Suicide in a clinical and a general population, with focus on comorbidity. Studies from the Lund Suicide Research Center and the Lundby Study.

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2016

Document Version:
Publisher's PDF, also known as Version of record

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Studies from the Lund Suicide Research Center and the Lundby Study

Cecilia Holmstrand

LUND
UNIVERSITY

DOCTORAL DISSERTATION
by due permission of the Faculty of Medicine, Lund University, Sweden.
To be defended at Konferensrum 12, Baravägen 1C, Lund
on 21 April 2016 at 09.00.

Faculty opponent
Prof. Bo Runeson, Karolinska Institutet, Stockholm, Sweden.

Organization LUND UNIVERSITY	Document name: Doctoral thesis
	Date of dissertation: 21 April, 2016
Author: Cecilia Holmstrand	Sponsoring organization

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Conclusions: Comorbid conditions are confirmed to be important risk factors for suicide in both the clinical and general populations examined. People with mental disorders, often complicated by personality disorder and a long period with recurrent psychiatric impairment, psychiatric care and suicide attempts, seem to be at a high risk of suicide. For patients with dysthymia, pain appear to be a risk factors for suicide. Results in this thesis also suggest that men with alcohol use disorder should be followed carefully and attention paid to additional mental disorders, especially depression, which seem to elevate the suicide risk significantly for many years ahead. In most disorders, the risk of suicide will persist during lifetime, but in persons suffering from depression, suicide usually occurs early in the course. Intensive interventions are apparently necessary for a long time.

Key words: suicide, suicide attempt, risk factors, comorbidity, depression, dysthymia, alcohol use disorder		
Classification system and/or index terms (if any)		
Supplementary bibliographical information		Language: English
ISSN and key title: 1652-8220		ISBN 978-91-7619-272-6
Recipient's notes	Number of pages	Price
	Security classification	

Signature _____ Date _____

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Cover photo by Sander Broström

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2016:46

ISBN 978-91-7619-272-6
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2016

“I am terrified by this dark thing

That sleeps in me;

All day I feel its soft, feathery turnings, its malignity.”

— Sylvia Plath, from *Ariel*, published posthumously in 1965.

Contents

Errata

Page 22. Third paragraph, the sixth line should be: In 1999 WHO/EURO Multicentre Study group adapts the outcome-based classification……(De Leo, Burgis et al. 2006).

Page 26. At the penultimate line: 'Population attributed risk' should be 'Population attributable Risk'.

Page 31. Second paragraph, fourth line should be: A somewhat lower annual incidence rate was seen in the same study in 1972-1997 compared to 1947-1972…..

Page 37. Section 2.9.2. ICD-8 and ICD-9 references are missing. Should be (World Health Organization 1968) and (World Health Organization 1987) respectively.

Page 38. Last paragraph, second line: Reference is missing: Eaton, W. W., D. A. Regier, B. Z. Locke and C. A. Taube (1981). "The Epidemiologic Catchment Area Program of the National Institute of Mental Health." Public Health Rep **96**(4): 319-325.

Page 39. Second paragraph, second line. Reference missing: Gruenberg, E. M. (1965). "A Review of Mental Health in the Metropolis: The Midtown Manhattan Study." Int J Psychiatry **1**: 77-86.

Page 48. Second paragraph, penultimate sentence should be: It could better differentiate suicide cases from controls than SIS, MADRS and BHS….

Page 58. Tenth line: (Figure 2) should be (Figure 3).

Page 60. 4.3.4.5. In line 4: 'chronic fatigue syndrome' should be excluded as not in DSM-IV.

Page 62. 4.3.8: First line should be …..each of the 62 suicide victims…….

Page 69: First line should be: The following (DSM-III-R, Axis I) comorbidities …

Page 85. 6.4, second paragraph, last line should be: .....in a systematic review (comorbid mental disorders 31-48% and comorbidity between mental disorders and substance use 21-57%)…..

Page 95. Third paragraph, first sentence should be: Persons with dysthymia severe enough to have been admitted to a psychiatric ward after a suicide attempt differ from MDD inpatient suicide attempters…..

Page 95. Penultimate paragraph, first sentence should be: ……., though the risk was increased with comorbid disorders, but non-significantly if the diagnoses were analysed separately.

Page 123. The fifth reference at the page. Community Medicine Institution, Lund University (2004)…..

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Original papers

1. **Holmstrand C, Niméus A, Träskman-Bendz L.** Risk factors of future suicide in suicide attempters – A comparison between suicides matched survivors. Nord J Psychiatry, 2006;60:162-167.
2. **Holmstrand C, Engström G, Träskman-Bendz L.** Disentangling dysthymia from major depressive disorder in suicide attempters – suicidality, comorbidity and symptomatology. Nordic Journal of Psychiatry, 2008;62:25-31.
3. **Holmstrand C, Bogren M, Mattisson C, Brådvik L.** Long-term suicide risk in no, one or more mental disorders: the Lundby Study 1947-1997. Acta Psychiatr Scand. 2015 Dec;132(6):459-69. doi: 10.1111/acps.12506. Epub 2015 Sep 24.
4. **Holmstrand C, Bogren M, Mattisson C, Brådvik L.** First and additional lifetime mental disorders in suicide victims - the Lundby Study 1947-1997. Manuscript 2015. Submitted to Archives of Suicide Research.
5. **Holmstrand C, Bogren M, Mattisson C, Brådvik L.** Time span from onset of first mental disorder to suicide – the Lundby Study 1947-2011 (Brief report, manuscript).

Abbreviations

BHS	The Beck Hopelessness Scale
CDC	United States Centers for Disease Control and Prevention
CI	Confidence interval
CPRS	Comprehensive Psychopathological Rating Scale
CSF	Cerebrospinal fluid
DALY	Disability-adjusted life years
DSM	Diagnostic and Statistical Manual for Mental Disorders
ECA	Epidemiologic Catchment Area
GABA	Gamma-aminobutyric acid
GAF	Global Assessment of Functioning
5-HIAA	5-hydroxyindoleacetic acid
HPA axis	Hypothalamic-pituitary-adrenal axis
HVA	Homovanillic acid
ICD	International Classification of Diseases
MADRS	Montgomery-Asberg Depression Rating Scale
MDD	Major depressive disorder
MEIU	Medical Emergency Inpatient Unit
NSSI	Non-suicidal self-injury
NSSIB	Non-suicidal self-injurious behaviour
OR	Odds ratio
PAR	Population attributable risk
PASW	Predictive Analytic Software

PPV	Positive predictive value
REM	Rapid eye movement
SBU	Statens beredning för medicinsk och social utvärdering
SUAS	Suicide Assessment Scale
WHO	World Health Organization
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
SSRI	Selective serotonin reuptake inhibitors

1. Introduction

Every suicide is a tragedy. Usually, the suicide event is preceded by a long period of suffering for the individual, who sees no other way out of a seemingly unbearable situation. Afterwards, relatives and friends are usually left in despair, asking themselves whether anything could have been done to prevent the irrevocable event.

More than 800,000 people around the world kill themselves annually. For every completed suicide event, around 20 persons attempt suicide (World Health Organization 2014).

For several decades, researchers and healthcare professionals have tried to learn more about risk factors and warning signs in an attempt to prevent suicide. Familial factors (hereditary or environmental), difficult experiences in childhood, and personality characteristics may influence the risk of future suicide. Factors arising later in life, such as mental and physical disorders, stressful life events, lack of social network and feelings of hopelessness about the situation, may also be significant. There are protective factors that may counteract the influence of risk factors.

Psychological autopsy studies have shown that about 90% of suicide victims had suffered from one or more mental disorders (Isometsa 2001, Cavanagh, Carson et al. 2003, Arsenault-Lapierre, Kim et al. 2004). Mood disorders, substance use disorders and schizophrenia have been found to be the most frequent diagnoses (Bertolote and Fleischmann 2002), and psychiatric comorbidity is also common (Henriksson, Aro et al. 1993, Isometsa 2001, Bertolote and Fleischmann 2002).

The risk of dying by suicide is greatly increased in persons who develop major depression, eating disorders, and personality disorders, especially borderline personality disorder, bipolar disorders, substance use disorders and schizophrenia (Harris and Barraclough 1997, Chesney, Goodwin et al. 2014).

Assessment instruments designed to measure the severity of psychiatric symptoms, suicide ideations or suicide intent could be useful in the often difficult task of evaluating suicide risk (Nimeus, Alsen et al. 2000, Lindqvist, Nimeus et al. 2007, Freedenthal 2008, Stefansson, Nordstrom et al. 2012). However, no single instrument should be crucial for the choice of interventions for the suicidal patient and, in a recent systematic Swedish review, no rating scale has provided scientific

evidence to predict suicide (Statens beredning för medicinsk och social utvärdering 2015).

Various methods may be used in suicide research. Large populations could be studied in already existing national official registers. Community populations could be followed longitudinally or investigated in cross-sectional epidemiological projects. Another way is to study samples of in- or outpatients. Psychological autopsy is commonly used, where the researchers try to find information about the suicide victims after death, examining life and health conditions. Different methods and perspectives could be of benefit in order to introduce the correct measures in preventive work.

In this thesis two kinds of perspectives have been used. First, by examining individuals with a high risk of suicide, such as patients admitted after a suicide attempt at a specialised psychiatric ward. Second, the suicide risk is also analysed in a general population, including persons with and without mental illness over a very long perspective, but without previously being selected for suicide risk. The main issues have been to study mental disorders, comorbidity, symptomatology, and hospital care as possible risk factors for future suicide.

2. Background

2.1 Epidemiology and history of suicide – a short summary

Suicide is a global problem, but reliable statistics are lacking in many countries. International and national suicide prevention programmes have been devised, aimed at reducing the suicide rate. The WHO Mental Health Action Plan 2013-2020 stated that member countries should work towards the global target of reducing the suicide rate by 10% by 2020. The WHO world suicide report, *Preventing Suicide: A Global Imperative*, was published in 2014; in this report, there were estimated to be 804,000 suicides in 2012. Suicide accounted for 1.4% of all deaths, and the highest age-standardised suicide rate was found in low- and middle-income member states and especially in the South-East Asian region (World Health Organization 2014).

Suicide is more common in men than women (Bertolote and Fleischmann 2005, Hawton and van Heeringen 2009, Murphy, Xu et al. 2013).This is especially the case in richer countries, where three times more men than women die by suicide, but in low- and middle-income countries the male-to-female ratio is only 1.5:1 (World Health Organization 2014).

Suicide attempts are far more common, and are reported to be 10-20 times the rate of suicide (World Health Organization 2014). One study estimated the lifetime prevalence of a suicide attempt worldwide to be 2.7% (Nock, Borges et al. 2008). The occurrence of non-fatal suicidal behaviour is known to be higher in women in most countries and for all ages (Bertolote and Fleischmann 2005, Hawton and Harriss 2008, Angst, Hengartner et al. 2014). Some studies have found no significant difference in gender with regard to suicide ideation or suicidal behaviour (Petronis, Samuels et al. 1990, Kuo, Gallo et al. 2001).

Globally the suicide rate is higher in persons 70 years and older, but suicide is still the second leading cause of death in people aged 15-29 and even the leading cause in high-income countries and low- and middle-income countries in South-East Asia. The overall suicide rate fell between 2000 and 2012, but countries vary greatly, and age-standardised suicide rates ranged from a decline of 69% to an increase of 270% (World Health Organization 2014).

Classification and registration of suicide as a cause of death, and availability of data on suicide attempts from hospital-based systems and surveys, need to be improved, to provide better estimates of prevalence and effective suicide prevention. Illegality, taboo and stigma associated with suicide and suicide attempts are other problems that may cause misclassification and underestimation of the frequency, and might stop people seeking help.

Work to prevent suicide should be performed at three different levels (Maris 2002, Nordentoft 2011, World Health Organization 2014). A primary/universal level is directed towards the public (the nation, the county, the community, the school, etc.), providing information and facilitating access to care and influence help-seeking behaviour. The secondary/selected level includes strategies that address subsets of the total population, focusing on groups identified as having a higher suicide risk. The tertiary/indicated level is directed towards persons in the population who have high risk for suicide, as shown for example by attempted suicide.
The preventive work can be improved with research done on the basis of the three different perspectives.

2.1.2 History

The word 'suicide' comes from Latin, and derives from the words 'su´us' that means 'of oneself' and 'caedere' that means 'to kill'. 'Suicidum' means the act when a person kills herself/himself.

Throughout history, the phenomena of suicide have been discussed from different perspectives, with various definitions and explanatory models. Philosophers were considering moral, existential and autonomy aspects already in ancient times. The world religions have had more or less pronounced attitudes or rules regarding suicide, and they have mostly been negative or condemning. In Christianity, suicide has been condemned since the middle of the 10th century after the Donatists were said to have praised the acts as a martyrdom (Minois 1999). However, the Bible contains no clear prohibition of suicide. In Sweden, suicide and suicide attempts were punishable till 1864 and it was not until 1908 that legislation regarding burial of suicide victims was repealed.

The sociologist Durkheim argued that suicide could be attributed to the individual's relation to society and its environments and norms. In 1897, he formulated a definition that has influenced subsequent nomenclature (Durkheim 1993): "All cases of death resulting directly or indirectly from a positive or negative act of the victim himself, which he knows will produce this result".

In the field of psychology, Freud presented a theory of suicide in his work *Trauer und Melancholie* in 1917; he described suicide as a consequence of non-acceptable feelings of anger against the lost object which had been transformed to self-censure and the wish to harm one-self (for review, see (Brådvik 2000)).

Shneidman, a psychologist, described suicide as an act to escape from unbearable psychological pain, and formulated the following definition: "Suicide is a conscious act of self-induced annihilation, best understood as a multidimensional malaise in a needful individual who defines an issue for which suicide is perceived as the best solution" (Shneidman 1985).

The Swedish philosopher Anderberg conducted extensive research on the phenomena of suicide using a multidisciplinary approach, and considered definitions, causes and values. He proposed the following definition: "A person has committed suicide if he has instigated a course of events, of which he is an active or passive participant, where the great majority of his simple actions (or action constituents) are performed with the intention to shorten life, for whatever motive, good or bad, and from which death follows in the way he has planned or at least in a way he could accept" (Anderberg 1989).

Research within psychiatry and psychology has further developed explanatory models about suicide. This has also opened the possibility to help people contemplating or planning suicide because of mental pain and despair. It has been shown that such feelings are often caused by underlying mental disorder or comorbid conditions.

2.2 Nomenclature

2.2.1 Suicide, suicidal behaviour and self-harm.

The question of whether persons who harm themselves repeatedly (but not lethally) and people who harm themselves and die as a consequence of the act, should be seen as belonging to a continuum or to separate groups with different characteristics has been debated for a long time (Linehan 1986). The heterogeneous and unclear nomenclature of suicide and self-destructive behaviour has been a problem in the communication, both in research and in healthcare.

A relative consensus on distinguishing between behaviour with and without the 'intent to die' has resulted in a distinction in the recently developed classification systems. Examples are 'Suicidal' vs. 'Non-suicidal' in a nomenclature of self-injurious behaviour by Posner at el. (Posner, Oquendo et al. 2007) and behaviour 'with intention to die' or 'without intention to die' in the nomenclature of 'fatal' and 'non-

fatal suicidal behaviour' (De Leo, Burgis et al. 2006). Another system distinguishes between behaviour, communication or ideations with 'some degree of suicidal intent', 'undetermined intent' or 'without suicidal intent' in *Nomenclature of self-injurious thoughts and behaviours* by Silverman et al. (Silverman, Berman et al. 2007). As a contribution to the attempt to develop uniform definitions, the United States Centers of Disease Control and Prevention (CDC) have devised nomenclature dealing with different kinds of self-inflicted behaviour, intent and desire to die, including terms like 'Suicidal' vs. 'Non-suicidal' self-directed violence/self-injurious behaviour (Crosby, Ortega et al. 2011).

Most researchers and professionals agree that the intent of the behaviour is an essential variable for distinction. However, a person considering or performing a suicidal act often has an ambivalent intent to die. And the 'non-zero' wish to die by the behaviour has been suggested as being sufficient to classify the act as a suicide attempt (O'Carroll, Berman et al. 1996). Another aspect to consider is the person's beliefs about the result of the act, based on knowledge of lethality. For example, a low-dose intake of a mild painkiller could be a seriously meant suicide attempt in a person without medical knowledge. The actual physical harm or the putative physical harm of the behaviour is not always an appropriate discriminator of the seriousness of the attempt, as the circumstances could be changed by interruption or by external events. For example, the branch of the tree could have given way when a person tried to hang him or herself, or someone could have been rescued by a family member. According to CDC, a self-interrupted attempt should be classified as an attempt (Crosby, Ortega et al. 2011).

Non-suicidal self-injurious behaviour (NSSIB) is distinguished from a suicide attempt in terms of intent, method, lethality and pattern (Favazza 1998), but they share self-injury as an outcome. This behaviour is associated with borderline personality disorder, but can also be a way to regulate overwhelming and negative effects and emotions in, for example, anxiety, depression or other psychiatric conditions (In-Albon, Burli et al. 2013). ICD-10 published in 2007 adapts the outcome-based classification of 'fatal' and 'non-fatal' suicidal behaviour, as the intention is not always known. The distinction between 'non-suicidal self-injury' and 'suicidal behaviour' was subsequently incorporated in DSM-5 (American Psychiatric Association 2013). Authors have argued for a distinction between 'suicidal' and 'non-suicidal' self-harm, but there are overlapping phenomena regarding suicidality and etiology (Wichstrom 2009, Andover, Morris et al. 2012). An inpatient-study of adolescents showed that 70% of the persons with NSSIB had attempted suicide at some point of their lives (Nock, Joiner et al. 2006). NSSIB increases the risk of both suicide attempts and suicide, and this also applies after controlling for other known risk factors (Zahl and Hawton 2004, Andover and Gibb 2010, Whitlock, Muehlenkamp et al. 2011, Wilkinson, Kelvin et al. 2011).

2.4 Models of understanding the suicidal process of suicidal behaviour

Various explanatory models of the suicidal process have been described. Most of them consider the influence of different risk factors, and they overlap to some extent. They are described in brief below.

2.4.1 A stress-diathesis model of suicidal behaviour

Multiple factors in the individual's life may lie behind a person's suicidal behaviour, and in some cases they could contribute to a final suicide. In the multifactorial Model of Diseases developed by Mościkici, risk factors based on previous epidemiologic studies are divided into 'proximal' and 'distal' factors. She pointed out that risk factors often co-occur and interact, and argued that the best method for preventing suicide is one that includes the individual as well as his or her physical and psychosocial environment (Moscicki 1997).

The categorisation has been developed further. Distal factors could include genetic loading, personality characteristics, events in foetal life and childhood, and neurobiological disturbances. Proximal factors could include psychiatric disorder, physical disorder, psychosocial crisis, and availability of means (Hawton and van Heeringen 2009). The impact of the different risk factors can be described in an explanatory model of suicide, such as the 'stress-diathesis model'. This model has not only been used for understanding suicidal behaviour (Mann, Waternaux et al. 1999), but also as a general model of how genes and environment may contribute to the genesis of different types of psychopathology (Mann 2003). The diathesis consists of predisposing factors such as genetic and biological traits, personality, cognitive, psychological and social traits. These factors make a person vulnerable for subsequent stressors, which might trigger or potentiate a disorder or a behaviour.

Epigenetics is an interesting and expanding field of research, and deals with processes that alter the expression of genes without changing the DNA sequences (Weaver, Cervoni et al. 2004). These phenomena are coherent with, and might explain, some processes in the stress-diathesis model. A model of an interaction and interdependence between stressors and diathesis is possibly the most useful, and a 'kindling effect' on suicide attempts has been suggested (van Heeringen 2012). In this context it could mean that the risk of a new suicide attempt will increase with the number of previous suicide attempts. The inclusion of impulsivity and aggression in the diathesis of the suicidal model has been debated.

2.4.2 Risk factors/protective factors by Maris

Maris describes a multifactorial scheme of predictors and risk factors (proximal/state), as a supplement to the predisposing factors (distal/chronic/trait) (Maris 2002). Risk factors interact and may potentiate each other. Protective factors for the individual can include positive health aspects, early and effective treatments for possible illnesses, supportive social network, and a satisfactory economic situation. Trigger factors could acutely elevate the suicide risk, and might push the individual beyond the pain threshold until they are ready to complete suicide. Maris argues that the clinical evaluation of the patient's history must be the starting point, followed by useful assessment instruments and a physical examination. Based on these, treatments should be initiated, along with stress reduction and other measures, including trying to strengthen protective factors.

Primary prevention, secondary prevention and tertiary prevention could be inserted at the three different levels of factors.

2.4.3 The suicidal process described by Beskow and O´Connell

The process may start with thoughts of hopelessness or with a wish to escape from an intolerable situation. The suicidality might progress step by step via suicide ideations and suicide plans to completed suicide. The different steps could persist for a variable length of time, and most people never proceed from suicide ideation to the level of concrete suicidal plans or suicidal behaviour. Possible external or internal risk factors are not involved in the actual model. In Sweden, the process was described by Beskow in 1979 and since then has often have been used in clinical practice (Beskow 1979). O'Connell's model of suicidality is similar, and was originally described in a paper on suicide among elderly people (O'Connell, Chin et al. 2004).

