1997). Estimates of life time prevalence of DSM-III or DSM-III-R schizophrenia in USA have been 1.1-1.3% (Keith et al 1991, Kendler et al 1996), while the range across studies and countries has been from 0.2% to 2.0% (APA 1994). In Finland, the prevalence of schizophrenia is estimated to be 1.3 % (Lehtinen et al 1990a, Hovatta et al 1997). In Finland and Sweden some local genetic isolate populations have been found to have a notably higher prevalence of schizophrenia (Böök et al 1982, Hovatta et al 1997).

Although the lifetime prevalence of schizophrenia is approximately only 1% in the general population of most countries, it imposes a large burden of suffering and need for services due to the enormous morbidity and long-term chronic disability of persons with it, but it also burdens carers, the health service and society at large (Murray & Lopez 1997). In UK in 1992/93, patient care, pharmaceuticals and social services for schizophrenia cost £810.0 million, accounting for 2.8% of all National Health Service budget. Besides, not all the costs of schizophrenia can be expressed in monetary terms, but are significant in terms of quality of life for the patient and carer (Knapp 1997). In Finland, about 20% of schizophrenic patients have been evaluated as having unmet needs related to the basic self-care skills needed for living independently in the community, and 25% of the patients´ unmet needs concerned assessment or intervention of psychotic symptoms. Two-thirds of the relatives experienced a burden related to the patients´ illness (Honkonen 1995).

2.3 Etiology of schizophrenia

The observation that schizophrenia is differentially distributed in certain populations has led to the identification of markers for high risks. *Genetic factors* interacting with the environment are an established marker for high risk of schizophrenia. A genetic contribution to schizophrenia has been shown in family studies, where biological relatives of patients are at increased risk of the disorder.

This is also supported by findings from adoption studies, as well as twin studies (McGuffin et al 1995, Cannon et al 1998). However, there is not yet information regarding the specific genetic base of schizophrenia. The problems that genetic studies face concern an inadequate description of the phenotype, and division of various phenotypes into relevant subgroups (Hovatta 1998).

Evidence of a *neurodevelopmental basis* for schizophrenia is substantial, and comes from findings of studies on maternal influenza during mid-pregnancy, gestational and obstetric complications, minor physical abnormalities, as well as neuropathological deviations in postmortem studies, structural and functional imaging studies in patients with schizophrenia. A higher frequency of winter and spring births among subjects with schizophrenia may reflect the higher rate of viral infections during the second trimester of maternal gestation. The findings suggestive of neurodevelopmental etiology in schizophrenia are still being challenged for definition of the nature of the primary etiological events and also to specify their relation to the evolution of symptoms and illness course (Mednick et al 1988, Waddington 1993, Isohanni et al 1995, Weinberger 1995).

Neurochemical theories of schizophrenia have long centered around altered dopaminergic function. Studies using positron emission tomography for visualizing the binding of antipsychotic drugs to dopamine receptors in the brain have given strong support for the hypothesis that neuroleptic action is related to interference with dopamine receptors in the brain. However, the precise role of dopamine in the pathophysiology of schizophrenia remains unclear (Sedvall & Farde 1995). There is much evidence also to suggest interactions between brain monoaminergic systems, whereby they can effectively alter dopaminergic activity (Owen & Simpson 1995). Clinical studies have yielded benefits of serotonin 5-HT_2 antagonists in schizophrenic patients, and the search for disturbed mechanisms of the serotonin system continues (Sedvall & Farde 1995). Glutamate is the primary excitatory neurotransmitter of pyramidal neurones within the cerebral cortex. It functions in integrating the cortical association areas. There is evidence for alteration in glutamatergic transmission in schizophrenia, too. Some neuropeptides have also been shown to interact with dopamine in the brain. Clinical evidence of therapeutic efficacy supporting the glutamate or cholecystokinin peptide hypotheses has not been validated (Owen & Simpson 1995, Sedval & Farde 1995).

Immunological basis for schizophrenia has been suggested on the basis of findings of abnormalities of immune function due to virus infection altering the genome, immunopathology activated by a viral infection, autoimmune mechanisms, and a secondary influence of maternal viral infection (Carpenter & Buchanan 1994).

Psychosocial theories of causal inferences in schizophrenia have been difficult to evaluate scientifically. There is considerable interest in how the psychosocial stresses and vulnerability to schizophrenia precipitate psychosis, emphasizing the importance of monitoring the patients´ reactions to their environment rather than childhood psychosocial factors (Carpenter & Buchanan 1994). Although the evidence for life events as an etiological factor for schizophrenia remains uncertain, the onset of the illness and changes in its symptoms have both been associated with stressful life events (Lukoff et al 1984, Norman & Malla 1993a, Bebbington et al 1993). The importance of life events in schizophrenia relapse may depend on patients´ characteristics, e.g. illness course, medication status, treatment status and social factors (Birley & Brown 1970, Leff 1973, Lukoff et al 1984, Ventura et al 1992, Hirsch et al 1996). Expressed emotion (EE) is a measure of negative emotional family environment (Vaughn & Leff 1976). This has been demonstrated to be a reliable psychosocial predictor of relapse in schizophrenia (Butzlaff & Hooley 1998), supported by the Finnish adoption study finding of higher rates of schizophrenia among adoptees of dysfunctional adoptive families (Tienari 1991).

2.4 Mortality in schizophrenia

Schizophrenia is associated with an increased risk of premature death from both natural and unnatural causes. It is not known how the mortality of schizophrenia has been affected by the introduction of antipsychotic drugs or by deinstitutionalization. The mortality rate of more recent cohorts with schizophrenia is lower than those of asylum cohorts, but due to the effects of confounding variables and selection bias, reliable comparisons cannot be made. Meta-analyses of follow-up mortality studies in schizophrenia since the 1950´s have reported that 38%-41% of the total excess mortality is accountable for by unnatural causes, which is 4.3 times more than expected (Brown 1997, Harris & Barraclough 1998). 28% of the excess mortality in schizophrenia, and 12% of all deaths were attributable to suicide, which is the largest cause of premature death in schizophrenia (Brown 1997). The risk of suicide in schizophrenia has been estimated to be 8.4 - 9 times that expected in follow-up (Brown 1997, Harris & Barraclough 1998), while the excess natural mortality may be explained by unhealthy diet, lack of exercise, or frequent use of tobacco and alcohol (Simpson 1988, Brown 1997).

2.5 Outcome in schizophrenia

2.5.1 Outcome and phenomenology of schizophrenic symptoms

Signs and symptoms are essential to the diagnosis of schizophrenia in most nosologic systems. In DSM- III-R, DSM-IV and ICD-10 the predominant cross-sectional qualitative symptoms of schizophrenia are further classified as subtypes. By these classifications, subtypes may change over time. The distinction in severity tends to be most robust between paranoid and disorganized subtypes. Despite the wide use of these traditional subtypes , only some characteristics of cross-sectional psychopathology have significance in the long-term outcome of schizophrenia. In general, these characteristics have yet to prove useful for the purposes of treatment, explaining pathophysiologic processes, or genetics (Carpenter & Buchanan 1994, Möller & Zerssen 1995, Liebermann 1995).

In the 1970s, Strauss and coworkers prompted the revival of of the ideas of a 19th century neurologist, Jackson, about symptom distinctions in schizophrenia (Strauss et al 1974). They proposed three symptom manifestations in schizophrenia to be relevant for prognosis and outcome: positive symptoms, negative symptoms, and disordered relationships. Crow´s formulation of positive/negative syndrome hypothesis attracted more attention in 1980 (Crow 1980). It produced many studies that subsequently refined the model to include the third symptom constellation of disorganization. This three symptom domain model has later been validated (Liebermann 1995, Andreasen et al 1995b). Positive symptoms include hallucinations, and delusions; disorganized symptoms often included under positive symptoms comprise disorganized speech/ positive formal thought disorder, disorganized behavior, and inappropriate affect, and negative symptoms include anhedonia, avolition, affective flattening and alogia. The negative symptom domain has been further elucidated to include a group of primary negative symptoms, " a deficit state" (Carpenter et al 1988). There is already some evidence for the symptoms in each domains are differentially associated with specific neurobiological, illness course, and treatment response measures (Liebermann 1995, Davidson & McGlashan 1997, Ratakonda et al 1998). However, the specificity of these symptom domains for schizophrenia diagnosis has recently been questioned (Ratakonda et al 1998).

2.5.2 Outcome and premorbid, illness onset, and illness course measures

It is difficult to compare follow-up studies of schizophrenia due to differences of method, and to varying diagnostic criteria, outcome definitions, instrumentation, strategies for dealing with missing and deceseased subjects, protocols for collecting of follow-up information, and treatment eras. In addition, when course is an element of the definition, circular reasoning may take place (Strauss & Carpenter 1972, Angst 1988, McGlashan 1988).

A review of follow-up studies within the last 8 years concluded that there seems to be heterogeneity in long-term outcome for individuals with schizophrenia within each study sample, regardless of treatment setting. (Davidson & McGlashan 1997). The onset may be abrupt or insidious, but the majority of the patients show some type of prodromal phase of illness, and eventually the appearance of some active-phase symptoms marks the disturbance as schizophrenia. Some persons display exacerbations and remissions, while others remain chronically ill. If deterioration occurs, it does so in the early years, with stabilization of impairment after 5 to 10 years of illness and some gradual improvement subsequently (Ciompi 1980, Carpenter & Kirkpatrick 1988, Breier et al 1991). An active disease and deterioration process seems to be established by the onset of psychosis. Late in the illness there is a tendency for the psychotic symptoms to become less intense. In 5 to 15 % of patients, a relatively severe psychosis is continuous (Carpenter & Buchanan 1994, Davidson & McGlashan 1997). These findings on illness course are also in line with findings in a follow-up study of a Finnish DSM-III schizophrenia sample (Kuusi 1986).

Specific psychopathological predictors seem weaker in their predictive power for the overall outcome than the clinical history and social adaptation. The favourable prognostic significance of better premorbid social and work functioning, as well as acute illness onset, older age at onset, and precipitating factors at the time of illness onset have been reported by several studies (Ram et al 1992, Möller & von Zerssen 1995, Davidson & McGlashan 1997). McGlashan (1986) suggested that outcome in schizophrenia also varies at different follow-up points. In the first decade of follow-up premorbid functioning, in the second decade family functioning, and in the third decade and beyond family genetics, have the greatest impact on outcome . The sociocultural setting was the best predictor of outcome in the WHO studies at 2- and 5-years follow-up. A more favourable outcome for individuals with schizophrenia in the non-industrialized than industrialized world was reported (Leff et al 1992), although this finding was later questioned (Edgerton & Cohen 1994).

2.5.3 Outcome and comorbidity

2.5.3.1 Depressive syndrome

Mood disorders are conventionally viewed as nosologically distinct from schizophrenia, yet depressive signs and symptoms are evident during the course of schizophrenia. In a review by Siris (1995), estimates of depressive syndrome during the illness course of schizophrenia vary from 7% to 65% depending on the patient sample and criteria used for definition of depression, the modal rate being at 25 %. The rate of depressive syndrome has been estimated to range within 25% -50% among patients in the active phase of illness (Barnes et al 1989). First episode schizophrenia patients in the active illness phase are reportedly frequently depressed, the depression often resolving as the psychosis remits (Leff et al 1988, Koreen et al 1993). Depressive symptoms during the acute phase and short term follow-up in the first episode were more severe than among a multiepisode group of schizophrenic patients (Addington et al 1998).

Depressive symptoms have also been reported to occur as a "postpsychotic depression" during remission from an acute episode (McGlashan & Carpenter 1976, APA 1994). Patients on maintenance neuroleptic treatment for schizophrenia and having comorbid depressive syndrome in the postpsychotic illness phase have been found to have higher rates of relapse (Johnson 1988), suicide attempts and suicide (Roy et al 1983a, Drake et al 1984). However, somewhat contrasting with this, affective symptoms during the illness course appear to be predictive of a more favourable outcome overall (Davidson & McGlashan 1997). This discrepancy may be related to the stage of illness at which the patients were assessed (Koreen et al 1993).

2.5.3.2 Psychoactive substance use disorders

Psychoactive substance use disorders are common comorbid conditions in patients with schizophrenia. In clinical patient samples the life time prevalence of DSM-III-R diagnosis of alcohol use disorders have been estimated at about 50%, with DSM-III-R current alcohol use disorders affecting among 18% - 35% (Mueser 1990, Drake et al 1990, Fowler et al 1998). Alcohol use disorders have often been associated with various poor outcomes: treatment non-compliance, more frequent relapses and hospitalizations, depressive symptoms, suicide, violent and criminal behavior, homelessness, and increased rates of tardive dyskinesia, although the direction of influence is unknown in these (Rich et al 1988, Drake et al 1990, Eronen et al 1996a, Fowler et al 1998). However, some studies have not found a high rate of substance dependence or abuse to be

strongly associated with adverse illness course in schizophrenia. This has been explained by selection biases in some clinical patient samples towards more negative outcomes (Fowler et al 1998).

2.5.4 Outcome and treatment of schizophrenia

In follow-up studies, good outcome in schizophrenia has often been predicted by treatment measures: shorter duration of first hospitalization, shorter duration of untreated illness, and rapid treatment response (Ram et al 1992, Möller & von Zerssen 1995, Davidson & McGlashan 1997). Research has started to focus on early detection and intervention during or prior to the first schizophrenia episode due to the mounting evidence for the presence of an active illness and deterioration process early in the course of illness, and for the negative impact of untreated psychosis on outcome (Davidson & McGlashan 1997). While medication generally produces a faster remission of the illness with a considerable decrease in the severity of positive symptoms, the majority of patients cannot be considered cured (Hirsch & Barnes 1995). Despite routine use of neuroleptics and other contemporary therapies, reported average clinical outcomes have worsened in the past decade. This may be due to diagnostic changes, biased availability of more chronic or severe cases in follow-up studies as an effect of responsiveness to treatment, or changes in treatment organizations (Hegarty et al 1994).

The general goals of treatment are to decrease the frequency, severity, and psychosocial consequences of the episodes in order to maximize psychosocial functioning between them. The specific goals of the treatment depend on the phase of the illness and other specific characteristics of the patient (APA 1997). In line with this, the Finnish National Schizophrenia Project has emphasized the "need-adapted" treatment of schizophrenic psychoses, to stress the importance of integrating various treatment modalities according to both the patients´ and their families actual and changing needs (Alanen et al 1991, Alanen 1997).

2.5.4.1 Antipsychotic treatment

Conventional antipsychotic medications act by blocking dopamine D_2-receptors at high rates throughout the brain, and their therapeutic activity is presumably related to such blockade in the mesolimbic system. With conventional dopamine-blocking antipsychotics about 30% - 40 % of the patients have an inadequate or poor response (Pickar 1995), although the percentage would be considerably higher if the definition of poor treatment response also included negative symptoms

and cognitive dysfunction. A smaller proportion of patients (5% - 20%) have been refractory to treatment from their first episode of illness, whereas the remainder develop resistance over the course of their illness (Lieberman et al 1998, Meltzer et al 1998a). All types of acute extrapyramidal syndromes have been common in 2% to 90% of patients, whereas the prevalence of tardive dyskinesia occurring during extended neuroleptic therapy is estimated to be 15% - 20% (range 0.5% - 100%)(Casey 1991).

The comparison of clinical efficacy of various antipsychotic drugs faces the familiar problems of converting dose equivalents (Rey et al 1989). In subsequent studies, no significant differences in the efficacy of the various conventional neuroleptics have emerged (Kane 1996). However, in patients who have been treatment resistant for conventional neuroleptics, an effective response to clozapine has been reported in 30% - 61% (Kane et al 1988, Lieberman et al 1994). During the 1990s clozapine-like "atypical antipsychotics" that are less likely to produce neurological side-effects have been developed. This characteristic is suggested to be due to the balance of low D_2/ high 5-HT_2A receptor antagonism. There is a hope that better tolerance of these drugs and maybe better efficacy in preventing relapses and in reducing negative symptoms would improve the overall outcome in schizophrenia (Huttunen 1995, DeQuardo & Tandon 1998).

There is plenty of evidence of the short-term efficacy of both conventional and atypical antipsychotics is in reducing positive symptoms, but it is quite limited for other outcomes (Schooler 1997). Approximately 60% of patients in the acute illness phase treated with conventional antipsychotic medication improve substantially, compared to only 20% of patients treated with placebo (Gilbert et al 1995). Long-term efficacy has usually been measured by reductions in either relapse rate or rehospitalization rates among treated patients over the course of several years. Double-blind studies show that 30-80% of patients relapse if they are untreated with conventional antipsychotics in a follow-up of one to two years (Kane et al 1982, Crow et al 1986, Jolley 1990, Herz et al 1991, Hogarty & Ulrich 1998). A meta-analysis of neuroleptic withdrawal in schizophrenic patients showed relapse rate increasing with the length of follow-up (Gilbert et al 1995). There is not yet enough available evidence to evaluate the long-term efficacy of atypical neuroleptics in the outcome of schizophrenia (Schooler 1997). There is little evidence that adding adjunctive agents to standard neuroleptics will dramatically change the somatic treatment of schizophrenia. Adjunctive agents that have shown some promise are benzodiazepines, lithium, and carbamazepine. Electroconvulsive treatment (ECT) is most likely to benefit those with catatonia, affective symptoms, or a short duration of illness (Johns & Thompson 1995, APA 1997).

Effectiveness in practice may be substantially less than efficacy in clinical trials, possibly owing to patient heterogeneity, prescribing practices, and noncompliance (Dixon et al 1995a). In the clinical setting, the individual patient´s acceptance or rejection of prescribed medication has often been the stongest determinant of the treatment´s effectiveness. Noncompliance is a multifactorial problem with an estimated prevalence of 50% - 75%. It is affected by psychopathology, medication related factors, available social support, substance abuse comorbidity and quality of therapeutic alliance in patients with schizophrenia (Wilson & Enoch 1967, McEvoy et al 1984, Bartkó et al 1988, Buchanan 1992, Bebbington 1995, Weiden et al 1995, Fenton et al 1997a), and accounts for at least 40% of all relapses in schizophrenia (Weiden & Olfson 1995).

2.5.4.2 Psychosocial treatment

Although pharmacotherapy is effective for treating acute symptoms and reducing vulnerability to relapses, it does not effectively alleviate psychosocial deficits in schizophrenia, such as impairments in social skill. Behavioral family therapy or psychoeducation is the most extensively studied area among the psychosocial treatment modalities in schizophrenia (Penn & Mueser 1996). There is substantial evidence that long term psychoeducational family interventions may reduce the rate of patient relapse. These interventions may also improve patient functioning and family well-being (Dixon & Lehman 1995b, Penn & Mueser 1996). The role of EE as a significant factor in relapse of schizophrenic illness supports the importance of psychosocial treatments (Butzlaff & Hooley 1998). There have been few controlled trials of individual or group psychotherapies for persons with schizophrenia. Such studies are compromised by methodological problems that limit their generalizability. Reality-orientated approaches appear to be superior to dynamic, insight-orientated psychotherapies, but further research is needed (Scott & Dixon 1995). Research on longterm psychosocial skills training models shows that target skills can be trained and maintained over time, but the clinical benefit of these treatments still needs to be demonstrated (Scott & Dixon 1995, Penn & Mueser 1996). There has been some promise of efficacy for cognitive therapy techniques in reducing residual delusionally psychotic symptoms, but inconsistent findings in improving information-processing skills (Penn & Mueser 1996). It has been suggested that psychosocial treatment would have a strong additive effect on reducing relapse rates in schizophrenia when used with maintenance drug therapy, but that without medication it would be as ineffective as placebo (Hogarty & Ulrich 1998).

2.5.4.3 Treatment of comorbidity

The etiology of depression in schizophrenia is likely to be complex and heterogenous. The treatment of depression in schizophrenia is still quite controversal. It has been shown that acute treatment with conventional neuroleptics has often improved the mood symptoms during the active illness phase (Remington 1995). Atypical antipsychotic agents have indicated efficacy in both depressive and psychotic symptoms during the active illness course (Tran et al 1997), and also improved efficacy compared with the conventional antipsychotics (Tollefson et al 1998). However, up to 25% of patients have shown depression independent of acute exacerbation (Siris 1995). When depression is considered primary i.e. not related to side-effects of antipsychotic treatment, to organic factors, or to negative symptoms, some groups of patients are likely to benefit from antidepressants as adjunctive treatment in the postpsychotic phase of the illness (Siris et al 1987, Siris 1996). Lithium may have efficacy in the treatment of postpsychotic depression, although research evidence for this is sparse (Siris 1996). Desipramine has been reported to improve chronic anxiety and depression in schizophrenia (Hogarty et al 1995). ECT has also shown some efficacy in the treatment of affective symptoms in schizophrenia (Johns & Thompson 1995).

Clozapine treatment has been noted to reduce substance abuse among treatment resistant patients, suggesting a need for further study (Buckley et al 1994).

2.5.4.4 Deinstitutionalization

Since the 1950s there has been an international trend to reduce mental hospital treatment and expand community care. This has been supported by various arguments for better quality of life among the patients with schizophrenia. The development of local mental health centers near patients homes started at the same time, with recognition of the need for a wide range of services to meet the needs of the mentally ill (Muijen & Hadley 1995). However, it seems, that with seriously ill people, particularly those with schizophrenia, have had difficulties engaging with the community based services (Bacharach 1982). There has also been concern that the reduction in hospital care has been too rapid as reflected in homelessness, increased crime rates, revolving door admission patterns, and the consequences of these (Leff 1993, Lamb 1993). It has been suggested furthermore, that the reduction of psychiatric hospital beds has led to shorter and more frequent admissions, and thus to an increased risk of suicide (Rossau & Mortensen 1997).

On the other hand, according to a review of studies of varying treatment models, suggested that good community services can reduce the number of hospital admissions and length of stay, and are preferred by users and carers. However, in the absence of adequate resources community care exposes discharged patients to disadvantages (Muijen & Hadley 1995). These are supported by the the evaluations of discharged patients and their care by studies from England (Leff et al 1996). It has also been suggested that in Finland the deinstitutionalism process has been succesful in that patients with schizophrenia have not been neglected (Salokangas & Saarinen 1998, Tuori et al 1998). However, in Finland the deinstitutionalization process has began a lot later, during the 1980s, than in many other western countries, providing a substantially shorter follow-up time for patient outcomes (Salokangas & Saarinen 1998).

3. SUICIDE IN SCHIZOPHRENIA

3.1 Suicide mortality in schizophrenia

The risk of suicide in schizophrenia is high; in follow-up studies it is estimated that 10%-13% of all sufferers commit suicide (Caldwell & Gottesman 1992, Brown 1997). Suicide rates in schizophrenia vary in follow-up mortality studies between 147-750 per 100 000 persons per year (Evenson et al 1982, Morrison 1982, Wilkinson 1982, Pokorny 1983, Lim & Tsoi 1991). However, a recent methodological report claimed that the life time figures for suicide rates are often quoted too high in the literature for mental disorders. In this article the life time risk for suicide in schizophrenia was estimated at 4% (Inskip et al 1998). Several factors contribute to variance in suicide rates across studies, including age and phase of illness of subjects included in the study, duration of follow-up, source of subjects, and diagnostic methods. Suicide rates are consistently found to be higher among men than women with schizophrenia (Brown 1997, Räsänen et al 1998).

The prevalence of schizophrenia among general population suicides has varied from 2% to 12% (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Hagnell et al 1979, Chynoweth et al 1980, Arato et al 1988, Rich et al 1988, Henriksson et al 1993, Cheng 1995). The standardized mortality ratio (SMR) represents the risk of death compared with the general population of similar age and sex. In recent meta-analyses, SMRs for suicide in schizophrenia were shown to be 8.4 -

9.0 times higher than in the general population (Brown 1997, Harris & Barraclough 1997, Harris & Barraclough 1998). Some studies have reported higher SMRs for women than men with schizophrenia (Allebeck & Wistedt 1986a, Black & Fisher 1992, Mortensen & Juel 1993).

