Self-harm in patients with schizophrenia; risk factors and clinical characteristics

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Contents

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Summary

<u>Background and aims</u>: Although risk factors for self-harm in individuals with schizophrenia have been identified, our knowledge about pathways into self-harm in general, or into suicide attempts in individuals with schizophrenia, is still limited. The overall aim of this thesis has been to describe the prevalence and clinical characteristics of a lifetime history of self-harm in patients with schizophrenia, and to investigate whether such clinical characteristics vary according to gender or the type of self-harm. In this thesis self-harm includes both non-suicidal self-harm and suicide attempts. The first study had three aims: (1) to report the prevalence of a lifetime history of self-harm within a large, clinical sample of patients with schizophrenia; (2) to investigate the clinical characteristics associated with such a history in patients with schizophrenia; and, (3) to investigate whether the clinical characteristics associated with a lifetime history of self-harm in patients with schizophrenia vary according to gender. The second study had two aims: 1) to investigate whether patients with schizophrenia with a lifetime history of both suicide attempts and non-suicidal self-harm have an earlier onset of clinical symptoms or 2) report more current symptoms than patients with schizophrenia with a lifetime history of suicide attempts only, or than non-attempters. The third study had two aims: 1) to investigate whether a lifetime history of both suicide attempts and non-suicidal self-harm was associated with childhood trauma in patients with schizophrenia; and, 2) to investigate to what extent a link between childhood trauma and a lifetime history of both suicide attempts and non-suicidal self-harm would diminish when adjusting for early symptom onset and current levels of symptoms.

<u>Method</u>: Using a naturalistic cross-sectional design, three partly overlapping samples of 388, 251 and 208 schizophrenia patients treated at standard outpatient and inpatient psychiatric units at hospitals in the Oslo area and at Innlandet Hospital Trust, Norway, were interviewed about and assessed on relevant clinical characteristics and grouped based on their lifetime history of self-harm (study I) or lifetime history of suicide attempts and non-suicidal self-harm (study II and III).

<u>Results</u>:

Study I: The prevalence of a lifetime history of self-harm (49%), frequency of repetition (58%) and the severity of the most recent episode of self-harm were high. Self-harm was associated

with female gender, having had a depressive episode, a younger age at psychosis onset, alcohol abuse or dependence in the last six months, current suicidality, an awareness of illness and low adherence to prescribed medication in the multivariate analysis. Gender significantly modified the effect of two clinical characteristics associated with self-harm: greater insight into illness (awareness of having a mental disorder) was associated with self-harm in men only, while emotional dysregulation (measured with PANSS G14, hereafter referred to as impulsive aggression) was associated with self-harm in women only.

Study II: Patients with a history of both suicide attempts and non-suicidal self-harm were more frequently women, younger at the onset of psychotic symptoms, had a longer duration of untreated psychosis, and higher levels of current impulsive aggressive and depressive symptoms than patients with suicide attempts only.

Study III: Patients with both suicide attempts and non-suicidal self-harm had elevated scores on all subtypes of childhood trauma compared to patients with no self-harm, and they had higher scores on childhood sexual abuse compared to patients with suicide attempts only. The association of childhood emotional abuse with a history of both suicide attempts and non-suicidal self-harm was no longer significant after adjusting for onset of depressive and psychotic symptoms and current symptoms of impulsive aggression and depression.

Conclusions: Self-harm was frequent in patients with schizophrenia and varied in important ways according to gender. Patients with schizophrenia and a history of both suicide attempts and non-suicidal self-harm represent a distinct subgroup with elevated childhood exposure to trauma, early onset of psychotic symptoms, significant treatment delay, a high rate of repeated suicidal behaviour, and elevated levels of current depressive and impulsive aggressive symptoms compared to other patients with schizophrenia. We hypothesize that childhood trauma may be linked to suicide attempts in patients with non-suicidal self-harm through early onset of depressive or psychotic symptoms and current depressive or impulsive aggressive symptoms.

List of papers

Paper I

Mork E, Mehlum L, Barrett EA, Agartz I, Harkavy-Friedman JM, Lorentzen S, Melle I, Andreassen OA, Walby FA: Self-harm in patients with schizophrenia spectrum disorders. Arch Suicide Res 2012, 16(2):111-123.