2.4.4 The interpersonal theory of suicide by Joiner.

The basis of the interpersonal theory of suicide is the assumption that people die from suicide because they can and because they want to (Joiner 2005, Van Orden, Witte et al. 2010). Three dimensions are described. Suicidal desire originates from two constructs, 'thwarted belongingness' and 'perceived burdensomeness', in combination with feelings of hopelessness. The third construct is the successively acquired 'capability for suicide'. Observable multiple risk factors contribute to the development of the constructs and to their consolidation via causal pathways. Proximal risk factors could be seen as indicators of the significance of the constructs to the individual.

Distal risk factors such as childhood maltreatment may also be relevant for development of the constructs of thwarted belonging and perceived burdensomeness.

According to this model, the capacity to kill oneself requires the individual to, in some way, lose the innate fear of death. This could happen through repeated exposure and practice, with the result that the individual may habituate to the physical painful and fearful aspects of self-harm and death. Several studies have tested the hypothesis (Van Orden, Witte et al. 2010).

2.5 Risk factors for suicide

Risk factors and protective factors should be identified and further investigated on different levels for effective interventions in healthcare systems, in societies/communities, at an individual level (World Health Organization 2014). The most important known risk factors at the individual level are described below.

2.5.1 Previous suicide attempt

Suicide attempts might be the strongest predictor for subsequent death by suicide (Owens, Horrocks et al. 2002, Oquendo, Galfalvy et al. 2004, Nordentoft 2007, Runeson, Haglund et al. 2015). In a meta-analysis the risk was estimated to be 38 times higher than expected (Harris and Barraclough 1997). The risk is considered to be particularly elevated during the first year after a suicide attempt and after discharge from hospital care (Nordstrom, Samuelsson et al. 1995, Ostamo and Lonnqvist 2001, Hawton, Zahl et al. 2003, Tidemalm, Langstrom et al. 2008). A five-year Swedish follow-up showed a suicide risk of 8.3% among men and 4.3% among women who had all been hospitalised in psychiatry after a suicide attempt (Nordstrom, Samuelsson et al. 1995). The elevated risk persists for a long time, perhaps for decades (Jenkins, Hale et al. 2002, Bradvik 2003, Suominen, Isometsa et al. 2004).

A suicide attempt could be classified as 'violent' and 'non-violent', depending on the chosen method (Traskman, Asberg et al. 1981). Intoxication or single wrist-cut are classified as non-violent methods. Hanging, strangulation, drowning, jumping from a height, or use of a firearm are examples of methods which are usually regarded as violent methods. A violent method often indicates a strong intent to die and a higher risk of subsequent suicide (Holley, Fick et al. 1998, Hawton, Bergen et al. 2008, Runeson, Haglund et al. 2015, Stenbacka and Jokinen 2015). Individuals who have attempted suicide by hanging, strangulation, or suffocation are found to have the worst prognosis (Runeson, Tidemalm et al. 2010).

Suicide attempts classified as serious should be considered as constituting a high risk for completed suicide (Beautrais, Joyce et al. 2000). In a serious attempt, a violent method not always is used. Intoxication can result in death or need of intensive care but, according to the definition above, is a non-violent attempt. By Beautrais, a medically serious suicide attempt has been define as one required hospital admission for longer than 24 hours and met one of specified criteria regarding medical interventions (Beautrais 2002). An attempt should also be assessed as serious if the individual had ensured seclusion during the act. A higher suicide risk must be suspected after a medically severe suicide attempt (Rosen 1976, Suokas and Lonnqvist 1991). Persons who make violent or serious suicide attempts often share the characteristics of suicide completers, such as more frequently being male and having a family history of suicidal behaviour (Giner, Jaussent et al. 2014).

Repeated suicide attempts have been shown to correlate more strongly to later suicide (Hawton and Fagg 1988, Ostamo and Lonnqvist 2001)

2.5.2 Mental disorders

Mental disorder is a strong, well-known risk factor for suicide (Harris and Barraclough 1997, Chesney, Goodwin et al. 2014, World Health Organization 2014). In a recent meta-review, the suicide rate was substantially increased (more than ten times higher) in persons with borderline personality disorder, depression, bipolar disorder, opioid use, and schizophrenia, and in eating disorder and alcohol use disorder in women (Chesney, Goodwin et al. 2014). An earlier meta-analysis showed risk was 23 times higher than expected in anorexia nervosa, 20 times higher in major depressive disorder, 8.5 times higher in schizophrenia, and almost six times higher for alcohol use disorders (Harris and Barraclough 1997). In another meta-analysis of mortality follow-up studies, the lifetime suicide risk was estimated to be 7% in alcohol use disorders, 6% in affective disorders and 4% in schizophrenia (Inskip, Harris et al. 1998).

Psychological autopsy studies of suicide victims have shown that around 90% of the cases have suffered from mental disorders (Barraclough, Bunch et al. 1974, Henriksson, Aro et al. 1993, Foster, Gillespie et al. 1997, Isometsa 2001, Cavanagh, Carson et al. 2003), and the figure was even higher in elderly persons (Waern, Runeson et al. 2002). Mood disorders are reported as the most common mental disorders in suicide victims, followed by substance use disorders, most often alcohol use disorder (Henriksson, Aro et al. 1993, Lesage, Boyer et al. 1994, Cheng 1995, Isometsa 2001). A Swedish study showed that depression was especially dominant in female cases (Asgard 1990). The presence of a mood disorder was associated with a population attributed risk (PAR) of 74%, the proportion of late life suicides that would be prevented if affective illness were eliminated from the population (Conwell,

Duberstein et al. 2002). Suicide in persons with bipolar disorder often occurs in a depressive phase (Isometsa 2005). Comorbidity between mental disorders is common in suicide victims (Henriksson, Aro et al. 1993, Foster, Gillespie et al. 1997, Isometsa 2001, Cavanagh, Carson et al. 2003).

A review showed that only 0.1% of suicide victims in a psychiatric inpatient population, and 3.2% in a general population, had no established psychiatric diagnosis (Bertolote and Fleischmann 2002).

2.5.3 Physical disorders and pain

Suicide risk is elevated in several physical disorders (Harris and Barraclough 1994). Comorbidity with depression or substance use disorders is thought to increase the risk considerably. However, in one study, people who had been hospitalised for physical illness were found to have an elevated risk for subsequent suicide (incidence rate ratios 2.13) compared to matched controls, and this was still significant after adjustment for psychiatric history and socio-economic status (Qin, Webb et al. 2013). In physical illness, development of a comorbid mental illness substantially increases the suicide risk (Qin, Hawton et al. 2014). Some neurological disorders with permanent or progressive disability entail a multi-fold increase in suicide risk, apart from Parkinson's disease (Stenager and Stenager 2009). The disability caused by the disorder rather than the illness itself seems to lie behind the higher suicide risk (Kaplan, McFarland et al. 2007).

Moderate or severe pain in non-psychiatric illness has been found to increase the suicide risk in elderly persons (Juurlink, Herrmann et al. 2004). Studies also have shown that chronic pain elevates the risk for suicide (Fishbain, Goldberg et al. 1991, Penttinen 1995, Tang and Crane 2006), lifetime suicide attempts (Scott, Hwang et al. 2010) and self-harm (Theodoulou, Harriss et al. 2005). In many cases, an essential link between pain and suicide could be depression. Pain complaints are common in depressed patients (Corruble and Guelfi 2000) and are sometimes more dominant than main characteristics of depression, such as depressed mood (Blumer and Heilbronn 1982, Lipowski 1990). Common pathogenic pathways, possibly involving serotonin, have been suggested (Blier and Abbott 2001).

2.5.4 Neurobiology

Abnormality in the serotonergic system of the brain has been a suspected risk factor for suicide for about three decades. Low levels of the serotonin metabolite 5-HIAA were found in suicide attempters (Asberg, Traskman et al. 1976, Nordstrom,

Samuelsson et al. 1994) and seemed to be specifically associated with violent suicide attempts (Traskman, Asberg et al. 1981).

The noradrenergic and dopaminergic pathways have been studied. There are indications for dysregulation of these systems in depression and possibly in persons with suicidal behaviour, but results have not been conclusive (Mann 2003). The neurotransmitters glutamate and GABA have also been in focus, and there is support for their involvement in suicidal behaviour (Fiori, Ernst et al. 2014).

Studies have been published where monoamines or their metabolites, monoamine transporter, receptor binding capacity in different regions in the brain, expression of genes involved and possible genetic polymorphism are shown to be related to suicide. The results have not been conclusive, but trends could be discerned (Fiori, Ernst et al. 2014).

The hypothalamic-pituitary-adrenal axis (HPA-axis) interacts with hormones, neurotransmitters, and the inflammatory system, and the impact has been studied in different mental disorders, as well as in suicide and suicidality (Westrin 2000)). Levels of inflammatory parameters have been found to be changed in depressive patients who have made a suicide attempt (Nassberger and Traskman-Bendz 1993, Lindqvist, Janelidze et al. 2009, Janelidze, Mattei et al. 2011).

2.5.5 Violence, aggression, impulsivity

Epidemiological studies have shown a strong link between interpersonal violence and self-inflicted aggression in young people, as well as in suicidal behaviour (Centers for Disease Control and Prevention 2004, Swahn, Simon et al. 2008). A person's choice of a violent method in the process of taking his or her life will increase the risk of lethality and death as an outcome. A shared underlying biological mechanism between aggression/violence and suicidal behaviour has been discussed (Traskman-Bendz, Alling et al. 1993, Virkkunen, Goldman et al. 1995, Virkkunen, Eggert et al. 1996, Engstrom, Persson et al. 1999, Westling, Ahren et al. 2004). In a recent review, evidence of co-occurrence of aggression and self-harm was found (O'Donnell, House et al. 2015).

2.5.6 Familial – genetic and environmental risk factors

The risk of suicide is elevated in an individual if suicide has previously occurred in the family. A two to threefold increase in risk has been found if a parent has died by suicide or has made a suicide attempt (Qin, Agerbo et al. 2002, Runeson and Asberg 2003, Niederkrotenthaler, Floderus et al. 2012). In these cases, mental disorder is often found in several persons in the family, which strongly contributes to the suicide

risk, but studies have shown that there are other familial factors involved that are independent of mental disorders (Brent, Bridge et al. 1996, Runeson and Asberg 2003).

Support for an existing genetic predisposition has been found in twin and adoption studies (Bondy, Buettner et al. 2006), but interpersonal and environmental factors also seem important (Fu, Heath et al. 2002, Tidemalm, Runeson et al. 2011). The environmental factors (such as family conflicts, physical or sexual abuse) might have an aggravating effect on the genetic predisposition and increase the risk of suicidal behaviour (Caspi and Moffitt 2006, Moffitt, Caspi et al. 2006)

2.5.7 Socioeconomical factors

Many suicide victims have lived alone (Barraclough, Bunch et al. 1974, Monk 1987, Nordentoft 2007). Higher suicide rates are reported for separated/divorced/ widowed persons (especially in men) than for married or never married persons (Smith, Mercy et al. 1988, Kposowa 2000). Poor social network was found to be one of the predictors for reattempt in a sample of admitted suicide-attempters (Johnsson Fridell, Ojehagen et al. 1996). Some studies have shown that unemployment and low income have been associated with a higher suicide risk (Brown, Beck et al. 2000, Duberstein, Conwell et al. 2004).

2.5.8 Stressful life events

A wife's death has been identified as a risk factor in elderly men (Erlangsen, Jeune et al. 2004). Life events such as separations or other interpersonal difficulties, the death of a spouse or another loved one, financial and legal problems might elevate the risk of suicide (Hagnell and Rorsman 1980, Brent, Perper et al. 1993, Cavanagh, Owens et al. 1999).These could often be seen as aggravating factors adding to other individual risk factors (Rowe, Walker et al. 2013). The personal experience of the event, the psychiatric response and a possible underlying mental disorder are important for the impact on the risk of suicide and suicidal behaviour (Rich, Warstadt et al. 1991, Blakely, Collings et al. 2003, Mann 2003, Wilcox, Storr et al. 2009).

2.5.9 Feeling of hopelessness

A feeling of hopelessness has been described as a risk factor for suicide (Beck, Steer et al. 1985, McMillan, Gilbody et al. 2007), especially in persons with depression (Hawton, Casanas et al. 2013) and bipolar disorders (Hawton, Sutton et al. 2005).

Rated hopelessness in patients with major depressive disorder (MDD) was reported as high in persons who later committed suicide, and Beck et al. have described hopelessness as a modulating factor between depression and suicide intent (Beck, Weissman et al. 1974). It has also been found to be an important prediction factor in suicide ideation in terminally ill persons after controlling for the level of depression (Chochinov, Wilson et al. 1998).

2.6 Protective factors

Protective factors are not so well studied, but are important in the preventive work to reduce suicide. Factors considered include accessibility to care for mental disorders and psychological distress. Many suicide victims with mental disorder are untreated or inappropriately pharmacologically treated at the time of suicide. Recent reports have shown that adequate pharmacological treatment for depression (Mann, Apter et al. 2005, Barbui, Esposito et al. 2009), lithium in bipolar disorder (Goodwin, Fireman et al. 2003, Collins and McFarland 2008), clozapine in schizophrenia (Meltzer, Alphs et al. 2003), cognitive-behavioural therapy (Brown, Ten Have et al. 2005), dialectical behavioural therapy (Linehan, Comtois et al. 2006) and psychodynamic therapy (Clarkin, Foelsch et al. 2001) have a protective effects on suicidal behaviour. The availability of specific means for suicide affects the national pattern of suicide methods, applying to, for example, firearms in the US (Brent 2001, De Leo, Milner et al. 2013) and pesticides in rural areas (De Leo, Milner et al. 2013, World Health Organization 2014). Reducing the availability of lethal means such as firearms is thought to reduce the overall suicide rate (Miller, Azrael et al. 2006).

Religious and cultural beliefs, as well as social support of different kinds (i.e. family and friends), could be protecting factors (Neeleman and Lewis 1999, Chioqueta and Stiles 2003, Lawrence, Oquendo et al. 2015, Wu, Wang et al. 2015).

2.7 Mental disorders of particular focus in this thesis

2.7.1 Epidemiology of depression, alcohol use disorder and psychosis

Depression is the most common mental disorder in suicide victims (Cavanagh, Carson et al. 2003). Depressive disorders are a great burden to health worldwide as they are common, sometimes recurrent, and lead to disability, reduced quality of life, medical morbidity and mortality (Spijker, Graaf et al. 2004, Ustun, Ayuso-Mateos et

al. 2004). WHO estimated lifetime prevalence of major depressive episode at 14.6% in high-income countries and 11.1% in low-income countries. The median age of onset was estimated to be around 25 years (Kessler and Bromet 2013).

In the Lundby Study, between 1972 and 1997, cumulative probability for developing a depression of at least medium grade impairment was 30.7% in women and 22.5% in men (Mattisson, Bogren et al. 2005). A somewhat lower annual incidence rate was seen in the same study in 1947-1972 compared to 1972-1997, indicating that a previously seen increase had stabilised. In another epidemiologic study in the US, the prevalence rates rose for females between 1981 and 2004, but incidence rates in the period 1993-2004 were lower than during the period 1981-1993, suggesting the rise in prevalence is due to increasing chronicity (Eaton, Kalaydjian et al. 2007). Recurrence rate in the long term has been shown to be 30-40% (van Weel-Baumgarten, Schers et al. 2000, Mattisson, Bogren et al. 2007).

Alcohol and other substance use disorders are often the second most common mental disorders in psychological autopsy studies of suicide victims. Globally, alcohol causes a considerable disease burden and 3.2% of the deaths and 4.0% of the disability-adjusted life years (DALY) could be attributed to alcohol consumption in 2000 (Rehm, Room et al. 2003). The lifetime prevalence of alcohol dependence was found to be 20.1% in men and 8.2% in women in a general population in the US (Kessler, McGonagle et al. 1994). In the Lundby Study, the cumulative probability for any alcoholism over the 50-year period was 24.4% for men and 4.0% for women (Mattisson, Bogren et al. 2010). In the same study, overall mortality was shown to be 52% higher among subjects with an alcohol use disorder, compared to other participants (hazard ratio = 1.52)(Mattisson, Bogren et al. 2011). Women are especially vulnerable (Mattisson, Bogren et al. 2010, Chesney, Goodwin et al. 2014). Dual diagnoses are shown to be particularly common in people with alcohol dependence (Kessler, Crum et al. 1997, Berglund and Ojehagen 1998).

Together with personality disorder, psychotic disorders are often mentioned after depression/affective disorders and substance use disorder/alcohol use disorder as most frequently occurring in suicide victims (Isometsa 2001, Arsenault-Lapierre, Kim et al. 2004). These disorders are more commonly found in psychiatric inpatient samples than in general populations (Bertolote and Fleischmann 2002). Psychotic disorders often refer to schizophrenia, other non-affective psychosis, and schizophreniform psychosis, but also sometimes include affective psychosis. However, several mental disorders may have psychotic features, and psychotic symptoms may appear due to intoxications, medical conditions and during the course of primary degenerative brain disorders. In the Lundby Study, lifetime prevalence of any psychotic or bipolar disorder was reported to be 2.82 per 100, of which 1.38 per 100 was for non-affective psychotic disorder (Bogren 2009). A previous Finnish study estimated the lifetime prevalence of psychotic disorders to be somewhat more than 3% (Perala, Suvisaari et

al. 2007). In reviews the life time prevalence of schizophrenia have been estimated around 4.0-5.5 per 1000 individuals (Goldner, Hsu et al. 2002, Saha, Chant et al. 2005).

Suicide risk in different mental disorders has mostly been investigated in clinical samples (Inskip, Harris et al. 1998, Nordentoft, Mortensen et al. 2011, Chesney, Goodwin et al. 2014). This gives a biased and often overestimated picture of suicide risk. Only a few epidemiological longitudinal studies in the world contribute to knowledge about the risk in a general population.

2.7.2 Dysthymia – historical and clinical aspects relating to suicidality

For several decades there has been great interest in trying to understand long-term depressive conditions and to more clearly define the diagnosis 'dysthymia'. Together with co-workers, Akiskal presented a nomenclature of different chronic depressive subtypes (Akiskal, Rosenthal et al. 1980, Akiskal 1983). Winokur underlined that depressions are heterogeneous syndromes, and proposed a way to sub-classify them (Winokur 1997).

More than 75% of dysthymia patients will at least once in their life suffer from a major depression (MDD), sometimes co-occurring, and then often denoted 'superimposed major depression' or 'double depression' (Keller, Klein et al. 1995, Klein, Schwartz et al. 2000). Literature supports a strong link between dysthymic disorder and double depression and that they are probably different phases of the same condition (Klein and Hayden 2000).

In several studies, early onset of dysthymia has been associated with comorbidity of Axis II (Markowitz, Moran et al. 1992, Garyfallos, Adamopoulou et al. 1999, Klein, Schatzberg et al. 1999). These persons more frequently have a history of major depression (Barzega, Maina et al. 2001), and longer episodes of superimposed MDD (Klein, Schatzberg et al. 1999). Emotional and cognitive symptoms have dominated in dysthymia rather than neurovegetative ones (Keller, Klein et al. 1995, Serretti, Jori et al. 1999, Barzega, Maina et al. 2001).

Studies comparing groups of dysthymia and episodic depressive disorders have shown that persons with dysthymia more often have psychiatric comorbidity (Haykal and Akiskal 1999, Bell, Chalklin et al. 2004) and especially personality disorders (Pepper, Klein et al. 1995, Spalletta, Troisi et al. 1996, Garyfallos, Adamopoulou et al. 1999), earlier age of onset (Haykal and Akiskal 1999), and familial loading (Klein, Riso et al. 1995, Haykal and Akiskal 1999). At follow up, they are more likely to have been hospitalised and to have attempted suicide or to have shown other suicidal behaviour (Klein, Schwartz et al. 2000).

Persons with comorbid personality disorder seem to have more severe depressive symptomatology (Klein, Taylor et al. 1988, Garyfallos, Adamopoulou et al. 1999). Dysthymia and cluster B personality disorder have been proposed to co-occur because of shared etiological factors according to family data (Klein, Riso et al. 1995, Riso, Klein et al. 1996).

In a meta-analysis, the suicide risk was about 12 times higher than expected for dysthymia, but with variation between studies of 3-100 times (Harris and Barraclough 1997). Lifetime prevalence of suicide attempts in a group of military outpatients with dysthymia was 17% (Spalletta, Troisi et al. 1996).

It has been concluded that there is little evidence of qualitative distinctions in symptomatology between dysthymia and MDD, but rather a question of quantity (Klein, Kocsis et al. 1996). A two-dimension system was proposed by Klein, referring to severity and chronicity (Klein 2008). Consequently, the release of DSM-5 meant a modification in the aimed direction.

2.7.3 Comorbidity and suicide risk

2.7.3.1 Co-occurring diagnoses

According to autopsy studies, comorbidity of mental disorders is common among suicide victims (Henriksson, Aro et al. 1993, Foster, Gillespie et al. 1997, Isometsa 2001, Cavanagh, Carson et al. 2003), and the most frequent combination is depression and alcohol/substance use disorder (Cheng 1995, Berglund and Ojehagen 1998, Isometsa 2001, Bertolote and Fleischmann 2002). An increased suicide risk has also been found in depression/mood disorder combined with alcohol/substance use disorders (Murphy, Wetzel et al. 1992, Cheng 1995, Conner, Beautrais et al. 2003, Dumais, Lesage et al. 2005). A study of persons who had contact with mental health services showed that, in all groups of mental disorders, comorbid substance abuse disorder increased the cumulative incidence of suicide, except among men with schizophrenia (Nordentoft, Mortensen et al. 2011). Comorbid affective disorder also increased the cumulative risk of suicide in all diagnoses. A higher suicide risk has been reported in persons with schizophrenia who have depression or depressive symptoms (Hor and Taylor 2010) and, in a meta-analysis, previous depression in schizophrenia was estimated to increase the suicide risk (De Hert, McKenzie et al. 2001, Hawton, Sutton et al. 2005). However, in a study of hospitalised patients with schizophrenia, comorbid substance use disorder did not show to increase the suicide risk (Reutfors, Brandt et al. 2009).