High suicide mortality in schizophrenia reflects the great burden of the illness on the patient as well as the consequences for their families. T he monetary costs of suicidal behavior in schizophrenia are also high (Wyatt et al 1995).

3.2 Previous research on suicide in schizophrenia

In 1911 Eugen Bleuler (1950) described the "suicidal drive" to be the most serious of schizophrenic symptoms. Although the estimated life time suicide risk in schizophrenia approaches that for affective disorders, the study of suicide in schizophrenia has not received comparable attention to that in affective disorders (Miles 1977, Tsuang & Woolson 1978). As in affective disorders, knowledge about suicide related factors in schizophrenia is important for obtaining better quality of care in terms of reducing the rate of suicidal behavior in schizophrenia. Moreover, in the search for models of causative and protective factors for suicide and suicidal behavior, focusing the studies on all high-risk groups is important.

The classification of suicide in psychoses with command hallucinations or bizarre delusions has been suggested to be even more difficult than among non-psychotic states due to problems in determining the intentionality of self-destructive deaths (Banen 1954). Suicide during psychoses may be more often classified as accidental or undetermined deaths (Weiden & Roy 1992). However, in a meta-analysis of mortality in mental disordes, SMRs (observed number of deaths divided by expected number of deaths and multiplied by 100) for violent deaths other than suicide in schizophrenia (227, 95% CI 207-248) were found to be somewhat similar to those in major depression (233, 95% CI 166-318), but smaller than in alcohol dependence or abuse (389, 95% CI 368-412; Harris & Barraclough 1998).

Many studies of clinical characteristics of suicide victims with schizophrenia have been compromised by the relatively small numbers of subjects and thus inadequate representation of many clinically important subgroups for comparisons, the heterogenous diagnostic criteria used, selection of suicides among clinical or regional settings and data based mainly on patient records. Only eight studies (Table 1.) have so far investigated completed suicides using record data and

samples of 15 or more suicide victims with DSM-III or DSM-III-R schizophrenia (Roy 1982, Breier & Astrachan 1984, Drake et al 1984, Allebeck et al 1987, Cheng et al 1990, Hu et al 1991, Lim & Tsoi 1991, Fenton et al 1997b, Peuskens et al 1997). However, four of these studies also included schizo-affective disorder (Breier & Astrachan 1984, Allebeck et al 1987, Fenton et al 1997b, Peuskens et al 1997) and three included schizophreniform disorder in the sample (Breier & Astrachan 1984, Allebeck et al 1987, Fenton et al 1997b). Four ICD-8 or ICD-9 based studies of clinical characteristics of suicide victims with schizophrenia with a sample size of 15 or more have been published (Wilkinson & Bacon 1984, Wolfersdorf et al 1989, Cannon et al 1991, Rossau & Mortensen 1997). Psychological autopsy studies of the general population have not been able to investigate the clinical characteristics of suicide victims with schizophrenia due to small sample numbers varying from 3 to 17 victims (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Chynoweth et al 1980, Mitterauer 1981, Arato et al 1988, Rich et al 1988, Henriksson et al 1993, Cheng 1995, Saarinen 1995, Foster et al 1997).

In the 1960s and 1970s three studies applied the psychological autopsy interview method to investigate suicide among clinical samples of patients with schizophrenia, as diagnosed with varying criteria (Farberow et al 1961, Virkkunen 1974, Yarden 1974). Farberow et al (1961) studied suicide in 30 males with schizophrenia (non-defined criteria) that occurred during hospital treatment in 1955-58 in USA. A study from New York described DSM-II schizophrenia patients at a clinical regional mental health care setting; 20 suicides occurred during the five year follow-up after inpatient treatment (Yarden 1974). Virkkunen (1974) studied 82 suicides with schizophrenia and paranoid psychoses that occurred among psychiatric patients during 1969 - July 1971 in the Uusimaa, Finland (province with the highest number and density of people with a population of 1,014,000 inhabitants in 1969). In this study schizophrenia diagnoses were based on 10 typical symptoms.

3.3 Risk factors for suicide in schizophrenia

The clinical retrospective studies with sufficient numbers of suicide victims for individual level analyses have been mainly cross-sectional evalutions of factors or markers at index hospitalization, or at other clinical reference points using record based data. Thus, the current knowledge of time related suicide risk factors during the longitudinal illness course among persons with schizophrenia is very limited. Further, given the broad scale of symptoms, outcomes, and heterogeneity of illness courses within and between persons with schizophrenia, very little is known about possible varying

suicide risks among specific subgroups of patients. Compared to affective disorders, very little is known about possible illness-specific suicide risk factors in schizophrenia (Haas 1997).

3.3.1 Sociodemographic risk factors for suicide in schizophrenia

Among living subjects with schizophrenia female sex and older age at onset are related to characteristics of good outcome (Bardenstein & McGlashan 1990). As in the general population, male sex (but younger age) is usually associated with heightened suicide risk in schizophrenia (Caldwell & Gottesman 1990, Newman & Bland 1991). In the previous studies using DSM-III or DSM-III-R, the range of mean age was 23.3 years to 41 years at the time of suicide (Roy 1982, Breier & Astrachan 1984, Drake et al 1984, Cheng et al 1990, Hu et al 1991, Lim & Tsoi 1991, Fenton et al 1997b). However, the overall effect of high suicide risk at younger age has been suggested to be less important than other risk factors such as male sex and clinical illness history (such as: previous suicide attempts, depression, severe physical disorders, and psychiatric hospitalization patterns) (Rossau & Mortensen 1997). Knowledge about the association and interaction of age and sex with other clinical characteristics in suicide is still lacking in schizophrenia, because most studies have been compromised by the relatively small numbers of subjects and thus inadequate representation of women as well as elderly persons for comparisons.

Persons with schizophrenia are often unmarried and living alone, which applies more often to men than women (Andia & Zisook 1991). In schizophrenia, the relative risk of suicide among single males has not been found to be elevated (Breier & Astrachan 1984, Drake et al 1984), but among women with schizophrenia unmarried, divorced, or widowed status raised the risk of suicide by almost ten times the expected (Allebeck et al 1987), in line with the general population trend of marital status and suicide.

3.3.2 Illness related risk factors for suicide in schizophrenia

3.3.2.1 Schizophrenia subtypes and symptoms

Earlier descriptive studies suggested an association of suicide risk with paranoid features of schizophrenia (Drake et al 1985), with support from a later controlled study by Fenton et al (1997b), that also indicated for high suicide risk in DSM-III-R paranoid type compared to other types of schizophrenia. The positive symptoms of suspiciousness and delusions in particular have been associated with an elevated long-term risk of suicide in follow-up (Fenton et al 1997b). There

is some evidence for lowered suicide risk in long-term follow-up of patients with a prominent negative symptom component of schizophrenia, and particularly for the deficit type (Fenton et al 1997b), which is supported by a similar trend in another follow-up study (Black & Fisher 1992).

3.3.2.2 Illness duration, phases, and course

Illness durations of five to ten years tend to characterize many suicide victims with schizophrenia (Caldwell & Gottesman 1990). Suicide risk in cohorts of first-admission schizophrenic patients was particularly elevated during the first year after the index admission (Mortensen & Juel 1993). However, the follow-up time of the subjects and the selection of patients from clinical samples may affect these findings, since in long-term follow-up, elevated suicide mortality throughout the whole span of the illness was found (Tsuang & Woolson 1978).

During the course of schizophrenia three distinct phases have been suggested: early phase with a deteriorating course, middle phase with relatively stable illness course, and later phase that may be characterized by gradual improvement. Different illness phases during the course of schizophrenia have also been related to varying predictors of outcome (McGlashan 1986, Breier et al 1991). The effect of illness duration with its different phases has not been studied in relation to clinical characteristics and their association with suicide risk.

Little is known about the course specifiers in schizophrenic suicide due to the small numbers of suicide victims in most studies, and also to the frequent selection of patients from hospital settings for follow-up. It has been suggested that suicide risk is higher in chronic RDC schizophrenia with the gradual type of onset than in other types (Westermeyer et al 1991). Roy (1982) found chronic illness course with acute exacerbations to increase the risk of suicide four times the expected rate. In line with this, Rossau & Mortensen (1997) found suicide risk to rise with the number of psychiatric admissions during the last year. Also, among parasuicidal schizophrenic patients suicidal behavior was found to occur in the initial phase of psychosis or during subsequent exacerbations, and occurred more frequently among patients with recurring or periodic type of illness (Planansky & Johnston 1971).

3.3.3 Comorbidity and suicide risk in schizophrenia

Comorbid depressive symptoms are among the most frequently cited features of schizophrenic patients who commit suicide according to the majority of studies over the past 30 years (Galdwell

& Gottesman 1990). The estimates for recent depressive symptoms among suicide victims with DSM-III or DSM-III-R schizophrenia from patient records of last contact before suicide have varied from 9% - 80 %. Depression has consistently been found to increase the risk of suicide in schizophrenia (Roy 1982, Drake et al 1984, Cheng et al 1990, Hu et al 1991, Peuskens et al 1997). The large range of reported depressive symptoms is likely to be explained by varying patient samples, classification of depressive states, and data of varying accuracy and detail in patient records. At index hospitalization, the proportion of schizophrenic patients with depressive symptoms among those who committed suicide (12 %) in follow-up was the same as among those who did not (Lim & Tsoi 1991). A history of depressive episodes has been reported among 27% - 58% , which is significantly more often than among living comparison patients with schizophrenia (Roy 1982, Cheng et al 1990, Hu et al 1991), although this is not found in all studies (Allebeck et al 1987). The proportion of suicide victims with schizophrenia suffering from current depressive symptoms at the time of suicide is not yet known.

In contrast to depressive syndrome, the findings from substance abuse and suicide risk in schizophrenia are less consistent. Substance use disorder rates are infrequently reported in studies of completed suicides in schizophrenia, and those that have been reported vary greatly, maybe due to selection characteristics of regional and clinical populations. Drake et al (1984) reported a history of substance abuse among a smaller proportion of suicide victims (33%) than nonsuicides (44%), supported by a similar finding of less (6% versus 23%) from a study of hospital suicides in patients with schizophrenia at admission (Wolfersdorf et al 1989). In line with this, Rossau & Mortensen (1997) did not find comorbid substance abuse relating to high suicide risk when some other risk factors where taken into account. Only Allebeck and coworkers (1987) have found a history of alcohol abuse (19%) to increase the risk for suicide in schizophrenia, but only among male patients. Rich et al (1988) reported a high rate (73%) of current substance abuse among suicide victims with schizophrenic psychoses (N=8/11) in San Diego, USA. A higher rate of comorbidity with substance abuse was reported among suicidal patients with schizophrenia than among non-suicidal controls (Dassori et al 1990). As for current depressive symptoms, there is little information about the rate of current substance abuse among suicide victims with schizophrenia. The comorbidity patterns possibly vary with age, sex and their interaction among suicide victims with schizophrenia, but these are still largely unknown.

The extent and consequences of comorbidity with physical illness in patients with schizophrenia are generally underrecognized, and it has been suggested that they receive less than adequate health care for their medical problems (Jeste et al 1996). Natural causes account for 59% of the excess

of illness pathology was associated with suicidality, including both suicidal thoughts and suicide attempts, whereas the risk for suicidality was lower among patients with no awareness of these aspects. However, general awareness of having a mental disorder did not predict suicidality.

3.3.6 Adverse life events and suicide in schizophrenia

The onset of schizophrenia and changes in its symptoms have both been associated with stressful life events (Lukoff et al 1984, Norman & Malla 1993a, Bebbington et al 1993). Compared to the general population, the impact of life events on suicide among schizophrenic subjects has been little explored (Johns et al 1986). Only seven retrospective studies have reported on life events and completed suicide in schizophrenia (Yarden 1974, Shaffer et al 1974, Breier & Astrachan 1984, Rich et al 1988, Salama 1988, Cheng et al 1989, Modestin et al 1992b). Subjects who had experienced life events prior to suicide varied from 12% to 64%. This large variation is probably partly caused by methodological variations between the studies. Studies involving comparison groups have reported fewer life events for suicides in schizophrenia, compared with both psychotic and non-psychotic non-schizophrenic suicides (Breier &Astrachan 1984, Rich et al 1988). No significant differences in life events between living and completed suicide patients with schizophrenia have been found (Shaffer et al 1974, Salama 1988, Modestin et al 1992b). However, knowledge about life events and suicide among subjects with schizophrenia remains sparse, especially in different illness phases.

3.3.7 Familial factors and suicide in schizophrenia

Family history of suicide has been shown to associate with suicide among psychiatric patients, particularly in those with depression, but the evidence for higher familial suicide risk in schizophrenia has not been very strong (Roy 1983b, Tsuang 1983). Studies on clinical patient samples have not found significant differences between living patients and suicide victims with schizophrenia, although underreporting may have caused bias in these studies (Roy 1982, Breier & Astrcahan 1984, Drake et al 1984, Cheng et al 1990, Hu et al 1991).

3.3.8 Biological markers for suicidal behavior in schizophrenia

The evidence for neurochemical abnormalities specific to suicide in schizophrenia is more limited than in suicide and depression. There is preliminary evidence that neurochemical alterations may have a role in suicidality among persons with schizophrenia, although the findings have been partly contradictory. There is some evidence that reduced 5-HIAA in cerebrospinal fluid is also associated with suicidal patients with schizophrenia (Cooper & Kelly 1992, Mann & Arango 1992). Indirect support for serotonergic dysfunction in suicidal behavior of schizophrenia has been suggested by findings of an association between rapid eye movement (REM) sleep abnormalities and suicidal behavior in schizophrenia (Keshavan et al 1994, Lewis et al 1996). The results from the studies of dopamine and benzodiatzepine receptor densities among suicide victims with schizophrenia do not obviously support the modifications of these receptor systems being related to suicide, but rather the neuroleptic treatment effects (Ruiz et al 1992, Pandey et al 1997). Aggressive and impulsive behavior is often associated with self-destructive behavior, and there is some indirect evidence for biological linkage in these (Linnoila & Virkkunen 1992, Marzuk 1996). Schizophrenia has been shown to raise the risk for both aggressive (Eronen et al 1996b) and suicidal behavior (Allebeck & Wistedt 1986, Räsänen et al 1998). However, the biological basis for linkage of these theories in schizophrenia remains unresolved, and it is likely to interact with environmental factors (Marzuk 1996).

3.4 Suicide prevention in schizophrenia

The knowledge of risk factors for suicide in schizophrenia is still quite limited and somewhat inconsistent. The studies are characterized by small numbers of suicide victims, which creates difficulties in making general inferences about the findings. The heterogeneous nature of the long-term illness is likely to imply several high-risk subgroups relating to sex, age, illness characteristics and life circumstances though, so far relevant data on this are very sparse. The knowledge of proximate risk factors for suicide is also limited in schizophrenia, compared to that in affective disorders. Effective reduction of suicide mortality in schizophrenia is still likely to remain very difficult due to these shortcomings in relevant research.

In contrast to non-psychotic mental disorders, the majority of people with schizophrenia have been in contact with health care and also received treatment during their illness (Lehtinen et al 1990a, Regier et al 1993). Measures for suicide prevention in schizophrenia are suggested on the basis of

the evidence on treatment related factors and also by the suicide methods used by people with schizophrenia. As with psychiatric suicide prevention in general, treatment related issues are the only feasible targets for suicide prevention in schizophrenia at the moment.

3.4.1 Treatment related factors and suicide risk in schizophrenia

3.4.1.1 Drug treatment

Although most suicide victims with schizophrenia have been receiving antipsychotic medication at the time of suicide (Yarden 1974, Roy 1982, Drake et al 1984, Wilkinson & Bacon 1984). However, the role of such treatment in suicides has remains unclear (Johns et al 1986). Case reports have suggested that high doses of neuroleptics may associate with suicidal behavior via side effects, especially akathisia (Shear et al 1983, Schulte 1985, Drake & Ehrlich 1985), while some controlled studies in living patients have suggested an association of neuroleptics with depressive states (Siris 1996). Dose comparisons of prescribed neuroleptics between suicide victims and living patients with schizophrenia have yielded inconsistent findings. It has been suggested that the reason for victims found to have received higher doses may be explained by more severe illness, whereas victims with lower doses may have had more prevalent depressive symptoms (Cohen et al 1964, Warnes 1968, Roy 1982, Hogan & Awad 1983, Cheng et al 1990, Taiminen & Kujari 1994). This disparity in dosing findings may be due to the selection of patients in different clinical settings. Furthermore, the adequacy of antipsychotic treatment in terms of victim´s current psychopathology has not been explored in previous studies. There are no studies addressing antidepressant medication and suicide risk in schizophrenia (Kane 1996).

There is some suggestion that treatment related factors protect against suicidality and suicide, at least in certain patient subpopulations. A register based linkage study on clozapine use and mortality showed that among patients with current clozapine treatment the risk of suicide was smaller than among past clozapine users (Walker et al 1997). Somewhat similarly Meltzer et al (1995) found that the risk of suicidal ideation and suicide attempts decreased during maintenance treatment of clozapine among treatment resistant patients with schizophrenia. It remains unknown, whether the specific nature of this suicide rate reducing effect relates to the treatment setting, selection of patients, and/or drug efficacy.

Among factors influencing treatment outcome, non-compliance has rarely been addressed in the context of suicide, although many factors associated with drug non-compliance have also been

related to suicide in schizophrenia: a negative attitude toward treatment, compulsory admission to hospital, paranoid symptoms, high level of positive symptoms, and comorbid alcoholism (Wilson & Enoch 1967, McEvoy et al 1984, Bartkó et al 1988, Pan & Tantam 1989, Buchanan 1992, Allebeck et al 1987, Fenton et al 1997a). A study by Peuskens et al (1997) reported an increased risk of suicide among non-compliant than compliant patients in a young adult patient cohort. There is no knowledge of the role of treatment refractoriness in completed suicide in schizophrenia. However, it has been suggested that treatment resistance may associated with heightened suicide risk (Haas 1997, Meltzer 1998b). This has been supported indirectly by preliminary data findings from the University of Pittsburgh study, which reported that when parasuicidal patients with schizophrenia were hospitalized for acute care, they had taken higher doses of antipsychotics than other patients, and had had more frequent admissions compared to non-suicidal patients (Haas 1997). Findings from another study comparing neuroleptic-responsive and neuroleptic-resistant patients showed however no difference between the groups in terms of a history of suicidal behavior (Meltzer & Okayli 1995).

3.4.1.2 Treatment phase

Suicide in people with schizophrenia has usually occurred in the context of psychiatric treatment. In clinical samples of suicide victims with schizophrenia, a high proportion (10-44%) have occurred during inpatient treatment (Yarden 1974, Roy 1982, Drake et al 1984, Wilkinson & Bacon 1984, Allebeck et al 1986, Hu et al 1991). For suicide prevention in psychiatric care, patients with schizophrenia occupy an important focus. They have usually comprised the largest proportion (31% - 76%) of psychiatric hospital suicides (Lönnqvist et al 1974, Copas & Robin 1982, Goh et al 1989, Wolfersdorf et al 1989, Taiminen &Lehtinen 1990, Modestin et al 1992b, Roy & Draper 1995, Proulx et al 1997). Suicide in patients with schizophrenia during psychiatric inpatient treatment may be preceded by more severe illness and a greater tendency to previous suicidal behavior than among living patients with schizophrenia (Wolfersdorf et al 1989, Modestin et al 1992b). Mistrust in the treatment relationship, discharge plans, or other treatment changes, particularly among long-stay patients, have been common prior to suicide among victims with schizophrenia (Niskanen et al 1974, Virkkunen 1976, Goh et al 1989, Roy & Draper 1995).

Further, a substantial proportion (33-55%) of suicides among clinical samples of schizophrenics have occurred within three months of discharge (Yarden 1974, Roy 1982, Drake et al 1984), the risk being highest immediately after discharge (Rossau & Mortensen 1997). Uncontrolled studies have suggested that discharge may be experienced as an adverse life event by subjects with

schizophrenia, resulting in depression or exacerbation of psychotic symptoms, and also that high levels of psychopathology and functional impairment, or brief hospitalizations, associate with suicide after discharge (Lindelius & Kay 1973, Stein 1982, Caldwell & Gottesman 1992). Frequent psychiatric admissions during the preceding year have been found to increase the suicide risk in schizophrenia, which suggests that "revolving door" admission patterns associate with high suicide risk (Rossau & Mortensen 1997).

A suggestion for suicide prevention in schizophrenia at the population level, has been offered by register-based studies from Denmark. These reported an increase in suicide rates among patients with schizophrenia concurrent with reductions in facilities for in-patient treatment, as well as a co-occurring trend toward shorter and more frequent admissions. These studies imply that increased suicide rates among patients with schizophrenia may be an indicator of adverse effects of deinstitutionalism (Munk-Jørgensen & Mortensen 1992, Mortensen & Juel 1993, Rossau & Mortensen 1997).

3.4.2 Suicide methods

In many clinical samples of suicide victims with schizophrenia, violent suicide methods have been used most often (Roy 1982, Breier & Astrachan 1984, Allebeck 1986b), which may suggest less ambivalence in motivation for suicide (Breier & Allebeck 1984). A Danish nationwide register-based study reported that poisoning had been the commonest suicide method, whereas violent suicide methods were used substantially more often during inpatient treatment (Rossau & Mortensen 1997). There is a distinct lack of studies and detailed information about the use of medication as a suicide method in schizophrenia.

III. AIMS OF THIS STUDY

The purpose of this study was to examine suicide in schizophrenia, and to compare antecedents of suicide between victims with and without schizophrenia in a nationwide representative suicide population. This study is comprised of four original publications, in which the aims were:

(I) To study the clinical illness characteristics and suicide related factors in suicide victims with schizophrenia, and to examine the effects of age, sex and illness duration in these suicides. Also to describe suicide methods used by victims with schizophrenia.

(II) To examine whether suicide victims with schizophrenia made their suicidal intent less known than others before suicide. In order to determine specifically whether psychotic symptoms affect communication of suicidal intent (CSI), schizophrenic victims in the active illness phase were compared to definitely non-psychotic victims.

(III) To examine the prevalence of recent life events among victims with schizophrenia and to compare it with non-schizophrenic suicide victims. Also to explore whether recent life events occur at different rates among suicide victims with schizophrenia according to illness phase, medication status, treatment setting and social factors.

(IV) To study and compare patients with schizophrenia who committed suicide and their clinical characteristics in different treatment phases (inpatients, recently discharged, and other outpatients). Also, to examine the drug treatment prescribed and the adequacy of antipsychotic treatment in relation to the current clinical state of the suicide victim prior to suicide.

IV SUBJECTS AND METHODS

1. The National Suicide Prevention Project in Finland

This study forms part of the National Suicide Prevention Project in Finland (Lönnqvist 1988, Lönnqvist et al 1993). The classification of suicide was based on the results of medicolegal examination and police investigation as required by Finnish law, but these were more detailed than usual during the research project. The classification of suicide in Finland was derived from the official cause of death classification based on ICD-9. All officially classified suicides in medicolegal investigations were considered as suicides (Lönnqvist 1988). All suicides committed in Finland between April 1, 1987 and March 31, 1988 (n=1397) were carefully examined using the psychological autopsy method (Litman et al 1963, Shneidman 1981).

Ethical aspects for the project were approved by the National Board of Health and the Ethics Committee of the National Public Health Institute in 4.11.1987.

1.1 Psychological autopsy method

The interview process was always initiated by fully explaining to the interviewee the nature and procedures of the study project.Informed consent was always requested written and documented in a structured format. The data on the suicide victims were gathered in four types of interview: 1) Interviews with next-of-kin conducted face-to-face, usually at their homes, using a semi-structured questionnaire containing 234 items concerning the suicide process, victim´s everyday life and behaviour, recent life-events, family history, alcohol and psychoactive substance use and help-seeking behavior; 2) Structured interview with the attending health care professional, usually face-to-face at their office, containing 113 items about the victim´s health status, suicidal behavior and treatment received. This included also a cross-sectional psychiatric symptom questionnaire; 3) Interview with suicide victim´s last health or social care contact based on a separate semi-structured questionnaire and conducted by telephone or face-to-face; 4) Additional unstructured interview(s) when needed, usually by telephone. The interviewers were mental health professionals specially trained for the psychological autopsy research project.