Paper II

Mork E, Walby FA, Harkavy-Friedman JM, Barrett EA, Steen, NE, Lorentzen S, Andreassen OA, Melle I, Mehlum L: Clinical characteristics in schizophrenia patients with or without suicide attempts and non-suicidal self-harm - a cross-sectional study. BMC Psychiatry 2013, 13:255.

Paper III

Mork E, Walby FA, Harkavy-Friedman JM, Aas M, Andreassen OA, Melle I, Mehlum L: The association of childhood trauma with a history of both suicide attempts and non-suicidal self-harm in patients with schizophrenia. Submitted BMC Psychiatry November, 2013

List of papers

Abbreviations

ANOVA	Analysis of variance
BIS	Birchwood insight scale
BPD:	Borderline personality disorder
CDSS	Calgary depression scale for schizophrenia
CTQ	Childhood trauma questionnaire
DSM-IV	Diagnostic and statistical manual of mental disorders – Fourth edition
DUP	Duration of untreated psychosis
FEP	First episode of psychosis
FES	First episode of schizophrenia
GAF	Global assessment of functioning scale
ICD-10	Classification of mental and behavioural disorders
ICC	Intraclass correlation
MARS	The medication adherence report scale
NoSA	No suicide attempt
NSSH	Non-suicidal self-harm
PANSS	Positive and negative syndrome scale
SA	Suicide attempt
SCID-I	Structured clinical interview for DSM-IV axis I disorders
SCI-PANSS	Structured clinical interview for the positive and negative syndrome scale
SH	Self-harm
TOP	Thematically organized psychosis study
WHO	World health organization

Errata

Paper II:

In the Abstract section, results, 1st sentence it says: Suicide attempts were present in 88 patients (35%), 52 had suicide attempts only (29%) …

This should read: Suicide attempts were present in 88 patients (35%), 52 had suicide attempts only (21%) …

1 Introduction

Non-fatal self-harm is a powerful sign of the distress a person experiences, a sign that their ability to cope in healthy ways is under strong pressure. Working with a suicidal patient towards regaining his ability to cope is one of the most demanding tasks in clinical practice. At the same time, watching a client recover and regain his or her faith in a life worth living is one of the most rewarding experiences as a clinician. The presence of a wide range of non-fatal self-harm behaviours in patients with schizophrenia was described in the early days of schizophrenia (then called dementia praecox) research a century ago. In "Dementia præcox and paraphrenia", translated into English from the original German *Textbook of Psychiatry*, Kraepelin (1919) refers more than 20 times to suicide or non-fatal self-harm behaviours in his patients. He notes that "thoughts of suicide often rise to the surface…" (p. 95), that "they frequently make attempts at suicide," (p. 106), and that "…unexpected suicide, especially in the first period of malady, is not infrequent" (p. 211). Kraepelin also described non-fatal self-harm behaviours that seem to be non-suicidal in nature. He describes "…damage which patients inflict on themselves" (p. 211) and provides detailed descriptions of a range of non-suicidal self-harm behaviours, from low lethality behaviours such as a patient who "scratched himself with his knife in order to lessen the influences" (p. 98) and another who "…beat his head against the wall…" (p. 114), to "the most frightful mutilations of themselves carried out often with incredible rapidity and energy" (p.211). Research over the following one hundred years has confirmed that patients with schizophrenia have strongly elevated rates of completed suicide compared to the general population (Saha, Chant, & McGrath, 2007). This research has also shown that non-fatal self-harm is highly prevalent among patients with schizophrenia (Nordentoft et al., 2002; Radomsky, Haas, Mann, & Sweeney, 1999; Suokas et al., 2010) and that past self-harm is a robust risk factor for completed suicide among patients with schizophrenia (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005). Although risk factors for suicide or non-fatal self-harm in schizophrenia have been identified, we still lack knowledge to develop more effective prevention and treatment interventions. One explanation for this continuing challenge is that non-fatal self-harm is linked to heterogeneous, multiple, and interacting biological and psychological etiological factors as well as the psychosocial and cultural context within which we live. Thus, it should come as no surprise that simple models fall short in explaining why some people with schizophrenia become self-destructive and others do not (Hooley, 2008). Thus, further understanding of the pathways

into non-fatal self-harm in patients with schizophrenia is needed to guide the development of better treatment and prevention strategies.