In another study, comorbid personality disorders in persons with psychosis were independently associated with an increased risk for suicide and suicide attempts (Moran, Walsh et al. 2003). Isometsä et al. reported that suicide victims with

personality disorders had a concomitant depressive syndrome and/or a substance use disorder in 95% of cases (Isometsa, Henriksson et al. 1996). Henriksson et al. found that 31% of patients with major depression who later committed suicide had a personality disorder (Henriksson, Aro et al. 1993). In a Danish ten-year follow-up study, comorbid personality disorder was independently associated with an increased suicide rate (relative hazard 3.41) in patients with major depression (Hansen, Wang et al. 2003).

The impact of comorbidity on the risk of suicide attempts has also been highlighted. In a study by Hawton et al., persons with comorbidity of psychiatric and personality disorders were more often repeaters, and were more depressed and felt more hopeless at an index suicide attempt than those without comorbidity (Hawton, Houston et al. 2003). Psychiatric consultation patients who had made a suicide attempt more often had depression and comorbid substance use than those without self-harm (Dhossche, Meloukheia et al. 2000).

2.7.3.2 Comorbidity in the long term – co-occurring or separate episode during life

The long-term comorbidity and the temporal sequence of psychiatric diagnosis in patients with suicidal behaviour only seem to have been studied in a few projects. In a Swedish autopsy study, Runeson et al. found that major depression was important as a background factor in 41% of the young suicide cases; it was primary to other disorders in 22% of the cases, and secondary in 19% of the cases (Runeson 1989). Co-occurring substance use disorder occurred in 47%, most often secondary to another disorder. In a Taiwanese study, Cheng et al. (1995) found that the clinical history in the suicide victims indicated that alcohol use disorder usually preceded depression (Cheng 1995).

One study showed that alcohol-dependent individuals with a history of suicide attempts and independent depression had a higher number of suicide attempts than persons with alcohol-induced mood disorders (Preuss, Schuckit et al. 2002). According to another study, participants with lifetime major depressive disorder and substance use disorder tended to report an onset of major depressive disorder prior to the onset of the substance use disorder. When studying different subtypes of major depressive disorders, the authors found that persons with 'suicidal major depressive disorder' at some time in their lives were particularly likely to report that their first major depressive disorder developed prior to a substance use disorder (Marmorstein 2011).

2.8 Assessment instruments for prediction and prevention

2.8.1 Assessment instruments in the clinical evaluation of suicide risk

Assessing suicide risk and the risk for possible other self-harming acts is difficult, requiring knowledge about distal and proximal risk factors and counteracting protecting factors. Several instruments for assessment of suicidality *per se* and symptoms associated with suicidal ideations and behaviours have been constructed, and been validated to various extents. They have sometimes been reported as being useful in predicting suicide or suicide attempts. Some of the instruments are described below. Undoubtedly, a trusting conversation is important in obtaining information from the patient regarding risk factors, protecting factors and warning signs. A dialogue is also a prerequisite for a treatment alliance in the clinical setting. A rating scale can only be a complement to an assessment by a clinician.

The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) (Statens beredning för medicinsk och social utvärdering 2015) recently published a review of the usefulness of rating instruments to predict suicide. One of the conclusions was that none of the studies provided scientific evidence to support that any instrument had sufficient accuracy to predict future suicide with 80% sensitivity and 50% specificity. There were insufficient studies to assess the reliability of some of the instruments.

2.8.2 Suicide Intent Scale (SIS)

This rating scale was first constructed by Beck et al. in 1974 (Beck, Herman et al. 1974) and concerned circumstances around a suicidal act and the person's self-report of his/her state of mind at the time. The scale was later modified by Pierce (Pierce 1981). The scale has been evaluated in some studies and has been found useful in identifying a higher risk of suicide after a suicide attempt (Nimeus 2000, Stefansson, Nordstrom et al. 2012).

2.8.3 Beck Suicide Ideation Scale

This is a 19-item clinical research instrument designed to quantify and assess suicidal ideation. It can also be used to monitor patient´s response to interventions over time (Beck, Kovacs et al. 1979).

2.8.4 The Columbia-Suicide Severity Rating Scale (C-SSRS)

This scale was developed as a standard method for accessing both suicidal ideation and behaviour, to identify those at risk of suicide and to track treatment response. The purpose was to distinguish the domains of suicidal ideation and suicidal behaviour. It quantifies the severity (including intent) and intensity of suicidal ideation, as well as behaviour and its lethality (Posner, Brown et al. 2011). The scale is now frequently used in the US.

Studies have indicated that persons with high level of severity of suicide ideation have higher odds for attempting suicide at follow-up (Posner, Brown et al. 2011, Gipson, Agarwala et al. 2015).

2.8.5 The Suicide Assessment Scale (SUAS)

SUAS was constructed with the aim of measuring suicidality independent of any specific diagnosis, and it should be sensitive to change over time (Stanley, Traskman-Bendz et al. 1986). The authors initially found interrater reliability to be 0.78-0.88. The scale estimates both reported and observed symptoms, and consists of 20 items dealing with affect, bodily states, control and copying, emotional reactivity as well as suicide thoughts and behaviour, which are answered in a 5-point scale.

2.9 Changes in the relevance of diagnostic systems

2.9.1 Diagnostic and Statistical manual of Mental disorders (DSM)

The Diagnostic and Statistical Manual of Mental Disorders (DSM) has been revised over the years. Some examples relevant to this thesis are discussed in this section.

In DSM-5 the 'chronic major depressive disorder' and 'dysthymic disorder' of DSM-IV (American Psychiatric Association 1994) were consolidated into 'persistent depressive disorder', which might then be specified by for, instance, age of onset and the concepts of 'with pure dysthymic disorder', 'with persistent major depressive (American Psychiatric Association 2013).

In Papers 1 and 2 of this thesis, the axes in the multiaxial system from DSM-III-R (American Psychiatric Association 1987) and DSM-IV are used (Axis I for mental disorders, Axis II for personality disorders, and Axis III for physical disorders), as they were current when the papers were written. The multiaxial system was removed in

DSM-5, which was published in 2013. Since then personality disorders have been classified together with the other mental disorders.

New diagnoses dealing with self-harm are introduced as conditions of further study in DSM-5. One of them is 'suicidal behaviour disorder', which applies if a person had made a suicide attempt within the past two years, so the diagnosis could be used independently of other mental disorders (American Psychiatric Association 2013).The other introduced condition is 'non-suicidal self-injury (NSSI)' and refers to deliberate self-harm without suicidal intent.

2.9.2 International Classification of Disease (ICD)

In the International Classification of Disease ICD-8 and ICD-9, the expression 'Suicide and self-inflicted injury' was used as a sub-category of 'Supplementary classification of external causes of injury and poisoning and specified by means'(E950-E959). ICD-10 includes 'Suicide and suicide attempt' in the chapter 'Injury, poisoning and certain other consequences of external causes and intentional self-harm in the chapter external causes of morbidity' (X60-X84).

2.9 Methods of studying mental disorders and suicidality

2.9.1 Studies in clinical samples

Studying a sample of persons in contact with psychiatric care has the advantage of more easily finding people with the focus on outcome. This facilitates a direct meeting with the participants, and a more detailed examination of medical history and psychiatric and physical examinations. Such samples mostly have a relatively severe grade of mental illness, especially if admitted to a psychiatric ward, and an acute event could have aggravated the condition.

In suicide research, important studies could be carried out involving persons with high suicide risk. However, these samples are not usually representative if the aim is to improve the knowledge of all grades and frequencies of mental disorders in general, as many people with a mental illness are not found within psychiatry. Similarly, not all persons who kill themselves had contact with psychiatric care. Research only based on inpatient populations will overestimate suicide risk in a specific disorder.

Another method is to use regional or national registers for studies of samples of in- or outpatients; this makes it possible to gather many people with the outcome of interest.

2.4.2 Psychiatric epidemiology

The way of studying mental disorders and suicidality in an in- or outpatient differs from studies in general population.

In an epidemiological study, a total population (or as compete as possible) in a specified area could be investigated, for instance in the form of a cross-sectional approach. Prevalence of mental disorders or suicide could be examined and defined as occurrence in the population at a specified time (Fletcher and Fletcher 2014). A longitudinal approach could also be used, with repeated identical or similar surveys of the population. This would enable estimating the incidence, defined as the number of new cases during an observation period (a specified time unit, usually years) divided by the total time free from outcome (often a sum of all person observation years). If all individuals have been followed for the same length of time, an occurrence or risk could be estimated as the proportion of affected individuals in the population.

Studying a general population in this way makes it possible to see how mental illnesses and disorders develop over time. By assessing individuals who participate in a general population, it becomes easier to form an opinion of the mental health regardless of the availability of psychiatric hospitals or other specialised psychiatric care units, primary care units, and care-seeking behaviour in society, as well as personal attitudes to mental illness and psychiatric care. One disadvantage is that the outcome could be rare relative to the number of individuals examined. However, there is less risk of selection bias when a total general population is examined.

There are only a few internationally well-known studies in epidemiological psychiatry. One of them is the Stirling County Study, started by Leighton in 1952 (Murphy 1994), and is comparable to the Lundby Study in that it followed a general rural population. There were two follow-ups, as opposed to four in the Lundby Study. The region is a county in Atlantic Canada with 200.000 inhabitants. The study includes three samples of people selected in 1952 and in 1962 (1628 subjects), 1970 (1369 subjects) and 1992 (1700 subjects). Cross-sectional surveys were carried out, as well as panel follow-up of members in an earlier cross-sectional study. The persons included were 18 years or older and the information came from scheduled interviews held by trained laymen; the county's general physicians were interviewed by psychiatrists about the subjects in the sample. The researchers also developed a diagnostic computer program based on algorithms.

The Epidemiologic Catchment Area Program (ECA) is another epidemiologic multi-site study with five sites in the US. The studies, started in the late 1970s, were carried out in collaboration with the National Institute of Mental Health to provide accurate data on mental health status in the nation. The programme involved at least two rounds of interviews (by trained laymen) with the same person in both community and institution surveys, enabling estimates of incidence, relapse and remission of

mental disorders according to the DSM system. The final diagnoses were made using a computer algorithms program.

The Midtown Manhattan Study in New York is another study commonly mentioned together with the Swedish Lundby Study. The aim of the study was to chart mental health and illness, not least in a social psychiatric perspective, and considered socioeconomic status, ethnicity, gender and civil status. The study, which began in the 1950s, involved interviewing a representative sample of 1911 persons aged 20-59 from the area. The standardised interviews were carried out by psychologists, social workers and students, and psychiatrists later estimated the subjects' mental health and illness. Additional information was obtained from case reports or key informants.

The Lundby Study is one of a few epidemiological projects in the world where mental health in a general population was monitored over a long period. The study will be described in the Methods section of this thesis.

3. Aims of the thesis

The overall aim was to identify possible suicide risk factors in a clinical sample and suicide risk in a general population, with primary focus on mental disorders, signs, symptoms and comorbidity. Different approaches have been used. The first involved studying an inpatient population of persons who have attempted suicide (tertiary/indicated level), and the second involved investigating a general population (secondary/selected level). All five studies in this thesis were mainly carried out in a prospective manner, and the main themes were suicidality and comorbidity of mental disorders.

The specific aims were:

Paper 1: To investigate whether patients admitted after suicide attempts and who later died by suicide had more complicated and severe psychiatric states and courses compared to suicide attempters who are still alive.

Paper 2: To find variables disentangling dysthymia patients from those with MDD in terms of psychiatric symptoms, comorbidity and suicidality in an inpatient population of suicide attempters. Our hypothesis was that suicidal persons with longstanding depressive states (dysthymia) have more complicated symptomatology than those with major depression.

Paper 3: To estimate very long-term suicide risk in persons with no mental disorder and in persons with one or more mental disorders in a general population, and to consider gender aspects in a general population. Our hypothesis was that more diagnoses during lifetime would increase the risk of subsequent suicide.

Paper 4: To investigate the first-time diagnosis and subsequent additional diagnoses during lifetime in suicide victims; and to investigate the temporal sequence of alcohol use disorder and other mental disorders a) among suicide victims, b) among persons with an additional diagnosis, as an impact of suicide risk, and c) in the community population. Alcohol use disorder and depression were investigated separately.

Brief report (5): To describe the age of onset, age at suicide, and timespan from onset until suicide in persons with different mental disorder in a community population, and possible differences between mental disorders.

4. Materials and methods

4.1 Inpatients sample

The subjects in Papers I and II have all been admitted to a psychiatric ward in the Lund Suicide Research Center.

Every year during the study periods (1987-1994 in Paper 1 and 1987-2000 in Paper 2), about 190 persons older than 18 years arrived in the Medical Emergency Inpatient Unit (MEIU) of the University Hospital in Lund (now Skåne University Hospital) after a suicide attempt (Nimeus 2000, Backman, Ekman et al. 2003). About 215,000 persons lived in the catchment area of the hospital in these years.

The patients met a consultant psychiatrist within 24 hours. On weekdays, approximately half of the patients met a consultation team from a specialised ward for affective disorder and suicide prevention. Semi-structured interviews were held by a psychiatrist and a social worker from the specialised ward for an evaluation. An estimation of suicidality was made, including an assessment with the Suicide Intent Scale (SIS) (Beck, Herman et al. 1974). However, about two-thirds of the consultations took place during evenings, weekends or holidays, when this consultation team was not on duty. In a medically stable condition, about 50% of the suicide attempters who met the consultation team were referred to the above ward (Figure 1). About 10% were referred to psychiatric wards elsewhere. Roughly 40% were treated as outpatients. Patients who were discharged from the specialised ward after a few days (about 3%), or were in a severe condition/treated under commitment/in need of immediate medical treatment (about 8%), did not take part in the study (Magne-Ingvar, Ojehagen et al. 1992).

Within a week of arriving in the ward, the patients were informed about the research programme and asked to participate. Approximately 9% of patients declined (Magne-Ingvar, Ojehagen et al. 1992), and the rest gave their informed consent to join the whole programme, or part of it.

The definition of suicide attempt described by Beck et al. was used (Beck, Davis et al. 1972): *"those situations in which a person has performed an actually or seemingly life-threatening behaviour with the intent of jeopardizing his life, or to give the appearance of such an intent, but which has not resulted in death"*. Psychiatric and

somatic diagnoses were usually determined by two independent psychiatrists according to the DSM-III-R (American Psychiatric Association 1987) and from 1994 according to DSM-IV (American Psychiatric Association 1994). If the diagnoses were not in accordance, they were decided by consensus after a discussion. The actual suicide attempt was called the 'index suicide attempt'. The research programme included many parameters, such as physical examination, blood sample analyses, urine analysis, lumbar puncture with cerebrospinal fluid analyses of, for example, monoamine metabolites, and different rating scales and questionnaires. The blood sampling and the lumbar puncture were carried out after a wash-out period of 5-35 days depending on type of self-poisoning, current pharmacotherapy and the psychiatric condition of the patient. Except for possible oral contraceptives or benzodiazepines, the subject was free from medication.

The representability of the sample of patients evaluated by the consultation team was studied by other researchers in the group. No significant differences were found in gender or age distribution or in the proportion of persons with repeated suicide attempts/deliberate self-harm in one sub-sample studied in comparison with the total sample of persons admitted to MEIU for a suspected suicide attempt (Backman, Ekman et al. 2003). In another study, no differences in age, gender and frequency of ongoing or previous psychiatric treatment were seen in the sub-sample (Ojehagen, Regnell et al. 1991).

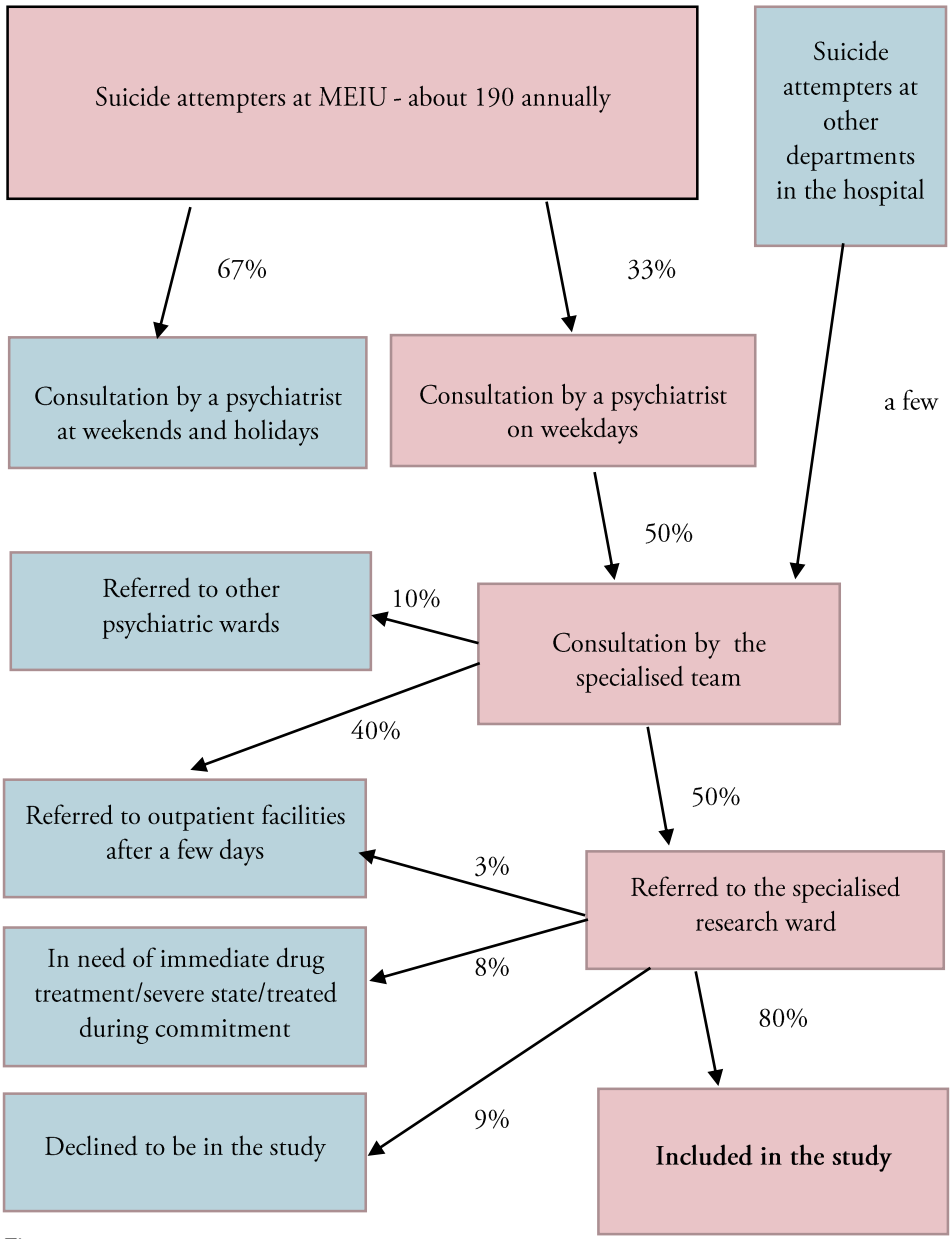

Figure 1.
Recruitment of a patient to the research programme

4.1.1 Paper 1

Information on completed suicides among the subjects was retrieved from the Department of Forensic Medicine in Lund as well as the Cause of Death Register (National Board of Health and Welfare 2015) in 1994. There were no undetermined deaths. Suicide cases ('completers') were matched with suicide attempters from the research programme who were still alive ('non-completers'), according to gender, age (five-year intervals) and main Axis I diagnosis. This procedure was performed by an independent person in the research team. Where more than one control patient was found, the control was randomly selected. Fifteen pairs of subjects were found, giving a sample of 30 subjects. Ten of the pairs were women and five men. The mean age at index was 43.6 years (SD ±14.1) and ranged from 22 to 76 years. At the index suicide attempt, most of the subjects had used a non-violent method according the criteria described by Träskman et al. (Traskman, Asberg et al. 1981). One man used a method that was regarded as a violent method (deep cut in his neck).

Seven (47.7%) of the 15 suicide victims had used a non-violent suicide method, and seven of the victims killed themselves during the first year after index. The mean time from index to suicide was 632 (SD ± 665 days), i.e. about 1 year and 9 months. The person who had lived for the shortest time after index lived for 113 days, and the longest time from index to suicide was 2207 days (slightly more than six years). Ten of the 15 persons who had killed themselves had made one or more suicide attempts before the index suicide attempt, and were classified as repeaters (66.7%). Six of the persons still alive were repeaters (40.0%) which is a non-significant difference (Fisher´s exact test). Persons who had made repeated suicide attempts were often women (13 of 16 repeaters). The main diagnoses for suicide completers and non-completers at the index suicide attempt are presented in Table 1.

Table 1.