Suicide notes, medical, social agency and police records, and other data, such as hospital charts and toxicological test results, were also utilized as information sources on suicide victims (Marttunen et al 1991, Lönnqvist et al 1993)

1.2 Retrospective diagnostic procedure for suicide victims with schizophrenia

The subjects for this study were identified in three phases from the total of 1397 suicide victims. In the *first phase,* all the information collected on each of the 1397 suicide victim was carefully reviewed by the author to identify all persons with any symptoms, illness patterns, behavior or medications during their lifetime possibly related to a psychotic disorder. In 578 cases such evidence existed. All 1397 suicides were then identified from the Finnish Hospital Discharge Register (FHDR), which covers all discharges from general, mental and private hospitals in Finland since 1969 (Keskimäki & Aro 1991), including ICD-8 and/or DSM-III-R diagnoses (Kuoppasalmi et al 1989). Among these, 149 suicide victims with a 295-code diagnosis of schizophrenic psychoses were detected. The author checked the sensitivity of this first phase screening against the FHDR. The sensitivity was found to be good: the 578 suspected psychotic cases in the present study included 98% (146/149) of the suicide cases identified from the Hospital Discharge Register with a 295-diagnosis code during the year of the National Suicide Prevention Project.

In the *second phase* these 578 suspected cases were categorized by the author into three groups, first excluding the DSM-III-R organic psychoses (n=66) and then categorizing the remaining cases into either a suspected schizophrenia group (n=233) or other psychosis group (n=279). A suicide victim was included in the suspected schizophrenia group if there was any evidence of current or lifetime history of the DSM-III-R criteria A for active phase symptoms of schizophrenia.

In the *third phase* the retrospective diagnostic evaluation of the 233 subjects with suspected schizophrenia was made by pairs of psychiatrists (author, Martti Heikkinen, Markus Henriksson, Erkki Isometsä and Mauri Marttunen) according to DSM-III-R criteria by combining and weighing all available information. Multiple diagnoses were assigned if applicable. This suspected schizophrenia group was found to include all 16 cases diagnosed earlier as schizophrenia in the study of a random sample of suicide victims in the nationwide suicide population (Henriksson et al 1993). Whether the subject´s schizophrenic symptoms fulfilled the DSM-IV criteria for schizophrenia was also evaluated. The interrater reliability of these provisional diagnoses was measured by kappa statistic (Fleiss 1975), and found to be good (kappa=0.79, 95% confidence interval 0.71-0.87). Kappa values for schizophrenia subtypes of the provisional diagnoses were also calculated. The reliabilities achieved for paranoid (kappa=0.62, 95% CI=0.47-0.77), disorganized (kappa=0.60, 95% CI=0.26-0.95) and residual (kappa=0.65, 95% CI=0.47-0.84)subtypes were good, and for undifferentiated (kappa=0.45, 95% CI=0.27-0.64) moderate. The kappa value for catatonic schizophrenia was not calculated because of its low prevalence. The

kappa for DSM-III-R acute exacerbation was 0.58 (95% CI=0.42-0.73). A third psychiatrist reanalyzed all cases with diagnostic disagreement to achieve the final best estimate research diagnoses which were determined in consensus meetings.

2. Subjects in the present studies

2.1 Suicide victims with schizophrenia (study I)

Altogether, there were 92 suicide victims with DSM-III-R schizophrenia (90 of them also fulfilling DSM-IV schizophrenia criteria), for whom interviews with relatives or next-of-kin were conducted in 84% (n=77), with attending health care professionals in 79% (n=73), and with last contact to health care in 79% (n=73). Data from psychiatric records as well as the forensic examination results were available for 100% (n=92) of the suicide victims in the present study. 16% (n=15) left a suicide note.

Part (N=17) of the suicide victims with schizophrenia, who lived in Kuopio province in Finland, have been reported elsewhere previously (Saarinen 1995). The diagnostic procedure, as well as the study design, were different between Kuopio suicide sample and the present study.

2.2 Suicide victims with interview data on communication of suicidal intent (study II)

The study subjects were identified from the nationwide total of 1397 suicide victims by the availability of semi-structured interview data for suicide communication to 1) next-of-kin and 2) attending health care professional(s) (II: Table 1). The person thought to provide the most complete information on the suicide victim had been selected as the next-of-kin interviewee, and if there were several, the person who best knew the final circumstances. Among those who had had a treatment relationship during their last year, the principal treatment setting was defined according to the health care contacts the victim had had. If the victim had had treatment contacts with several facilities which included any form of psychiatric care, he/she was included only in the relevant psychiatric care group. Schizophrenic victims more often had mother (44% versus 20%) and non-schizophrenic victims spouse (11% versus 33%, respectively) as informants.

2.2.1 Suicide victims with schizophrenia

Semi-structured responses of next-of-kin concerning the suicide process were available in 84% (77/92) of suicide victims with schizophrenia. After excluding health care or other professionals as next-of-kin interviewees, the number of study subjects with schizophrenia was 73. Semi-structured responses of the attending health professionals were available in 73/92 (79%) of these victims.

2.2.2 Non-schizophrenic suicide victims

The non-schizophrenic victims numbered 1305. In 819 suicides no evidence of psychotic disorder was apparent, and these victims formed the group of non-psychotic subjects. The semi-structured responses of next-of-kin concerning the suicide process were available in 82% (1074/1305) of non-schizophrenic victims. After excluding health care or other professionals as next-of-kin interviewees, the number of study subjects was 1065. The semi-structured responses of the attending health professionals were available in 539/1305 (41%) of non-schizophrenic victims.

2.3 Suicide victims with interview data on life events (study III)

Life event data on victims with schizophrenia were gathered by interviewing the mother in 31(43%) cases, father in 6 (8%), spouse in 8 (11%), sibling in 16 (22%), adult child in 4 (6%), and other next-of-kin in 7 (9%). The respective figures for non-schizophrenic victims were 52(24%), 15(7%), 77(36%), 29(13%), 16(7%) and 27(12%). There were significant differences in the proportions of mothers (χ^2=9.5, df=1, p=0.0021) and spouses (χ^2=15.6, df=1, p<0.0001) as informants. The mean time interval between death and interview was equal (schizophrenia: 152.0 days, sd= 89 versus non-schizophrenia: 157.6 days, sd=102; t test, two-tailed, p=0.66).

2.3.1. Suicide victims with schizophrenia

Life event data were available for 76 (83%) subjects with schizophrenia; the missing data were mainly due to relatives´ refusal to be interviewed. Four subjects were subsequently excluded because the interviewers considered the reporting of life events as insufficiently reliable. Thus, a total of 72 (78%) subjects formed this study group. The included and excluded groups were similar in terms of: age, proportions living alone, in primary or secondary family, and being

married; illness duration and number of psychiatric hospitalizations, illness phase, comorbid alcoholism and depressive symptoms, current treatment status, and timing of the last hospital discharge. The excluded group contained more women (9/20[45%] versus 15/72 [21%]; χ^2=4.7, df=1, p=0.029), and subjects were more often employed (4/20 [20%] versus 3/72[4%]; Fisher´s exact test, two tailed, p=0.038).

2.3.2 Non-schizophrenic suicide victims

Among suicide victims without schizophrenia 82% (1067/1305) had available life event data, and 76% (n=995) were assessed as reliable by the interviewers. Among all the victims with reliable life event data, those with schizophrenia were significantly younger than the non-schizophrenic subjects (n=72; mean age=39.6, sd=13.4 versus n=995; mean age: 44.6, sd=17.1; t-test two tailed, p=0.0038). Men were equally represented among both groups (n=57/72[79%] versus n=768/995 [77%]). To control for the confounding effect of age, we randomly selected three comparison suicides for each subject with schizophrenia from a list of non-schizophrenic victims containing only age and sex data, and matched each of these 216 victims by age (within $\pm$ 1 year) and sex with their paired schizophrenia case. The mean age of all matched suicide victims with life event data was 39.6 years (sd=13.4, median 37 years, range 19-77 years), 79% (n=228) were men and 21% (n=60) women.

2.4 Suicide victims with schizophrenia in different treatment phases (study IV)

This study included 88 suicide victims with DSM-III-R schizophrenia after excluding those with no treatment contact at the time of suicide (n=4/92 [4%]). They were divided according to current treatment phase into three categories: (1) psychiatric inpatient care (n=25), (2) recent discharge ($\leq$three months) from psychiatric inpatient care (n=28), (3) other outpatients: discharge over three months ago from psychiatric ward (n=35). The third group included one victim with no lifetime psychiatric hospital treatment.

Interview data from attending health care professionals during the last year (hospital: 84%, recent discharge: 89%, other outpatients: 71%; χ^2=3.4, df=2, p=0.18), and with the last health care contact (hospital: 76%, recent discharge: 86%, others: 80%; χ^2=0.8, df=2, p=0.66) were available equally for all suicide victims with schizophrenia in different treatment phases, whereas the data from next-of-kin were less often available for hospital suicides than others (hospital:18/25[72%], recent

discharge: 27/28[96%], other outpatients: 30/35[86%]; χ^2=6.3, df=2, p=0.043). Data from psychiatric records and the forensic examination results were available for all victims (hospital:100%, recent discharge: 100%, others: 100%). Although the proportion of interviewed next-of-kin was smaller among inpatients than others, no major bias is likely in the treatment or psychopathology related variables, since the rates of interviewed health care professionals were similar for victims in all treatment phases.

3. Classification of study variables

3.1. Suicide, suicidality and suicide methods

The definition of *suicide* in the present study was based on the results of medicolegal examination and police investigation as required by Finnish law, but these were more detailed than usual during the research project. The official classification of suicide (ICD-9) in Finland at that time defined suicide as a death resulting from an intentional self-inflicted injury. *Suicidality* (suicidal ideation, communication, threats, or suicide attempts; in study IV) was assessed according to all available information, and primarily according to the semi-structured responses of the attending health care professional in the fourth study. *Communication of suicide intent* (CSI e.g. threats, ideation, and plans; in study II) was assessed using the responses to the semi-structured interviews in the second study. If the interviewee´s interpretation of the victim´s behavior or verbal communication indicated to them an indirect suicidal preoccupation, it was recorded as an *indirect suicide communication.* Violent *suicide methods* used included hanging, jumping from high place, shooting a firearm, cutting, burning and traffic deaths; non-violent methods included suicide by drugs, drowning, inhaling carbon monoxide, and hypothermia under the influence of alcohol and neuroleptic drugs.

3.2 Sociodemographic variables

In the first study, suicide victims with schizophrenia were divided into three equal sized *age groups* 1)young: 16-32 years (n=32), 2)middle: 33-44 years (n=30), and 3)old: 45-77 years (n=30), in order to examine any variation in clinical characteristics between suicide victims of different ages. These groups did not differ significantly in the sex distribution.

Social factors and living arrangements were explored by six items in the interview with the next-of-kin in the third study of life events and suicide (study III). These factors were having had a *companion* of the opposite sex, having had *children*, a *confidant*, *friends* sharing common interests, being *employed* and *living alone*. If the victim had been married, cohabiting, engaged or steadily dating we decided that he or she had had a companion. If the victim had had a friend in whom to confide, and whose company and friendship was important, he or she was regarded as having had a confidant. Being employed excluded those who were retired, on sick leave or pension, unemployed, in school, or working at home.

3.3 Illness related factors and comorbidity

Illness duration was classified as the time between the first psychiatric contact and suicide. In study I, the schizophrenic suicide victims were divided into three equal sized groups by illness duration: 1) short: 0-10 years (n=32), 2) medium: 11-18 years (n=29), and 3) long: 19-43 years (n=30) according to the 3-stage phasic model of Breier et al (1991) for the course of schizophrenic illness: early deteriorating phase (first 5-10 years), stabilization phase, and gradual improvement phase. There were no significant differences in the sex distribution of the three illness duration groups. DSM-III-R definitions of *active and residual illness phases* and *acute exacerbation* were used for classifying current illness course.

The cross-sectional classification of *positive and negative schizophrenia symptoms* was based on all available data, but mainly on the interview of the attending health care professional during the last year using a 35-item structured psychosocial symptom questionnaire. These were assessed only among suicide victims with a treatment relationship during their last year (study IV). Positive symptoms were recorded if at least two of the following were present: (1) hallucinations, (2) delusions, (3) thought disorder, or (4) bizarre behavior, while at least two of the following were required for negative symptoms: (1) avolition, (2) anhedonia, or (3) affective flattening.

DSM-III-R classification allows a diagnosis of depressive disorder with schizophrenia confined to the residual phase of the illness, i.e. as a depressive disorder NOS. We also evaluated the presence during the active phase of *depressive symptoms* defined as depressed mood plus at least one other symptom of DSM-III-R major depressive episode. The presence of comorbid current *alcoholism* was classified according to DSM-III-R definitions of alcohol abuse or dependence. In study III,

in the comparison of suicide victims with and without schizophrenia, *alcohol misuse* was recorded if the victim was reported to have been drunk at least once or twice a week during the last year (Heikkinen et al 1995). This information on the victim´s use of alcohol was obtained from the structured next-of-kin interview form.

3.4 Treatment related factors

The principal *treatment setting* of the mental disorders was defined according to the health care contacts the victim had had during his or her last year. In study I, the principal treatment setting was divided into four categories: 1) psychiatric hospital care, 2) psychiatric outpatient treatment: contacts with mental health care center, psychiatric hospital outpatient department or private psychiatrist, 3) general practice: treatment contacts with primary care, municipal health center or home nursing, 4) no treatment contact with health care: absent or irregular and scarce contact with health care without a known person in charge of the treatment during the last year. If the victim had had treatment contacts with several facilities which included any form of psychiatric care, he was included only in the relevant psychiatric care group.

The current *treatment phase* was classified in three categories according to the proximity of the last psychiatric hospitalization to suicide. This is based on previous research findings of high suicide risk among recently discharged patients from psychiatric hospital. The three categories were: (1) psychiatric inpatient care, (2) recent discharge (≤three months) from psychiatric inpatient care, (3) other outpatients: discharge over three months ago from psychiatric ward.

Adequacy of neuroleptic treatment was assessed using chlorpromazine (CPZ) equivalents (Baldessarini 1985, Bollini et al 1994). When conversion formulas were missing from these sources, other sources were used for calculating CPZ equivalents. They produced the following: levomepromazine (75mg = 100mg CPZ), melperone (50 mg = 100mg CPZ), pericyazine (5mg = 100 mg CPZ), pipotiazine (30 mg = 100mg CPZ), promazine (100 mg = 100mg CPZ), remoxipride (60 mg = 100 mg CPZ), sulpiride (200 mg = 100 mg CPZ) and zuclopenthixol (10 mg = 100 mg CPZ). Neuroleptic medication of at least 300 mg CPZ equivalents was classified as adequate in the active illness phase, and at least 100 mg CPZ equivalents in the residual illness phase for maintenance treatment (Baldessarini et al 1988, Marder et al 1991, Bollini et al 1994, APA 1997).

In study IV, *treatment non-compliance* during the last three months was assessed by the attending health care professional as follows: (1) Appointment non-compliance (minority of appointments kept, or none), and (2) drug non-compliance (had quit neuroleptic medication entirely, or for most of the time). This classification was made independent of current illness symptoms. The opinion of the attending health care professional was validated against the toxicological analyses of liver and blood (thin layer and gas-liquid-chromatography) in forensic examination at the time of suicide. The finding of no neuroleptic in toxicological analyses despite a prescribed detectable dose only referred to non-compliance among non-drug overdose cases (n=55/88 [63%]), in which analyses were available in 47/55 (85%).

Suicide victims were classified as *treatment non-responders* if there were current active illness phase symptoms despite a prescribed amount of CPZ equivalents of 700 mg or more according to the upper limit of recommended sufficient CPZ equivalent dosage (Baldessarini 1988) at the time of suicide, and while any type of neuroleptic medication had been prescribed at least during the previous six months (study IV).

Attitude toward treatment (negative, indifferent or positive) during the last hospitalization was recorded by a structured question in the interview of the attending health care professional and in the hospital chart data. An indifferent attitude was classified as negative (study IV).

3.5 Life event categories

Data concerning life events during the last three months and final week of the victim´s life were obtained during the interview with the next of kin (study III) via a list of structured questions initially developed for an epidemiologic survey in Finland (Lehtinen et al 1985). The *life event questionnaire* in the present study is based on the Recent Life Change Questionnaire by Rahe (Rahe 1977), and modified somewhat by items presented by Paykel and coworkers (Paykel et al 1983). The questionnaire contains 33 structured questions on adult life. Thirty-two items were used in the analysis; the item "change in get-togethers with friends" was omitted because of its ambiguity and symptom-like character (Lehman 1978, Heikkinen et al 1995).

Life event items generally considered as adverse - representing loss rather than gain - were categorized according to the area of life (III: Table 1). The metacategory of *any life event* comprised 32 life event items, and included also three positive items: marriage, engagement, and

financial status substantially improved. Subjects with more than one life event in a single category were counted only once for that category. The author also checked the validity of the life event data questionnaire obtained from next-of-kin against all other available information, and no additional information was found on life events during the final three months. If an event was reported to have begun during the last 3 months, the informant was asked whether this had taken place within the final week. Items were classified *a priori* on logical grounds into either *independent* or *possibly dependent* according to the possibility of the victim´s own behavioral influence on the life events. The independent events were categorized as death, somatic illness of the suicide victim, separation due to work, illness in the family, and own/partner´s miscarriage.

4. Statistical analyses

Two non-paired groups were compared using the chi-square test with Yates´ correction or Fisher´s exact test when appropriate, the two-sample t test, two-tailed, the median test or the Mann-Whitney U-test, two-tailed. Multiple class comparisons were made using the chi-square test or Fisher´s exact test, two-tailed, when appropriate. Kruskall-Wallis tests were used for comparisons of ordinal categorical variables. The comparisons of matched groups of suicide victims were performed by logistic regression analysis and the Wilcoxon rank sum test. Logistic regression analyses were performed to derive odds ratios and confidence intervals for the independent variables studied, and also to adjust the suicide victims with possible confounding factors. Factorial analysis of variance was also used for investigating the main effects of sex and illness duration on the variation in the number of hospital treatments. Kappa statistics were used to assess the diagnostic reliability. The results were considered statistical significant at alpha level <0.05. SAS (SAS Inc. 1990), SPSS (SPSS Inc. 1993) and MEDSTAT (1991) software were used.

V RESULTS

1. Sociodemographic and clinical characteristics of suicide victims with schizophrenia (study I)

1.1 Sociodemographic factors

The mean age was 40 years (sd=13.2, range=61) among suicide victims with schizophrenia. The mean age of women (n=24; 43.2 years, sd=12.9, range=51) did not differ significantly from men´s (n=68; 38.8 years, sd=13.2, range=61; two-tailed t=-1.39 df=90 p=0.17). Social and vocational impairment was characteristic of both sexes at the time of suicide (I: Table 1).

1.2 Illness related factors

The mean age at first referral to psychiatric care was 24.4 years (median=23.0, sd=6.6). The mean illness duration from first psychiatric contact to suicide was 15.5 years (median=14.0, sd=10.2): there was no significant difference between men (mean=14.7 years; median=13.0; sd=10.5) and women (mean=17.8 years; median=17.5; sd=9.4; Mann-Whitney test: Z=-1.7, two-tailed p=0.89).

Lifetime psychiatric hospital admissions for all suicide victims with schizophrenia averaged 7.9 (median=6.0; sd=7.9; range=49). Only 3 suicide victims (3%) had not attended psychiatric hospital during their lifetime. Women had more admissions than men: 11.5 (median=9.0) versus 6.6 (median=5.0; Mann-Whitney test: Z=-2.73; two-tailed p=0.006). To investigate if some longer illness duration would explain the excess hospitalizations among women, factorial ANOVA was performed. This indicated that only sex had a significant mean effect on the variation in hospital admissions (F=4.4; df=1,86; p=0.039), whereas illness duration (F=2.7; df=2,86; p=0.076) did not. No significant interaction was found between sex and illness duration (F=0.09; df=2,86; p=0.99).

At the time of suicide almost one-third of the victims with schizophrenia were receiving psychiatric in-patient care, over half had a psychiatric outpatient treatment contact, seven (8%) were being treated by general practitioners, and eleven (12%) had no treatment contact. Almost half of the outpatient victims committed suicide during the first three months after discharge (I: Table 1). 50%(n=45/89) of the suicide victims with schizophrenia had their last contact with health care

within four days before suicide, 70%(n=62/89) within two weeks, 82%(n=73/89) within one month, and 96%(n=85/89) within three months. For 3% (n=3) the exact date of the last contact with health care was not known.

Three-fourths of suicides were committed during an active phase of illness. About two-thirds of women but only one-third of men committed suicide during an acute exacerbation. Paranoid and undifferentiated types comprised the majority of all schizophrenic suicides. Almost every tenth victim suffered from current suicide-commanding hallucinations (I:Table 1). The proportion of victims with current prominent positive schizophrenia symptoms was 70% (n=52/74), while 61% (n=44/72) had suffered prominent positive as well as negative symptoms at the time of suicide (IV: Table 2).

1.3 Comorbidity

A depressive syndrome (depressive disorder, not otherwise specified (NOS): n=11[13%]) during the residual phase of the illness and depressive symptoms (n=42[51%] during the active phase) were found among two-thirds, and alcoholism (alcohol abuse: n=8 [9%] and dependence: n=11 [12%]) among one-fifth of the suicide victims with schizophrenia. Other substance abuse was rare: only 3 victims had a diagnosis of drug abuse. Young and old men suffered more often from depressive syndrome than the middle-aged, among whom alcoholism was more frequent. Unlike men, middle-aged and young women were more often depressed compared to older women (I: Table 2). The respective groups of illness duration among women and men had a similar, but statistically non-significant effect on the depressive syndrome. Illness duration was significant only in terms of alcoholism among men: the medium illness duration group (n=8[40%]) had alcoholism significantly more often compared to the short (n=7[26%]) and long illness duration groups (n=1[5%]; χ^2=6.8, df=2, p=0.033).

1.4 Suicide methods

Drug overdose was the most common suicide method for both sexes (I: Table 3). In logistic regression analysis middle age (Waldχ^2=10.5; p=0.0012; OR=3.5; df=1, 95%CI=1.6-7.4), and female sex (Waldχ^2=8.8, df=1, p=0.0030; OR=7.0; 95%CI=1.9-25.3) were found to raise the risk of using drug overdose as a suicide method, whereas hospital treatment status (Waldχ^2=5.5; df=1,

p=0.019; OR=0.15, 95%CI=0.031-0.71) and living alone (Waldχ^2=5.2, df=1, p=0.023, OR=0.27, 95%CI=0.085-0.83) decreased it. A neuroleptic drug caused the lethal intoxication among 79% of the overdose victims (n=27/34): a low-potency preparation among 74% (n=25/34). Three poisonings were due to antidepressants, two to antihypertensives (beta-blockers), one to barbiturates and one to benzodiazepines. Violent suicide methods were used by two-fifths of the suicide victims with schizophrenia (I: Table 3). Young age was the only significant variable found to increase the risk of using a violent suicide method (I: Table 2).

2. Antecedents of suicide among people with schizophrenia (study II)

Schizophrenic victims more often had their mother (schizophrenia: 44% versus non-schizophrenia: 20%) and non-schizophrenic victims their spouse (sch:11% versus non-sch: 33%) as informants. Both groups were similar in sex distribution (77% men) and living alone (sch:35% versus non-sch:27%), but differed in age (sch:median=37 versus non-sch:42 years) and cohabiting (sch:31% versus non-sch:73%). For comparison of next-of-kin communication, suicide victims with and without schizophrenia were adjusted for age, sex, cohabiting, and mother and spouse as informants in the logistic regression model (II:Table 2).