Previous research into risk factors for non-fatal self-harm in individuals with schizophrenia has measured either suicide attempts or non-fatal self-harm irrespective of the intent of the behaviour (Haw, Hawton, Sutton, Sinclair, & Deeks, 2005; Simms, McCormack, Anderson, & Mulholland, 2007). Little research has studied the role of non-suicidal self-harm in individuals with schizophrenia. The limited existing research has focused on extreme self-injury such as self-enucleation, which is extremely rare (Large, Babidge, Andrews, Storey, & Nielssen, 2009). However, research based on non-psychotic clinical samples suggests that individuals with a history of both suicide attempts and non-suicidal self-harm may have more severe symptoms than individuals with suicide attempts only (Stanley, Gameroff, Michalsen, & Mann, 2001).

Thus, the overall aim of this thesis is to generate new hypotheses about pathways into non-fatal self-harm in patients with schizophrenia. Firstly, by describing clinical characteristics associated with non-fatal self-harm according to gender. Secondly, by examining whether patients who have carried out suicide attempts and non-suicidal self-harm differ from other schizophrenia patients according to clinical characteristics.

1.1 Schizophrenia

1.1.1 Schizophrenia - definitions and classification

Schizophrenia is a severe and often lifelong mental disorder with disturbances in perception, thoughts, feelings, and/or the way in which the individual experiences reality. The severity of the symptoms and the often long-lasting pattern result in reduced functioning in one or more areas in life. This thesis presents data on non-fatal self-harm in the narrow schizophrenia spectrum disorders - schizophrenia, schizoaffective and schizophreniform disorder - as they are described in the *Diagnostic and statistical manual of mental disorders*, Fourth edition (DSM-IV) (American Psychiatric Association, 2000). These disorders are defined by abnormalities in two or more (only one if delusions are bizarre) of the following five symptom domains in the active phase of the disorder: delusions, hallucinations, disorganized speech, grossly disorganized or

catatonic behaviour and negative symptoms. In addition, a schizophrenia diagnosis requires that the person has a social or occupational dysfunction markedly below the level prior to the onset of symptoms (or below the expected level of functioning) for a significant portion of time since the onset of the disorder. The criteria for schizophreniform disorder are identical to those of schizophrenia, except that the total duration of the illness is shorter (between one and six months) and that impairment in social or occupational functioning is not required. Schizoaffective disorder is a disorder where an uninterrupted period with concurrent active phase schizophrenia symptoms and a mood episode (major depressive, manic, or mixed) is preceded or followed by a period of at least two weeks of delusions or hallucinations without prominent mood symptoms.

There is no single pathognomonic symptom of schizophrenia and individuals with schizophrenia, schizoaffective, and schizophreniform disorder vary greatly in their combination of disorganized, positive, and negative symptoms across time and across individuals (MacDonald & Schulz, 2009). As such these disorders are best viewed as heterogeneous clinical syndromes (American Psychiatric Association, 2013). Some of the associated features of schizophrenia are of particular interest in relation to non-fatal self-harm, since these features are considered risk factors of self-harm in other populations. Most notably, mood symptoms or episodes are common in individuals with schizophrenia. Thus, the assessment and treatment of mood symptoms and episodes are considered important in all patients with schizophrenia. Individuals with schizophrenia may also have other expressions of mood or emotional dysregulation that are potentially linked to self-harm. Anxiety and irritability are common and some have episodes of inappropriate affect (American Psychiatric Association, 2013). Individuals with schizophrenia may also lack insight into the symptoms of schizophrenia. This lack of insight into illness has been associated with poorer outcomes in several domains such as non-adherence to treatment, higher relapse rates and worse psychosocial functioning. On the other hand, greater insight into illness has been suggested as a risk factor for suicidal behaviour in psychotic disorders (Crumlish et al., 2005). In this thesis, the term schizophrenia will be used to refer to schizophrenia, schizoaffective, and schizophreniform disorder, unless specified otherwise.