Distribution of main diagnosis (DSM-III-R) at the index suicide attempt for the paired subject.

	Pairs (N)	% of all subjects	Men (N)	Women (N)
Major depression	8	53.3	2	6
Dysthymia	3	20.0	0	6
Adjustment disorders	1	6.7	2	0
Psychotic syndrome	1	6.7	2	0
Anxiety	1	6.7	2	0
Depressive disorder UNS	1	6.7	0	2

4.1.1.1 Rating scales – CPRS-MADRS, BHS, SUAS

After admission to the psychiatric ward, and after the wash-out period and the biochemical measures, the patients completed the Beck Hopelessness Scale (BHS), and were rated according to the Comprehensive Psychopathological Rating Scale (CPRS) (Asberg, Montgomery et al. 1978), from which the Montgomery-Asberg Depression Rating Scale (MADRS) was extracted (Montgomery and Asberg 1979). The Suicide Assessment Scale (SUAS) was also completed (Stanley, Traskman-Bendz et al. 1986).

The Beck Hopelessness scale (BHS) measures negative attitudes to the future and comprises 20 statements with a total range of 0-20 (Beck, Weissman et al. 1974). The creator found that a cut-off score of 9 could distinguish persons who had a high risk of completed suicide (Beck, Steer et al. 1985, Beck, Brown et al. 1990). Hopelessness has long been seen as a strong risk factor for suicide and suicide attempt. In a meta-analysis the pooled sensitivity was 0.80 [95% confidence interval (CI) 0.68-0.90], pooled specificity was 0.42 (95% CI 0.41-0.44), and the pooled diagnostic OR was 3.39 (95% CI 1.29-8.88) regarding ability to predict suicide (McMillan, Gilbody et al. 2007). However, in a previous study form our group, the authors did not find BHS a satisfactory instrument in predicting future suicide (Nimeus, Traskman-Bendz et al. 1997).

The Comprehensive Psychopathological Rating Scale (CPRS) comprises 65 items that apply to psychiatric symptoms of various types (Asberg, Montgomery et al. 1978).

The symptoms are rated on a four-point scale (0-3), so can be quantified in relation to each other. In 40 of the items, the patient's answers are recorded in an interview and the rest are evaluated by the observer. The CPRS has been validated (Perris 1979) and is one of the most used scales for general psychopathology in Sweden. 'The Montgomery and Asberg Depression Rating Scale' (MADRS) comprises the ten items from the CPRS dealing with the core-symptoms of depression.

The Suicide Assessment Scale (SUAS) was devised to measure suicidality independent of any specific diagnosis, and it should be sensitive to change over time (Stanley, Traskman-Bendz et al. 1986). The interrater reliability was initially found to be 0.78-0.88 by the authors. It estimates both reported and observed symptoms, and comprises 20 items dealing with affect, bodily states, control and copying, and emotional reactivity, as well as suicide thoughts and behaviour, which are answered on a five-point scale. The predictive value was tested in suicide attempters, and a cut-off value of 39 could significantly differentiate the suicide victims who killed themselves within one year from matched controls (sensitivity 75.0%, specificity 86.3%, PPV 19.4%). It could better differentiate suicide cases from controls was a better than SIS, MADRS and BHS (Nimeus 2000). A score over 30 was associated to repetition of suicide attempt in a sample of people who were admitted to emergency wards after a suicide attempt, and was the best predictor in those with ongoing psychiatric treatment at follow-up (Waern, Sjostrom et al. 2010).

4.1.1.2 Case record evaluation

The paper case records were scrutinised to compare the occurrence of subsequent suicide attempts, as well as different factors reflecting psychiatric treatment and care that might indicate progress of morbidity or comorbidity over time. The information was manually extracted from the case records and prescription lists. The number and length of the hospitalisation episodes, the number of drugs used for treatment (occasional medicines given when needed were left out), possible psychotherapy, and the number of suicide attempts during the observation period were counted. The observation period for each matched pair was counted from the index suicide attempt to death of the suicide completer within the pair. Consequently, the length of observation time was the same for both individuals, but different from one pair to another. The shortest observation period was 113 days and the longest 2207 days. The mean observation time was 632 days (SD±665) and median 485 days.

4.1.1.3 Statistical methods

Non-parametric statistics were used for comparing categorical variables (groups). The Wilcoxon signed-rank test was used for pairwise comparisons of continuous or ranking data (not normally distributed), i.e. variables such as number of hospitalisations, total time (days) at a psychiatric ward, results from the various rating scales, number of diagnoses, number of suicide attempts, number of diagnoses, or

number of prescribed drugs. The Mann-Whitney U-test was performed when not making matched-pair comparisons but comparisons between groups such as 'men' vs 'women' or 'suicide cases during the first year after index' vs 'suicide cases after the first year'. When comparing categorical data between groups, for example the presence or absence of comorbid diagnosis, the Chi-squared or Fisher's exact test (two-tailed) were used.

4.1.2 Paper 2

Diagnostics of low-grade depressive states have changed over time. When this study began, DSM-III-R was the prevailing diagnostic system, so the methods, subject and results are presented according to this. The sample of study patients between 1986 and 2000 included 81 patients whose main diagnosis was major depression (MDD) and 35 patients were diagnosed with dysthymia. These two groups were studied in Paper II. Two subjects had a double depression (dysthymia with additional major depression) and were therefore excluded from the study, as the aim was to find discriminators for the two diagnoses. Mean age and gender did not differ significantly between the study sample (mean age: 43.4 years, SD±15.7, median 42.5; 64% women and 36% men), and for those subjects with these diagnoses who were not referred to the research ward but diagnosed at the MEIU (mean age: 47.3 years, SD±18.7; 62% women and 38% men).

Comorbidity of DSM-III-R Axis I, Axis II and Axis III and possible repeated suicide attempts and/or completed suicide were recorded for the subjects in the two diagnostic groups for comparisons. Overdoses and single wrist-cuts were considered to be non-violent methods, and other methods or combinations of methods were categorised as violent (drowning, hanging, shooting, carbon monoxide intoxication, and several deep cuts) (Traskman, Asberg et al. 1981).

The ratings from CPRS, MADRS and SUAS (described above) were used to compare symptomatology. Unfortunately, not all of the subjects had been evaluated according to the scales. In the MDD group there were results from CPRS and MADRS in 62 of the 81 subjects, and there were SUAS results from 57 of the subjects. In the dysthymia group of 35 persons we had CPRS and MADRS ratings from 31 individuals and SUAS ratings from 25 of them.

4.1.2.1 Statistical methods

Age was compared by the Student's t-test. For categorical variables the chi-squared test or Fisher's exact test (two-tailed) were used for cross-tabulation. Group differences in results of rating scale and values of separate items were evaluated using the Mann-Whitney U-test. The CPRS items that showed significant differences between the dysthymia group and the MDD group were dichotomised into two

categories (<1.0 and ≥1) and entered into the subsequent stepwise backward logistic regression analysis together with gender and age. The divider of 1 point at the scale was chosen because lower value than this is considered to be a non-pathological grade of symptom. The p-value for removal from the model was 0.1. Tolerance for each independent variable was calculated as a test for collinearity. Tolerance below 0.2 was considered to indicate collinearity. Tolerance for the variables in the final step was calculated, and the result showed 0.80-0.97, indicating no collinearity problem. The results were considered significant when $P<0.05$. All tests were two-tailed. The SPSS (Statistical Program for Social Sciences) software was used for the statistical calculations (Norušis 1990).

4.1.4 Ethical considerations

The persons included in the study after a suicide attempt were probably in a more or less acute crisis, either due to events preceding the attempt or by the suicide attempt itself and the consequences. Some could have been disappointed to be alive, others grateful to have survived, and others could feel ambivalent about life. Some could have been experiencing feelings of guilt or shame in relation to others. Inclusion in a research project should be preceded by informed content, which was obtained in all cases.

It could be speculated whether the subjects were in a mental state to make a rational decision about whether to take part in a scientific study at the time they were asked, or whether the subjects accepted because they lacked the energy or peace of mind to understand the issue, consider any advantages and disadvantages and if they felt free to say no. The researchers and the staff at the ward carefully chose a time when the person was responsive to the information. The subjects could choose to only accept one part or parts of the research programme.

Greater knowledge about suicidality is important, both for clinical psychiatry and for society, in order to reduce the suicide rate. In suicide prevention, it should be seen as important to also study a person's condition around the time of a suicide attempt. As long as the inclusion procedure provides opportunities for the patient to make a well-considered decision, while respecting the patient's autonomy and integrity, the study should be seen as ethically justifiable. Naturally, the subjects must not be exposed to exorbitant risks by participating in the study. Participants may have found questions and rating scales inconvenient, and the research might have aroused unpleasant feelings or aggravated psychiatric symptoms in some individuals. Other persons might have positive experiences of being carefully examined and through engaging in dialogue with staff during the examination.

4.3 The Lundby Study

4.3.1 The Lundby population

In 1947, Erik Essen-Möller, professor in psychiatry in Lund, started the Lundby project. He was aiming to investigate the psychiatric health in a general population to obtain accurate information on mental illness, in a study not affected by the selection bias often seen in investigations of inpatient populations. One of the main aims was to find out the frequency of various mental disorders and, as a successor of Professor Henrik Sjöbring, he was also interested in examining the subjects according to the theory of a personality traits by Sjöbring (Sjöbring 1904).

The intention was that all inhabitants of the area should be interviewed and examined, persons with known mental disorders as well as seemingly healthy persons, independent of age, and to discover how mental disorders and personality traits were interrelated. The first field investigation started in 1947 and was performed by Essen Möller and three co-workers, also psychiatrists. They included and met 98.8% of the inhabitants. People in the Lundby area had already heard about the study from authorities such as the dean before the start.

The researchers formulated all the semi-structured interviews and assessments. The interview started with questions about health, sleep and work capacity. The interviewees were then asked to describe previous diseases and contacts with healthcare facilities, and psychiatric symptoms. They were asked to describe their health throughout life, their childhood, education, career choice, pregnancies and hobbies. Information about possible mental retardation, substance abuse, physical illnesses, heredity and socio-economic factors that might influence mental health was also collected. The interviews ended with 30 specific questions about health. The psychiatrists also made observations about mental status and behaviour during the interview. Additional information was obtained from so-called 'key informants' (for example, family members, clergymen, general practitioners, teachers, work supervisors), and external sources such as in- and outpatient case notes and official registers of alcohol abuse and socioeconomic conditions.

Subjective data from the interviews, and observed and collected data was then merged, and led to a conclusion about any former or ongoing episode of mental disease. The original sample comprised 2550 persons. Between 1947 and 1957, 1013 newcomers were included in the study (new-born inhabitants and people who had moved into the area), giving two overlapping cohorts with a total of 3563 individuals.

In 1972, some new diagnostic schedules, such as an assessment of alcohol and drug problems (the CAGE questionnaire) (Mayfield, McLeod et al. 1974) and a checklist

of certain signs in status and behaviours during the interview, were introduced. In 1997, supplementary self-rating questionnaires were added (Nettelbladt, Bogren et al. 2005), for example 'Hopkins Symptom Check-list-25' measuring anxiety and depression (Derogatis, Lipman et al. 1974) and a Mini-mental Test performed if cognitive impairment was suspected (Folstein, Folstein et al. 1975).

In some respects, more available external information was available about the participants in the earlier field investigations, particularly information from key informants, access to archives in nearby hospitals and direct information from local outpatient clinics. In the follow-up between 1972 and 1997, informants were usually family members; case-reports could be requested as a follow-up to information arising during the interviews, or information could be obtained after a hit in any of the available registers: the National Patient Register (inpatient care) (National Board of Health and Welfare 2015), the Cause of Death Register (National Board of Health and Welfare 2015) and a local outpatient care register covering the Lund district (University 2004).

The socioeconomic level was described according to the Swedish standard by Statistics Sweden, 'Swedish socio-economic classification' (Statistiska centralbyrån 1982) using the following three groups:

i) Blue-collar workers: unskilled and semi-skilled workers and skilled workers.

ii) White-collar workers: Assistant non-manual employees, intermediate non-manual employees, and employed and self-employed professionals, higher civil servants and executives.

iii) Self-employed (other than professionals).

Between 1947 and 1997, about 50% of the inhabitants left the area (Figure 2). They had mostly moved to other parts in the south of Sweden and often to neighbouring districts. The fieldworkers always tried to complete the follow-up by travelling to the subjects' new places of residence.

During the entire follow-up period that ended in 1997, 1766 individuals died (Figure 2). For persons who had died since the most recent field investigation, the researchers tried to find information about the person's health and life events between the final interview and death. This information was obtained from key informants and various registers, and by studying death certificates, the Cause of Death Register (National Board of Health and Welfare 2015) and autopsy reports. If no interview was possible at follow-up, information from at least two of the other sources was required for inclusion in the follow-up. Where there was insufficient information for inclusion, the subject was regarded as dropped-out from the study.

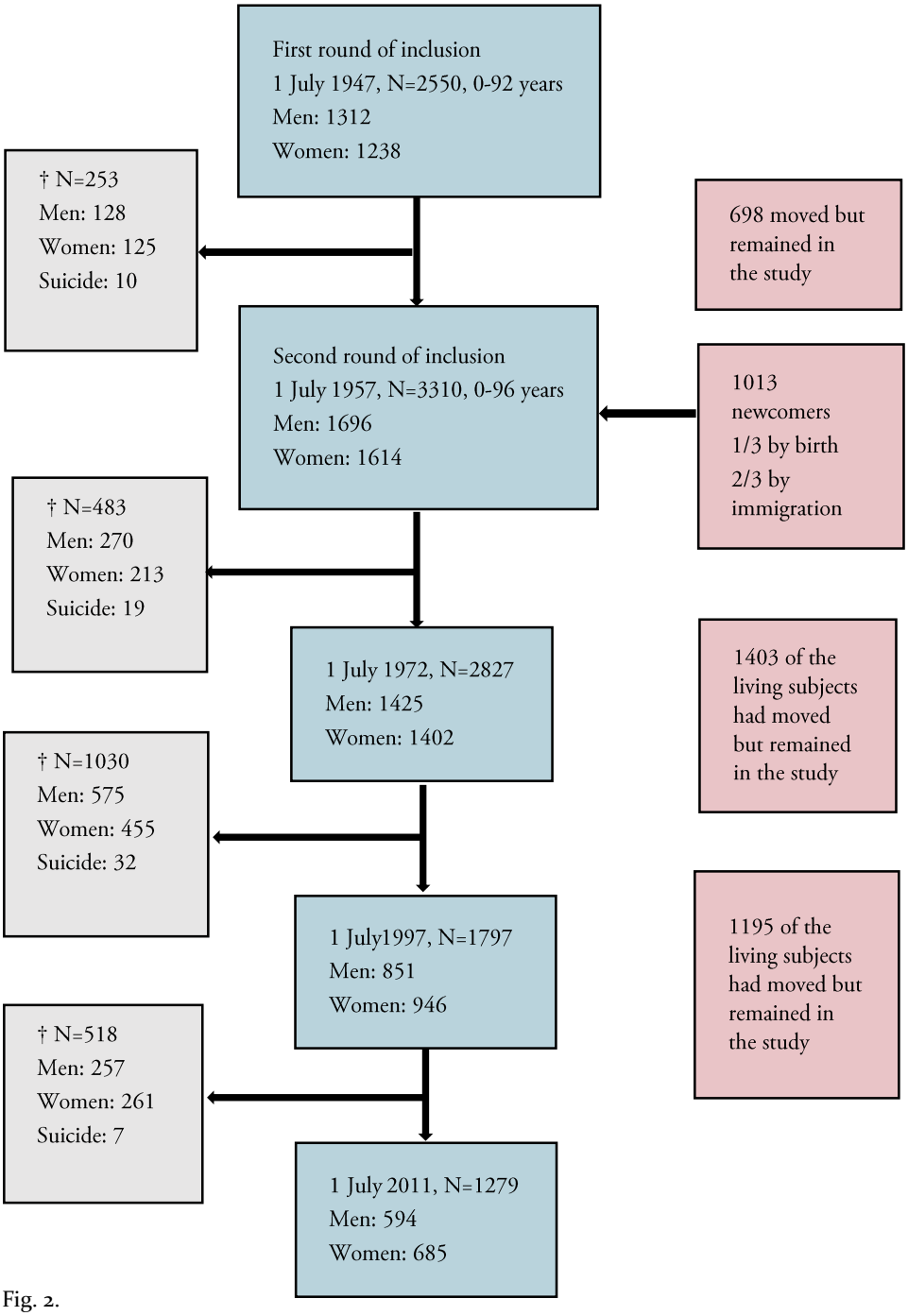

Fig. 2.
The Lundby population – inclusion, deaths and attrition during the follow-up 1947-1997.

Some of the participants could not be traced, and others had died between the two field investigations. In the latter two cases, enough information could sometimes be found from other sources. Missed interviews meant that the drop-out rate was 1.2% in 1947 1.5%, in 1952, 1.8% in 1972, and 13% in 1997 among living subjects, but by using information from at least two other data sources, the actual drop-out rates were 0.7%, 0.6%, 0.1%, 8.7% respectively. When persons who had died between the field investigations and all sources of information were included, the attrition rates were 0.5%, 1.1%, 0.2%, 5.9% respectively (Bogren 2009). Overall, about 1% between 1947 and 1972 and 6% between 1972 and 1997, when all sources of information were used.

The mean age at the times of the different follow-ups can be seen in Table 2. The mean age and median age differed, at the most, 1.5 years between men and women at the time of the field investigations.

Table 2.
Age at follow-ups, men and women combined.

	1/7 1947 N=2500	1/7 1957 N=3310	1/7 1972 N=2827	1/7 1997 N=1797
Mean (SD)	35.0 (±22.4)	36.3 (±21.4)	46.2 (±18.0)	61.8 (±12.6)
Median	34.0	34.0	45.0	61.0
Range	0-92	0-96	15-97	40-96

SD= standard deviation

Overviews of socioeconomic and marital status in the population are shown in Table 3 and Table 4. The proportion in the white-collar group increased and the group of self-employed (for example farmers) decreased over time.

Not unexpectedly, inhabitants moved from the area during the course of the study. From the start of the study to the second follow-up, 698 of the still-living subjects had moved away. At the follow-up in 1972, 1403 of the living persons lived elsewhere and, in 1997, 1195 persons lived elsewhere. Overall, 1817 (about 50%) persons had moved from the Lundby area between the start of the study and 1997. Most people still lived in the south of Sweden, usually in another part of the county, but some of them had migrated to other regions of Sweden or abroad.

Tabel 3.
Socioeconomic index in the Lundby population at each follow-up.

	1/7 1947		1/7 1957		1/7 1972		1/7 1997	
	N	%	N	%	N	%	N	%
White collar	177	5	395	11.1	656	18.4	617	17.3
Blue collar	1260	35.4	1667	46.8	1744	48.9	982	27.6
Self-employed	494	13.9	526	14.8	424	11.9	197	5.5
missing*	619	45.8	975	27.4	739	20.7	1767	49.6
	2550	100	3563	100	3563	100	3563	100

*Children, retired, unemployed, dead.

Tabel 4.
Marital status of the Lundby population at each follow-up.

	1/7 1947		1/7 1957		1/7 1972		1/7 1997	
	N	%	N	%	N	%	N	%
Unmarried	1246	35.0	1447	40.6	453	25.2	111	3.1
Married/cohabiting	1158	32.5	1644	46.1	1261	70.2	1108	31.1
Divorced/separated	18	0.5	49	1.4	60	3.3	168	4.7
Widowed	128	3.6	170	4.8	23	1.3	218	6.1
Deceased	-		253	7.1	736	20.7	1958†	55.0
Total	2550	100	3563	100	3563	100	3563	100

† deceased or had withdrawn from the study.

4.3.2 Lundby area

The two selected parishes were located in the catchment area of the University Hospital in Lund, where the hospital-based psychiatric department used for patients with minor psychosis, neurosis, alcohol problems and social problems had recently opened. There was also a state-run mental hospital driven (St Lars Hospital) and institutions for mentally retarded, chronic diseases, persons who were blind and deaf-mute persons. There was also a forensic unit.

At the start of the study, the area was mainly agricultural, but there was also one industry and a couple of smaller companies. During the period of the Lundby Study, the area became increasingly urbanised, and more of the population earned their livelihoods from work in factories or in the service and administration sector, instead of farming, crafts or small businesses as before. Easier transport and fewer jobs in the neighbourhood has resulted in more people now commuting to nearby cities. The area and its inhabitants have been influenced by industrial and social developments in the same way as other developing regions in the western world.

4.3.3 Suicide and undetermined death

As a new category, self-inflicted death by undetermined intent, E980–989, was introduced in 1968. In the Lundby Study uncertain suicides according to this definition were also noted after 1968. Suicide was defined by the International Classification of Diseases (ICD) codes, from revisions 6 to 9 (World Health Organization 1949, World Health Organization 1955, World Health Organization 1968, World Health Organization 1987) Information about suicide cases was retrieved from the Cause of Death Register (National Board of Health and Welfare 2015). Before 1994 the classification codes E950-E959 for obvious suicide, and E980-989 for undetermined death in ICD 8 and ICD-9 were used. From 1994 until 2011 ICD 10 was used, with the categories X60-X84 for obvious suicides and Y10-Y34 for event of undetermined intent (World Health Organization 1992).