Among those with a treatment relationship during their last year, the principal treatment setting was defined according to the health care contacts the victim had had. In the case of treatment contacts with several facilities which included any form of psychiatric care, he/she was included only in the relevant psychiatric care group.Victims with schizophrenia had more often been treated in psychiatric outpatient (51% versus 27%) and inpatient (33% versus 17%) care compared to victims without schizophrenia who had been treated more often in general practice (19% versus 7%). For comparing suicide communication to attending health care professional between suicide victims, odds ratios were adjusted for age, sex and treatment setting (psychiatric hospital care, psychiatric outpatient care and general practice) in the logistic regression analyses (II:Table 2) .

A history of communication of suicide intent (CSI) was equally common among victims with schizophrenia (45/86, 52%) and others (609/1101, 55%) according to both the attending health care professional and/or next-of-kin (II: Table 2). A history of previous suicide attempts and/or CSI was more frequent among victims with schizophrenia (72/86, 84%) than among other victims (776/1109, 70%; χ^2=7.3, df=1, p=0.007), but similar during the last three months (39/81, 48% versus 470/1086, 43%, respectively; χ^2=0.7, df=1, p=0.5). However, actively ill schizophrenic

victims more frequently had CSI and/or suicide attempts (33/59, 56%) than non-psychotic victims (267/655, 41%; χ^2=5.1, df=1, p=0.03) during the last three months.

Times (categorical variable) from the first and the last suicide attempts to completed suicide were also similar between the victim groups (first: Kruskall-Wallis test: χ^2=3.5, df=1, p=0.06; last:Kruskall-Wallis test: χ^2=0.8, df=1, p=0.38). Suicide had usually been experienced as unexpected by next-of-kin of both schizophrenic (54/73[74%]) and non-schizophrenic victims (857/1061[81%]; χ^2=1.6, df=1, p=0.2), as well as by attending health care professionals (51/71[72%] versus 393/533[74%], respectively; χ^2=0.04, df=1, p=0.84).

3. Life events among suicide victims with schizophrenia

3.1 Comparison of recent life events between suicide victims with and without schizophrenia

Subjects with schizophrenia had seldom had companions, children or friends compared with the other victims; they had misused alcohol less often, and had rarely been employed, but had more commonly lived with their parents. The groups were similar only in proportions living alone and having had a confidant (III: Table 1).

The proportion of victims with at least one recent life event prior to suicide was markedly higher in the non-schizophrenia (83%) than the schizophrenia (46%) group, as were the mean numbers of life events during the last three months (n=2.5, sd=2.3, range 0-11 versus n=0.9, sd=1.3, range 0-5; Wilcoxon rank sum test with continuity correction, Z=-6.2, p=0.0001), and the last week (n=1.2, sd=1.7, range 0-8 versus n=0.5, sd=0.9, range 0-5; Wilcoxon rank sum test with continuity correction , Z=-3.8, p=0.0001). Within the groups, no sex differences were found in the total occurrence of recent life events. The proportion of victims with schizophrenia was lower in almost all life event categories, except for illness in the family and death of a close person, which both formed part of the independent life event category (last week: sch:n=8/71[11%] versus non-sch: n=11/205[5%]; Waldχ^2=2.7, df=1, p=0.098; last three months: sch: n=15/72[21%] versus non-sch: n=37/206[18%]; Waldχ^2=0.29, df=1, p=0.59).

A logistic regression analysis was performed to control for any confounding effects generated by the significant differences in sociodemographic factors and alcohol misuse between the victims

VI DISCUSSION

1. Methodology

1.1 General study design

The lack of a control group of living subjects with schizophrenia precluded the possibility of using the results of this study for estimating the specific risk factors for suicide among persons with schizophrenia (Myllykangas et al 1997). However, it was possible to study the occurence of antecedents for suicide, and to estimate whether the suicidal process was different in terms of risks for certain antecedents between suicide victims with and without schizophrenia. The possible changes in treatment practices during the last ten years may limit the generalization of some of the results of the present study to date. Despite the application of multivariate analyses in the relevant circumstances, the use of many statistical tests may have led to some spurious associations (Grove & Andreasen 1982).

1.2 Psychological autopsy method and diagnostic methods

The validity and reliability of retrospective, indirect interview methods for psychiatric diagnoses have been studied in the context of epidemiologic and genetic research, and in psychological autopsy studies. Both underreporting and overemphasizing of psychiatric symptoms and life events may occur for various reasons (Andreasen et al 1986, Paykel 1988, Brent 1989). Compared to direct interviews, indirect methods are shown to have high specificity but moderate sensitivity, leading to probable underreporting of mental disorders (Andreasen et al 1986).

Underreporting may result from insufficient knowledge of the deceased by the informant or from otherwise incomplete information. Overreporting may be due to psychological reactions that suicide has triggered in informants; for example "effort after meaning" reasoning for the cause of suicide, which may also occur among interviewers (Paykel 1988, Brent 1989). Interpreting the events in the light of subsequent experiences may occur, and varying levels of accuracy and detail may be obtained between informants. These may weaken the reliability and validity of the data (Paykel 1989, Brent 1989, Clark & Horton-Deutsch 1992). The validity of the information has been found to vary with the informants´ mental status (Kendler et al 1991). However, Brent (1989)

and Lesage and coworkers (1994) did not find depression of the informant to significantly affect the estimated rate of mental disorders among the deceased. Furthermore, the use of different sources of information and integration of all available data is likely to enhance the general level of information, and thus improve the validity of the information (Brent 1989, Clark & Horton-Deutsch 1992, Brent et al 1993c).

Overall, the availability of interview data was good for the whole research part of the National Suicide Prevention Project in Finland: next-of-kin information was available for 83% of all suicide victims (Lönnqvist et al 1993). Among persons with schizophrenia a similar proportion of next-of-kin interview data was available, but also a high rate of health care professional interview data and hospital record based data (study I). In study IV, suicide victims with schizophrenia were compared according to their treatment phases. Although the proportion of interviewed next-of-kin was smaller among inpatients than others, no major bias was likely in the treatment or psychopathology related variables, since the rates of interviewed health care professionals were similar for victims in all treatment phases.

In the present thesis the validity of the retrospective provisional diagnoses was found to be excellent after comparison with the clinical schizophrenia diagnoses of the Finnish Hospital Discharge Register (study I). In addition, the proportion of suicide victims with schizophrenia in this study (6.6%) was similar to that in the random sample of the suicide population (7%) in the National Suicide Prevention Project, in which the diagnostic procedure was performed somewhat differently from more heterogeneous base population (Henriksson et al 1993). Overall, the stringent documentation required for diagnoses and the lack of standardized interview methods has probably led to underestimation of both schizophrenic (especially negative) and comorbid symptoms. The proportion of concurrent negative symptoms among schizophrenic suicide victims may have been inflated by the high rate of partly overlapping depressive symptoms.

Interrater reliabilities of best-estimate axis I diagnoses have been moderately good in the family interview studies (Leckman et al 1982, Maziade et al 1992), as has been the re-test reliability of the diagnoses (Klein et al 1994). The retrospective best-estimate diagnostic procedure method, sharing features with the LEAD standard (Longitudinal, Expert, All Data) proposed by Spitzer (1983), was used in the assessment of the psychiatric diagnoses in the random sample of suicide victims in the National Suicide Prevention Project in Finland (Henriksson 1996). This was applied in the present study after a short period of training by the diagnosticians and before the diagnosis assessment began. The diagnostic method proved to have good reliability for the representative sample of the

Finnish National Suicide Prevention Project in the most important diagnostic categories (Henriksson et al 1993). The schizophrenia diagnoses in the studies for the present thesis were assessed with a similar diagnostic method. A high rate of agreement measured by kappa value was found for schizophrenia diagnoses, although the reliability was not assessed in a heterogenous base population, but in a more homogenous sample of subjects with suspected psychotic symptoms (study I).

Underreporting of life events may occur due to forgetting, but the inter-rater reliability of reporting, especially of severe life events, has been found to be good in some studies (Parry et al 1981, Brown & Harris 1982). Moreover, a short recall period of three months prior to suicide is likely to minimize the fall-off in recall (Paykel 1983). In line with this, the consistency of the diagnostic data obtained by psychological autopsy studies suggests that major recall biases will not occur if the interviews are performed within 2-6 months of the suicide (Brent 1989), as in the present study (Lönnqvist et al 1993). Information bias may also occur when recall maybe impaired as among subjects with schizophrenia (Norman & Malla 1993b), in which case the use of other informant may reduce such bias. Over-reporting of life events may also result from the tendency to report life events closer to the death than they actually were when using overlapping time periods of three months and one week before suicide, as in our study, instead of asking actual dates of event onset.

1.3 Classification of suicide and suicidality

The classification of suicide in the present thesis was based on official death causes, and the identification of suicides among patients with schizophrenia was likely to be accurate. In some previous studies derived from clinical patient samples of suicide victims with schizophrenia, the classification of suicide or identification of suicide victims has not been explained or has been inconsistent (Hu et al 1991, Cannon et al 1991). The classification of suicidality in this thesis (study IV) is likely to be sensitive to any type of suicidal behaviour, including acts of self-harm, rather than those with exact specificity to high suicidal intention. This may have led to high rates of suicidality in our study. Overall, the use of interview and hospital chart data probably rather underestimates than overestimates CSI (communication of suicidal intent), as well as the number of previous suicide attempts, but equally among all suicide victims. However, a shorter time from the last health care appointment to suicide among victims with schizophrenia may cause more CSI among them, if the duration of the suicidal intention is shorter before suicide. Since CSI has further

varied with some of the characteristics found different between schizophrenic and non-schizophrenic victims (Allebeck et al 1987, Isometsä et al 1995), the odds ratios for victims with and without schizophrenia were adjusted accordingly in the analyses.

1.4 Life event data (study III)

The strength of this study over previous studies on life events and suicide in schizophrenia was the use of the psychological autopsy study method with data collection by interviews using a structured life event instrument, and classification of events according to the person´s possible behavioral influence on them. In addition, the large sample size of suicide victims with schizophrenia allowed us to examine life events among victims with varying clinical characteristics. Nevertheless, several methodological limitations need to be addressed.

The validity of the life event data questionnaire in the present study was checked against all other available information, and no additional life events details were found during the final three months. Life event measurement via face-to-face interview, as in this study, has been proven more reliable compared with self-report questionnaires (Paykel 1983). An attempt to control for possible bias created by the differing proportions of mothers and spouses as informants between schizophrenic and non-schizophrenic victims was performed by adjusting these in the logistic analysis in the present study.

Life event scales were originally developed to measure life events among people of the general population, commonly with an active social life, rather than in more isolated subjects with schizophrenia. Treatment associated events that often occur among schizophrenia subjects are not covered by these schedules (Lukoff et al 1984). Life event stressors may also include comparatively ordinary daily occurrences and minor daily stressors (Donovan et al 1975, Norman & Malla 1991), since schizophrenic patients may experience more stress than others in response to an event, due to a limited capacity to negotiate everyday problems (Norman & Malla 1993b). This study was not able to measure minor life events among suicide victims, since detecting them via retrospective next-of-kin interview is likely to be very unreliable, and also because our life event scale was originally designed only for measuring the occurrence of discrete major life events.

1.5 Methodological issues concerning treatment variables (study IV)

The use of CPZ equivalents for evaluating adequacy of antipsychotic treatment in schizophrenia is compromised by the well known problems in defining the concept of drug equivalence (Rey et al 1989). The classification of compliance in this study was based on clinician interviews, which tend to underestimate the magnitude of non-compliance (Weiden et al 1995). However, it is not known whether this underestimation occurs in interviews of clinicians whose patients have committed suicide. The use of negative results from toxicological analyses in classifying non-compliance among other suicides than those by overdoses creates uneven information among the suicide victims, but it does increase the overall level of information. The classification of non-responder in the present study also differed from the classification of treatment resistance used in the clozapine trial study for neuroleptic resistance (Kane et al 1988), being closer to broader definitions of treatment refractoriness (Marder 1995). This represents a cross-sectional estimate without the possibility of longitudinal evaluation in the quantity of symptoms. The concept of non-responder in the present study tends toward an underestimation, since it was used only if the current CPZ equivalent dose was 700 mg or more, thus definitely eliminating the victims for whom adequate dosing had been prescribed previously without effect; or the ones who had not yet been prescribed sufficient neuroleptic dose for maximum effect. This study focused on the pharmacological treatment before suicide, for which reliable data were available. Thus, an estimation of the role of other, possibly important and interacting non-pharmacological treatments on drug response and non-compliance in the suicide process was not possible.

2. Sociodemographic and clinical characteristics of suicide victims with schizophrenia (study I)

In this study a prevalence of 6.6% for schizophrenia among all suicide victims in Finland was found, which accords with the prevalence reported in previous unselected psychological autopsy studies (Robins et al 1959, Dorpat & Ripley 1960, Barraclough et al 1974, Chynoweth et al 1980, Arato et al 1988, Rich et al 1988, Henriksson et al 1993, Cheng 1995). The unique representativeness of this study sample allowed us to investigate variation of comorbid symptoms and disorders among suicide victims with schizophrenia

2.1 Sociodemographic factors

Previous research has emphasized that suicide victims with schizophrenia tend to be young adults. Suicide in schizophrenia has been suggested to be age dependent and not often to occur later in life due to changes in the character of the illness (Black & Winokur 1990). We found, however, that suicides had occurred over large ranges of age and illness duration. In addition, the high risk group of young suicide completers among persons with schizophrenia characterized in many previous studies (Lim & Tsoi 1991, Roy 1982, Breier & Astrachan 1984, Drake et al 1984, Cheng et al 1990) was very similar to the youngest group in our study in terms of mean age, male dominance, depressive symptoms and violent suicide methods. The higher mean age in our study than in most earlier studies is probably explained by the unselected nature of our study population.

In the majority of outcome studies on schizophrenia, women tned to have a more favourable illness course than men as measured by social functioning (Bardenstein & McGlashan 1990). In this study the sexes did not differ significantly in sociodemographic parameters. Unmarried status and living alone were strongly related to suicide among women with schizophrenia in one previous controlled study (Allebeck et al 1987) which accords with our finding. Further, unlike non-suicidal women with schizophrenia (Andia & Zisook 1991), women in the present study had more hospital admissions than men which was not explained by their some longer illness duration. Perhaps women are more prone to seek help and thus to have more hospital admissions. On the other hand, in this study the sexes were alike in their treatment variables. The sexes also differed in the timing of suicide in relation to illness relapse: women were more likely to commit suicide during acute exacerbations of the illness. The findings for sex, sociodemographic features and illness characteristics might imply that female suicide victims with schizophrenia tend to have a very severe illness course with frequent relapses and poor social outcome.

2.2 Illness related factors and comorbidity

Drake et al (1984) reported that young persons with schizophrenia are at greatest risk for suicide during the non-psychotic depressed phase. However, in this study the majority of suicide victims were in the active phase of schizophrenia at the time of suicide, regardless of their age and illness duration. This may be due to the comprehensive data collection in our study, which included information on mental state close to the time of suicide. The rate of current depression in the present study was found to accord with previous studies documenting an average of 60% of suicide

victims suffering from affective symptoms (Yarden 1974, Virkkunen 1974, Roy 1982, Drake 1984, Drake et al 1986, Hu et al 1991, Cannon et al 1991).

While the first ten years of illness are reportedly the highest risk period for suicide among young subjects with schizophrenia associated with depressive symptoms (Roy 1992), the possibly, clinically important relationships of later illness stages (Breier et al 1991) and older age with depression have remained obscure. Depressive syndromes were most commonly found among the young and old men, and in the young and middle aged women. Illness duration had similar effects on the variation of depressive symptoms in both sexes. The later peak in the prevalence of depressive syndrome among women is perhaps explained by their later age of onset of schizophrenic illness. Due to the small number of women the findings of age-specificity in the clinical characteristics are only suggestive, although they do derive from a representative sample of female suicide victims with schizophrenia.

Although the proportions of alcoholism and substance abuse among victims with schizophrenia have been rarely reported and found highly variable. Record based studies have reported comorbid alcoholism among 3% to 19% (Roy 1982, Allebeck et al 1987), but the psychological autopsy study by Rich and coworkers (1988) found substance use disorders in as many as 73%. Both substance dependence and abuse (3%) and alcohol dependence and abuse (21%) were moderately infrequent in the present study compared with these figures of Rich et al (1988). The present study included a higher number of victims with schizophrenia, both sexes, all age groups and both rural and urban living settings, which may explain these disparities. In this study the proportion of comorbid alcoholism was highest among middle aged men (46%). This was similar to the rate of alcoholism (43%) in the representative random sample of all suicides among the general population in Finland during the same time period (Henriksson et al 1993), whereas the overall rate of alcoholism was lower among suicide victims with schizophrenia.

2.3 Suicide methods

Previous studies on suicides among subjects with schizophrenia have reported violent suicide methods to be the most common (Roy 1982, Breier & Astrachan 1984, Allebeck & Wistedt 1986b, Cheng et al 1990), whereas drug overdose was found as the most frequent method in the present study. Female sex, age between 33-44 years, and a probably easier availability of psychotropic medication among outpatients than in-patients were strongly associated with lethal drug overdose.

The unselected population in the present study included substantially more females, minimal selection related to treatment status and a larger proportion of older suicide victims than previous studies, which might explain the disparity in the type of main suicide method.

Breier et al (1984) reported that victims with schizophrenia tended to use more lethal and violent suicide methods than non-schizophrenic victims, suggesting less ambivalence in their motivation to kill themselves. However, the methods used in the present study were significantly less violent overall (due to the high number of drug overdoses) than in non-schizophrenic suicides in Finland. Besides the unselected nature of our schizophrenia victims, the relatively easy access to cardiotoxic low-potency neuroleptic drugs probably explains the particularly high proportion of fatal drug overdoses among them. This finding is congruent with an earlier discovery of a higher proportion of drug overdoses among suicide victims with bipolar disorder (35%), who were significantly more often receiving psychiatric treatment than unipolar suicide victims (13%; Isometsä et al 1994a).

The cardiotoxicity of low-potency neuroleptics in overdose is well known, including their ability to cause sudden death (Mehtonen et al 1991, Buckley et al 1995). However, little attention has been paid to the toxicity of low-potency neuroleptics in the treatment of suicidal patients with schizophrenia, compared with the highly focused issue of toxic antidepressants in the treatment of depressive patients.

3. Antecedents of suicide among victims with and without schizophrenia (study II)

This is the first study to examine communication of suicidal intent (CSI) in schizophrenia and other suicides using a representative, nationwide sample of suicide victims. Against the common belief of unexpected suicides among subjects with schizophrenia (Johns et al 1986, Barraclough & Hughes 1987, Murphy 1994), it was found that they (52%) communicated suicidal intent as often as non-schizophrenic victims (55%) to next-of-kin and/or an attending health care professional. Moreover, victims with active phase schizophrenia (56%) had even more CSI and/or suicide attempts than non-psychotic victims (41%) during the last three months. Also, on the population level, as victims with schizophrenia were more likely to have received treatment than others during their last year, they actually had more CSI (34%) to attending health care professionals than other victims (14%).

In our study, CSI to either next-of-kin or attending health care professional was recorded with similar frequency in schizophrenic and non-schizophrenic victims. In line with our finding, the San Diego study using the psychological autopsy method reported CSI as frequently among 11 schizophrenic victims as among other victims (Rich et al 1988). Further, in the psychological autopsy study of Virkkunen (1974) a similar finding of CSI in a sample of suicide victims with schizophrenia and paranoid psychoses and in a control group of victims with other psychiatric disorders was reported. However, record based studies suggest that suicides of persons with schizophrenia have seldom been preceded by CSI compared with other suicides (Breier & Astrachan 1984, Nathan & Rousch 1984, King 1994). The different findings of CSI in schizophrenia and other suicides between interview based or record based studies may result from the patient selection in smaller samples, less recorded suicide communication in patient charts than in interviews, or the possible effects of treatment of patients with less suicide communication in adequate psychiatric care. Contrasting with the suggestion of Rich et al (1988) of less CSI to attending health care professionals and more to next-of-kin among schizophrenics, we found that schizophrenics communicated almost equally to both.

4. Life events among suicide victims with and without schizophrenia (study III)

Almost half the victims with schizophrenia had had one or more life events 3 months prior to suicide. The type of event (independent, possibly dependent or any) varied according to age, having had a companion, illness phase, pattern of neuroleptic use, and treatment setting. However, life events seemed to present less prominently before suicide among victims with schizophrenia compared to those without, of whom the majority had had life events.

4.1 Comparison of suicide victims with and without schizophrenia

To evaluate the possible influence of the victim´s own behavior on event onset, which may also be affected by his or her psychiatric symptoms, we categorized the life events as possibly dependent or independent, in an attempt to distinguish whether the stressors themselves may reflect increased symptomatology. The independent life event categories were classified as death, illness in the family, separation due to work, somatic illness of the victim and own/partner´s miscarriage. This classification caused asymmetry in the comparison of victims with and without schizophrenia:

the reporting of somatic illness among victims with schizophrenia was very low (III: Table 2). However, this may be associated with the familiar problems of under-recognizing and underdiagnosing medical comorbid illness among patients with schizophrenia (Jeste et al 1996, Mäkikyrö et al 1998).

Another interesting question is whether the lower rate of adverse life events prior to suicide was due to schizophrenia and factors related to it, such as fewer social contacts and consequently a lower probability of life event exposure, or whether it is a common phenomenom in psychosis in general. We compared victims with affective psychosis (bipolar psychotic disorder and psychotic major depression) (Isometsä et al 1994a, Isometsä et al 1994b) from the representative nationwide suicide population in Finland and victims with active phase schizophrenia during the same time period. We found that victims with current affective psychosis (55%) were similar to active illness phase schizophrenics (45%) in the relatively low rate of any type of recent life events before suicide compared to other suicide victims (83%). This seems to imply that the suicide process among currently psychotic subjects is less affected generally by adverse life events prior to the suicide than among other suicide victims.

In the present study almost half of the victims with schizophrenia had had recent life events prior to suicide, which was significantly less than among the four-fifths of non-schizophrenic comparisons. This accords with the finding of Rich et al (1988), who mentioned the unknown nature of the difference in life event prevalence. Neither did they classify the events according to the possibility of the subject´s own influence on them, nor study the social discriminants between the victims. We found that the difference in occurrence of life events between the suicide groups was clearer with the possibly dependent events, which are more susceptible to the subject´s own behavior or illness, than with the independent events. When significantly discriminating social factors and alcohol misuse were controlled for, the two groups were no longer differentiated by the prevalence of independent life events. This finding supports Brown and Birley´s (1968) study, in which rates of independent life events correlated with household size. This also indicates that the role of independent events before suicide may be equally important among victims with or without schizophrenia, and is further supported by our finding that the event categories of death of a close person or illness of a family member were equally common among both schizophrenic (21%) and non-schizophrenic (18%) suicide victims.

4.2 Recent life events among suicide victims with schizophrenia

The occurrence of stressful life events among living patients with schizophrenia is reportedly higher among inpatients than outpatients (Lukoff et al 1984). Unexpectedly, of all the variables investigated in the present study outpatient status was the strongest single predictor of any life event prior to suicide among subjects with schizophrenia, independently of the illness phase: 83% of active phase and all residual phase victims with any life events were outpatients. This accords indirectly with Modestin et al (1992b), who found no differences in life events between inpatient suicides and non-suicides with schizophrenia. One explanation may be that the suicidal potential associated with relapse preceded by a life event is treated effectively, and suicide prevented, by hospitalization. However, the possible protective effect of in-patient treatment for suicide among patients with schizophrenia who had had stressful life events prior to hospitalization would be very difficult to estimate.

It has been suggested that life events in the course of schizophrenia would have a greater influence in patients discharged from hospital with non-psychotic symptoms such as anxiety, depression and somatic concerns (Schwartz & Myers 1977). This may correspond to a syndrome described as "demoralization" (Dohrenwend & Egri 1981), which has also been associated with motivation for suicide among subjects with schizophrenia (Bartels & Drake 1988). Roy et al (1983a) found that living chronic schizophrenic outpatients whose illness was controlled with neuroleptics were at risk of depression if they had had recent life events. However, in our study we found no excess of any type of recent life events among victims who had suffered from comorbid depressive symptoms. This may imply that schizophrenic suicide completers with recent life events do not present clear-cut depressive syndrome.