1.1.2   Incidence and prevalence of schizophrenia

The median lifetime prevalence of schizophrenia across studies worldwide is approximately 0.7% and the median incidence of schizophrenia is 15 per 100,000 persons (Saha, Chant, Welham, & McGrath, 2005). The TIPS study (Early Intervention in Psychosis) in Norway found incidence rates in the Rogaland area of 16.5 per 100,000 in 1993-94 and 25.5 per 100,000 persons in 1997-98 after implementing a systematic public awareness campaign (Johannessen, 2011; Johannessen et al., 2001; Larsen et al., 2001). A Finnish general population study (Perala et al., 2007) found a lifetime prevalence of 0.87% for schizophrenia, 0.32% for schizoaffective disorder, and 0.07% for schizophreniform disorder, indicating a lifetime prevalence of about 1.3% for the three disorders combined in Finland. If the lifetime prevalence in Norway is also above 1% and with an estimated point prevalence of about 200 per 100,000 persons (Johannessen, 2011), about 10,000 individuals fulfil the criteria of a diagnosis of schizophrenia at any given time, and more than 50,000 individuals in Norway develop schizophrenia, schizoaffective disorder or schizophreniform disorder during their lifetime. Schizophrenia is found universally (McGrath, Saha, Chant, & Welham, 2008), but contrary to earlier interpretations of the literature, recent reviews indicate that the incidence and prevalence of schizophrenia vary markedly across countries, gender and samples (Saha et al., 2005). The male to female ratio is about 1.4 to 1 (Aleman, Kahn, & Selten, 2003). Higher prevalence is also found among migrants compared to the native-born, individuals from urban areas compared to individuals from rural areas, and in developed countries compared to developing countries (McGrath et al., 2008).

1.1.3   Etiology and course of schizophrenia

The heterogeneity of schizophrenia probably contributes to the fact that the etiology of schizophrenia is not fully understood. There seems to be agreement among most researchers that both environmental and genetic factors are involved in the development of schizophrenia and related disorders. Linkage studies have suggested a number of regions of the genome that increase the risk of developing schizophrenia, such as 8p and 22q and others (Andreassen & Steen, 2011; MacDonald & Schulz, 2009). Furthermore, the unexpressed genetic liability to schizophrenia, as measured in the patient's non-psychotic relatives, affects cognitive and brain functioning. Examples of such findings are impairments in executive functioning and smaller grey matter or hippocampal volume. A number of environmental risk factors have also been

found to be associated with schizophrenia, such as migrant status, older fathers, toxoplasmosis antibodies, prenatal famine, lifetime cannabis use, obstetrical complications, urban rearing, and winter or spring birth. However, the way in which these and other unknown factors interact, and whether they are independent or interrelated, is not well understood (for further details, see MacDonald & Schulz (2009)).

The development of schizophrenia can be described in phases: a premorbid phase, the prodromal phase, and the first episode of schizophrenia (FES) or psychosis (FEP). The onset of schizophrenia is usually in early adulthood with a peak age of onset in men in the early to mid-twenties, and in women in the late twenties. Men also tend to have a worse course of illness with lower premorbid functioning, a lower level of education, more negative symptoms and more pronounced cognitive impairment. The onset may be abrupt but most individuals have a slow onset and a variety of clinical symptoms in the prodromal phase. More than half experience depressive symptoms in the prodromal phase. While positive psychotic symptoms tend to be episodic, negative symptoms and cognitive impairment may persist and are more closely associated with the disability the individual experiences over time (American Psychiatric Association, 2013).

Treatments that have shown an effect on psychotic symptoms include antipsychotic medication and psychosocial treatments such as social-skills training, family interventions, and cognitive behavioural therapy/ training (MacDonald & Schulz, 2009). Based on follow-up studies, it is estimated that about one quarter of people with schizophrenia have only one episode of illness, one quarter have a chronic lifelong course of illness and the remainder fall in-between these two categories (Häfner & an der Heiden, 1999; Johannessen, 2011). Longer duration of untreated psychosis is associated with a poorer treatment response which has led to the development of many projects for early intervention in psychosis.