During the entire follow-up (until 1 July 2011) there were 68 suicide cases, including 19 undetermined deaths. Between 1 July 1947 and 1 July 1957, there were 10 suicide cases; between 1 July 1957 and 1 July 1972, 19 cases; between 1 July 1972 and 1st July 1997, 32 cases; and from then until 1 July 2011, 7 cases.

4.3.4 Lundby diagnostics

When the Lundby Study started in 1947 there was no universal classification system for mental disorders. Professor Essen-Möller devised a classification system of mental disorders where clusters of symptoms were categorised into different disorders; the system was further developed in 1957 together with co-investigator Hagnell. All mental disorders were included in the main group 'Diagnosis I', which was meant to represent acquired disorders with a perceptible onset and mostly termination.

The main classes were 'organic brain disorders', 'psychoses' and 'neuroses' (Nettelbladt, Bogren et al. 2005). The main classes can be further divided into main categories such as 'dementia', 'schizophrenia', 'depression' and 'anxiety', and then to even more specific sub-categories. This is a hierarchical system allowing only one diagnosis per episode; for example, dementia rules out psychosis. For the class 'neuroses', the researchers also devised sub-categories for comorbid psychiatric symptoms, such as 'depression + other psychiatric symptoms'.

In the modified diagnostic system used in 1957, the 18 sub-categories of the main classes were structured as shown in Figure 3. Mental retardation and habitual conditions rooted in personality, alcohol problems and psychosomatic complaints were included in 'Diagnosis II'. In the Lundby classification, a subject could only be given one 'Diagnosis I', but one or more 'Diagnosis II' or one 'Diagnosis I' and one or more 'Diagnosis II' in the same period of time.

In the Lundby Study the diagnoses have always been based on information from all available sources (best estimate). Since 1957, the diagnosis was decided after discussion and consensus between the researchers. At the last follow-up, the diagnosis was set after discussion between all the researchers, using all available information, resulting in a 'best estimate consensus diagnosis'. In the field investigation in 1997, diagnoses were decided on the basis of the Lundby classification system, the DSM-IV-system (American Psychiatric Association 1994) and ICD-10 (World Health Organization 1992)In the field investigation in 1997 all episodes of mental disorders in 1972 were re-evaluated, but only for most first-incidence episodes from the earlier investigations and for episodes of impairment grade 3 (described below). This re-evaluation included most first episodes of neurotic disorders 1947-1957, and all episodes 1972-1997.

All episodes of depression and psychosis over the entire study period have been re-evaluated/evaluated and a diagnosis set according to DSM and ICD, but anxiety was less often evaluated systematically. The decision to re-evaluate episodes was due to the differing aims of the various Lundby projects that have been carried out over the years.

The procedure of validation of the diagnostic agreement between previous researchers and the field investigators in 1997, and how Lundby diagnoses correspond to DSM-IV diagnoses, has been discussed previously (Nettelbladt, Bogren et al. 2005). In brief, 200 randomly selected subjects from the cohorts in 1947 and 1952 were blindly diagnosed by the two main field investigators. They found a lack of conformity between episodes of certain diagnostic categories before 1972 compared to after 1972 (tiredness/tiredness+, mixed neurosis, schizophrenia and organic syndrome). These categories were then re-evaluated. The researchers also condensed the 18 original categories to 11, in order to comply better with DSM-IV and ICD-10, which were used in parallel to the traditional Lundby diagnostics (Figure 2). There was good agreement between major Lundby diagnoses, such as psychosis, depression and alcohol use disorders, and DSM IV (Mattisson, Bogren et al. 2009, Bogren, Mattisson et al. 2010, Mattisson, Bogren et al. 2011, Mattisson, Bogren et al. 2015).

In this thesis, the following Lundby categories were used: 'organic brain disorder', 'psychosis', 'depression', 'anxiety disorder' and 'alcohol use disorder' ('Diagnosis II' as described above). The remaining 'Diagnoses I' are combined into 'Other psychiatric disorders'. In the field investigation in 1997, diagnoses according to Lundby, DSM-IV (American Psychiatric Association 1994) and ICD-10 (World Health Organization 1992) were assessed.

4.3.4.1 Organic brain disorder

'Organic brain disorder' represents disorders with clearly disturbed cognitive functions or a clear deterioration of personality or behaviour in which the etiology is unquestionably organic. This is divided into the main category 'dementia' with its sub-categories 'vascular/multi-infarct dementia', 'senile dementia', and the main category 'organic syndrome', which represents conditions not reaching the dementia threshold and other organic brain disorders due to, for example, medical conditions, injury or illegal drugs.

Original diagnostic categories (1957)	Simplified Lundby diagnostic categories, in order to fit DSM-IV and ICD 10	Diagnostic categories in this study
Diagnosis I		
Depression proper	Depression proper	Depression
Depression + Other psychiatric symptoms	Depression + Other psychiatric symptoms	
Anxiety proper	Anxiety proper	Anxiety
Anxiety and other psychiatric symptoms	Anxiety + Other psychiatric symptoms	
Schizophrenia	Schizophrenia	Psychosis
Other psychosis	Other psychosis	
Epilepsy + psychiatric syndrome		
Vascular/Multi-infarct dementia		
Senile dementia	Organic syndrome	Organic brain disorder
Age neurosis	Dementia	
Mixed neurosis		
Mixed neurosis 'deeper'		
Tiredness + nervous stomach	Tiredness	
Tiredness proper	Tiredness with other psychiatric symptoms	Other psychiatric disorders
Tiredness + other psychiatric		
Neurosis + stomach illness	Mixed neurosis	
Child neurosis		
Diagnosis II		
Alcoholism	Alcohol abuse/dependence	Alcohol use disorder
Character neurosis		
Abnormal personality		
Psychopathy		
Mental retardation		

Figure 3.
List of diagnoses in the Lundby Study and in this thesis (Papers 3-5).

4.3.4.2 Psychosis

According to the Lundby Study, 'psychotic disorder' consists of 'schizophrenia' and 'other psychosis'. When the Lundby diagnoses were re-diagnosed according to DSM-IV in 1997, the latter group included other non-affective psychosis, psychotic disorder due to a general medical condition (including delirium/confusion), substance induced psychosis, and manic conditions (Bogren, Mattisson et al. 2009).

4.3.4.3 Depression

The Lundby diagnosis 'depression' has two sub-categories: 'depression proper' and 'depression +', which means 'with other psychiatric symptoms', such as anxiety, obsessive or psychotic symptoms. Subjects with 'depression with psychotic symptoms' were included in the 'depression' group, following the DSM-IV main classification of 'Mood disorders' and the original Lundby classification of 'depression+'. In the majority of cases, the depression group could be approximated to major depressive disorder in DSM-IV if the medium and severe degree of impairment (see below) was used to select cases. However, subjects sometimes better fulfilled the criteria for other DSM-IV diagnoses with depressive symptoms, such as dysthymia, depression NOS, bipolar depression, depression due to general medical condition or substance-induced depression. Twelve (2.4% of individuals with Lundby depression) cases were re-evaluated as bipolar disorder. In some cases, the DSM diagnosis corresponding with the Lundby diagnosis was not included in the DSM-IV mood disorders, for example adjustment disorder and somatoform disorder with depressive features.

4.3.4.4 Anxiety

'Anxiety' was subdivided into 'Anxiety proper' and 'Anxiety + other psychiatric symptoms' (in which anxiety should always be the predominant symptom). In the DSM-IV evaluation, the main category 'anxiety' corresponded with disorders such as panic disorder, generalised anxiety disorder, phobias, anxiety NOS and some other disorders in which anxiety may be prominent, such as obsessive compulsive disorder, somatoform disorder, and adjustment disorder.

4.3.4.5 Other psychiatric disorders

The remaining group, which we call 'Other psychiatric disorders' in this study, represents the Lundby diagnoses 'Tiredness' and 'Mixed neurosis'. The group is heterogeneous, and includes persons whose diagnoses according to DSM-IV could be classified as 'chronic fatigue syndrome', 'social phobia' and 'somatoform/somatization disorder', 'adjustment disorders', 'phobias', 'sleep disorders' and 'anorexia nervosa'.

4.3.4.6 *Alcohol use disorder*

Alcohol problems in the Lundby Study were categorised as 'alcoholism' in the main group 'Diagnosis II', and corresponds to the DSM-IV criteria for 'alcohol abuse' or 'alcohol dependence'. A subject was assessed as a case of the broader category 'alcohol use disorder', if he or she met the criteria for 'Alcohol abuse' or 'Alcohol dependence', at any time between 1947 and 1997. In addition, an estimated duration of disorder of at least one year was needed. In this study we have used the category 'Alcohol use disorder'.

More detailed descriptions of the criteria of the Lundby diagnoses may be found in previously published articles (Hagnell 1966, Grasbeck, Hagnell et al. 1993, Mattisson, Bogren et al. 2005, Mattisson, Bogren et al. 2011).

4.3.5 Grade of impairment

The functional impairment of the episodes of mental disorders between 1947 and 1997 have been estimated according to the principles put forward by Leighton, who defined five levels of impairment: minimal, mild, medium, severe and very severe impairment (Leighton, Harding et al. 1963). Medium impairment (number 3) or higher, was a criterion for suffering from mental illness or 'caseness' (Nettelbladt, Bogren et al. 2005, Bogren, Mattisson et al. 2007), in accordance with proposals by Eaton et al. (Eaton, Anthony et al. 1997). This corresponds to a GAF score between 60-51 or less out of hundred (American Psychiatric Association 1994).

4.3.6 Specific methods in Paper 3

In Paper III we studied persons with no, one, and two or more Lundby diagnoses and the occurrence of suicide in the long term (54-64-year follow-up). Of the 3563 participants, 1528 had suffered from mental disorders during lifetime at the time of the last field investigation in 1997. Specific diagnosis of mental disorders (Lundby diagnosis) were studied. At the time of the latest check of the National Cause of Death Register (Epidemiological Centre, National Board of Health and Welfare) on 1 July 2011, 2284 of the 3563 persons had died (64%).

There were 68 cases of suicide (19 undetermined death included) of which six have never had an episode of mental disorder pronounced sufficient to have reached the level of 'caseness'. Suicide risk, expressed as the proportion of persons who had killed themselves, was analysed for the diagnostic groups. In the logistic regression analyses, the suicide risk as OR was calculated for the Lundby diagnoses (with and without long-term comorbidity), then also by gender. Diagnoses with the highest proportion of suicides (psychosis and depression with additional alcohol use disorder) were analysed in more detail.

4.3.6.1 Statistics

Category variables were compared with Pearson's chi-squared test or Fisher´s exact test in a cross-tabulation for estimating which variables were suitable for entering in multivariate analyses. As we intended to examine whether a mental disorder increased the suicide risk, and the influence of additional diagnoses of mental disorders over time, the Lundby diagnosis groups 'organic brain disorder', 'psychosis', depression',

'anxiety', 'other psychiatric disorders' and 'alcohol use disorder' were entered in a logistic regression analyses with a backward stepwise elimination of non-significant results. In one of the procedures, the existence of only '1 diagnosis' or '≥2 diagnoses' during the observation period was included as a variable. Variables where a diagnosis was combined with gender were used in some of the analyses. Results were considered as statistically significant for p-values below 0.05. The PASW Statistics 18 (Norušis 2011) and version IBM SPSS Statistics 21 (Armonk, New York, USA) software were used for the statistical calculations.

4.3.7 Specific methods in Paper 4

In this study we investigated the temporal sequence of diagnoses in the very long-term perspective in the 68 suicide cases (19 undetermined death included), in the Lundby population, and whether primary or secondary forms of alcohol use disorders in relation to other mental disorder was most common. We also analysed whether the temporal sequence of diagnoses in the 191 persons who had alcohol use disorder with comorbid mental disorder influences the suicide risk. In the final step, we studied the presence of primary and secondary alcohol use disorder in the entire population of 3563 individuals.

4.3.7.1 Statistics

We used Fisher´s exact test or Pearson chi-squared test in cross-tabulation when examining the category variables. Results were considered as statistically significant for p-values below 0.05. In some of the subjects with 'alcohol use disorder' debuting before inclusion in the study, the age of onset was unknown. In these cases, the age of at onset was regarded as the age at inclusion, when assessing the temporal sequence of diagnoses.

The PASW Statistics 18 (Norušis 2011) and version IBM SPSS Statistics 21 (Armonk, New York, USA) software were used for the statistical calculations.

4.3.8 Specific methods in Paper 5 – a brief report

The first Lundby diagnosis in each of the 61 suicide victims with a mental disorder was investigated, and the median age of onset, median age at suicide and the median timespan between these years in the various first diagnosis groups were compared. Some of the groups contained very few individuals in some of the groups, and the distribution of values was not normal, so a non-parametric test was used. We merged the groups with 'organic brain disorder', 'psychosis', 'anxiety' and 'other psychiatric disorders' into a larger group that we called 'all other psychiatric disorders', which

contained 16 individuals. The above variables were compared using Kruskal-Wallis test for independent samples.

We also studied whether the suicide victims had an ongoing episode of mental disorder at time of the suicide event. This information was obtained from interviews with family members or other relatives, case recordings or in- and outpatient care registers at the time of follow-up. This could only be examined in persons who had killed themselves before 1 July 1997, 61 out of the 68 suicide cases.

4.3.9 Ethical considerations

As always before starting a study, it is necessary to consider whether the subjects or their relatives could be disturbed in one way or another. Autonomy and integrity of the participants must always be protected. Researchers must do everything possible to ensure that the subject will be given support if the interview awakens unpleasant memories or lead to mental suffering in other ways. The secrecy of collected data must also be assured. The investigators must not publish data in an identifiable way.

At the field investigations in 1947 and 1952, some parts of the project may not have been approved from an ethical point of view compared with today's standards. The Lundby Study started at a time when people generally obeyed the authorities in society. The project was supported by the government and agencies. The people in the two parishes were informed about the planned investigation of all inhabitants, by the dean and the general physician, and information was sent to everyone in writing. Participation was to be free of charge, no physical examination was involved, and the information would be used with discretion and for scientific purposes. It is hard to know the extent to which people felt they were totally free to abstain from participation in the study or parts of it.

In the follow-up in 1997, the project had received approval from the Research Ethics Committee of the Medical Faculty at the University of Lund. Before the field investigation, a letter was sent to the subjects, stating that participation was optional and professional secrecy would be observed, and that the ethical committee had approved the study. Participants also received information about the content of the interview. The interview was held after the participant had signed an informed consent.

Attitudes to individual autonomy and integrity in general, and in healthcare have developed since 1947. Today there are recommendations and regulations regarding ethical aspects in medical research. At the end of the Second World War, research ethics principals were enshrined in the Nuremberg Code and, later, the World Medical Association (WMA) developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects (World Medical

Association 2013. The Swedish Act (2003:460) concerning the Ethical Review of Research Involving Humans came into effect in 2003, making ethical approval mandatory in medical research {Sveriges riksdag, #575).

Guidelines and legislation protecting human safety, autonomy, and integrity in medical research and in society have been introduced. The approach used in the Lundby Study has changed and has been further developed. The best approach is probably to preserve all the information about the persons who participated in the Lundby Study, and use the extensive work of the previous Lundby researchers in new studies, with the aim of helping to improve knowledge about mental illness.

4.4 Ethical approval

The studies presented in Papers I and II are parts of a large multidimensional investigation on suicidal behaviour, which was approved by the Research Ethics Committee of the Medical Faculty at the University of Lund.

Before the field investigation in the Lundby Study performed in 1997, the project received approval from the Research Ethics Committee of the Medical Faculty at the University of Lund.

5. Results

5.1 Paper 1

5.1.1 Results

There were no significant differences regarding comorbidity at index between suicide-completers and non-completers. About 60% of the subjects had personality disorders. DSM-III-R Cluster B personality disorder (Antisocial, Borderline, Histrionic and Narcissistic) tended to dominate in the suicide completer group (8 persons) compared to the non-completer group (3 persons, Fisher´s exact test, p=0.056).

Of the rating scales examined in this study (CPRS, MADRS, BHS and SUAS), only SUAS at index differed between the groups in terms of the total sum. A higher value was seen in the suicide group, with a mean of 43.2 (SD ±16.4) compared to 23.1 (SD±11.0) in the non-completer group (p=0.017), and the rating was significantly higher in persons who killed themselves within the first year after index. MADRS ratings at index tended to be higher in the completer group (p=0.056). No significant differences was observed between men and women.

From the case record investigation, completers had a greater number of hospitalisations than non-completers during the observation period (P=0.012) and the total time spent in a psychiatry ward was longer (P=0.005, Table 4). The number of prescribed psychotropic drugs used after index tended to be higher among completers (P=0.073). In the completer group, seven out of 15 had received psychotherapy, compared with six of the non-completers (NS). In the case records, we also identified the age of onset of psychiatric illness, which was similar in completers and non-completers (NS). Subjects who later committed suicide made more suicide attempts after index (P=0.018) than non-completers. Seven of the completers made additional attempts during the observation period, but only one of the persons still alive.

Nine of the completers had an 'increased comorbidity' (1-3 new diagnosis) during the observation period compared to one (1 new diagnosis) of the non-completers (p=0.007). Seven of the suicides (47%) occurred during the first year after index.

Table 4.
Chart showing variable comparisons between completers and non-completers (15 pairs, Wilcoxon signed-ranks test).

	Completers mean (SD)	Non-compl. mean (SD)	Completers median (rank)	Non-compl. median (rank)	Z	p two-tailed
Age of onset	32 (±12.9)	32 (±10.2)	30 (14-64)	33 (16-49)	-0.57	0.570
Hospitalisation[1] (N)	5.0 (±4.1)	2.0 (±1.6)	3.0 (1-15)	1 (1-5)	-2.51	0.012
Inpatient duration (days)[2]	211 (±253)	48 (±46.3)	125 (2-884)	26 (2-154)	-2.78	0.005
Post-index suicide attempts (N)	2 (±4.0)	0 (±0.3)	0 (0-14)	0 (0-1)	-2.38	0.018
Drugs (N)[3]	5 (±3.1)	3 (±3.1)	6 (0-12)	2 (0-12)	-1.80	0.073

1. Index hospitalisation included
2. Index hospitalisation included
3. Drugs prescribed from index suicide attempt

5.1.2 Further results

Not reported in Paper I, we also compared whether there was any difference in marital status at the end of the follow-up period, i.e. how many lived alone (widowed, divorced, separated or single) and how many who lived with at least one other person (married, cohabiting). There was no significant difference between the groups.

5.2 Paper 2

5.2.1 Results

No significant differences between MDD patients and those with dysthymia were seen regarding occurrence of comorbid diagnosis according to Axis I or III, number of 'repeaters' before index, or violent suicide methods at index. No significant differences were found in the frequency of completed suicide during the observation period (3-16 years) or in the number of suicides within the first year after index. Noteworthy is that four out of five suicide events in the dysthymia group occurred within the first year. None of the cases were registered as undetermined deaths.

Personality disorders according to DSM III-R (Axis II) were common in both groups, but significantly more common among dysthymia persons (P=0.003, Pearson´s chi-squared). The results are presented in Table 5. The difference was especially pronounced regarding Cluster B (Antisocial, Borderline, Histrionic and Narcissistic, $p<0.001$). The combination of comorbid personality disorder and history of repeated suicide attempts was more common among dysthymia patients ($p=0.014$).

The total value for the rating scales CPRS, MADRS and SUAS did not differ between the MDD group and the dysthymia group, but a few single items did. Reported 'aches and pains' (#24), as well as observed 'increased speech flow' (#53), 'agitation' (#61) and 'vegetative symptoms' (#46) were significantly more common among the dysthymia patients than among those with an MDD. The MDD group had significantly higher scores with regard to the reported CPRS items of 'worrying over trifles' (#9), 'indecision' (#13), 'lassitude' (#14) and 'concentration difficulties' (#16). The only item from SUAS that differed significantly was the item dealing with 'somatic complaints' (#10), which had a higher value in the dysthymia group.

Table 5.

Characteristics of the samples, suicidality and comorbidity. Comparisons between the dysthymia group and the MDD group (Fisher´s exact test or Pearson´s Chi-squared test).

		Dysthymia n=35		MDD n=81		p-value
		N	(%)	N	(%)	
Gender	Men	12	(34.3)	30	(37.0)	NS
	Women	23	(65.7)	51	(63.0)	NS
Suicide before June 2000		5	(14.3)	8	(9.9)	NS
Suicide the first year after index		4	(11.4)	3	(3.7)	NS
Previous suicide attempts		19	(54.3)	35	(43.2)	NS
Violent suicide attempt method		5	(14.3)	20	(25.3)	NS
Comorbidity Axis I		6	(17.1)	17	(21.0)	NS
Comorbidity Axis II		29	(82.9)	42	(51.9)	0.003
Axis II + repeated suicide attempts		17	(48.6)	19	(23.5)	0.014
Comorbidity Axis III		8	(22.9)	20	(24.7)	NS

In a logistic regression analysis, the variables 'age', 'aches and pains', 'increased speech flow', increased 'agitation', less tendency to 'worry over trifles' remained independently associated with dysthymia. Further analysis showed that the prominence of the symptoms in the dysthymia group was not dependent on simultaneous Cluster B personality disorders, but instead were linked with dysthymia. As many as 54.3% of persons with dysthymia had 'aches and pains' according to the CPRS rating, compared to 30.6% of the MDD patients (Fisher´s exact test; p=0.037).