Previous studies on suicide and schizophrenia have not reported life events in DSM-III-R illness phases of schizophrenia. In the present study, the proportion of subjects in the residual illness phase with independent life events (40%) was found to be almost significantly larger than the proportion of victims in the active illness phase (17%), thus matching the proportion of non-schizophrenic suicide victims with independent life events (40%). The total percentage of schizophrenic suicide victims with life events in the present study was similar to that in Breier and Astrachan´s study (1984), whereas the majority of life events they recorded were illness-related, such as: "could not return to family´s home", and the victim´s illness phase was not reported. In contrast to their conclusion of a weak utility of life events as an indicator of suicide, we suggest that major independent life events may indeed associate with suicide among subjects in residual

phases. However, in active illness phases the motivation for suicide does not seem to associate with an "external" independent life event, but may be more due to "internal" illness related factors as reflected by the moderate proportion of victims with possibly dependent life events. Somewhat analogously, Nyman and Jonsson (1986) suggested that schizophrenic suicides characterized by residual states or chronic symptomatology were possibly triggered by "personal crises". In addition, the possibly dependent life events may play an important role in suicides of active illness phase victims, since shame and hopelessness may be related to or worsened by self-inflicted life events (Isometsä et al 1995b).

Recent life events were found to vary with the pattern of neuroleptic medication use in different schizophrenic illness phases before suicide. Among the victims in the residual phase only those on neuroleptic medication had experienced life events prior to suicide. This parallels a finding from life event and relapse studies in schizophrenia which suggests a role for maintenance neuroleptic medication as a buffer against everyday life stress among subjects with schizophrenia: those with medication had more major life events preceding relapse than those without (Ventura et al 1992).

5. Treatment received among suicide victims with schizophrenia (study IV)

In this study 57% of schizophrenic suicide victims in the active illness phase were either not prescribed adequate neuroleptic treatment or were not using it, and a further 23% were estimated as compliant non-responders. Schizophrenic suicide victims in different treatment phases differed significantly in their current clinical and treatment related characteristics. Recently discharged victims were found to have a significant clustering of known risk factors for suicide.

5.1 Antipsychotic treatment

We found that an average of 512 mg CPZ equivalents was prescribed for our schizophrenic suicide victims, which falls in the range of previously reported CPZ equivalents (183 mg to 688 mg) among suicide victims with schizophrenia (Yarden 1974, Hogan & Awad 1983, Cheng et al 1990, Taiminen & Kujari 1994). However, despite the adequate average amount of the prescribed neuroleptics, only about a half (54%) of all suicide victims in the active illness phase were

prescribed adequate antipsychotic treatment according to the modest requirement of 300 mg of CPZ equivalents in our study. Further, the figure of 43% for the proportion of actively ill victims with adequate treatment who had actually taken the prescribed treatment is probably an over estimation. Since most suicides (78%) occurred during the active illness phase, we suggest that pharmacological undertreatment of psychotic symptoms may be a serious problem in the management of suicidal schizophrenics.

The majority of suicide victims in this sample suffered from both positive and negative symptoms simultaneously (61%). In the present sample, recent suicidality was strongly associated with the presence of current positive, but not negative symptoms. This supports the findings of Fenton and McGlashan (1997), who suggested that suicide may be more often connected with prominent positive symptoms, and that among patients with only prominent negative symptoms the suicide risk may be low. Positive symptoms are considered to react better to antipsychotic treatment than negative symptoms (Kane & Mayerhoff 1989), emphasizing the importance of treatment of active psychotic symptoms among suicidal schizophrenic patients.

Unfortunately, the issue of neuroleptic side-effects could not be reliably examined in this suicide sample due to lack of structured data on possible side-effects, especially akathisia. According to all available information on the suicide victims, there were no spontaneous reports of current neuroleptic side-effects. Akathisia is usually associated with higher neuroleptic doses in about 24% of patient samples (Halstead et al 1994), but in the present sample the majority tended to be undertreated with neuroleptics or non-compliant, rather than receiving high doses of neuroleptics. This suggests, that neuroleptic side-effects are not a major factor in suicides among patients with schizophrenia, although they may play an important role in occasional cases.

5.2 Antidepressant treatment among suicide victims with schizophrenia

Depression among patients with schizophrenia is found in among approximately 25% of cases during the longitudinal course of schizophrenia, but its presence varies according to the diagnostic methods and patient samples used, and it is associated with functional impairment, morbidity and mortality (Siris 1996). There is evidence that tricyclic antidepressants can be effective when used in conjunction with neuroleptic medication after the the acute phase has resolved (Siris 1996, APA 1997). However, in our sample, only three of nine depressive victims in a stable illness phase (after half a year from hospital discharge) were on antidepressive treatment at the time of suicide.

Besides, the doses of prescribed antidepressants were often inadequate. The rates of antidepressants use have varied (12%, 47%) in previous studies (Roy 1982, Cheng et al 1990), but it is difficult to compare the treatment standards, since these studies did not report the antidepressant usage among stabilized depressive schizophrenic patients. Depressive symptoms are an important risk factor for suicide in schizophrenia (Caldwell & Gottesman 1992), but there is a lack of knowledge about the role of antidepressant treatment in suicide prevention among depressive patients with schizophrenia.

5.3 Treatment compliance and response

In the present study one-third of suicide victims were assessed as drug non-compliant. Non-compliance was associated with alcoholism, as previously reported among living patients (Bebbington 1995, Weiden & Olfson 1995), but not with other factors known to associate with both suicide and non-compliance in schizophrenia, such as negative attitude toward treatment during hospitalization, paranoid subtype, depressive syndrome or acute exacerbations of illness. Non-compliance may not be a specific character of suicidal patients with schizophrenia, but it certainly plays an important role in schizophrenic relapse (Weiden & Olfson 1995), often leading to a cycle of hospital admissions and discharges, treatment phases of high suicide risks.

Meltzer and Okayli (1995) have suggested that neuroleptic-resistant patients with schizophrenia who suffer from persistent and severe positive and negative symptoms of schizophrenia, and may thus feel hopeless, have a particularly high risk for suicide. They have reported that among neuroleptic-resistant patients clozapine treatment decreased suicidality. In this study, a considerable proportion of suicides occurred in hospital among a subgroup of severely and chronically ill patients with recent suicidality. Further, 44% of inpatient suicides were found to be non-responders to typical neuroleptics. However, none of the suicide victims had been prescribed clozapine before suicide. During the same period in Finland, it can be estimated that about 1150 patients were using clozapine, as derived from DDD (defined daily dose) values and approximations of the average usage time per year per patient (Erkki Palva, Research director, National Agency for Medicines, Finland, personal communication 14.4.1997) among the roughly 50 000 patients with a diagnosis of schizophrenia (Isohanni et al 1998). Lithium is also recommended for augmenting the efficacy of antipsychotic drugs in the treatment of positive symptoms among patients with schizophrenia (Karper & Krystall 1996), but it was not prescribed for any of these suicide victims. For suicide prevention in psychiatric hospitals, the treatment of severely ill and recently suicidal schizophrenic

patients needs further study, but the use of alternative and augmenting treatment options, when typical neuroleptics in adequate dosages do not yield good response, is to be encouraged on the basis of the present findings.

5.4 The clinical characteristics of suicide victims with schizophrenia in different treatment phases

Recently discharged schizophrenics were found to differ from others in having more suicide risk factors such as paranoid symptoms, alcoholism, and suicide attempts during their last year. Among all psychiatric patients, alcoholism has also been associated with higher suicide risk during recent discharge than in inpatient care (Modestin & Hoffman 1989). Unexpectedly, all suicide victims with schizophrenia in different treatment phases were similar in the proportions of depressive symptoms. Further, recently discharged schizophrenic victims had the highest number of hospitalizations per year during their illness duration and the shortest median duration of last hospital treatment. Unfortunately, our data do not allow us to reliably estimate the total time spent in hospital during the whole illness, or the exact rate of hospitalizations per year. However, our findings may imply that the revolving door syndrome in schizophrenic suicides may be associated with the recent discharge period. This is in line with the finding of a recent study by Rossau and Mortensen (1997) that revolving door admission patterns are associated with increased suicide risk in schizophrenia. Attitudes of inpatient suicide victims toward treatment were more often negative or indifferent and they were more often treated against their will, which is similar to previous reports (Virkkunen 1974). The disparities which emerged in this study between schizophrenic suicide victims in different treatment phases suggests the possibility of varying suicide risk among distinct subgroups of schizophrenic patients in different treatment phases. It may also suggest that longer hospital treatment could offer some protection against suicide among younger subjects with revolving door admission patterns and other known suicide risk factors. However, these issues need to be further studied with a controlled study design. For suicide prevention, these findings imply that when planning discharge, suicidality should be assessed carefully.

6. Implications for suicide prevention in schizophrenia

Schizophrenia is very often a severely disabling and chronic illness with onset in young adult life, and still lacking effective or curative treatment. In this study, suicide victims with schizophrenia were characterized by severe illness course, a history of suicidal behavior and depressive symptoms at the time of suicide. Suicide prevention among persons with schizophrenia is a major concern in psychiatric care, since at the time of death the majority of suicide victims had been in psychiatric treatment: 53% of suicide victims in psychiatric outpatient care and 27% in hospital care. A minority (8%) had had treatment contact in primary health care.

Providing patients with schizophrenia a need adapted, good quality of care is an essential task in psychiatry. For suicide prevention in schizophrenia, particular focus on the adequacy of comprehensive care is crucial especially among actively psychotic patients with recent suicidal behavior and depressive symptoms. Close monitoring of treatment and adequate antipsychotic drug treatment is of special importance during inpatient treatment and shortly after discharge from psychiatric hospital. Attention should be paid to problems in treatment contact, as well as to achieving better treatment compliance. For patients with poor antipsychotic drug treatment responses, active trials of second-line treatment options, such as clozapine or augmenting treatments, are important. The use of newer antipsychotic drugs with less side-effects, better compliance, and possible antidepressant properties may be also beneficial when treating suicidal and depressed patients with schizophrenia.

Prescribing large amounts at the time of antipsychotics potentially toxic in overdose should be avoided for high-risk patients, particularly at the time of hospital discharge. A good continuity of care between psychiatric hospital and outpatient settings is important, since a third of all suicides in this study occurred within three months of discharge.

As among other psychiatric patients, a history of suicidal behavior and communication of suicidal intent are of great importance when evaluating suicide risk among patients with schizophrenia. In this study, schizophrenic patients with stabilized illness on regular medication resembled non-schizophrenic suicide victims in having had recent adverse life events at higher rates prior to suicide than actively ill schizophrenic patients. This suggest that adverse life events may be of clinical importance when assessing suicide risk among schizophrenic patients in stabilized illness phases.

7. Implications for further studies

For suicide prevention in schizophrenia, further knowledge of the possible high-risk subgroups among patients, and of clinical short term risk factors would be very important. The present studies have been able to describe suicide victims with schizophrenia with different clinical characteristics relating to sex, age, illness phases, and treatment phases. Clinical characteristics among suicide victims with schizophrenia were found to vary with age and phases of treatment and illness. These findings may be of importance for future controlled studies aiming to specifically identify risk factors for suicide during the illness course of schizophrenia.

Suicides occurred throughout the entire course of schizophrenia in this study, though most often in the active illness phase. Women committed suicide significantly more often during an acute exacerbation of illness. Middle aged women had depressive symptoms and suicide attempts during the year before suicide most often, whereas middle aged men haddepressive symptoms, but instead the highest proportion of alcoholism least often . The use of violent suicide method was highest among the young; whereas drug overdose was commonest among middle aged men and old women. The possibility that the risk factors for suicide among subjects with schizophrenia vary according to sex and age should be further investigated.

Schizophrenic suicide victims in different treatment phases differed significantly in their current clinical and treatment related characteristics. Inpatient suicide victims had the highest proportion of negative or indifferent treatment attitudes, whereas recently discharged suicide victims had the highest prevalence of comorbid alcoholism, paranoid subtype, recent suicidality, as well as the highest number of hospitalizations per year during their illness course and the shortest last hospitalization. These findings suggest the possibility of varying suicide risk in different treatment phases among patients with schizophrenia. It may also imply that longer hospital treatment could offer some protection against suicide among younger subjects with revolving door admission patterns and other known suicide risk factors. These possibilities need to be further investigated with a controlled study design. The effect of deinstitutionalism on suicide mortality rates among patients with schizophrenia should be addressed (Veijola & Isohanni 1998).

The high rate of inadequate treatment (inadequate dosing, non-compliance and non-response) among suicide victims with schizophrenia suggests further controlled studies to address the potential protective effect of adequate antipsychotic treatment. The effect of newer antipsychotic drugs with fewer side-effects in suicidality should be addressed in future studies.

Most victims in high suicide risk periods of psychiatric hospitalization and recent discharge are, compared with other victims, characterized by depressive symptoms. There is a lack of consistent information about the role of antidepressants in the treatment of depressive syndrome in schizophrenia. Furthermore, as depression is an important risk factor for suicide in schizophrenia, and knowledge about the possible role of antidepressant treatment in suicide prevention among depressive patients with schizophrenia remains unknown, this issue needs to be addressed.

The proportions of subjects with recent life events seemed to vary in different clinical subgroups of suicide victims with schizophrenia. Outpatient suicides were more commonly preceded by life events, especially in a subgroup of residual phase patients who had regularly used neuroleptic medication. As with non-schizophrenic suicide victims, there may be a subgroup of compliant schizophrenic outpatients with stable illness course in whom life events may present a risk factor for suicide. This needs to be further examined using a controlled study design.

VII SUMMARY

The present thesis forms part of the National Suicide Prevention Project in Finland, during which all suicides committed in Finland over one year were examined using the psychological autopsy method. The purpose of the present studies was to examine clinical characteristics in suicide victims with schizophrenia, and to compare some antecedents of suicide between suicide victims with and without schizophrenia in a nationwide suicide population.

Data concerning suicide victims with and without schizophrenia was collected using the psychological autopsy method: comprehensive interviews of the relatives and attending health care professionals and also data from all available records. Retrospective best-estimate DSM-III-R diagnoses of schizophrenia were carefully assessed on the basis of all available information collected on the victims.

There were 92 suicide victims with DSM-III-R schizophrenia, representing 6.6% of all suicides in Finland. The mean age was 40 years among 24 women and 68 men, and the mean illness duration from the first psychiatric contact to suicide 15.5 years. Three-fourths of suicides were committed during an active phase of illness, and two-thirds were currently having depressive symptoms. About two-thirds of women but only one-third of men committed suicide during an acute exacerbation. A history of suicide attempts was common (71%). At the time of suicide almost one-third of the victims with schizophrenia were receiving psychiatric in-patient care, over half had a psychiatric outpatient treatment contact, seven (8%) were being treated by general practitioners, and eleven (12%) had no current treatment contact. Almost half of the outpatient suicide victims committed suicide during the first three months after hospital discharge. For suicide prevention, these findings imply that when planning discharge, suicidality should be assessed carefully.

Drug overdose was the most frequent suicide method among both sexes (37%). A neuroleptic drug caused the lethal intoxication among 79%, and a low-potency neuroleptic drug among 74% of the overdose victims. Female sex, age between 33-44 years and outpatient status were strongly associated with suicidal drug overdose. When treating high-risk patients with schizophrenia, prescribing large amounts of antipsychotics potentially toxic in overdose should be avoided.

In contrast to the previous suggestions of unexpected suicides among subjects with schizophrenia, it was found that 52% had communicated suicidal intent as often as non-schizophrenic victims

(55%) to next-of-kin and/or an attending health care professional. Further, victims with active phase schizophrenia (56%) had even more communication of suicidal intent and/or suicide attempts than non-psychotic victims (41%) during the last three months. Thus, the suicide process in terms of previous suicide attempts and communication of suicidal intent known by next-of-kin and an attending health care professional is similar among victims with or without schizophrenia. In suicide prevention, a history of communication of suicidal intent and suicide attempts is an important factor in the evaluation of suicide danger among persons with schizophrenia, as it is among others.

In comparison to non-schizophrenic suicides, it was found that adverse life events seemed to present less prominently before suicide among victims with schizophrenia. Almost half the victims with schizophrenia had had one or more life events three months before suicide, compared to the majority of the non-schizophrenic subjects. This difference may be at least partly due to the fewer social contacts, low rate of employment, and less alcohol misuse among persons with schizophrenia. The proportions of subjects with life events varied in different clinical subgroups of suicide victims with schizophrenia. Outpatient suicides were more commonly preceded by life events, especially in a subgroup of residual phase patients who had regularly used neuroleptic medication. Similarly with non-schizophrenic suicide victims, there may be a subgroup of compliant schizophrenic outpatients with stable illness course in whom life events may present a suicide risk.

Over half (57%) of schizophrenic suicide victims in the active illness phase were either not prescribed adequate neuroleptic treatment or were not using it, and a further 23% were estimated as compliant non-responders. This suggests the need for better psychopharmacological treatment of schizophrenia, especially in the active illness phase.

Suicide victims with schizophrenia in different treatment phases differed significantly in their current clinical and treatment related characteristics. Inpatient suicide victims had the highest proportion of negative or indifferent treatment attitudes, whereas recently discharged suicide victims had the highest prevalence of comorbid alcoholism, paranoid subtype, recent suicidality, as well as the highest number of hospitalizations per year during their illness course and the shortest last hospitalization. These findings suggest that suicide risk factors may vary in different treatment phases among patients with schizophrenia, and need to be further studied.

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IX REFERENCES

Addington D, Addington J, Patten S. Depression in people with first-episode schizophrenia. Br J Psychiatry 172:90-92, 1998.

Ahrens B, Muller-Oerlinghausen B, Grof P. Length of lithium treatment needed to eliminate the high mortality of affective disorders. Br J Psychiatry 163 (suppl 21): 27-29, 1993.

Ahrens B, Linden M. Is there a suicidality syndrome independent of specific major psychiatric disorder? Results of a split half multiple regression analysis. Acta Psychiatr Scand 94:79-86, 1996.

Alanen YO. Schizophrenia. Its Origins and Need-Adapted Treatment. Karnac Books:London, 1997.

Alanen YO, Lehtinen K, Räkköläinen V, Aaltonen J. Need-adapted treatment of new schizophrenic patients: experiences from the Turku Project. Acta Psychiatr Scand 83: 363-372, 1991.

Allebeck P, Varla A, Kristjansson E, Wistedt B. Risk factors for suicide among patients with schizophrenia. Acta Psychiatr Scand 76, 414-419, 1987.

Allebeck P, Wistedt B. Mortality in schizophrenia. A ten-year follow-up based on the Stockholm county inpatient register. Arch Gen Psychiatry 43:650-653, 1986 (a).

Allebeck P, Varla A, Wistedt B. Suicide and violent death among patients with schizophrenia. Acta Psychiatr Scand 74:43-49, 1986 (b).

Amador XF, Harkavy-Friedman J, Kasapis C, Yale SA, Flaum M, Gorman JM. Suicidal behavior in schizophrenia and its relationship to awareness of illness. Am J Psychiatry 153:1185-1188, 1996.

Andia AM, Zisook S. Gender differences in schizophrenia. A literature review. Annals Clin Psychiatry 3:333-340, 1991.

Andreasen NC. Schizophrenia. Symptoms, signs, and diagnosis of schizophrenia. Lancet 346:477-481, 1995 (a).

Andreasen NC. The evolving concept of schizophrenia: from Kraepelin to the present and future. Schizophr Research 28:105-109, 1997.

Andreasen NC, Arndt S, Alliger R, Miller D, Flaum M. Symptoms of schizophrenia. Methods, meanings, and mechanisms. Arch Gen Psychiatry 52:341-351, 1995(b).

Andreasen N, Rice J, Endicott J, Reich T, Coryell W. The family history approach to diagnosis: how useful is it? Arch Gen Psychiatry 43:421-429, 1986.

Angst J. European long-term follow up studies of schizophrenia. Schizophr Bull 14: 501-513, 1988.

APA 1980. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition. American Psychiatric Association: Washington DC, 1980.

APA 1987. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Revised Edition. American Psychiatric Association: Washington DC, 1987.

APA 1994. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. American Psychiatric Association: Washington DC, 1994.

APA 1997. American Psychiatric Association: Practice guideline for the treatment of patients with schizophrenia. Am J Psychiatry Suppl. 154, Vol. 4, 1997.

APA 1998. American Psychiatric Association. DSM-IV Sourcebook. American Psychiatric Association: Washington DC, 1998.

Appleby L. Suicide in psychiatric patients: risk and prevention. Br J Psychiatry 161:749-758,1992.

Arango V, Underwood M, Mann JJ. Biologic alterations in the brainstem of suicides. Psychiatr Clin North America 20:581-593, 1997.

Arato M, Demeter E, Rihmer Z, Somogyi E. Retrospective psychiatric assessment of 200 suicides in Budapest. Acta Psychiatr Scand 77:454-456, 1988.

Babigian HM, Odoroff CL. The mortality experience of a population with psychiatric illness. Am J Psychiatry 126:52-61, 1969.

Bacharach LL. Assessment of outcomes in community support systems: results, problems, and limitations. Schizophr Bull 8:39-60, 1982.

Baldessarini RJ, Cohen BM, Teicher MH. Significance of neuroleptic dose and plasma level in the pharmacological treatment of psychoses. Arch Gen Psychiatry 45:79-91, 1988.

Baldessarini RJ. Antipsychotic agents. In Baldessarini RJ (ed.). Chemotherapy in Psychiatry. Principles and Practice. Harvard University Press: Cambridge, 1985.

Banen DM. Suicide by psychotics. J Nerv Ment Dis 120:349-357, 1954.

Bardenstein KK, McGlashan TH. Gender differences in affective, schizoaffective, and schizophrenic disorders: A review. Schizophr Res 3:159-172, 1990.

Barnes TRE, Curson DA, Liddle PF, Patel M. The nature and prevalence of depression in chronic schizophrenic in-patients. Br J Psychiatry 154:486-491, 1989.

Barraclough BM, Bunch B, Nelson B, Sainsbury P: A hundred cases of suicide: clinical aspects. Br J Psychiatry 125:355-373, 1974.

Barraclough BM, Pallis DJ. Depression followed by suicide: a comparison of depressed suicides with living depressives. Psychol Med 5:55-61, 1975.

Barraclough B, Hughes J. Mental illness and suicide. In Suicide: Clinical and Epidemiological Studies. Croom Helm: USA, 1987.

Bartels SJ, Drake RE. Depressive symptoms in schizophrenia: comprehensive differential diagnosis. Compr Psychiatry 29: 467-483, 1988.

Bartkó G, Herczeg I, Zádor G. Clinical symptomatology and drug compliance in schizophrenic patients. Acta Psychiatr Scand 77:74-76, 1988.

Beasley CM, Dornseif BE, Bosomworth JC, Sayler ME, Rampey AH, Heiligenstein JH, Thompson VL, Murphy DJ, Masica DN. Fluoxetine abd suicide: a meta-analysis of controlled trials of treatment for depression. BMJ 303: 685-92, 1991.

Bebbington P, Wilkins S, Jones P, Foerster A, Murray R, Toone B, Lewis S. Life events and psychosis. Initial results from the Camberville collaborative psychosis study. Br J Psychiatry 162:72-79, 1993.

Bebbington PE. The content and context of compliance. Int Clin Psychopharmacol 9:5:41-50, 1995.

Beck AT, Steer RA, Kovacs M, Garrison B. Hopelessness and eventual suicide: a 10-year prospective study of patients hospitalized with suicidal ideation. Am J Psychiatry 142:559-563, 1985.

Beck AT, Steer RA. Clinical predictors of eventual suicide: a 5- to 10-year prospective study of suicide attempters. J Affect Disord 17:203-209, 1989.

Beck AT, Brown G, Berchick RJ, Stewart BL, Steer RA. Relationship between hopelessness and ultimate suicide: a replication with psychiatric outpatients. Am J Psychiatry 147:190-195, 1990.

Beskow J, Runeson B, Åsgård U. Psychological autopsies: methods and ethics. Suicide and Life-Threat Behavior 20: 307-323, 1990.

Bille-Brahe U, Schmidtke A, Kerkhof AJFM, De Leo D, Lönnqvist J, Platt S. Background and introduction to the study. In Attempted suicide in Europe. Findings from the multicentre study on parasuicide by the WHO regional office for Europe. DSWO Press, Leiden University: The Netherlands, 1994.

Birley JLT, Brown GW. Crises and life changes preceding the onset or relapse of acute schizophrenia: clinical aspects. Br J Psychiatry 116:327-333, 1970.

Black DW, Warrack G, Winokur G. Excess mortality among psychiatric patients. The Iowa record-linkage study. JAMA 253:58-61, 1985.

Black DW. The Iowa record-linkage experience. Suicide LifeThreat Behav 91:78-88, 1989.

Black DW, Fisher R. Mortality in DSM-III-R schizophrenia. Schizophr Res 7:109-116, 1992.

Bleuler E. Dementia praecox or the group of schizophrenias. International Universities Press, New York, 1950.

Bolin RK, Wright RE, Wilkinson MN, Lindner CK. Survey of suicide among patients on home leave from a mental hospital. Psychiatr Quart 42:81-89, 1968.

Bollini P, Pampallona S, Orza MJ, Adams ME, Chalmers TC. Antipsychotic drugs: is more worse? A meta-analysis of the published randomized control trials. Psychol Med 24: 307-316, 1994.

Breier A, Astrachan BM. Characterization of schizophrenic patients who commit suicide. Am J Psychiatry 141:206-209, 1984.

Breier A, Schreiber JL, Dyer J, Pickar D. National Institute of Mental Health longitudinal study of chronic schizophrenia. Arch Gen Psychiatry 48:239-246, 1991.

Brent DA, Perper JA, Goldstein CE, Kolko DJ, Allan MJ, Allman CJ, Zelenak JP. Risk factors for adolescent suicide. A comparison of adolescent suicide victims with suicidal inpatients. Arch Gen Psychiatry 45:581-588, 1988.

Brent DA. The psychological autopsy: methodological considerations for the study of adolescent suicide. Suicide Life Threat Behav 19:43-57, 1989.

Brent DA, Perper JA, Moritz G, Allman C, Friend A, Roth C, Schweers J, Balach L, Baugher M. Psychiatric risk factors for adolescent suicide: a case-control study. J Am Acad Adolesc Psychiatry 32:521-529, 1993 (a).

Brent DA, Perper JA, Moritz G, Allman CJ, Roth C, Schweers J, Balach L. The validity of diagnoses obtained through the psychological autopsy procedure in adolescent suicide victims: use of family history. Acta Psychiatr Scand 87:118-122, 1993 (c).

Brent DA, Perper JA, Moritz G, Baugher M, Roth C, Balach L, Schweers J. Stressful life events, psychopathology, and adolescent suicide: a case control study. Suicide Life Threat Behavior 23:179-187, 1993 (b).

Brent DA, Perper JA, Moritz G, Baugher M, Schweers J, Roth C. Suicide in affectively ill adolescents: a case-control study. J Aff Disord 31:193-202, 1994.

Brent DA, Bridge J, Johnson BA, Connolly J. Suicidal behavior runs in families. A controlled family study of adolescent suicide victims. Arch Gen Psychiatry 53:1145-1152, 1996.

Brown GW, Birley JLT. Crises and life changes and the onset of schizophrenia. J Health Soc Behavior 9:203-219, 1968.

Brown GW, Harris T. Fall-off in the reporting of life events. Soc Psychiatry 17:23-28, 1982.

Brown S. Excess mortality of schizophrenia. A meta-analysis. Br J Psychiatry 171:502-508, 1997.

Buchanan A. A two-year prospective study of treatment compliance in patients with schizophrenia. Psychol Med 22:787-797, 1992.

Buckley P, Thompson P, Way L, Meltzer H. Substance abuse among patients with treatment-resistant schizophrenia: characteristics and implications for clozapine therapy. Am J Psychiatry 151:385-389, 1994.

Buckley NA, Whyte IM, Dawson AH: Cardiotoxicity more common in thioridazine overdose than with other neuroleptics. Clin Toxicology 33:199-204, 1995.

Bunch, J. Recent bereavement in relation to suicide. J Psychosom Res 16: 361-366, 1972.

Butzlaff RL, Hooley JM. Expressed emotion and psychiatric relapse. Arch Gen Psychiatry 55:547-552, 1998.

Böök JA, Modrzewska K. Schizophrenia and suicide in a North Swedish isolate, 1890-1980. Clin Genetics 22:280-283, 1982.

Caldwell CB, Gottesman II. Schizophrenics kill themselves too: a review of risk factors for suicide. Schizophr Bull 16:571-588, 1990.

Caldwell CB, Gottesman II. Schizophrenia - a high risk factor for suicide: clues to risk reduction. Suicide Life Threat Behav 22:479-493, 1992.

Canetto SS, Sakinofsky I. The gender paradox in suicide. Suicide Life Threat Behav 28:1-23, 1998.

Cannon M, Buckley P, Larkin C. Suicide in schizophrenia. Irish J Psychological Med 8:19-21,1991.

Cannon TD, Kaprio J, Lönnqvist J, Huttunen M, Koskenvuo M. The genetic epidemiology of schizophrenia in a Finnish twin cohort. A population-based modeling study. Arch Gen Psychiatry 55:67-74, 1998.

Carpenter WT, Heinrichs DW, Wagman AMI. Deficit ann non-deficit forms of schizophrenia: the concept. Am J Psychiatry 145:578-583, 1988.

Carpenter WT Jr., Kirkpatrick B. The heterogeneity of the long-term course of schizophrenia. Schizophr Bull 14:645-652, 1988.

Carpenter WT, Buchanan RW. Schizophrenia. N Engl Med J 330:681-690, 1994.

Casey DE. Neuroleptic drug-induced extrapyramidal syndromes and tardive dyskinesia. Schizophr Res 4:109-120, 1991.

Cheng ATA. Mental illness and suicide. A case-control study in East Taiwan. Arch Gen Psychiatry 52:594-603, 1995.

Cheng KK, Leung CM, Lo WH, Lam TH. Suicide among Chinese schizophrenics in Hong Kong. Br J Psychiatry 154:243-246, 1989.

Cheng KK, Leung CM, Lam TH. Risk factors of suicide among schizophrenics. Acta Psychiatr Scand 81:220-224, 1990.

Chynoweth R, Tonge JI, Armstrong J. Suicide in Brisbane - a retrospective psychological study. Aust N Z J Psychiatry 14:37-45, 1980.

Ciompi L. Catamnestic long-term study on the course of life and aging of schizophrenics. Schizophr Bull 6:606-618, 1980.

Clark DC, Horton-Deutsch SL. Assessment in absentia: The value of psychological autopsy method for studying antecedents of suicide and predicting future suicides. In Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and prediction of suicide. Guilford Press: New York, 1992.

Cohen S, Leonard CV, Farberow NL. Tranquilizers and suicide in the schizophrenic patient. Arch Gen Psychiatry 11:312-321, 1964.

Conwell Y, Duberstein PR, Cox C, Herrman JH, Forbes NT, Caine ED. Relationships of age and axis I diagnoses in victims of completed suicide: a psychological autopsy study. Am J Psychiatry 153:1001-1008, 1996.

Copas JB, Robin A. Suicide in psychiatric in-patients. Br J Psychiatry 141:503-511, 1982.

Cooper SJ, Kelly CB, King DJ. 5-Hydroxyindoleacetic acid in cerebrospinal fluid and prediction of suicidal behavior in schizophrenia. Lancet 340: 940-941, 1992

Crow TJ. Molecular pathology of schizophrenia: more than one disease process? BMJ 280:66-68, 1980.

Crow TJ, MacMillan JF, Johnson AL, Johnstone EC. The Northwick Park study of first episodes of schizophrenia, II: a randomised controlled trial of prophylactic neuroleptic treatment. Br J Psychiatry 148:120-127, 1986.

Dassori AM, Mezzich JE, Keshavan M. Suicidal indicators in schizophrenia. Acta Psychiatr Scand 81:409-413, 1990.

Davidson L, McGlashan TH. The varied outcomes of schizophrenia. Can J Psychiatry 42:34-43; 1997.

Dennehy JA, Appleby L, Thomas CS, Faragher EB. Case-control study of suicide by discharged psychiatric patients. BMJ 312: 1580, 1996.

De Moore GM, Robertson AR. Suicide in the 18 years after deliberate self-harm. A prospective study. Br J Psychiatry 169:489-494, 1996.

DeQuardo JR, Tandon R. Do atypical antipsychotic medications favorably alter the long-term course of schizophrenia? J Psychiatric Res 32:229-242, 1998.

Diekstra RFW. The epidemiology of suicide: aspects of definition, classification and preventive policies. In Crepet P, Ferrari G, Platt S, Bellini M (eds.). Suicidal Behavior in Europe. Recent research findings. John Wiley CIC: Rome, 1992.

Dixon LB, Lehman AF, Levine J. Conventional antipsychotic medications for schizophrenia. Schizophr Bull 21:567-577, 1995 (a).

Dixon LB, Lehman AF. Family interventions for schizophrenia. Schizophr Bull 21: 631-643, 1995 (b).

Dohrenwend BP, Egri G. Recent stressful life events and episodes of schizophrenia. Schizophr Bull 7:12-23, 1981.

Donovan JM, Dressler DM, Geller RA. Psychiatric crisis. A comparison of schizophrenic and nonschizophrenic patients. J Nerv Ment Dis 161: 172-179, 1975.

Dorpat TL, Ripley HS. A study of suicide in the Seattle area. Compr Psychiatry 1:349-359, 1960.

Drake RE, Gates C, Cotton PG, Whitaker A. Suicide among schizophrenics. Who is at risk? J Nerv Ment Dis 172, 613-617, 1984.

Drake RE, Gates C, Whitaker A, Cotton PG. Suicide among schizophrenics: a review. Compr Psychiatry 26:90-100, 1985.

Drake RE, Ehrlich J. Suicide attempts associated with akathisia. Am J Psychiatry 142:499-501, 1985.

Drake RE, Cotton PG. Depression, hopelessness and suicide in chronic schizophrenia. Br J Psychiatry 148:554-559, 1986.

Drake RE, Osher FC, Noordsy DL, Hurlbut SC, Teague GB, Beaudett MS. Diagnosis of alcohol use disorders in schizophrenia. Schizophr Bull 16:57-67, 1990.

Eaton WW. Epidemiology of schizophrenia. Epidemiol Rev 7:105-126, 1985.

Edgerton RB, Cohen A. Culture and schizophrenia: the DOSMD challenge. Br J Psychiatry 164:222-231, 1994.

Eronen M, Tiihonen J, Hakola P. Schizophrenia and homicidal behavior. Schizophr Bull 22:83-89, 1996 (a).

Eronen M, Hakola P, Tiihonen J. Mental disorders and homicidal behavior in Finland. Arch Gen Psychiatry 53:497-501, 1996 (b).

Evenson RC, Wood JB, Nuttall EA, Cho DW. Suicide rates among public health patients. Acta Psych Scand 66:254-264, 1982.

Farberow N, Shneidman E, Leonard C. Suicide among schizophrenic hospital patients. In Farberow N, Shneidman E (eds.). The Cry for Help. McGraw-Hill: New York, 1961.

Fawcett J, Scheftner W, Clark D, Hedeker D, Gibbons R, Coryell W. Clinical predictors of suicide in patients with major affective disorders: a controlled prospective study. Am J Psychiatry 144:35-40, 1987.

Fawcett J, Scheftner WA, Fogg L, Clark DC, Young MA, Hedeker D, Gibbons R. Time-related predictors of suicide in major affective disorder. Am J Psychiatry 147:1189-1194, 1990.

Feighner JP, Robins E, Guze SB, Woodruff RA, Winokur G, Munoz R. Diagnostic criteria for use in psychiatric research. Arch Gen Psychiatry 26, 57, 1972.

Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull 23(4):637-651, 1997 (a).

Fenton WS, McGlashan TH. Antecedents, symptom progression, and long-term outcome of the deficit syndrome in schizophrenia. Am J Psychiatry 151:3:351-356, 1994.

Fenton WS, McGlashan TH, Victor BJ, Blyler CR. Symptoms, subtype, and suicidality in patients with schizophrenia spectrum disorders. Am J Psychiatry 154:2:199-204, 1997 (b).

Fernando S, Storm V. Suicide among psychiatric patients of a district general hospital. Psychol Med 14:661-672, 1984.

Fleiss J.L. Statistical methods for rates and proportions. John Wiley and Sons: New York, 1975.

Foster T, Gillespie K, McClelland R. Mental disorders and suicide in Northern Ireland Br J Psychiatry 170:447-452, 1997.

Fowler IL, Carr VJ, Carter NT, Lewin TJ. Patterns of current and lifetime substance use in schizophrenia. Schizophr Bull 24:443-455, 1998.

Garrison CZ. Demographic predictors of suicide. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and prediction of suicide. Guilford Press: New York, 1992.

Gilbert PL, Harris MJ, McAdams LA, Jeste DV. Neuroleptic withdrawal in schizophrenic patients. A review of the literature. Arch Gen Psychiatry 52:173-188, 1995.

Goh SE, Salmons PH, Whittington RM. Hospital suicides: are there preventable factors? Profile of the psychiatric hospital suicide. Br J Psychiatry 154:247-249, 1989.

Goldacre M, Seagroatt V, Hawton K. Suicide after discharge from psychiatric inpatient care. Lancet 31: 342:283-286,1993.

Goldney RD. The IASP Adelaide declaration on suicide prevention. Crisis, editorial 19/2, 1998.

Goldstein RB, Black DW, Nasrallah A, Winokur G. The prediction of suicide. Sensitivity, specificity, and predictive value of a multivariate model applied to suicide among 1906 patients with affective disorders. Arch Gen Psychiatry 48:418-422, 1991.

Gould MS, Fisher P, Parides M, Flory M, Shaffer D. Psychosocial risk factors of child and adolescent completed suicide. Arch Gen Psychiatry 53:1155-1162, 1996.

Gould MS, Shaffer D. The clinical prediction of adolescent suicide. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and Prediction of Suicide. Guilford Press: New York, 1992.

Greenfield SF, Reizes JM, Magruder KM, Muenz LR, Kopans B, Jacobs DG. Effectiveness of community-based screening for depression. Am J Psychiatry 154:1391-1397, 1997.

Grove WM, Andreasen NC. Simultaneous tests of multiple hypotheses in exploratory research. J Nerv Ment Dis 170:3-8, 1982.

Gunnel D, Frankel S. Prevention of suicide: aspirations and evidence. BMJ 308: 1227-1233, 1994.

Gunnel DJ, Peters TJ, Kammerling RM, Brooks J. Relation between parasuicide, suicide, psychiatric admissions, and socioeconomic deprivation. BMJ 311: 226-30, 1995.

Haas GL. Suicidal behavior in schizophrenia. In Maris RW, Silverman MM, Canetto SS (eds.). Review of Suicidology. The Guilford Press: USA, 1997.

Hagnell O, Rorsman B. Suicide in the Lundby Study: a comparative investigation of clinical aspects. Neuropsychobiology 5:61-73, 1979.

Hagnell O, Rorsman B. Suicide in the Lundby Study: a controlled prospective investigation of stressful life events. Neuropsychobiology 6:319-332, 1980.

Halstead SM, Barnes TRE, Speller JC. Akathisia: prevalence and associated dysphoria in an in-patient population with chronic schizophrenia. Br J Psychiatry 164:177-183, 1994.

Harris EC, Barraclough BM: Suicide as an outcome for medical disorders. Medicine 73:281-296, 1994.

Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. Br J Psychiatry 170:205-228, 1997.

Harris EC, Barraclough B. Excess mortality of mental disorder. Br J Psychiatry 173:11-53, 1998.

Hawton K. Assessment of suicide risk. Br J Psychiatry 150:145-153, 1987.

Hawton K, Arensman E, Townsend E, Bremner S, Feldman E, Goldney R, Gunnel D, Hazell P, Van Heeringen K, House A, Owens D, Sakinofsky I, Träskman-Bendtz L. Deliberate self harm: systematic review of efficacy of psychosocial and pharmacological treatments in preventing repetition. BMJ 317:441-447, 1998.

Hawton K, Fagg J. Suicide, and other causes of death, following attempted suicide. Br J Psychiatry 152:751-761, 1988.

Hegarty JD, Baldessarini RJ, Tohen M, Wternaux C, Oepen G. One hundred years of schizophrenia: a meta-analysis of the outcome literature. Am J Psychiatry 151:1409-1416, 1994.

Heikkinen M, Aro H, Lönnqvist J. Review article: Life events and social support in suicide. Suicide Lif Threat Behavior 23:343-358, 1993.

Heikkinen ME, Isometsä ET, Marttunen MJ, Aro HM, Lönnqvist JK. Social factors in suicide. Br J Psychiatry 167:747-753, 1995.

Henriksson M. Mental Disorders in Suicide: a Comorbidity Approach. Publications of the National Public Health Institute, NPHI A 15/ 1996. Hakapaino: Helsinki, 1996.

Henriksson MM, Aro HA, Marttunen MJ, Heikkinen MH, Isometsä ET, Kuoppasalmi KI, Lönnqvist JK. Mental disorders and comorbidity in suicide. Am J Psychiatry 150:935-940, 1993.

Henry JA, Alexander CA, Sener EK. Relative mortality from overdose of antidepressants. BMJ 310:221-224, 1995.

Herz MI, Glazer WM, Mostert MA, Sheard MA, Szymanski HV, Hafez H, Mirza M, Vana J. Intermittent vs maintenance medication in schizophrenia. Arch Gen Psychiatry 48:333-339, 1991.

Hintikka J, Viinamäki H, Tanskanen A, Kontula O, Koskela K. Suicidal ideation and parasuicide in the Finnish general population. Acta Psychiatr Scand 98:23-27, 1998.

Hirsch S, Bowen J, Emami J, Cramer P, Jolley A, Haw C, Dickinson M. A one year prospective study of the effect of life events and medication in the aetiology of schizophrenic relapse. Br J Psychiatry 168:49-56, 1996.

Hirsch SR, Barnes TRE. The clinical treatment of schizophrenia with antipsychotic medication. In Hirsch SR, Weinberger DR (eds.). Schizophrenia. Blackwell Science Ltd: Oxford, 1995.

Hirschfield RMA, Davidson L. Risk factors for suicide. In Frances AJ, Hales R (eds.). Review of Psychiatry (Vol 7). American Psychiatric Press: Washington DC, 1988.

Hogan TP, Awad AG. Pharmacotherapy and suicide risk in schizophrenia. Can J Psychiatry 28:277-281, 1983.

Hogarty GE, McEvoy JP, Ulrich RF, DiBarry AL, Bartone P, Cooley S, Hammill K, Carter M, Munetz MR, Perel J. Pharmacotherapy of impaired affect in recovering schizophrenic patients. Arch Gen Psychiatry 52:29-41, 1995.

Hogarty GE, Ulrich RF. The limitations of antipsychotic medication on schizophrenia relapse and adjustment and the contributions of psychosocial treatment. J Psychiatric Res 32:243-250, 1998.

Honkonen T. Need for care and support in schizophrenia. A follow-up study of discharged schizophrenia patients. Acta Universitatis Tamperensis, Ser A Vol. 437. Tampere, 1995.

Hovatta I. Molecular genetics of familial schizophrenia and PLO-SL. Publications of the National Public Health Institute, KTL A20/1998, Helsinki 1998.

Hovatta I, Terwilliger JD, Lichtermann D, Mäkikyrö T, Suvisaari J, Peltonen L, Lönnqvist J. Schizophrenia in the genetic isolate of Finland. Am J Med Genetics 74:353-360, 1997.

Høyer G, Lund E. Suicide among women related to number of children in marriage. Arch Gen Psychiatry 50:134-137, 1993.

Hu W-H, Sun C-M, Lee C-T, Peng S-L, Lin S-K, Shen WW. A clinical study of schizophrenic suicides. 42 cases in Taiwan. Schizophr Res 5:43-50, 1991.

Humphrey JA. Social loss: A comparison of suicide victims, homicide offenders and non-violent individuals. Dis Nerv System 38:157-160, 1977.

Huttunen MO. The evolution of the serotonin-dopamine antagonist concept. J Clin Psychopharmacology 15: 4S-10S, 1995.

Häfner H, an der Heiden W. Epidemiology of schizophrenia. Can J Psychiatry 42:139-151, 1997.

Härö AS. Surveillance of mortality in Scandinavian countries 1947-1993. The Social Insurance Institution, Finland. Studies in social security and health 4. Hakapaino: Helsinki, 1995.

Inskip HM, Harris C, Barraclough B. Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. Br J Psychiatry 172:35-37, 1998.

Isacsson G, Bergman U. Does increased use of antidepressants reduce suicide rates? Abstract, 7th Symposium on Suicide and Suicidal Behavior. Gent, 9.-12. September, 1998.

Isacsson G, Bergman U, Rich CL. Antidepressants, depression and suicide: an analysis of the San Diego study. J Aff Disord 32:277-286, 1994.

Isacsson G, Bergman U, Rich CL. Epidemiological data suggest antidepressants reduce suicide risk among depressives. J Aff Disord 41: 1-8, 1996.

Isacsson G, Holmgren P, Druid H, Bergman U. The utilization of antidepressants - a key issue in the prevention of suicide: an analysis of 5281 suicides in Sweden during the period 1992-1994. Acta Psychiatr Scand 96:94-100, 1997.

Isohanni M, Hartikainen A-L, Moring J. Mitä tiedetään skitsofrenian syistä ja taustasta? Duodecim 111:1745-1752, 1995.

Isohanni M, Honkonen T, Vartiainen H, Lönnqvist J. Skitsofrenia. In: Lönnqvist J, Heikkinen M, Henriksson M, Marttunen M, Partonen T (Eds). Psykiatria. Duodecim Oy: Jyväskylä, 1999.

Isometsä E, Aro S, Aro H. Depression in Finland: a computer assisted telephone interview study. Acta Psychiatr Scand 96:122-128, 1997.

Isometsä E, Henriksson M, Heikkinen M,Lönnqvist J. Suicide after discharge from psychiatric inpatient care. Lancet 342:1055-1056, 1993 (letter).

Isometsä ET, Henriksson MM, Aro HM, Heikkinen ME, Kuoppasalmi KI, Lönnqvist JK. Suicide in major depression. Am J Psychiatry 1994, 151:530-536 (a).

Isometsä ET, Henriksson MM, Aro HM, Lönnqvist JK. Suicide in bipolar disorder in Finland. Am J Psychiatry 151:7:1020-1024, 1994 (b).

Isometsä ET, Heikkinen ME, Henriksson MM, Aro HM, Lönnqvist JK. Recent life events and completed suicide in bipolar affective disorder. A comparison with major depressive suicides. J Aff Disord 33:99-106, 1995 (b).

Isometsä ET, Heikkinen ME, Henriksson MM, Aro HM, Marttunen MJ, Lönnqvist JK. Parenthood, completed suicide, and mental disorders. Arch Gen Psychiatry 53:1061-1062, 1996 (letter).

Isometsä ET, Heikkinen ME, Marttunen MJ, Henriksson MM, Aro HM, Lönnqvist JK. The last appointment before suicide: is suicide intent communicated? Am J Psychiatry 152, 919-922, 1995 (a).

Isometsä ET, Lönnqvist JK. Suicide attempts preceding completed suicide. Br J Psychiatry 173:531-536, 1998.

Jablensky A. Schizophrenia: the epidemiological horizon, In Hirsch SR, Weinberger DR (eds.). Schizophrenia. University Press: Cambridge, 1995.

Jenkins R. Principles of prevention. In Paykel E, Jenkins R (eds.). Prevention in psychiatry. The Royal College of Psychiatrists: London, 1994.