The five dysthymia patients who later killed themselves had, on average, higher ratings for 'aches and pains' than the dysthymia patients who were still alive in June 2003 (p=0.025). This could not be seen in the MDD group. There was no significant difference in age between the MDD group and the dysthymia group (mean: 40.0 years, SD±17.6 vs. 44.9, SD±14.7) or in gender (65.7% vs. 63.0% women).

5.2.2 Further results:

The following (DSM-III-R, Axis III) comorbidities were found in the subjects at index. A subject could have more than one comorbid diagnosis.

- Dysthymia: found in 6 of 35 subjects: 2 persons had substance use disorder, 2 had anxiety disorder in combination with an 'other psychiatric diagnosis', 1 had two 'other psychiatric diagnoses' and 1 had one 'other psychiatric diagnosis'.
- MDD: found in 17 of 81 subjects: 9 persons had substance use disorder, 4 anxiety disorder (one with additional substance use disorder), 1 adjustment disorder, 3 other psychiatric diagnoses.

The following somatic disorders (DSM III-R, Axis-III) were found in the subjects:

- Dysthymia: found in 8 of 35 (22.8%) subjects: 1 person had asthma, 1 person had asthma as a child, 1 had epilepsy, knee damage, 1 had gastritis, 1 had hypertension, asthma and gastric ulcer, 1 had hepatic steatosis, 1 had migraine and urethra problems, 1 had migraine.
- MDD: found in 20 of 81 (24.7%) subjects: 1 person had angina pectoris, 1 had arthrosis, 1 had breast cancer, 1 had diabetes mellitus and hypothyreosis, 1 had epilepsy, 1 had pheochromocytoma, 1 had gastritis, 1 had hypertension, 1 had spastic hemiparesis, 1 had sciatic nerve pain, 1 had stomach pain, heart problems, pain, psoriasis, 2 had migraine, 1 had kidney stone problem, 1 had breast cancer and hypertension, 1 had polymyalgia, 1 had rheumatoid arthritis, tinnitus and had undergone a goiter operation, 1had pain, 1 had intestinal problems as a child, 1 had undergone a goiter operation.

The most recent check in the Cause of Death Register (in October 2006) showed that no more of the subjects with dysthymia had killed themselves, but two of the subjects with depression had done so.

5.3 Paper 3

5.3.1 Results

Description of the Lundby population and separate groups of mental disorder due to gender and age aspects could be seen in Table 6.

Table 6.
Description of the Lundby population and separate groups of mental disorder due to gender and age aspects

	Entire population N=3563	No diagnosis N=2035	Depression N=508	Alcohol use disorder N=427	Psychosis N=131	Anxiety N=300	Organic syndrome N=423	Other psychiatric disorders N=192
Gender, Men/Women %	1823/1740 51.2/48.8%	1017/1018 50.0/50.0%	196/312 38.6/61.4%	390/37 91.3/8.7%	72/59 55.0/45.0%	112/188 37.3/62.7%	225/198 53.2/46.8%	72/120 37.5/62.5%
Suicide M/ F	68 51/17	6 4/2	32 25/7	29 28/1	9, 7/2	10, 5/5	5, 5/0	6, 3/3
Age at onset known age N/ total N Mean (SD) Median range	-	-	507/508 48.9 (±17.2) 48.0, 10-89	348/427 34.7(±14.8) 32.0, 10-78	131/131 51.9 (±20.7) 51.0, 18-97	300/300 40.4 (16.3) 39.0, 14-85	419/423 74.6 (±13.9) 78.0, 18-97	192/192 38.2 (±19.4) 39.0, 4-97
Age at entry to the study Mean, SD Median range	31.9(±22.1) 31.0 0-95	30.24(±22.35) 27.0 0-92	27.2(±17.4) 29.0 0-65	31.8(±20.6) 30.0 0-83	33.3(±18.4) 35.0 3-64	24.0(±15.5) 22.0 0-62	53.5(±17.8), 53.0 0-64	21.25(±13.50) 18.0 0-81
Death rate on 1 July 2011	2284/3563	1189/2035	313/508	331/427	111/131	175/300	398/423	89/192
Death age- Mean (SD) Median, range	76.2(±13.1) 79.0, 6-102	75.6(±13.3) 78.0, 6-101	75.8(±13.2) 78.0, 22-100	71.1(±13.1) 72.0, 21-99	74.4(±13.9) 78.0, 22-99	75.7(±12.4) 79.0, 38-102	81.9(±9.6) 84.0, 32-101	76.6(±13.3) 78.0, 11-100
Death age at suicide Mean (SD), median, range	58.4(±17.2) 59.0, 22-91	69.5(±16.5) 74, 42-85	57.9(±18.1) 59, 22-91	58.4(±15.7) 60.0, 25-85	55.4(±17.8) 59.0, 22-85	57,2(±12.2) 56.5,42-77	57.2(±12.4) 61, 38-70	62.5(±13.8) 64.5, 46-81

The long-term risk for suicide in the Lundby population was 1.9% during the 64-year follow-up of causes of death. The risk with no mental disorder was 0.3%, with one diagnosis 3.4% and with two or more diagnoses 6.2%.

The association to suicide was high for persons with one mental disorder (OR: 11.76, 95% CI: 4.96–27.88, P < 0.0001) and even higher for those with two or more diagnoses (OR: 21.00, 95% CI: 8.48–52.04, P < 0.0001). In individuals with only depression, 6.0% had killed themselves; with only alcohol use disorder, 4.7%, and with only psychosis, 3.1%, but with long-term additional disorders, the suicide risk rose to 6.6%, 9.4% and 10.4% respectively (Table 7). There were no significant differences in persons who had a 'pure' diagnosis or in those who had any additional diagnosis.

Table 7.

Frequency of suicide cases in different diagnoses, with one diagnosis and with additional diagnoses in the Lundby population until 1 July 2011.

	In all persons with the diagnosis	In 1 diagnosis	In ≥ 2 diagnoses
Organic brain disorder	5/423, 1.2%	2/307, 0.7%	3/116, 2.6%
Psychosis	9/131, 6.9%	2/64, 3.1%	7/67, 10.4%
Depression	32*/508, 6.3%	17/281, 6.0%	15/227, 6.6%
Anxiety	10/300, 3.3%	4/158, 2.5%	6/142, 4.2%
Other psychiatric disorders	6/192, 3.1%	3/110, 2.7%	3/82, 3.7%
Alcohol use disorder	29/427, 6.8%	11/236, 4.7%	18/191, 9.4%
No diagnosis	6/2035, 0.3%		

*1 had bipolar disorder

'Psychosis' was equally associated with suicide in both men and women (OR: 2.98, CI: 1.35–6.57, P=0.007). For 'depression' the association was stronger in men (OR: 8.44, CI: 4.78–14.91, p<0.0001) than women (OR: 2.56, CI: 1.11–5.93, p= 0.028).

In men, 'alcohol use disorder' was associated to suicide but not to the same degree as 'depression' (OR: 3.81, CI: 2.17–6.69, p<0.001).

Another logistic regression with more specified variables in 'depression', 'alcohol use disorder' and both, showed a very strong association to suicide in men with long-term comorbidity of depression and alcohol use disorder (OR: 25.11, CI: 11.32–55.73, p<0.001). As seen in Table 8 the odds ratios for suicide in men with 'depression but

no alcohol use disorder' and 'alcohol use disorder but no depression' differed substantially from the OR in 'depression in men' and 'alcohol use disorder in men' respectively in the previous one. This is explained by how comorbidity or absence of comorbidity affects the outcome of the variables and the analysis as a whole.

Table 8.

The association with suicide in men with 'depression but no alcohol use disoder', 'alcohol use disorder but no depression' and men with both diagnoses.

	Odds Ratio (OR)	95% C I	P-value
No mental disorder	1		
Alcohol but no depression in men	7.14	3.64-14.03	<0.0001
Depression but no alcohol in men	17.83	8.71-36.52	<0.0001
Both alcohol and depression in men	25.11	11.32-55.73	<0.0001

Specified variables 'alcohol use disorder but no depression in men' and 'depression but no alcohol in men', 'depression and alcohol in men', ' depression in women', 'psychosis in men and women' and 'no mental disorder' were analysed in a logistic regression analysis (backward stepwise elimination). The table shows only the results for 'depression but no alcohol use disorder in men', 'alcohol use disorder but no depression in men' and both alcohol and depression in men.

5.4 Paper 4

5.4.1 Results

Among the 68 suicide victims in the Lundby population, 'alcohol use disorder' was most common as first diagnosis (26, 38.2%), followed by 'depression' (20, 29.4%) and 'anxiety' (7, 10.3%). In twenty-three of the cases (33.8%), the individual had also developed an additional mental disorder during the follow-up period of 50 years. The first diagnosis and additional diagnoses during the lifespan in the suicide victims are shown in Table 9.

Among the suicide victims it was more common that persons with alcohol use disorder later developed an additional Lundby diagnosis (15/26, 57.7%), than to start with another mental disorder and later in life develop alcohol use disorder (3/36, 8.33%, Fisher´s exact; $p<0.0001$). None of the individuals with primary 'alcohol use disorder' had a remission between the 'alcohol use disorder' and the start of the additional diagnosis, and only one of the persons with secondary 'alcohol use disorder' had a remission of their first diagnosis before developing the 'alcohol use disorder'.

We found a non-significant trend that it was more common to have alcohol use disorder first and later suffer from depression (9/26, 34.6%) than the other way around (2/20, 10.0%, Fisher´s exact, $p=0.08$). Among the suicide victims, only one woman had alcohol use disorder (no long-term comorbid diagnosis), so we could not make comparisons by gender.

When studying only the 191 individuals with long-term comorbid mental disorders, no significant difference was found between the proportion of individuals who had killed themselves in the group who had started with 'alcohol use disorder' (15/ 127, 11.8%) than in the group who had started with another Lundby mental disorder (3/ 64, 4.7%, Fisher´s exact test).

In persons with both 'alcohol use disorder' and 'depression' (85 persons) during the follow-up period, nine of the 54 persons with 'primary alcohol use disorder' had killed themselves (16.7%) and two of the 31 with secondary 'alcohol use disorder' (6.5%). However, the proportion of suicide did not differ significantly between the two groups.

Table 9.
First and additional diagnoses of suicide victims.

First diagnosis, N	Additional diagnosis I, N	Additional diagnosis II, N	Additional diagnosis III, N	Additional diagnosis IV, N
Organic brain disorder, 3	Depression, 1			
Psychosis, 2				
Depression, 20	Organic brain disorder, 1			
	Alcohol use disorder, 2			
Anxiety, 7	Psychosis, 1	Depression,1		
	Depression,1			
	Alcohol use disorder, 1			
Other psychatric disorder, 4	Anxiety, 1			
Alcohol use disorder, 26	Depression , 7			
	Psychosis, 6	Depression,1	Anxiety, 1	Other psychiatric disorder, 1
	Organic brain disorder, 1	Depression,1		
	Anxiety, 1			
No Lundby diagnosis, 6				

We also wanted to see how 'alcohol use disorder' was related to other mental disorders in the entire population. It was more common for a person who started with 'alcohol use disorder' to develop an additional other mental disorder (127/363, 35%) than for a person with start with another disorder and later develop alcohol use disorder (64/1155, 5.5%, $p<0.001$). Four of the 127 persons with primary 'alcohol use disorder' had a remission between the 'alcohol use disorder' and a subsequent disorder. In all these cases the additional diagnosis was 'organic brain disorder', more precisely dementia. Of the 64 individuals who had another diagnosis as their first diagnosis, 23 had ended the episode before the onset of 'alcohol use disorder'. However, there may have been other overlapping episodes.

There was also a higher proportion of individuals who had debuted with 'alcohol use disorder' and later developed 'depression' 54/363 (14.9%) than the other way round 31/384 (8.1%, Fishers exact test, p=0.004). None of those with primary 'alcohol use disorder' had remission before onset of 'depression'. Seven persons had remission of primary 'depression' before developing 'alcohol use disorder'.

One of the suicide victims with Lundby 'depression' first in life had a bipolar disorder.

5.4.2 Further results

Not reported in Paper IV, we also examined the marital status and socioeconomic demographic factors in suicide victims.

The latest known marital status in suicide victims (until 1997) and in persons who had not killed themselves is presented in Table 10. As there were sometimes few cases in the different groups, the variables were dichotomized into 'living alone' or 'married/cohabiting' in the comparisons. A comparison was also performed by dichotomizing to the groups 'separated' or 'not separated' (including persons who had never had been married and persons who were married/cohabiting). No significant differences in marital status were seen in persons who had killed themselves compared to those who had not, neither when the gender were calculated together nor when they were considered separately.

When studying whether there were significant differences in marital status within the specific Lundby diagnoses; the only significant difference found was that persons with 'depression' who had killed themselves had more often been married, cohabiting or living alone (in 28/32 of the cases, 87.5%), than had been divorced/separated (p=0.028). There were too few cases to perform calculations within specific diagnosis when the genders were separated.

No differences in socioeconomic status between suicide victims and other individuals in the Lundby population were found (Table 10). Nor when the different diagnostic groups were analysed separately (Pearson´s chi-squared test or Fisher´s exact test).

Table 10.
Marital and socioeconomic demographic factors in suicide victims

		Suicide cases				Non-suicide cases			
		Male		Female		Male		Female	
		N=51	%	N=17	%	N=1772	%	N=1723*	%
Marital status	Married/cohabitating	29	56.9	13	76.5	1193	67.3	948	55.0
	Living alone	22	43.1	4	23.5	579	32.7	773	44.9
	Unmarried	10	19.6	2	11.8	254	14.3	216	12.5
	Widowed	3	5.9	1	5.9	212	12.0	428	24.8
	Divorced/separated	9	17.6	1	5.9	113	6.4	129	7.5
Socioeconomic status	White-collar	9	17.6	6	35.3	479	27.0	490	28.4
	Blue-collar	31	60.8	8	47.1	1004	56.7	977	56.7
	Self-employed	8	15.7	3	17.6	279	15.7	253	14.7
	Unemployed/unknown	3	5.9	0	0	10	0.6	3	0.2

N= number, % = percent within suicide. * 2 missing cases

5.5 Brief report (5)

5.5.1 Results

During the follow-up period, 62 of the 68 suicide victims in the Lundby population had a mental disorder. Individuals with 'depression' as first diagnosis in life had a higher age at onset than those with 'alcohol use disorder' or any of 'all other disorders' ('organic brain disorder', 'psychosis', 'anxiety', 'other mental disorders') first.

The median span from onset of first mental disorder until suicide was 16 years, but differed essentially between the Lundby diagnoses. For persons with 'depression' as first diagnosis, the median time was 2.5 years, which was significantly shorter than both 'alcohol use disorder' and any of 'all other disorders', *but* the variance was great and the latest suicide occurred 42 years after onset (Table 11). 'Alcohol use disorder' showed a high median of 24 years from onset until suicide. The highest median was found in anxiety, with 32 years and a timespan up to 45 years.

There were no significant differences in the distribution of median 'age at onset' and 'time from onset of first diagnosis to suicide' and 'age at suicide' in men and women. Six suicides occurred within one year after onset of mental disorder, 25% of the suicide events within four years and 25% *after* 34.5 years. The survival curve (years from onset of first mental disorder until suicide) for the suicide victims is presented in Figure 4.

Fifty of the suicide victims had an ongoing episode of mental disorder at the time of suicide (73.5%). The diagnoses are shown in Table 11. 'Alcohol use disorder' (27/50, 54%) and 'depression' (21, 42%) dominated and 90% of them had the same diagnosis as their first diagnosis. Alcohol and co-occurring depression was found in six of the cases.

Table 11.
Age and time aspects of the first Lundby diagnosis in suicide victims.

First diagnosis, N	Age at onset Median Range	Time from age at onset until suicide Median Range	Age at suicide Median Range
In all suicide cases, 68	36.0 10-83, N= 61	16.0 1-54, N=61	59.0 22-91
Men, 51	35.5 (10-83), N=46	20.0 1-49, N=46	60.0 22-85
Women, 17	37.0 17-72, N=15	15.0 1-54, N=15	48.0 40-91
Organic brain disorder, 3	34.0 31-68	7.0 3-27	61.0 38-70
Psychosis, 2	26.0 18-34	14.5 4-25	40.5 22-59
Depression, 20	48.5 10-83	2.5 1-42	54.5 22-91
Anxiety, 7	23.0 17-44	32.0 4-45	51.0 42-77
Other psychiatric disorder, 4	29.5 18-61	18.0 9-54	59.5 46-81
Alcohol use disorder, 26	33.0 10-63, N=25	24.0 3-49, N=25	60.5 25-85
No Lundby diagnosis, 6			74.0 42-85

Age at onset: 'depression' vs. 'alcohol use disorder', Kruskal-Wallis; p =0.044

Age at onset: 'depression' vs. 'all other diagnoses'*, Kruskal-Wallis; p=0.033

Time from age at onset of mental disorder until suicide: 'depression' vs. 'alcohol use disorder' vs., Kruskal-Wallis; p<0.001

Time from age at onset of mental disorder until suicide: 'depression' vs. 'all other diagnoses'*, Kruskal-Wallis; p=0.005

* 'organic brain disorder', 'psychosis', 'anxiety' and 'other psychiatric disorders'

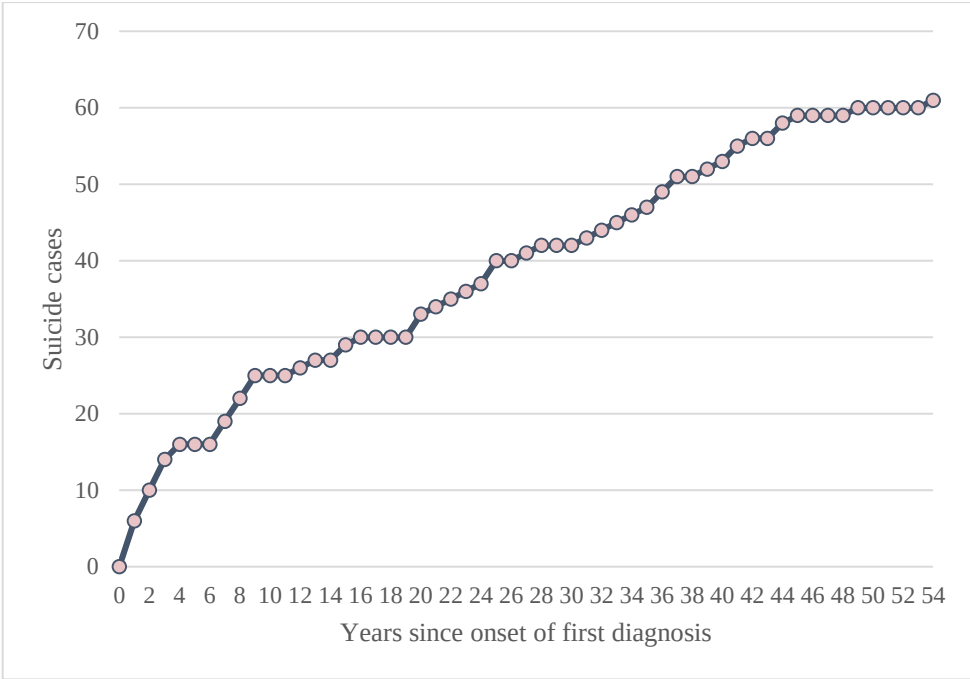

Figure 4.
Survival in years from onset of first mental disorder until suicide.

Table 11.
Diagnoses at time of suicide in the 68 suicide victims.

Diagnosis at suicide	Number	Same as the first diagnosis, N	Other first diagnosis
Organic brain disorder	3	2	Depression1
Psychosis	2	2	---
Depression	15	14	Organic brain disorder1
Anxiety	2	2	---
Other psychiatric disorder	1	1	---
Alcohol use disorder + another mental disorder	16 11*	16 8	---- Depression 2, anxiety 1
No known ongoing mental disorder	18		

*2 'psychosis', 6 'depression', 2 'anxiety' 1'other psychiatric disorder'.

6. Discussion

6.1 Paper 1

The suicide victims in the first study had more suicide attempts during the observation period than the subjects still alive. This might be explained by more severe mental disorders *per se*, but a possible kindling effect/sensitisation of suicidal ideations and suicidal behaviour has also been discussed. This could cause, for example, more severe suicidal ideation, increased number of attempts, and more lethal events over time (Joiner and Rudd 2000, Carter, Reith et al. 2005, Bradvik and Berglund 2011, van Heeringen 2012). The suicide completers in our study more often had additional diagnoses and/or changed diagnoses over time, which could be caused by severe psychopathology or complicated symptomatology, thereby making assessment and treatment harder.

Suicide completers also had a greater number of hospitalisations than non-completers, and the total time spent in a psychiatric ward was longer. One study has described that patients who killed themselves after psychiatric hospitalisation had more and longer hospitalisations and more previous suicide attempts (Goldney, Positano et al. 1985). Another study found a greater number of previous admissions in patients with major depressive disorder who had killed themselves compared to other depressed patients with and without a history of suicide attempts (Gladstone, Mitchell et al. 2001).

In a population of inpatients with affective disorders an increased suicide risk was found among those who had a history of multiple admissions (Hoyer, Olesen et al. 2004). A suicide attempt is known to be a very strong predictor for subsequent death by suicide, especially during the first year after a suicide attempt. One study found the highest risk within the first three months (Randall, Walld et al. 2014). Seven out of the 15 suicide events (47%) in our study occurred during the first year of follow-up, which are figures comparable with a Swedish cohort study of persons admitted after a suicide attempt (Tidemalm, Langstrom et al. 2008).