Jeste DV, Gladsjo JA, Lindamer LA, Lacro JP. Medical comorbidity in schizophrenia. Schizophr Bull 22:413-430, 1996.

Jick SS, Dean AD, Jick H. Antidepressants and suicide. BMJ 310:215-218, 1995.

Johns CA, Stanley M, Stanley B. Suicide in schizophrenia. Ann New York Acad Sciences 487, 294-300, 1986.

Johns CA, Thompson JW. Adjunctive treatments in schizophrenia: pharmacotherapies and electroconvulsive treatment. Schizophr Bull 21: 607-619, 1995.

Johnson DAW. The siginifance of depression in the prediction of relapse in chronic schizophrenia. Br J Psychiatry 152:320-323, 1988.

Jolley AG, Hirsch SR, Morrison E, McRink A, Wilson L. Trial of brief intermittent neuroleptic prophylaxis for selected schizophrenic outpatients: clinical and social outcome at two years. BMJ 301:837-842, 1990.

Jones JS, Stein DJ, Stanley B, Guido JR, Winchel R, Stanley M. Negative and depressive symptoms in suicidal schizophrenics. Acta Psychiatr Scand 89:81-87, 1994.

Joukamaa M, Lehtinen V, Karlsson H. The ability of general practitioners to detect mental disorders in primary care. Acta Psychiatr Scand 91:52-56, 1995.

Kane JM. Schizophrenia. N Engl J Med 4:34-40, 1996.

Kane J, Honigfeld G, Singer J, Meltzer H, Clozaril Collaborative Study Group. Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine. Arch Gen Psychiatry 45:789-796, 1988.

Kane JM, Mayerhoff D. Do negative symptoms respond to pharmacological treatment? Br J Psychiatry 155 (suppl 7):115-118, 1989.

Kane JM, Rifkin A, Quitkin F, Nayak D, Ramos-Lorenzi J. Fluphenazine vs placebo in patients with remitted, acute first-episode schizophrenia. Arch Gen Psychiatry 39:70-73, 1982.

Kaprio J, Koskenvuo M, Rita H. Mortality after bereavement: a prospective study of 95,647 widowed persons. Am J Public Health 77:283-287, 1987.

Karper LP, Krystall JH. Augmenting antipsychotic efficacy: new approaches. In Breier A (ed.) . The New Pharmacotherapy of Schizophrenia. American Psychiatric Press: Washington DC, 1996.

Kawachi I, Willett WC, Colditz GA, Stampfer MJ, Speizer FE. A prospective study of coffee drinking and suicide in women. Arch Intern Med 156:521-525, 1996.

Keller MB, Lavori PB, Klerman GL, Andreasen NC, Endicott J, Coryell W, Fawcett J, Rice JP, Hirschfeld RMA. Low levels and lack of predictors of somatotherapy and psychotherapy received by depressed patients. Arch Gen Psychiatry 43:458-466, 1986.

Kendler KS, Gallagher TJ, Abelson JM, Kessler RC. Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a US community sample. The National Comorbidity Survey. Arch Gen Psychiatry 53:1022-1031, 1996.

Kendler KS, Silberg JL, Neale MC, Kessler RC, Heath AC, Eaves LJ. The family history method: whose psychiatric history is measured? Am J Psychiatry 148:1501-1504, 1991.

Kerkhof A, Clark D. How to evaluate national suicide programs? Crisis 19:2-3, 1998.

Keith SJ, Regier DA, Rae DS. Schizophrenic disorders. In: Robins LN, Regier DA (eds). Psychiatric disorders in America: The Epidemiologic Catchment Area Study. The Free Press: New York, 1991.

Keshavan MS, Reynolds CF, Montrose D, Miewald J, Downs C, Sabo EM. Sleep and suicidality in psychotic patients. Acta Psychiatr Scand 89:122-125, 1994.

Keskimäki I, Aro S. Accuracy of data on diagnoses, procedures and accidents in the Finnish Hospital Discharge Register. Int J Health Sciences, 2:15-21 1991.

Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen H-U, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Arch Gen Psychiatry 51:8-19, 1994.

Kessler RC, Nelson CB, McGonagle KA, Swartz M, Blazer DG. Comorbidity of DSM-III-R major depressive disorder in the general population: results from the US National Comorbidity Survey. Br J Psychiatry 168:17-30, 1996.

Kessler RC, Olfson M, Berglund PA. Patterns and predictors of treatment contact after first onset of psychiatric disorders. Am J Psychiatry 155:62-69, 1998.

King E. Suicide in the mentally ill. An epidemiological sample and implications for clinicians. Br J Psychiatry 165: 658-663, 1994.

Kleck G. Miscounting suicides. Suicide Life Threat Behav 18:219-236, 1988.

Klein DN, Ouimette PC, Kelly HS, Ferro T, Riso LP. Test-retest reliability of team consensus best-estimate diagnoses of axis I and II disorders in a family study. Am J Psychiatry 151:1043-1047, 1994.

Klerman GL. Clinical epidemiology of suicide. J Clin Psychiatry 48(12 Suppl): 33-38, 1987.

Klerman GL, Weissman MM. Increasing rates of depression. JAMA 261:2229-2235, 1989.

Knapp M. Costs of schizophrenia. Br J Psychiatry 171:509-518, 1997.

Koreen AR, Siris SG, Chakos M, Alvir J, Mayerhoff D, Liebermann J. Depression in first-episode schizophrenia. Am J Psychiatry 150:1643-1648, 1993.

Kraemer HC, Kazdin AE, Offord DR, Kessler RC, Jensen PS, Kupfer DJ. Coming to terms with the terms of risk. Arch Gen Psychiatry 54:337-343, 1997.

Kraepelin E. Dementia praecox and paraphrenia. E and S Livingstone: Edinburgh, 1919.

Kreitman N. Suicide, age and marital status. Psychological Med 18:121-128, 1988.

Kuoppasalmi K, Lönnqvist J, Pylkkänen K, Huttunen M: Classification of mental disorders in Finland: a comparison of the Finnish classification of mental disorders with DSM-III-R. Psychiatr Fenn 20:65-81, 1989.

Kuusi K. Prognosis of schizophrenic psychoses in Helsinki in 1975-1983. Monographs of Psychiatrica Fennica No.13. Helsinki, 1986.

Lamb HR. Lessons learned from deinstitutionalism in the US. Br J Psychiatry 162:587-592, 1993

Landmark J, Cernovsky ZZ, Merskey H. Correlates of suicide attempts and ideation in schizophrenia. Br J Psychiatry 151: 18-20, 1987.

Leckman JF, Sholomskas D, Thompson D, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis. A methodological study. Arch Gen Psychiatry 39:879-883, 1982.

Leff J. Evaluating the transfer of care from psychiatric hospitals to direct-based services. Br J Psychiatry 162(Suppl 19): 6, 1993.

Leff JP, Hirsch SR, Gaind R, Rohde PD, Stevens BC. Life events and maintenance therapy in schizophrenic relapse. Br J Psychiatry 123:659-660, 1973.

Leff J, Tress K, Edwards B. The clinical course of depressive symptoms in schizophrenia. Schizophr Res 1:25-30, 1988.

Leff J, Sartorius N, Jablensky A, Korten A, Ernberg G. The international pilot study of schizophrenia: a five-year follow-up findings. Psychol Med 22:131-145, 1992.

Leff J, Trieman N, Gooch C. Team for the assessment of psychiatric services (TAPS) project 33: prospective follow-up study of long-stay patients discharged from two psychiatric hospitals. Am J Psychiatry 153:1318-1324, 1996.

Lehman RE. Symptom contamination of the schedule of recent life events. J Consult Clin Psychology 46:1564-65, 1978.

Lehtinen V, Joukamaa M, Jyrkinen E, Lahtela K, Raitasalo R, Maatela J, Aromaa A. Need for mental health services of the adult population in Finland: results from the Mini Finland Health Survey. Acta Psychiatr Scand 81: 426-431, 1990 (b).

Lehtinen V, Joukamaa M, Lahtela R, Raitasalo R, Jyrkinen E, Maatela J, Aromaa A. Prevalence of mental disorders among adults in Finland: basic results from the Mini Finland Health Survey. Acta Psychiatr Scand 81:418-425, 1990 (a).

Lehtinen V, Lindholm V, Veijola J, Väisänen E, Puukka P. Stability of prevalences of mental disorders in a normal population cohort followed for 16 years. Soc Psychiatry Psychiatric Epidem 26:40-46, 1991.

Lesage AD, Boyer R, Grunberg F, Vanier C, Morissette R, Mènard-Buteau C, Loyer M. Suicide and mental disorders: a case -control study of young men. Am J Psychiatry 151:1063-1068, 1994.

Lester D. The effectiveness of suicide prevention centers: a review. Suicide Life Threat Behav 27:304-310, 1997.

Lewis CF, Tandon R, Shipley JE, DeQuardo JR, Jibson M, Taylor SF, Goldman M. Biological predictors of suicidality in schizophrenia. Acta Psychiatr Scand 94:416-420, 1996.

Lewis G, Hawton K, Jones P. Strategies for preventing suicide. Br J Psychiatry 171:351-354, 1997.

Liebermann JA. Signs and symptoms. What can they tell us about the clinical course and pathophysiologic processes of schizophrenia. Arch Gen Psychiatry 52:361-363, 1995.

Lieberman JA, Safferman AZ, Pollack S, Szymanski S, Johns C, Howard A, Kronig M, Bookstein P, Kane JM. Clinical effects of clozapine in chronic schizophrenia: response to treatment and predictors of outcome. Am J Psychiatry 151:1744-1752, 1994.

Liebermann JA, Sheitman B, Chakos M, Robinson D, Schooler N, Keith S. The development of treatment resistance in patients with schizophrenia: a clinical and pathophysiologic perspective. J Clin Psychopharmacology 18(suppl 1):20S-24S, 1998.

Lim LCC, Tsoi WF. Suicide and schizophrenia in Singapore - a fifteen year follow-up study. Annals Acad Medicine 20:201-203, 1991.

Lindelius R, Kay WK. Some changes in the pattern of mortality in schizophrenia in Sweden. Acta Psychiatr Scand 49:315-323, 1973.

Lindeman S, Läärä E, Vuori E, Lönnqvist J. Suicides among physicians, engineers and teachers: the prevalence of reported depression, admissions to hospital and contributory causes of death. Acta Psychiatr Scand 96:68-71, 1997.

Linehan MM. Behavioral treatments of suicidal behaviors. Definitional obfuscation and treatment outcomes. Annals New York Acad Sciences 836:302-328, 1997.

Linnoila M, Virkkunen M. Biologic correlates of suicidal risk and aggressive behavioral traits. J Clin Psychopharmacology 12:19S-20S, 1992.

Litman RE. 500 psychological autopsies. J For Sciences 34: 638-646, 1989.

Litman RE, Curphey T, Shneidman ES, Farberow NL, Tabachnik N: Investigations of equivocal suicides. JAMA 184:924-929, 1963.

Lukoff D, Snyder K, Ventura J, Nuechterlein KH. Life events, familial stress, and coping in the developmental course of schizophrenia. Schizophr Bull 10:258-292, 1984.

Lönnqvist J. Suicide in Helsinki: an epidemiological and socialpsychiatric study of suicides in Helsinki in 1960-61 and 1970-71. Monographs of Psychiatria Fennica No. 8. Helsinki, 1977.

Lönnqvist JK. National suicide prevention project in Finland: a research phase of the project. Psychiatr Fenn 19:125-132, 1988 (b).

Lönnqvist J, Aro H, Marttunen M (toim.). Itsemurhat Suomessa 1987 - projekti: toteutus, aineisto ja tutkimustuloksia. STAKES: Tutkimuksia 25. Gummerus: Jyväskylä, 1993.

Lönnqvist J, Louhivuori K, Palonen K, Tuomaala A. Suicide mortality in Finland. Psychiatr Fenn 19:133-142, 1988 (a).

Lönnqvist J, Niskanen P, Rinta-Mänty R, Achté K, Kärhä E. Suicides in psychiatric hospitals in different therapeutic eras. A review of literature and own study. Psychiatr Fenn 265-273, 1974.

MacMahon B, Pugh TF. Suicide in the widowed. Am J Epidemiology 81(1):23-31, 1965.

Malone KM. Pharmacotherapy of affectively ill suicidal patients. Psychiatr Clin North America 20:613-624, 1997.

Mann JJ. The neurobiology of suicide. Nat Med 4:25-30, 1998.

Mann JJ, Arango V. Integration of neurobiology and psychopathology in a unified model of suicidal behavior. J Clin Psychopharmacology 12 (Suppl 2):2S-7S, 1992.

Mann JJ, Malone KM, Nielsen DA, Goldman D, Erdos J, Gelernter J. Possible association of a polymorphism of the tryptophan hydroxylase gene with suicidal behavior in depressed patients. Am J Psychiatry 154:1451-1453, 1997.

Marder SR, Wirshing WC, Van Putten T. Drug treatment of schizophrenia. Overview of recent research. Schizophr Res 4:81-90, 1991.

Marder S. Defining and characterising treatment-resistant schizophrenia. Eur Psychiatry; 10(suppl 1): 7-10, 1995.

Maris RM. The relationship of nonfatal suicide attempts to completed suicides. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and Prediction of suicide. Guilford Press: New York, 1992.

Marttunen M, Aro HM, Henriksson MM, Lönnqvist JK. Mental disorders in adolescent suicide. DSM-III-R axes and diagnoses in suicides among 13- to 19-year olds in Finland. Arch Gen Psychiatry 48:834-839, 1991.

Marzuk PM. Violence, crime and mental illness - how strong a link? Arch Gen Psychiatry 53:481-486, 1996.

Marzuk PM, Tardiff K, Leon AC, Tardiff K, Morgan EB, Stajic M, Mann JJ. The effect of access to lethal methods of injury on suicide rates. Arch Gen Psychiatry 49: 451-458, 1992.

Marzuk PM, Tardiff K, Leon AC, Hirsch CS, Stajic M, Hartwell N, Portera L. Use of prescription psychotropic drugs among suicide victims in New York city. Am J Psychiatry 152:1520-1522, 1995.

Maziade M, Roy M-A, Fournier J-P, Cliche D, Mèrette C, Caron C, Garneau Y, Montgrain N, Shriqui C, Dion C, Nicole L, Potvin A, Lavalleè J-C, Pirès A, Raymond V. Reliability of best-estimate diagnosis in genetic linkage studies of major psychoses: results from the Quebec pedigree studies. Am J Psychiatry 149:1674-1686, 1992.

McEvoy JP, Howe AC, Hogarty GE. Differences in the nature of relapse and subsequent inpatient course between medication-compliant and noncompliant schizophrenic patients. J Nerv Ment Dis 172:7:412-416, 1984.

McGlashan TH. Predictors of shorter-, medium-, and longer-term outcome in schizophrenia. Am J Psychiatry 143:50-55, 1986.

McGlashan T. A selective review of recent North American long-term follow-up studies of schizophrenia. Schizophr Bull 14:515-542, 1988.

McGlashan TH, Carpenter WT. Postpsychotic depression in schizophrenia. Arch Gen Psychiatry 33: 231-239, 1976.

McGuffin P, Owen MJ, Farmer AE. Genetic basis of schizophrenia. Lancet 346:678-682, 1995.

McIntosh JL: Methods of suicide. In Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and prediction of suicide. Guilford Press: New York, 1992.

Mednick SA, Machon RA, Huttunen MO, Bonett D. Adult schizophrenia following prenatal exposure to an influenza epidemic. Arch Gen Psychiatry 45:189-192, 1988.

MEDSTAT. Guide to MEDSTAT, Version 2.12, Statistical program for the analysis of the results of controlled therapeutic trials and other types of clinical research. Astra Group A/S, Copenhagen 1991.

Mehtonen O-P, Aranko K, Mälkönen L, Vapaatalo H: A survey of sudden death associated with the use of antipsychotic or antidepressant drugs: 49 cases in Finland. Acta Psychiatr Scand 84:58-64, 1991.

Meltzer HY, Okayli G. Reduction of suicidality during clozapine treatment of neuroleptic-resistant schizophrenia: impact on risk-benefit assessment. Am J Psychiatry 152:2:183-190, 1995.

Meltzer HY, Lee M, Cola P. The evolution of treatment resistance: biologic implications. J Clin Psychopharmacology 18:5S-11S, 1998(a).

Meltzer HY. Suicide in schizophrenia: risk factors and clozapine treatment. J Clin Psychiatry 59:15-20, 1998 (b).

Michel K. Suicide risk factors: a comparison of suicide attempters with suicide completers. Br J Psychiatry 150:78-82, 1987.

Miles CP. Conditions predisposing to suicide: a review. J Nerv Ment Dis 164:231-246, 1977.

Minkoff K, Bergman E, Beck AT, Beck RT. Hopelessness, depression, and attempted suicide. Am J Psychiatry 130(4):455-459, 1973.

Mitterauer B. Mehrdimensionale diagnostik von 121 suiziden im bundesland Salzburg im jahre 1978. Wien Med Wochenschr 131:229-234, 1981.

Modestin J. Antidepressant therapy in depressed clinical suicides. Acta Psychiatr Scand 71:111-116, 1985.

Modestin J, Hoffman H. Completed suicide in psychiatric inpatients and former inpatients. A comparative study. Acta Psychiatr Scand 79:229-234, 1989.

Modestin J, Schwartzenbach F. Effect of psychopharmacology on suicide risk in discharged psychiatric inpatients. Acta Psychiatr Scand 85:173-175, 1992.

Modestin J, Zarro I, Waldvogel D. A study of suicide in schizophrenic in-patients. Br J Psychiatry 160:398-401, 1992.

Monk M. Epidemiology of suicide. Epidem Rev 9:51-69, 1987.

Montgomery SA, Montgomery DB. Pharmacological prevention of suicidal behavior. J Aff Disord 4:291-298, 1982.

Morrison JR. Suicide in a psychiatric practice population. J Clin Psychiatry 43:9:348-352, 1982.

Mortensen PB, Juel K. Mortality and causes of death in first admitted schizophrenic patients. Br J Psychiatry 163:183-189, 1993.

Mościcki EK. Identification of suicide risk factors using epidemiologic studies. Psychiatr Clin North America 20:499-517, 1997.

Mościcki EK, O´Carroll P, Rae DS, Locke BZ, Roy A, Regier DA. Suicide attempts in the Epidemiologic Catchment Area Study. Yale J Biol Med 61:259-268, 1988.

Motto JA. Suicide prevention for high-risk persons who refuse treatment. Suicide Life Threat Behav 6:223-230, 1976.

Mueser KT, Yarnold PR, Levinson DF, Singh H, Bellack AS, Kee K, Morrison RL, Yadalam KG. Prevalence of substance abuse in schizophrenia: demographic and clinical correlates. Schizophr Bull 16:31-56, 1990.

Muijen M, Hadley T. Community care: parts and systems. In Hirsch SR, Weinberger DR (eds.). Schizophrenia. Blackwell Science Lt: Oxford, 1995.

Müller-Oerlinghausen B, Ahrens B, Grof E, Grof P, Lenz G, Schou M, Simhandl C, Thau K, Volk J, Wolf R, Wolf T. The effect of long-term lithium treatment on the mortality of patients with manic-depressive or schizo-affective illness. Acta Psychiatr Scand 86:218-222, 1992.

Müller-Oerlinghausen B, Wolf T, Ahrens B, Glaenz T, Schou M, Grof E, Grof P, Lenz G, Simhandl C, Thau K, Vestergaard P, Wolf R. Mortality of patients who dropped out from regular lithium prophylaxis: a collaborative study by the International Group for the Study of Lithium-Treated Patients (IGSLI). Acta Psychiatr Scand 94:344-347, 1996.

Munk-Jørgensen P, Mortensen PB. Incidence and other aspects of the epidemiology of schizophrenia in Denmark 1971-1987. Br J Psychiatry 161:489-495, 1992.

Murphy GE. On suicide prediction and prevention. Arch Gen Psychiatry 40:343-344, 1983.

Murphy GE. Suicide and attempted suicide. In Winokur G, Clayton PJ(eds.). The Medical Basis of Psychiatry. W.B. Saunders: Philadelphia, 1994.

Murray CJL, Lopez AD. Global mortality, disability, and the contribution of risk factors: global burden of disease study. Lancet 349:1436-1442, 1997.

Myllykangas M, Ruohonen P, Ryynänen O-P. Onko itsemurhien ehkäisy mahdollista? Itsemurhien ehkäisyprojektin tavoitteet ja toteutus. Suom Lääkäril 42:1251-1257, 1997.

Mäkikyrö T, Karvonen JT, Hakko H, Nieminen P, Joukamaa M, Isohanni M, Jones P, Järvelin M-R. Comorbidity of hospital-treated psychiatric and physical disorders with special reference to schizophrenia: a 28 year follow-up of the 1966 Northern Finland general population birth cohort. Public Health 112: 221-228, 1998.

Möller HJ, Von Zerssen D. Course and outcome of schizophrenia. In. Hirsch SR, Weinberger DR. (eds.). Schizophrenia. Blackwell Science Ltd: Oxford, 1995.

Nathan RG, Rousch AE. Which patients commit suicide? Am J Psychiatry 141, 1017, 1984 (letter).

Neeleman J, Halpern D, Lewis G. Tolerance of suicide, religion and suicide levels: an ecological and individual study in 19 Western countries. Psychol Med 27:1165-1171, 1997 (b).

Neeleman J, Wessely S. Changes in classification of suicide in England and Wales: time trends and associations with coroners´ professional backgrounds. Psychol Med 27:467-472, 1997(a).

Neeleman J, Wessely S, Wadsworth M. Predictors of suicide, accidental death, and premature natural death in a general-population birth cohort. Lancet 351:93-97, 1998.

Newman SC, Bland RC. Mortality in a cohort of patients with schizophrenia: a record linkage study. Can J Psychiatry 36:239-245, 1991.

Nielsen DA, Goldman D, Virkkunen M, Tokola R, Rawlings R, Linnoila M. Suicidality and 5-hydroxyindoleacetic acid concentration associated with a tryptophan hydroxylase polymorphism. Arch Gen Psychiatry 51:34-38, 1994.

Niskanen P, Lönnqvist J, Achté K. Schizophrenia and suicides. Psychiatr Fenn 223-229, 1973.

Niskanen P, Lönnqvist J, Achté K, Rinta-Mänty R. Suicides in Helsinki psychiatric hospitals in 1964-1972. Psychiatr Fenn 275-280, 1974.

Nordentoft M, Breum L, Munck LK, Nordestgaard AG, Hunding A, Bjældager PAL. High mortality by natural and unnatural causes: a 10 year follow up study of patients admitted to a poisoning treatment centre after suicide attempts. BMJ 306:1637-1641, 1993.

Nordström P, Samuelsson M, Åsberg M. Survival analysis of suicide risk after attempted suicide. Acta Psychiatr Scand 91:336-340, 1995 (a).

Nordström P, Åsberg M, Åberg-Wistedt A, Nordin C. Attempted suicide predicts suicide risk in mood disorders. Acta Psychiatr Scand 92:345-350, 1995 (b).

Norman RMG, Malla AK. Subjective stress in schizophrenic patients. Soc Psychiatry Psychiatric Epidemiology 26:212-216, 1991.

Norman RMG, Malla AK. Stressful life events and schizophrenia. I: A review of the research. Br J Psychiatry 162:161-166, 1993 (a).

Norman RMG, Malla AK. Stressful life events and schizophrenia. II: Conceptual and methodological issues. Br J Psychiatry 162:166-174, 1993 (b).

Nyman AK, Jonsson H. Patterns of self-destructive behavior in schizophrenia. Acta Psychiatr Scand 73:252-262, 1986.

Näyhä S. Short and medium-term variations in mortality in Finland. A study on cyclic variations, annual and weekly periods and certain irregular changes in mortality in Finland during the period 1868-1972. Scand J Soc Med 8(suppl 21), 1980.