People who had made repeated suicide attempts are usually considered to have a higher suicide risk (Hawton and Fagg 1988, Ostamo and Lonnqvist 2001). In our study the observation timespan differed between the pairs, but our results are in line with previous results, as the suicide victims had more suicide attempts after index.

The suicide completers and the survivors had no significant differences in the CPRS at index, which indicates that there was an equal grade of severity of mental illness at index. However, there was a trend towards higher values in MADRS, which could be interpreted as indicating more depressive symptoms in the completer group. However, the completers in our study had a significantly higher median value in SUAS (higher than the 39 which is suggested to be the cut-off) compared to the non-completers (whose median was below the cut-off). We found a significantly higher SUAS value in suicide victims who died within the first year after index compared to those who killed themselves later. Our results support that assessment of suicide risk by using SUAS in an inpatient population after a suicide attempt could be useful, and this has already been published by the research group (Nimeus, Alsen et al. 2000).

However, results from a rating scale could only be a complement to a careful and continuous psychiatric evaluation of the patient's condition, including all possible risk factors. The value of a rating scale like SUAS lies in describing a state more than a trait, so results may change over time. The Swedish Council on Health Technology Assessment and Assessment of Social Services (SBU) (Statens beredning för medicinsk och social utvärdering 2015) recently published a review dealing with the usefulness of rating instruments to predict suicide. One of the conclusions was that none of the instruments had sufficient accuracy to predict future suicide, but there were insufficient studies to assess the reliability of the Suicide Assessment Scale (SUAS).

This study shows that suicide attempters in a condition severe enough to be admitted to a specialised psychiatric ward, and who later commit suicide, often have had a period of months, but mostly years of long-lasting and frequent suffering from psychiatric illness before the suicide. They have repeatedly been hospitalised, spent many days on a psychiatric ward (often hundreds of days), and have been prescribed a great number of drugs, seemingly often without expected effect. New suicide attempts could possibly have been sensitizers for a future suicide.

6.2 Paper 2

In this selected group of dysthymia patients admitted after a suicide attempt, as many as 82.9% had an Axis II diagnosis. This was significantly more than persons with MDD, and these patients more often had a diagnosis within cluster B. In previous studies, comorbid personality disorder in dysthymia has often been reported as frequent (Markowitz, Moran et al. 1992, Klein, Schatzberg et al. 1999), particularly in patients with an early onset (Pepper, Klein et al. 1995, Garyfallos, Adamopoulou et al. 1999), and more often than in MDD (Spalletta, Troisi et al. 1996). Personality disorders within cluster B and C have been observed most frequently (Markowitz, Moran et al. 1992, Pepper, Klein et al. 1995). Results from a study comparing

dysthymia and borderline personality disorder suggest that depressive symptoms and borderline personality features in dysthymia arise from partially overlapping processes (Klein and Schwartz 2002). Our results indicate that previous results also apply for patients with dysthymia admitted after a suicide attempt.

In a Hungarian community sample, the risk of suicide attempt was high (OR 17.5) (Szadoczky, Vitrai et al. 2000) and the risk of completed suicide was found to be about 12 times more than expected in a meta-analysis (Harris and Barraclough 1997); this is less than has been shown in major depression. We found no significant differences in number of suicide attempts or suicide events among the subjects with dysthymia and MDD, but in both groups many had made repeated suicide attempts before index (54% and 43% respectively) and as many as 14% and 10% respectively, had died by suicide. This is probably because of the high risk sample in this study. Comorbidity between Axes I and II may contribute to higher risk of suicide (Hawton, Houston et al. 2003).

The variables 'aches and pains', 'increased speech flow', 'agitation', less tendency to 'worrying over trifles' remained independently associated with dysthymia, but not to MDD.

The mean value for 'aches and pains' (CPRS #24) was higher in dysthymia patients who later died by suicide, compared to non-suicides, and a trend of higher values of 'somatic concerns' (SUAS #10) was found. We suspect that perceived pain could be a complicating factor that elevates the suicide risk in patients with dysthymia. Several studies indicate that pain causes a higher suicide risk (Fishbain, Goldberg et al. 1991, Cattell and Jolley 1995, Penttinen 1995, Tang and Crane 2006, Hassett, Aquino et al. 2014). In a study on Canadian primary care patients, persons with comorbid dysthymia were compared to persons without any psychiatric disorder and the groups reported levels of pain which impaired their function in 34.3 and 15.3% respectively, which was a significant difference (Bell, Chalklin et al. 2004). To our knowledge, no one has studied pain in dysthymia and possible association with suicidality. Further studies in this field would be of interest.

The symptom item 'agitation' (CPRS #61) was independently associated with dysthymia. The authors in the Hungarian study above found that the only depressive symptom that increased the odds for a suicide attempt was 'agitation' in anxiety and affective disorders. A high value for this item might reflect anxiety. Anxiety and/or agitation were found in almost 80% of patients who had killed themselves while admitted to a psychiatric clinic (Busch, Fawcett et al. 2003). Pain and anxiety might be symptoms that aggravate the risk of suicidal behaviour in the dysthymic group in our study.

Over 50% of the dysthymia patients were repeaters and 10.5% of the repeaters died by suicide later (after 9-12 years). The complications associated with dysthymia may

easily be overlooked as depressive symptoms are milder. However, the long-term nature and the risk of comorbid mental disorders (not least personality disorders) may cause a complicated course of illness with suicidal behaviour, and the suicide risk in these cases must be carefully considered.

In this study it would have been interesting to know the age of onset of dysthymia and MDD, but unfortunately this information is unknown. An early average age at onset could be expected in these dysthymic patients due to a large proportion having a comorbid personality disorder, as has been described previously (Markowitz, Moran et al. 1992, Pepper, Klein et al. 1995, Garyfallos, Adamopoulou et al. 1999).

6.3 Paper 3

Our first finding was that the suicide risk (as a proportion of individuals who had killed themselves) in the group with no mental disorder in the Lundby-population was 0.3%. To the best of our knowledge, no previous longitudinal study has reported a risk of suicide over such a long period, approaching lifetime, among people without mental disorders. An estimation of suicide risk in the somewhat shorter perspective (follow-up of 15-36 years), but with a larger sample of a national total cohort, was made in a Danish study (Nordentoft, Mortensen et al. 2011). This study showed suicide risk in a non-psychiatric population to be 0.72% for men and 0.26% for women, compared with 0.39% and 0.20% in the present study. In a review by Bertolote and Fleischmann, 3.3% of suicide cases in general population studies had no established diagnosis and 0.1% in psychiatric inpatient samples (Bertolote and Fleischmann 2002). Consequently, our study gives further evidence of a very small suicide risk among mentally healthy people.

The figures we found for each diagnosis when additional diagnoses were not excluded were fairly similar to a previous meta-analysis of estimated lifetime risks (Inskip, Harris et al. 1998); 6.3% for Lundby depression versus 6% for affective disorders, 6.8% for Lundby alcohol use disorder versus 7% for alcohol dependence, and 6.9% for Lundby psychosis versus 4% for psychosis/schizophrenia. It should be noted that the study by Inskip et al. made a computerised estimate of lifetime mortality by suicide, while the present study is a long-term study where the entire population had not died.

In the present study we investigated suicide risk in exclusive diagnoses and compared it with the risk when there were additional diagnoses in a long-term perspective. When the diagnosis was only depression, the risk was 6.0%, only alcohol use disorders 4.7%, and only psychosis 3.1%, but with additional disorders the suicide risks were 6.6%, 9.4% and 10.4%, respectively. This means that each diagnosis has a

high suicide risk *per se*, but the risk is increased with comorbid diagnoses for alcohol use disorder and psychosis (but a non-significant difference).

Men who had both depression and alcohol use disorder diagnoses during lifetime had a very high risk of subsequent suicide, 16% (OR: 25.11). The Danish study (Nordentoft, Mortensen et al. 2011) showed a cumulative incidence of suicide risk in unipolar affective disorder combined with alcohol use disorder of 6.74% in men. The figures are not exactly comparable, due to different methods, but this appears to be lower than the figure shown in this study with a longer follow-up. Consequently, the risk may be very high when persons are followed up over a longer period. An additional or synergistic effect of alcohol use disorder and comorbid depression has been suggested (Cornelius, Salloum et al. 1995) that might increase the risk of suicide.

6.4 Paper 4

The finding that alcohol use disorder was the most common first diagnosis in the Lundby suicide victims was not expected, as mood disorders are often reported as the most common. However, in female suicide victims, depression dominated as first diagnosis in life, which is in agreement with a previous meta-analysis considering gender differences (Arsenault-Lapierre, Kim et al. 2004). In 15 of the 26 suicide victims who first had alcohol use disorder, an additional mental disorder developed later.

Comorbidity of mental disorders is known to be common in suicide victims (Henriksson, Aro et al. 1993, Foster, Gillespie et al. 1997, Isometsa 2001, Cavanagh, Carson et al. 2003) and is considered to elevate the suicide risk (Nordentoft, Mortensen et al. 2011). In this study, 23/68 (34%) of the suicide victims had long-term mental disorder comorbidity, which is similar to the proportion previously reported in a systematic review (comorbid mental disorders 41-52% and comorbidity between mental disorder and substance abuse 23-46%) (Cavanagh, Carson et al. 2003).

In previous studies the most frequently reported combination of mental disorders in suicide victims have been depression/mood disorder and alcohol/substance use disorder (Cheng 1995, Berglund and Ojehagen 1998, Isometsa 2001, Bertolote and Fleischmann 2002), which was also the most common long-term comorbidity in this study (11 of the 23 cases with comorbidity). One study reported that comorbid alcohol use disorder predicted inadequate treatment in depression after suicide attempt (Suominen, Isometsa et al. 1998). Another study has shown that successful

suicide prevention work in alcoholics must include a focus on depression as well as interpersonal factors (Conner, Beautrais et al. 2003).

We found that the alcohol use disorder usually preceded other mental disorders among suicide victims. However, when we studied persons with alcohol use disorder and comorbidity in the Lundby population, we did not find any significant difference in the proportion of suicide in those with alcohol use disorder first than in those with another mental disorder first.

In the entire Lundby population it was more common to have alcohol use disorder prior to another mental disorder, and alcohol use disorder was also more common prior to depression specifically. Some studies suggest that alcohol use disorder prior to depression is more common (Kessler, Crum et al. 1997, Gilman and Abraham 2001), and some authors argue that alcohol problems increase the risk of depression (Hasin and Grant 2002, Paljarvi, Koskenvuo et al. 2009). However, other studies indicate that persons with depression have a higher risk developing alcohol use disorder than the other way around (Kuo, Gardner et al. 2006).

Persons who develop alcohol use disorder before another mental disorder mostly had overlapping conditions, but there were fewer overlapping episodes when the other disorder preceded alcohol use disorder. In the suicide victims, only one person who had secondary alcohol use disorder had a remission between the episodes, and none of those with primary alcohol use disorder. This indicates that individuals with alcohol use disorder in the Lundby population had persistent and complicated courses of the disorder.

We emphasise that alcohol use disorder could be an essential risk factor for subsequent additional mental disorder and suicide in the very long perspective.

6.5 Brief report (5)

In the Lundby population, suicide victims with depression as first diagnosis in life distinguished themselves by having a relatively late age of onset, but a short time from then until suicide. The high risk of suicide early in the course of mental disorder has been studied (Nordentoft, Mortensen et al. 2011, Randall, Walld et al. 2014), especially in affective disorder (Sharma and Markar 1994, Hoyer, Olesen et al. 2004, Hunt, Kapur et al. 2006, Mattisson, Bogren et al. 2007) but also in schizophrenia and in (Gonzalez-Pinto, Aldama et al. 2007, Randall, Walld et al. 2014) Alzheimer's disease (Erlangsen, Zarit et al. 2008).

In this study, suicide early in course applies for those with depression as first diagnosis; of these subjects, six persons (30%) died within the first year and nine

persons (45%) before the end of the second. However, for the other diagnosis, the suicide events were spread over the observation period with a considerable number of suicide events decades after onset. Persons with alcohol use disorders and anxiety first usually lived two or three decades before suicide.

Age of onset of a mental disorder as a possible risk factor of suicide has been reported in some studies. Younger age has been associated with a higher risk of suicide in bipolar disorder (Latalova, Kamaradova et al. 2014) and schizophrenia (Popovic, Benabarre et al. 2014). In our study, a relatively low median age of onset was found in anxiety, but these subjects then lived for a long time before suicide. In contrast, suicide victims with depression first had a relatively high age of onset, but had a short time from onset to suicide. Individuals with alcohol use disorder were significantly younger than those with depression and mostly lived for at least two decades after onset before suicide.

In Paper 3, we found that 16% of men with depression and alcohol use disorder had killed themselves during the follow-up, which differed from the results in a Danish total cohort study with a cumulative incidence of 6.74% in men with unipolar affective disorder and comorbid substance use disorder up to 36 years after their first hospital contact (Nordentoft, Mortensen et al. 2011). The fact that we had a longer follow-up period may be one of the explanations, as we saw that suicide often occurred late in course of an alcohol use disorder. The considerable number of suicide events many years after onset of alcohol use disorder may be related to biochemical changes in the brain as a consequence of overconsumption of alcohol, but also the late psychosocial and economic effects of sustained alcohol abuse or dependence (Conner and Duberstein 2004, Sher 2006).

We found that as many as 25% of the suicide events occurred almost 35 years after the onset of the first episode of a mental disorder. Ninety percent of the suicide victims who had an ongoing mental disorder at time of suicide had the same diagnosis as at the first episode of mental disorder, often many years earlier in life. In everyday clinical practice, it is important to obtain information about previous episodes of mental illness, and to observe symptoms indicating relapse of a previous mental disorder throughout life, as well as try to detect current comorbidity, which further might elevate the suicide risk.

6.6 Methodological considerations in Papers 1 and 2

6.6.1 Sample strengths and limitations

The persons included in the research programme at the specialised ward constitute a selected group of people in a relatively severe psychiatric condition and who often had an intent to die. Other persons with milder self-destructive behaviour or with a less severe psychiatric state were usually referred to outpatient facilities. Consequently, the subjects in the two studies were in a relatively severe state, but still not severe enough to be excluded or unable to give informed consent for research.

Persons who entered the MEIU at weekends or during holidays, therefore not meeting a psychiatrist and social worker from the research team, were not admitted to the ward. This means there is a non-negligible drop-out. However, the group of patients evaluated by the research team were comparable to all persons who came to the MEIU after a suicide attempt in terms of age, gender, repeated suicide attempts and psychiatric treatment. Not all of these patients were included in these studies, but the study sample nevertheless represented a psychiatric inpatient population of suicide-attempters with substantial psychiatric suffering.

In Paper 1 there are very few pairs for comparison, which is a limitation. Fortunately, a completed suicide is a rare event, but this weakens the power in the analysis. On the other hand, one strength of the study is that we matched the pairs to age, gender and main diagnosis.

In Paper 2 the number of individuals in the groups differed. The dysthymia group had somewhat longer observation time (mean 10.7, SD± 2.8, median 9.5 years) from inclusions until the latest check at the Cause of Death Register compared to the MDD group (mean 8.9, SD± 3.3, median 11.0 years, Mann-Whitney U-test, p=0.008). One strength of the study is that the subjects were examined close to a suicide attempt in a standardised manner.

6.6.2 Collection of data and analyses – strengths and limitations

In Paper 1, the observation time differs between the pairs, but is the same within the pair, which gives the opportunity to study the history of the suicide-completer and the non-completer within the same time frame. In the still-living group, the psychiatric condition, the amount of psychiatric care, and suicidal behaviour could have changed since the study was performed. At the last check in the Cause of Death Register in 2006, one more person had killed himself, and belonged to the pair of psychotic syndrome. The suicide attempters could also have been given a new

diagnosis, could have made new suicide attempts, and experienced important life events, which could have influenced the course.

In most cases, the diagnoses after index are given after evaluation by other psychiatrists than those who met the patient at index, which may have been a contributing factor among the cases where diagnoses had changed over time. There is probably no recall bias, as the subjects were followed from index suicide attempt onwards. Information on the variables studied originated from case records, so we did not have to rely on the memories of the subjects. It cannot be excluded that some information could have been missing in the case records.

One of the non-completers had no known psychiatric contact after the index episode. In this case one cannot be sure that this person had no new psychiatric diagnoses or newly prescribed drugs, for example from primary care during the observation period of 589 days. Another subject, a suicide-completer, was referred to a psychiatrist in practice after the index inpatient episode, and had no contact with the psychiatric clinic before the suicide. Consequently, in these two cases, some information about a new diagnosis or new prescribed drug could have been missed.

The ICD-9 diagnoses recorded from the case records in some cases differed somewhat from the diagnoses given at the index evaluation mentioned above (DSM-III-R), mostly because of the use of different classification systems. This made it difficult to decide whether a possible progress or change of psychiatric disorder had occurred since the research diagnosis given at index. Consequently, we only studied the ICD diagnoses found in the case sheets when we assessed the number of diagnoses and possible increased comorbidity over time.

Data was missing in some cases with regard to rating scales, but if one individual in the matched pairs in Paper 1 had not been evaluated from one of the rating scales, the results from the pair were excluded from calculations. In Paper II, data was also missing from the rating scales in both the MDD group and the dysthymia group. However, there was no significant difference in missing items between the two groups. Missing data from the rating scales was often related to some of the patients' tiredness and lack of motivation (personal communication from research nurse at the ward). The subjects who had declined participation might have been those who were in the worst psychiatric condition. The reasons for missing data have not been systematically analysed.

Measurement bias in terms of expectations from the observer in interview-based ratings or in the diagnostic evaluation cannot be excluded. However, ratings made by the consultation team were made after a consensus discussion, and the diagnoses given for patients on the ward often given after a consensus discussion between two experienced psychiatrists, in order to minimise this kind of bias (personal communication).

In Paper 2, the MDD patients who were included in the study had their index suicide attempt between the years 1986-2000, and 94% of them occurred between the years 1986-1995. In the dysthymia group, all the index suicide attempts occurred between the years 1986-1995. The observation time for a possible subsequent completed suicide differed somewhat, and was an average of 8.9 years (SD±3.3) for the MDD group and 10.3 years (SD±3.2) for the dysthymia group (p=0.037). This means that the subjects with dysthymia had a longer mean time of observation regarding eventual suicide until June 2000 (when the last information regarding suicide cases was obtained). However, no significant difference in death by suicide was found between these diagnostic groups.

6.7 Methodological considerations in Papers 3, 4 and 5.

6.7.1 The sample – strengths and limitations

How representative is the Lundby population? A community population has the advantage of not being selected as an inpatient sample when it comes to estimating, for example, frequency of disorders and suicide risk. The Lundby area has changed from a rural to more suburban region. The inhabitants have also been influenced by the industrial and social developments in society, so is representative of a general population in Sweden during these years (1947-1997). However, the Lundby population is not representative of the younger or early middle-aged population of today, as most of them had reached late middle age or old age at the latest follow-up. There was very little influence of migrants from abroad. Drug abuse and criminality have been rare in the area during the follow-up.

As all inhabitants in the parishes were invited to take part of the study, no distinct sampling bias could be expected.

Overall, the attrition rate has been very low; 1% between 1947 and 1972 and 6% between 1972 and 1997. The attrition rate has risen somewhat over the years, for various possible reasons. People who are mentally healthy and people who are in a severe mental condition, might both have reasons to withdraw from study participation. Healthier persons are possibly more often younger, and could be busy with work and family life. They also might think that the study would not be of interest or of benefit to them. People with mental illness might be troubled by their symptoms and choose to withdraw from the attention of the researchers, but some might feel support from the interest of the interviewers and might be hopeful that involvement could help them. Some subjects might have thought that the interviews and questionnaires were too much trouble or would cause psychological discomfort.

6.7.2 Collection of data and analyses – strengths and limitations

Case findings in the study are based on an estimation of a subject's psychiatric status at the interview, but could also derive from a description of a passed episode, as well as from external information from case sheets or the National Patient Register (National Board of Health and Welfare 2015). Recall bias may be significant, as 10-25 years have passed between field investigations. The memory of events or mental sufferings may have faded in such a long time. Key informants and information from case records or registers can compensate for this bias.

The interviewer was always an experienced psychiatrist, which is a strength. Case finding method by personal meeting and evaluation by a psychiatrist is rarely used in other comparable epidemiological studies. Often, the diagnosis is given on the basis of questionnaires administered by laymen, sometimes assembled by computer algorithm (Henderson and Jablensky 2010). The assessment instruments and questionnaires used later in the Lundby Study are all well-known and validated. The diagnosis was given by consensus after a discussion with other psychiatrists in the research team. Multiple sources of information were used in the field investigation, which is a strength.

The Lundby Study involves a very long follow-up period of 50 years for mental illness and other health aspects, but as long as 64 years for causes of death. The long follow-up is a strength of the Lundby Study. The suicide risk in this long period is analysed in Paper 3, but many of the Lundby population were still alive. By 1 July 2011, 2284 persons had died (64%), but in the analyses life time risk is approached.

New diagnoses could have been added since the last field investigation, and more suicides might occur in the future. This is a limitation, but the suicide risk may not be affected much by this limitation, as the principal aim of the studies (Papers 3-5) was to investigate suicide cases. Seven of the 68 suicide cases killed themselves after the last investigation in 1997. However, there is usually information about the suicide victims from birth to death, due to the multiple sources of information, which is a strength.

The Lundby Study started almost 70 years ago, when there was no established universal diagnostic system for mental disorders. This might make it harder to compare the results with studies using current systems. However, this limitation has been compensated by re-evaluating many of the episodes according to the DSM- and ICD-classification systems (Nettelbladt, Bogren et al. 2005).The hierarchical diagnostic system of the Lundby Study did not allow more than one 'Diagnosis I' at the same episode (but an individual could have been diagnosed with 'depression + other psychiatric symptoms'), so there could be cases of concurrent or overlapping comorbidity in the suicide victims that not have been recognised in the studies presented in Papers 3-5. However, the Lundby diagnostics do allow diagnoses of

alcohol use disorder and another mental disorder to be given at the same time, thereby allowing detection of comorbidity in people with alcohol use disorder.

There are few women with alcohol use disorder in the Lundby Study. This may be due to women´s drinking habits changing over time, and alcohol problems in this group becoming gradually more common recently. Alcohol problems in women may have been more taboo when the early field investigations were carried out, which could have influenced the number of recorded alcohol use disorders.

Another limitation of our study might be that milder symptoms in those with less than impairment grade 3 were not included, so may have been overlooked as a possible contributing factor for developing an alcohol use disorder. Sub-threshold depressions may have preceded alcohol use disorder, in a condition that we have denoted as primary alcohol use disorder. The importance of subclinical depression prior to alcohol dependence was emphasised in a previous study (Gorman 1992), so a subclinical alcohol problem could have been undetected. On the other hand, the threshold for 'caseness' must not be so low that occasional or normal variations in mood are classified as a depressive disorder.

In the statistical analyses in Paper 3 we could not add other possible confounding factors than gender (such as age and socioeconomic status), due to loss of power, which is a limitation.

In the studies that make up Papers 4 and 5, the age at onset of alcohol use disorder was unknown in 79 of the 427 cases, which is a limitation. In 28 persons the onset of the disorder had already started before inclusion in the study. In these cases, the onset is approximated to the inclusion date when analysing the order of diagnoses. The age of onset was unknown in one of the suicide cases with alcohol use disorder as first diagnosis.

6.8 Inclusion of undetermined death

According to the ICD, 'certain' suicide cases are the cases where there is no doubt that the victim's intention was to kill him/herself, while the classification 'death by undetermined intent' is used when it is uncertain whether the death was accidental or where there is uncertainty about the victim's intention to die. Official statistics on suicide in Sweden, include uncertain suicides/undetermined death. Only including certain suicides is meant to underestimate the suicide rate (National center of Suicide research and prevention of Mental Ill-Health 2014). Similarity between groups of suicides and undetermined deaths have been shown in several studies (Evenson, Cho et al. 1988, Ohberg and Lonnqvist 1998, Linsley, Schapira et al. 2001, Gray, Coon et al. 2014), indicating that they should be included.

However, a register-based Swedish study found differences in background variables when comparing the groups, but was not able to clearly distinguish the two groups; the author suggested using separate analyses in future research. (Bjorkenstam, Johansson et al. 2014).

6.9 What can be learned from the two kinds of studies?

This thesis includes two different viewpoints in the field of suicidology. We have used different kinds of populations and different research methods with associated possibilities and problems. We studied a high-risk sample of persons with mental disorders, who were probably in a state of further mental affliction after a suicide attempt. The information from the index suicide attempt certainly reflects a state of emergency, which could change over days, weeks or months. Nevertheless, it is important to investigate this particular state, as well as the time afterwards, in order to identify possible factors predicting suicide.

A general entire population has been followed for a very long time. In the Lundby study, we had the opportunity to investigate mental illness during the lifespan with its different stages, and investigate suicide risk without selection bias. Not all persons who kill themselves have made a suicide attempt. In a psychological autopsy study, 56% of the victims had not made any previous suicide attempt (Isometsa and Lonnqvist 1998) and not all individuals at risk of future suicide come into contact with psychiatry.

Using different perspectives in research might help to ensure that adequate interventions could be suggested and performed at different levels of preventive work to reduce the suicide rate in society. Primary/universal prevention, which is directed to everyone, could include information about risk factors to inhabitants and describe availability of mental health care. Secondary/selective prevention deals with identifying risk groups and taking action, such as by arranging early treatment of people with mental disorders who have an elevated risk of suicide. Finally, tertiary/indicated prevention involves treatment and support directed to persons with suicidal behaviour and a high risk of suicide (Nordentoft 2011).

In this thesis the results presented in the studies could contribute to knowledge on two of the levels by identifying the risk of suicide in different groups with mental disorders in the population, and by investigating risk factors in a high-risk group of persons with mental disorders who have recently made a suicide attempt

7. Conclusions and future research

The results of this thesis may contribute to increased knowledge about suicidality. By extension, the results may help preventive work at the secondary/selected level (by identifying groups with elevated suicide risk in the general population) and the tertiary/indicated level (by identifying risk factors in a group of suicide attempters with high risk of subsequent suicide).

In a person with a history of admission to a psychiatric clinic after a suicide attempt, several episodes of worsening of the psychiatric condition with extensive psychiatric care could be warning signs for a high risk of suicide. The medical history could reveal a serious and complicated condition. The SUAS may be a useful complement (especially within the first year after a suicide attempt) in the urgent and often difficult assessment of suicide risk, regardless of main diagnosis.

Persons with dysthymia severe enough to have been admitted to a psychiatric ward after a suicide attempt differ from inpatient suicide attempters with a higher frequency of Axis II comorbidity, and especially Cluster B diagnoses. Our results indicate that these more severe cases of dysthymia have more symptoms of agitation, increased speech flow, aches and pains and somatic concerns, and less symptoms often associated with depressed mood such as lassitude, concentration difficulties, indecision and worrying over trifles. The clinical implication should be to carefully consider an underlying personality disorder, anxiety/agitation symptoms and pain (regardless of known somatic disorder) in this patient category. Pain may indicate increased the risk of suicide.

There was further evidence of a very low risk of suicide among people without mental disorders, a finding that emphasises the importance of mental disorders in the development of suicide risk.

Mental disorders like alcohol use disorder, depression and psychosis had a high suicide risk regardless of comorbidity, though the risk was increased with comorbid disorders. Comorbidity increased the risk, but a majority of suicide victims did not have a second disorder.

Men with depression and additional alcohol use disorder had a surprisingly high risk of suicide, as 16% of these men eventually committed suicide. Alcohol use disorder

appeared to be the most common first diagnosis during lifetime among male suicide victims, followed by depression and other disorders.

There may be many years from onset of mental disorders to suicide, sometimes decades, and the subjects often suffered from the same disorder at suicide. Depression was an exception, with a short median time to suicide, but even among depressives, suicide may occur after decades. People with mental disorders should be monitored for a very long time, as suicide risk seems to remain for many years after onset.

Depression has generally been seen as the most important disorder in suicide victims, but the role of alcohol use disorders should not be underestimated. This often appears to be the first mental disorder in men.

From a secondary suicide intervention perspective, prevention of alcohol use disorders in men may have an important preventative effect on suicide risk. It is also important to be observant of the development of secondary disorders, mainly depression, but also other conditions. Both disorders should be vigorously treated as part of the work to prevent suicide. Knowledge of the seriousness of this comorbid condition should be spread to healthcare providers as well as social workers, facilitating early identification of vulnerable individuals to enable early treatment at the adequate level of healthcare and to strengthen protective factors.

Healthcare professionals should be alert to the risk of suicide in the very long term course, and continually evaluate suicide risk. Not only concurrent or overlapping comorbidity should be taken into account when assessing the risk, but also comorbidity with separate episodes.

Larger studies of suicide attempters, where suicide completers and survivors are compared in terms of comorbidity, symptoms and signs and course of the condition, could validate the results from the first study in this thesis, which had only thirty subjects.

Future research on long-term pain in persistent depressive disorder and the association to suicide behaviour and suicide risk could be of interest. Another interesting area would be to investigate possible linkage to comorbid anxiety in persons with dysthymia with pain. There may be interventions that could improve the status in these persons and affect the long-term course.

An important topic for future research is what impact the increased consumption of alcohol in women may have on suicide risk. The pattern of comorbidity and its consequences for suicide risk in women should be explored. More research is also needed about the causes of secondary depression in men with alcohol use disorders, as there may be psychosocial problems resulting from the misuse or secondary brain damage. The right level of care in persons with this kind of comorbidity might be in psychiatric clinics.

There are very few studies on the temporal sequence of diagnoses and the association to suicide and suicidal behaviour. Another interesting subject could therefore be to examine the sequence of diagnoses during the lifespan and the occurrence of suicide attempts and suicide, in general populations as well as in clinical populations.

8. General summary in Swedish - populärvetenskaplig sammanfattning

Bakgrund: Suicid är en fruktad konsekvens vid psykisk sjukdom. Det är därför viktigt att finna prediktorer för dessa händelser. Psykisk sjukdom anses finnas hos ca 90% av de personer som tar sitt liv. Självmordsförsök är ansett som en av de allra viktigaste riskfaktorerna för fullbordat suicid och depression är en vanlig diagnos bland personer som gör icke–fatala eller fatala självmordsförsök. Dystymi (lättare grand av depressivitet men med långdraget förlopp) och så kallad egentlig depression (med mer uttalade depressionssymtom) utgör båda riskfaktorer för olika grad av suicidalitet. Alkohol missbruk/beroende är också en känd riskfaktor för självmord, men trots detta inte sällan förbisedd som en sådan. Förekomst av flera sjukdomar samtidigt ökar risken för självmord och mera kunskap behövs om hur olika faktorer hos individen själv eller i omgivningen kan öka risken över tid. Både grupper av personer vårdade inom psykiatri och av en allmän befolkning bör studeras.

Målsättning: Dels att studera riskfaktorer för självmord hos grupper av patienter som vårdats på psykiatrisk klinik efter suicidförsök (index vårdtillfälle) där fokus har varit framför allt på samsjuklighet, symtom och sjukhistoria. Även att undersöka risk för självmord i en allmän population. Fokus är framför allt på psykiska sjukdomar och samsjuklighet, särskilt vad gäller alkoholberoende, samt tidsaspekter.

Metod: I slutenvårdmaterialet (arbete 1-2) studerades samsjuklighet, symtombild, tidigare självmordsförsök och sjukvårdskonsumtion från data som insamlats vid indextillfället, samt från senare gjord journalgenomgång. I Lundbystudien har en allmän befolkning bestående av 3563 personer följts avseende psykiska hälsa under ca 50 år. I delprojekten (arbete 3-5) lades fokus på information från de fyra fältundersökningarna vad gäller psykiatriska diagnoser, samsjuklighet och risk för framtida självmord.

Slutenvårdsdata kunde jämföras med en allmän population.

Arbete 1. Personer som slutenvårdats efter självmordsförsök studerades. Individer som senare tagit sitt liv undersöktes beträffande om de haft ett svårare och mer vårdkrävande psykiatriskt tillstånd än de som fortfarande levde. Femton personer matchades med lika många överlevande beträffande ålder, kön och huvuddiagnos.

Olika variabler undersöktes under lika lång tidsperiod för de båda personerna i det matchade paret. Efter det självmordsförsöket vid studiens början, hade de som senare suiciderat fått mera psykiatrisk vård jämfört med kontrollerna. De hade också ökande psykiatrisk samsjuklighet över tid. Suicide Assessment Scale (SUAS–skalan) som utvecklats för att bedöma suicidrisk oberoende av psykiatrisk diagnos, visade sig vara en god prediktor för suicid hos dessa slutenvårdade patienter.

Arbete 2: Kliniska skillnader mellan dystymi och egentlig depression hos personer som gjort självmordsförsök studerades. Vår hypotes var att suicidala personer med dystymi har en mer komplicerad symtomatologi än de med egentlig depression.

Patienter med egentlig depression (81 personer) och dystymi (35 personer) skattades bl.a. enligt skalan SUAS. De bedömdes också enligt en symtomskattningsskala 'The Comprehensive Psychopathological Rating Scale' (CPRS) och delskalan 'The Montgomery and Asberg Depression Rating Scale' (MADRS) som består av frågor gällande depressionssymtom. Det fanns stora kliniska likheter mellan grupperna av personer med dystymi och egentlig depression. Självmordsbenägenheten utifrån SUAS-skattningen skilde sig inte signifikant. Dystymi–gruppen hade dock en större frekvens personlighetsstörningar. Symtombilden hos dem bestod oftare av agitation (d.v.s. motorisk rastlöshet), ökat talflöde och smärta/värk jämfört med dem med egentlig depression. Dystymipatienter som senare tog livet av sig, hade oftare värk och smärta enligt de genomförda skattningarna.

Arbete 3: Långtidsrisken för självmord hos personer utan psykisk sjukdom uppskattades, liksom risken med en eller flera psykiska sjukdomar i en allmän population.

Långtidsrisken var 0.3% för dem som inte hade haft någon psykisk sjukdom, 3.4% personer med en diagnos och 6.2% för dem med två eller flera diagnoser. Associationen till självmord var ca 12 gånger starkare om man haft en psykiatrisk diagnos och ca 21 gånger starkare om man haft två eller flera. Förekomsten av suicid var likvärdig i grupperna av personer som haft depression, alkoholism och psykos på ca 6-7%. Hos personer med endast depression var det 6,0%, med endast alkohol missbruk/beroende 4,7% och med endast psykossjukdom 3,1% som hade suiciderat. Men för dem med ytterligare diagnos var förekomsten 6.6%, 9.4% respektive 10.4%.

Samsjuklighet mellan alkoholism och depression under livet hade en mycket stark association till självmord hos män (ca 25 gånger starkare samband). Det går inte att uttala sig om inverkan av alkoholism hos kvinnor eftersom det var få kvinnor i populationen som fått en sådan diagnos (8,7 % av fallen) och bara 1 kvinna med alkoholism som tagit sitt liv.

Arbete 4: Ett syfte med studien var att undersöka vilken psykisk sjukdom personer som tagit sitt liv först drabbats av under livet och huruvida de fått efterföljande psykiatriska diagnoser under uppföljningstiden (ca 50 år) i Lundby-populationen.

Sedan undersöktes i vilken ordning alkohol och annan psykisk sjukdom uppkommit hos a) suicidoffer (68 personer) b) hos alkoholister med psykiatrisk samsjuklighet (191) och c) i hela Lundby-populationen.

Sextiotvå av 68 personer (91%) som tagit sitt liv hade haft någon psykisk sjukdom under livet. Bland personer som tagit sitt liv var det vanligast att först ha fått alkohol missbruk/beroende (38% av fallen). Näst vanligast var att först ha drabbats av depression och därefter kom ångestsjukdom. Bland dessa suicidfall var det vanligare att först ha haft alkoholism och sedan utvecklat en annan psykisk sjukdom än att ha insjuknat i omvänd ordning. Undersökte man de personer i Lundby-populationen som hade både alkoholdiagnos och annan psykisk sjukdom, såg man ingen skillnad i suicidförekomst beroende på om alkohol kom före eller efter annan diagnos.

Ordningen av alkoholsjukdom och annan psykisk sjukdom studerades också i hela populationen. Det var vanligare att först ha alkoholism och sedan få annan diagnos än att först ha annan diagnos och sedan får alkoholproblem. Detta gällde också för förhållandet alkoholsjukdom och depression.

Arbete 5: De 68 suicidfallen i Lundby-populationen undersöktes. Målsättningen med detta arbete var att undersöka debutålder för psykisk sjukdom, ålder vid suicid och tidsspannet mellan insjuknande i första diagnosen till suicid i en allmän population.

Personer med depression som första diagnos hade en högre debutålder än dem med alkoholsjukdom eller annan psykisk sjukdom. Hälften av de personer som hade en psykiatrisk diagnos hade suiciderat före 16 år från debut och hälften hade suiciderat efter (16 år således medianvärdet för tiden mellan debut och suicid), men med variation mellan olika diagnoser. För depression var mediantiden endast 2,5 år och signifikant kortare än tiden för dem som debuterat med alkoholism eller annan psykisk sjukdom. Längst tidsspann hade de som debuterat med ångest (median 32 år). Tjugofem procent av suiciden inträffade före 4 år efter debut och 25% efter 34,5 år. Detta tyder på en påtaglig spridning av självmorden under livet och ofta många år efter debut av psykisk sjukdom.

Slutsatser: I denna avhandling visar resultaten att de flesta som suiciderar har en psykisk sjukdom. Samsjuklighet var vanligt och kunde ses hos 1/3 av fallen i en allmän population, men i drygt 80% av fallen i gruppen som vårdats efter självmordsförsök tidigare. I arbetena baserade på Lundby-populationen har dock inte personlighetsstörningar undersökts.

Resultaten tyder på att personer som vårdats efter självmordsförsök och sedan tagit sitt liv ofta haft svårare, mer komplicerade och mer vårdkrävande sjukdomstillstånd än de som inte tar sitt liv.

Personer som slutenvårdats inom psykiatrin efter självmordsförsök och har diagnosen dystymi, förfaller ha större förekomst av personlighetsstörningar jämför med personer med egentlig depression, vilket särskilt bör uppmärksammas, med anledning av risk

för upprepade självmordsförsök. Det är angeläget med en noggrann uppföljning och behandling i öppenvård. De hade högre värden på skattningar av smärta och kroppsliga besvär liksom av agitation. Värkproblematik kan öka depressiva symtom och depressivitet kan å andra sidan förstärka smärtupplevelsen. Tidigare forskning har också visat på samband mellan långvarig värk och självmord. Värk och smärta förfaller kunna vara en riskfaktor för suicid hos dystymipatienter. Ökad förekomst av agitation kan vara ett tecken på ångest som bör behandlas. Agitation och ångest har i tidigare studier setts föregå självmordsförsök och självmord, vilket bör ses som en varningssignal.

Det är få studier i världen där psykisk sjukdom har följts prospektivt i en allmän population där man har kunnat undersöka uppkomna sjukdomar i under mycket lång tid. Psykisk sjukdom ökade associationen till självmord mer än 10 gånger och flera diagnoser mer än 20 gånger. Resultaten tyder på särskilt hög självmordsrisk hos män med kombination av alkoholism och depression under livet. Oftast ha alkoholproblemen kommit först (i trettioårsåldern) och självmordsrisken kvarstår under många år, till skillnad från hos dem som börjat med depression, som oftare tar sitt liv efter kortare tids sjukdom. Det är därför angeläget att ta reda på en persons sjukhistoria under livet och beakta även tidigare diagnoser när man bedömer behandlingsinsatser och självmordsrisk. Detta gäller inte minst män med alkoholmissbruk. Kunskaper om psykiatrisk samsjuklighet och riskfaktorer för självmord behövs både inom psykiatrin och i primärvården, då många med psykisk sjukdom inte kommer i kontakt med psykiatrin.

Acknowledgements

There are many people to whom I want to express my sincere gratitude. This thesis would never have seen the light of day without you all.

I particularly want to thank my supervisor and head of the Lundby Study, **Associate Professor Louise Brådvik** for sharing her deep knowledge and wisdom with me, and for always giving me excellent advice and rapid feedback. Without your never-ending support and encouragement, I don't know when, or even if, this dissertation would have been completed.

Also my warm thanks to my co-supervisor **Professor emerita Lil Träskman-Bendz**, who was my supervisor during the first years of this long journey. I'm very lucky to have been able to tap in to your enormous experience and knowledge in the field of suicidology. You've always believed in me, and it was your enthusiasm that lay behind my decision to become a PhD student.

Many thanks to my co-supervisors **Associate Professor Cecilia Mattisson** and **Mats Bogren, PhD.** You are fine role models for me in research, and I admire you very much for your solid and fastidious work in the Lundby field investigation in 1997. I am very grateful for valuable comments and ideas on early versions of the papers.

I want to thank **Associate Professor Åsa Westrin**, head of the research department, for her invaluable support. I remember my early years at the research team, and I appreciate all the rewarding and joyful conversations we had together with the other young researchers.

I thank my co-authors **Anders Nimeus** and **Gunnar Engström** for contributing with all their experience and helpful feedback on my work. I also want to thank you, Anders, for being such fine role model for me as a psychiatrist, but I know will never reach anywhere near your level. Gunnar, without your guidance and support in statistics, Paper 2 would never have been finished.

Thanks, also to Associate Professor and previous head of the Lundby Study **Per Nettelbladt**, who encouraged me to join the Lundby team. I am grateful for being given the opportunity.

Without **Anders Odensten's** knowledge about the Lundby data, his problem solving and his answers to all my questions, I would not have managed. Thank you.

I am grateful to the research nurses **Margot Alsén** and **Charlotta Sunnqvist**, for their support and for always keeping track of everything.

Thank you, **Ulla Persson,** for your valuable and accurate work in reading and correcting the language of my first manuscripts, and for seeking literature.

Many thanks to **Anna Lindgren**, the statistician who helped me with the analyses, and to **Leslie Walke, CommunicAID,** for language revision.

Special thanks to my supervisors and colleagues at the **Memory Clinic**. Without your support and encouragement, my graduate studies would never have been possible.

For me, it's an honour to have become involved in the excellent work that **Professor Erik Essen-Möller** started almost seventy years ago. He was a pioneer and an enthusiast in psychiatric epidemiology.

Thanks to following for providing financial support:

Medical Faculty, Lund University

County Council of Skåne

The Ellen and Henrik Sjöbring Memorial Foundation

The Söderström-Königska Foundation

The Bror Gadelius Foundation

The Sjöbring Foundation

The OM Persson Foundation

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