Obafunwa JO, Busuttil A. Clinical contact preceding suicide. Fellowship Postgrad Med 70, 428-432, 1994.

O´Carroll PW. Silverman MM, Berman AL. Community suicide prevention: the effectiveness of bridge barriers. Suicide Life Threat Behavior 24:89-99, 1994.

O´Carroll PW, Berman AL, Maris RW, Moscicki EK, Tanney BL, Silverman MM. Beyond the tower of Babel: a nomenclature for suicidology. Suicide Life Threat Behav 26:237-252, 1996.

Owen F, Simpson MDC. The neurochemistry of schizophrenia. In Hirsch SR, Weinberger DR (eds.). Schizophrenia. Blackwell Science Ltd: Oxford, 1995.

Pandey GN, Conley RR, Pandey SC, Goel S, Roberts RC, Tamminga CA, Chute D, Smialek J. Benzodiazepine receptors in the post-mortem brain of suicide victims and schizophrenic subjects. Psychiatry Res 71:137-149, 1997.

Pan P-C, Tantam D. Clinical characteristics, health beliefs and compliance with maintenance treatment: a comparison between regular and irregular attenders at a depot clinic. Acta Psychiatr Scand 79:564-570, 1989.

Parry G, Shapiro DA, Davies L. Reliability of life-event ratings: an independent replication. Br J Clin Psychology 20:133-134, 1981.

Paykel ES. Methodological aspects of life events research. J Psychosom Res 27:341-352, 1983.

Paykel ES, Dowlatshahi D. Life events and mental disorder. In Fisher S, Reason J.(eds.). Handbook of Life Stress, Cognition and Health. John Wiley & Sons: Colchester, 1988.

Paykel E, Myers J, Dienelt M, Klerman G, Lindenthal J, Pepper M. Life events and depression. Arch Gen Psychiatry 21:753-760, 1969.

Paykel ES, Myers JK, Lindenthal JJ, Tanner J. Suicidal feelings in the general population: a prevalence study. Br J Psychiatry 124:460-469, 1974.

Penn DL, Mueser KT. Research update on the psychosocial treatment of schizophrenia. Am J Psychiatry 153:607-617, 1996.

Peuskens J, De Hert M, Cosyns P, Pieters G, Theys P, Vermonte R. Suicide in young schizophrenic patients during and after inpatient treatment. Int J Ment Health 25:39-44, 1997.

Pickar D. Prospects for pharmacotherapy of schizophrenia. Lancet 345:557-562, 1995.

Pirkis J, Burgess P. Suicide and recency of health care contacts. A systematic review. Br J Psychiatry 173:462-474, 1998.

Planansky K, Johnston R. The occurrence and characteristics of suicidal preoccupation and acts in schizophrenia. Acta Psychiatr Scand 47:473-483, 1971.

Platt S. Unemployment and suicidal behaviour: a review of the literature. Soc Sci Med 19:93-115, 1984.

Pokorny AD, Kaplan HB. Suicide following psychiatric hospitalization - the interaction effects of defenselessness and adverse life events. J Nerv Ment Dis 162: 119-125, 1976.

Pokorny AD. Prediction of suicide in psychiatric patients. Report from a prospective study. Arch Gen Psychiatry 40:249-257, 1983.

Proulx F, Lesage AD, Grunberg F. One hundred in-patient suicides. Br J Psychiatry 171:247-250, 1997.

Rahe RH. Epidemiological studies of life change and illness. In Lipowski ZJ, Lipsitt DR, Whybrow PC (eds.) Psychosomatic Medicine. Current Trends and Clinical Applications. Oxford University Press: New York, 1977.

Ram R, Bromet EJ, Eaton WW, Pato C, Schwartz JE. The natural course of schizophrenia: a review of first admission studies. Schizophr Bull 18:185-207, 1992.

Ratakonda S, Gorman J, Yale SA, Amador XF. Characterization of psychotic conditions. Use of the domains of psychopathology model. Arch Gen Psychiatry 55:75-81, 1998.

Regier DA, Boyd JH, Burke JD, Rae DS, Myers JK, Kramer M, Robins LN, George LK, Karno M, Locke BZ. One-month prevalence of mental disorders in the United States. Based on five epidemiologic catchment area sites. Arch Gen Psychiatry 45:977-986, 1988.

Regier DA, Kaebler CT, Rae DS, Farmer ME, Knauper B, Kessler RC, Norquist GS. Limitations of diagnostic criteria and assessment instruments for mental disorders. Arch Gen Psychiatry 55:109-115, 1998.

Regier DA, Narrow WE, Rae DS, Manderscheid RW, Locke BZ, Goodwin FK. The de Facto US Mental and Addictive disorders service system. Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. Arch Gen Psychiatry 50:85-94, 1993.

Remington G. Understanding schizophrenia: the impact of novel antipsychotics. Can J Psychiatry 40(Suppl 2):S29-S32, 1995.

Rey M-J, Schulz P, Costa C, Dick P, Tissot R. Guidelines for the dosage of neuroleptics. I: Chlorpromazine equivalents of orally administered neuroleptics. Int Clin Psychopharmacology 4:95-104, 1989.

Rich CL, Motooka MS, Fowler RC, Young D: Suicide by psychotics. Biol Psychiatry 23:595-601, 1988.

Rich CL, Young D, Fowler RC. San Diego suicide study: I. Young vs old subjects. Arch Gen Psychiatry 43:577-582, 1986.

Rihmer Z, Barsi J, Arato M, Demeter E. Short communication. Suicide in subtypes of primary major depression. J Aff Disord 18:221-225, 1990.

Rihmer Z, Rutz W, Pihlgren H. Depression and suicide on Gotland. An intensive study of all suicides before and after a depression-training programme for general practitioners. J Aff Disord 35:147-152, 1995.

Robins E, Murphy GE, Wilkinson RH, Gassner S, Kayes J: Some clinical considerations in the prevention of suicide based on a study of 134 successful suicides. Am J Public Health 49:888-899, 1959.

Romanov K, Hatakka M, Keskinen E, Laaksonen H, Kaprio J, Rose RJ, Koskenvuo M. Self-reported hostility and suicidal acts, accidents, and accidental deaths: a prospective study of 21,443 adults aged 25 to 59. Psychosom Med 56:328-336, 1994.

Rorsman B. Mortality among psychiatric patients. Acta Psychiatr Scand 50:354-375, 1974.

Rosenberg ML, Davidson LE, Smith JC, Berman AL, Buzbee H, Gantner G, Gay GA, Moore-Lewis B, Mills DH, Murray D, O'Carroll PW, Jobes D. Operational criteria for the determination of suicide. J For Sciences 32(6):1445-1455, 1988.

Rossau CD, Mortensen PB. Risk factors for suicide in patients with schizophrenia: nested case-control study. Br J Psychiatry 171:355-359, 1997

Roy A. Suicide in chronic schizophrenia. Br J Psychiatry. 141:171-177, 1982.

Roy A. Family history of suicide. Arch Gen Psychiatry 40:971-974, 1983 (b).

Roy A. Suicide in schizophrenia. Int Rev Psychiatry 4:205-209, 1992.

Roy A, Draper R. Suicide among psychiatric hospital in-patients. Psychol Med 25:199-202, 1995.

Roy A, Mazonson A, Pickar D. Attempted suicide in chronic schizophrenia. Br J Psychiatry 144:303-306, 1984.

Roy A, Rylander G, Sarchiapone M. Genetics of suicide: family studies and molecular genetics. Ann New York Acad Sciences 836:135-157, 1997.

Roy A, Schreiber J, Mazonson A, Pickar D. Suicidal behavior in chronic schizophrenic patients: a follow-up study. Can J Psychiatry 31:737-740, 1986.

Roy A, Thompson R, Kennedy S. Depression in chronic schizophrenia. Br J Psychiatry 142:465-470, 1983 (a).

Ruiz J, Gabilondo AM, Meana JJ, Garcia-Sevilla JA. Increased (3H) raclopride binding sites in postmortem brains from schizophrenic violent suicide victims. Psychopharmacology 109:410-414, 1992.

Runeson B, Beskow J. Reactions of survivors of suicide victims to interviews. Acta Psychiatr Scand 83:169-173, 1991.

Rutz W, von Knorring L, Wålinder J. Long-term effects of an educational program for general practitioners given by the Swedish Committee for the Prevention and Treatment of Depression. Acta Psychiatr Scand 85:83-88, 1992.

Rutz W, Wålinder J, Eberhard G, Holmberg G, von Knorring A-L, von Knorring L, Wistedt B, Åberg-Wistedt A. An educational program on depressive disorders for general practitioners on Gotland: background and evaluation. Acta Psychiatr Scand 79:19-26, 1989.

Räsänen P, Tiihonen J, Isohanni M, Moring J, Koiranen M. Juvenile mortality, mental disturbances and criminality: a prospective study of the Northern Finland 1966 birth cohort. Acta Psychiatr Scand 97:5-9, 1998.

Saarinen P. Itsemurhavaaran tunnistaminen terveydenhuollossa. Prediction of suicide risk in health care. Kuopio University Publications D, Medical Sciences 73. Kuopio 1995.

Saarinen P, Viinamäki H, Lehtonen J, Lönnqvist J. Omaisten psyykkinen tilanne ja ammattiavun tarve läheisen itsemurhan jälkeen. Suomen Lääkäril 9:981-986, 1997.

Sainsbury P, Jenkins J. The accuracy of official reported suicide statistics for purposes of epidemiological research. J Epidemiol Commun Health 36:43-48, 1982.

Sakinofsky I. A survey of current international methods of suicide ascertainment. Presentation at the International Academy for Suicide Research, 7th European Symposium on Suicide and Suicidal Behaviour. Gent, September 9, 1998.

Salama A. Depression and suicide in schizophrenic patients. Suicide Life Threat Behav 18: 379-384, 1988.

Salokangas RKR, Saarinen S. Deinstitionalization and schizophrenia in Finland: I. Discharged patients and their care. Schizophr Bull 24:457-467, 1998.

SAS/STAT User´s Guide, Volume 2, version 6, 4th edition. Cary, NC, SAS Institute, 1990

Schwartz CC, Myers JK. Life events and schizophrenia: II. Impact of life events on symptom configuration. Arch Gen Psychiatry 34:1242-1245, 1977.

Schmidtke A, Bille-Brahe U, DeLeo D, Kerkhof A, Bjerke T, Crepet P, Haring C, Hawton K, Lönnqvist J, Michel K, Pommereau X, Querejeta I, Phillipe I, Salander-Renberg E, Temesvary B, Wasserman D, Fricke S, Weinacker B, Sampaio-Faria JG. Attempted suicide in Europe: rates, trends and sociodemographic characteristics of suicide attempters during the period 1989-1992. Results of the WHO/EURO Multicentre Study on Parasuicide. Acta Psychiatr Scand 90:53-64, 1996.

Schooler N. New antipsychotic medications: strategies for evaluation and selected findings. Schizophr Res 27:249-259, 1997.

Schulte JL. Homicide and suicide associated with akathisia and haloperidol. Am J For Psychiatry 3-7, 1985.

Scott JE, Dixon LB. Psychological interventions for schizophrenia. Schizophr Bull 21: 621-630, 1995.

Sedvall G, Farde L. Chemical brain anatomy in schizophrenia. Lancet 346:743-749, 1995.

Shaffer JW, Perlin S, Schmidt CW, Stephens JH. The prediction of suicide in schizophrenia. J Nerv Ment Dis 159: 349-355, 1974.

Shaffer D, Gould M, Fisher P, Trautman P, Moreau D, Kleinman M, Flory M. Psychiatric diagnosis in child and adolescent suicide. Arch Gen Psychiatry 53:339-348, 1996.

Shafii M, Carrigan S, Whittinghill JR, Derrick A. Psychological autopsy of completed suicide in children and adolescence. Am J Psychiatry 142:1061-1064, 1985.

Shafii M, Steltz-Lenarsky J, McDue Derrick A, Beckner C, Whittinghill JR. Comorbidity of mental disorders in the post-mortem diagnosis of completed suicide in children and adolescents. J Aff Disord 15:227-233, 1988.

Shear MK, Frances A, Weiden P. Suicide associated with akathisia and depot fluphenazine treatment. J Clin Psychopharmacology 3:235-236, 1983.

Shneidman ES. The psychological autopsy study. Suicide Life Threat Behav 11:325-340, 1981.

Simpson JC. Mortality studies in schizophrenia. In Tsuang MT, Simpson JC (eds.). Handbook of schizophrenia. Elsevier Science Publishers: 1988.

Siris SG, Morgan V, Fagerström R, Rifkin A, Cooper TB. Adjunctive imipramine therapy in the treatment of postpsychotic depression: a controlled trial. Arch Gen Psychiatry 44:533-539, 1987.

Siris SG. Depression and schizophrenia. In Hirsch SR, Weinberger DR (eds.). Schizophrenia. Blackwell Science Ltd: Oxford, 1995.

Siris SG. Treatment of depression in patients with schizophrenia. In The New Pharmacotherapy of Schizophrenia. Breier A (ed.). American Psychiatric Press: Washington DC, 1996.

Spitzer RL, Endicott J, Robins E. Research Diagnostic Criteria (RDC), 3rd edition. New York State Psychiatric Institute: New York, 1977.

Spitzer RL. Psychiatric diagnosis: are clinicians atill necessary? Compr Psychiatry 24:399-411, 1983.

SPSS for Windows Base System User's Guide and Advanced Statistics, Release 6.0. Norusis MJ, SPSS Inc: Chicago, 1993.

Stack S. Marriage, family, religion, and suicide. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and Prediction of Suicide. Guilford Press: New York, 1992.

Statistics Finland. Causes of Death 1996. Official Statistics of Finland, Health 1996:1. Statistics Finland: Helsinki, 1996.

Stein GS. Dangerous episodes occurring around the time of discharge of four chronic schizophrenics. Br J Psychiatry 141:586-589, 1982.

Stengel E. Some unexplored aspects of suicide and attempted suicide. Compr Psychiatry 1:71-79, 1960.

Strauss JS, Carpenter WT. The prediction of outcome in schizophrenia. Arch Gen Psychiatry 27:739-746, 1972.

Strauss JS, Carpenter WT, Bartko JJ. The diagnosis and understanding of schizophrenia, III: speculations on the processes that underlie schizophrenia symptoms and signs. Schizophr Bull 1:61-69, 1974.

Suokas J, Lönnqvist J. Outcome of attempted suicide and psychiatric consultation: risk factors and suicide mortality during a five year follow-up. Acta Psychiatr Scand 84:545-549, 1991.

Taiminen TJ, Kujari H. Antipsychotic medication and suicide risk among schizophrenic and paranoid inpatients. A controlled retrospective study. Acta Psychiatr Scand 90:247-251, 1994.

Taiminen T, Lehtinen K. Suicides in Turku psychiatric hospitals in 1971-1987. Psychiatr Fenn 21:235-247, 1990.

Tienari P. Interaction between genetic vulnerability and family environment: the Finnish adoptive family study of schizophrenia. Acta Psychiatr Scand 84:460-465, 1991.

Tollefson GD, Fawcett J, Winokur G, Beasley CM, Potvin JH, Faries DE, Rampey AH, Sayler ME. Evalution of suicidality during pharmacologic treatment of mood and nonmood disorders. Ann Clin Psychiatry 5:209-224, 1993.

Tollefson GD, Sanger TM, Lu Y, Thieme ME. Depressive signs and symptoms in schizophrenia. A prospective blinded trial of olanzapine and haloperidol. Arch Gen Psychiatry 55:250-258, 1998.

Tondo L, Jamison KR, Baldessarini RJ. Effect of lithium maintenance on suicidal bahvior in major mood disorders. Ann New York Acad Sciences 836: 339-351, 1997.

Tran PV, Hamilton SH, Kuntz AJ, Ptvin JH, Andersen SW, Beasley CM, Tollefson GD. Double-blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. J Clin Psychopharmacol 17:407-418, 1997.

Tsuang MT. Risk of suicide in the relatives of schizophrenics, manics, depressives and controls. J Clin Psychiatry 44:396-400, 1983.

Tsuang MT, Woolson RF. Excess mortality in schizophrenia and affective disorders. Do suicides and accidental deaths solely account for this excess? Arch Gen Psychiatry 35:1181-1185, 1978.

Tuori T, Lehtinen V, Hakkarainen A, Jääskeläinen J, Kokkola A, Ojanen M, Pylkkänen K, Salokangas RKR. The Finnish National Schizophrenia Project 1981-1987: 10 year evaluation of its results. Acta Psychiatr Scand 97:10-17, 1998.

Vaughn CE, Leff JP. The measurement of expressed emotion in the families of psychiatric patients. Br J Soc Clin Psychol 15:157-165, 1976.

Veijola J, Isohanni M. Katsaus suomalaiseen skitsofreniatutkimukseen. Sos.lääketiet aikakausl 35:166-170, 1998.

Ventura J, Nuechterlein KH, Hardesty JP, Gitlin M. Life events and relapse after withdrawal of medication. Br J Psychiatry 161:615-620, 1992.

Verkes RJ, Van der Mast RC, Hengeveld MW, Tuyl JP, Zwinderman AH, Van Kempen GMJ. Reduction by paroxetine of suicidal behavior in patients with repeated suicide attempts but not major depression. Am J Psychiatry 155: 543-547, 1998.

Virkkunen M. Suicides in schizophrenia and paranoid psychoses. Acta Psychiatrica Scandinavica (Suppl) 250, 1974.

Virkkunen M. Attitude to psychiatric treatment before suicide in schizophrenia and paranoid psychoses. Br J Psychiatry128:47-49, 1976.

Waddington JL. Schizophrenia: developmental neuroscience and pathology. Lancet 341:531-538, 1993.

Walker AM, Lanza LL, Arellano F, Rothman KJ. Mortality in current and former users of clozapine. Epidemiology 8:671-677, 1997.

Warnes H. Suicide in schizophrenics. Dis Nerv Sys 29 (suppl):5:35-40, 1968.

Wasserman IM. Economy, work, occupation and suicide. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (eds.). Assessment and Prediction of suicide. Guilford Press: New York, 1992.

Weiden PJ, Mott T, Curcio N. Recognition and management of neuroleptic noncompliance. In: Shriqui CL, Nasrallah HA (eds.). Contemporary Issues in theTreatment of Schizophrenia. American Psychiatric Press: Washington DC, 1995.

Weiden PJ, Olfson M. Costs of relapse in schizophrenia. Schizophr Bull 21:3:419-429, 1995.

Weiden P, Roy A. General versus specific risk factors for suicide in schizophrenia. In Jacobs D, (ed.). Suicide and Clinical Practice. American Psychiatric Press: Washington DC, 1992.

Weinberger DR. Schizophrenia. From neuropathology to neurodevelopment. Lancet 346:552-557, 1995.

Weishaar ME, Beck AT. Clinical and cognitive predictors of suicide. In: Maris RW, Berman AL, Maltsberger JT, Yufit RI (Eds). Assessment and Prediction of Suicide. Guilford Press: New York, 1992.

Westermeyer JF, Harrow M, Marengo J. Risk for suicide in schizophrenia and other psychotic and nonpsychotic disorders. J Nerv Ment Dis 179:259-266, 1991.

WHO 1992. World Health Organization. The ICD-10 Classification of Mental and Behavioral Disorders. Clinical Descriptions and Diagnostic Guidelines. World Health Organization: Geneva, 1992.

WHO 1993. World Health Organization. The ICD-10 Classification of Mental and Behavioral Disorders. Diagnostic criteria for research. World Health Organization: Geneva, 1993.

WHO 1998. World Health Organization. Annual Statistics 1995. World Health Organization, Geneva, 1998.

Wilkinson DG. The suicide rate in schizophrenia. Br J Psychiatry 40:138-141, 1982.

Wilkinson G, Bacon NA. A clinical and epidemiological survey of parasuicide and suicide in Edinburgh schizophrenics. Psychol Med 14:899-912, 1984.

Wing JK. Concepts of schizophrenia. In Hirsch SR, Weinberger DR (eds.). Schizophrenia. Blackwell Science Ltd: Oxford, England 1995.

Wilson JD, Enoch MD. Estimation of drug rejection by schizophrenic inpatients which analysis of clinical factors. Br J Psychiatry 113:209-211, 1967.
Wolfersdorf M, Barth P, Steiner B, Keller F, Vogel R, Hole G, Schuttler R. Schizophrenia and suicide in psychiatric in-patients. In Platt S, Kreitman N (eds.). Current research on suicide and parasuicide. Edinburgh University Press: Edinburgh, 1989.

Wyatt RJ, Henter I, Leary MC, Taylor E. An economic evaluation of schizophrenia - 1991. Soc Psychiatr Epidemiol 30:196-205, 1995.

Zahner GEP, Chung-Cheng H, Fleming JA. Introduction to epidemiologic research methods. In Tsuang MT, Tohen M, Zahner GEP (eds). Textbook in psychiatric epidemiology. John Wiley & Sons: New York 1995.

Yarden PE. Observations on suicide in chronic schizophrenics. Compr Psychiatry 15:325-333, 1974

Young MA, Fogg LF, Scheftner WA, Fawcett JA. Interactions of risk factors in predicting suicide. Am J Psychiatry 151:434-435, 1994.

Åsberg M. Neurotransmitters and suicidal behavior: the evidence from cerebrospinal fluid studies. Ann New York Acad Sciences 836:158-181, 1997.

Öhberg A, Lönnqvist J, Sarna S, Vuori E, Penttilä A. Trends and availability of suicide methods in Finland. Proposals for restrictive measures. Br J Psychiatry 166:35-43, 1995.

Öhberg A, Lönnqvist J. Suicide trends in Finland 1980-1995. Psychiatr Fenn 28:11-23, 1997.

Öhberg A. Suicide methods in Finland. Publications of the National Public Health Institute KTL A5/1998. Hakapaino Oy: Helsinki, 1998.

Table 1.

PREVIOUS DSM-III AND DSM-III-R STUDIES ON SUICIDE AND SCHIZOPHRENIA

AUTHOR	NUMBER OF SUICIDES	TYPE OF SAMPLE	TIME PERIOD	CONTROLS	DATA
Roy 1982, Canada	N=30	Retrospective follow-up of inpatients and outpatients with subchronic and chronic schizophrenia	1968-79	N=30; matched for age, sex, schizophrenia type	all available patient records
Breier and Astrachan 1984, USA	N=20	Retrospective follow-up of inpatients and outpatients, schizophrenic psychoses	1970-81	1) N=18; non-sch suicidal group 2) N=81; randomly selected schizophrenia group 3) N=20; schizophrenia	all available patient records
Drake et al 1984, USA	N=15	Retrospective follow-up of inpatients	1976-80	N=160 inpatients; excluding longstay, elderly and patients with brief admission	hospital records

Allebeck et al 1987, Sweden	N=32	inpatient cohort of schizophrenic psychoses	1971-81	N=64; 10% random sample of the cohort	inpatient register and medical records
Cheng et al 1990, Hong Kong	N=74	Retrospective follow-up of inpatients and outpatients;chronic and subchronic sch	1981-85	N=74; matched for age and sex	all available patient redords
Hu et al 1991,Taiwan	N=42	Retrospective follow-up of inpatients and outpatients	1972-87	1) N=84; matched for age, sex, and outpatient care length 2) N=60; first outpatient clinic visit in 1982, non- suicidal schizophrenic patients; follow-up of at least 5 years	patient records; family interviews

AUTHOR	NUMBER OF SUICIDES	TYPE OF SAMPLE	TIME PERIOD	CONTROLS OF STUDY	DATA
Lim et al 1991, Singapore	N=41	Prospective follow-up schizophrena cohort	1975-90	N=411	inpatient register and inpatient records at first admission
Fenton et al 1997, USA	N=19	Retrospective follow-up of a cohort of discharged patients with schizophrenia psychoses	1950-75	N=276	medical records, interviews with subjects and/or significant others
Peuskens et al 1997, Belgium	N=27	Retrospective follow-up of inpatients with schizophrenia and schizo-affective patients	1979-89	N=27 matched for age, sex, diagnosis subtype and time of first admission	hospital records