1.2 Non-fatal self-harm and suicide

1.2.1   Definitions and classification

The study of suicidal behaviour has been complicated by the lack of a unitary nomenclature and controversies, in particular over the classification of non-fatal self-harm. Although attempts have been made to establish a common nomenclature (O'Carroll et al., 1996; Silverman, Berman, Sanddal, O'Carroll, & Joiner, 2007), a consensus has not yet been reached. However, the essential element in all suicidal behaviour is suicidal intent: the intention to end one's life. The term *suicidal behaviours* will be used in this thesis to describe the wide range of behaviours or processes from suicidal ideation - thoughts of engaging in behaviours intended to end one's life, suicide plan (the formulation of a specific method through which one intends to die) (p.6, (Nock et al., 2012), suicide attempt, and suicide itself. There are several definitions of suicide. The following definition is commonly used in Norway: "*suicide* is a conscious and deliberate act, which the individual undertakes to injure him- or herself, and where the injuries have led to death" (translated from Norwegian) (Retterstøl, Ekeberg, & Mehlum, 2002).

The broad concept of "self-harm" *(*previously *"deliberate self-harm")* was chosen as an overarching term to describe non-fatal intentional self-harm. The self-harm concept has gained widespread use in Europe (Hawton, Rodham, Evans, & Weatherall, 2002; Madge et al., 2008) and Australia (Carter, Reith, Whyte, & McPherson, 2005) and is defined as any act of intentional self-poisoning or injury, irrespective of the apparent purpose of the act. Self-harm includes behaviours such as poisoning, asphyxiation, cutting, burning and other self-inflicted injuries and should be distinguished from accidentally inflicted self-harm. Furthermore, the term is not intended to cover harm arising from behaviours such as the excessive consumption of alcohol or recreational drugs, mismanagement of physical health conditions, body piercing or starvation arising from anorexia nervosa (Hawton et al., 2002; National Institute for Clinical Excellence, 2004). Research has shown that people report various and complex motives for self-harm episodes (Brown, Comtois, & Linehan, 2002; Hjelmeland et al., 2002). Thus an individual who cuts himself and reports suicidal intent ("I wanted to die") may also report seemingly contradictory motives or reasons for the self-harm behaviour, such as "I wanted to get away from unbearable emotions" and "I wanted to get help". The self-harm concept does not assume

any knowledge about the individual's possible suicidal motives and covers a spectrum of non-fatal, intentional self-harm behaviours. In this thesis, the term self-harm will be used as described above. Some older studies cited in this thesis use the concept *parasuicide* (Platt et al., 1992), which is similar to the self-harm concept. The term self-harm will be used in this thesis to describe the self-harm measure in these studies.

However, most researchers and clinicians further distinguish self-harm based on the presence or absence of any intent to die as a result of the behaviour. There is substantial evidence that suicide attempts and non-suicidal self-harm can to some degree be differentiated, in terms of intention, function, frequency and lethality (Andover, Morris, Wren, & Bruzzese, 2012; Guertin, Lloyd-Richardson, Spirito, Donaldson, & Boergers, 2001; Hamza, Stewart, & Willoughby, 2012; Klonsky, 2007; Muehlenkamp & Gutierrez, 2007). In line with most previous research, the presence of at least some suicidal intent is classified as a suicide attempt, also when seemingly contradictory, additional reasons are given for the behaviour. Thus, in this thesis, the term "suicide attempt" is defined as 'self-harm with the intent to die' and "non-suicidal self-harm" is defined as 'self-harm without suicidal intent'. Non-suicidal self-harm includes the behaviours covered by the concept of non-suicidal self-injury, which refers to "direct, deliberate destruction of one's own body tissue in the absence of intent to die" (Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006), a concept that has now been included in the DSM-V as a condition for further study (American Psychiatric Association, 2013). The term non-suicidal self-harm has been chosen in the present thesis, since the behaviours covered in this thesis also includes acts of self-poisoning.

1.2.2 Suicide in the general population and in individuals with schizophrenia

Suicide is a worldwide, major public-health issue. It is estimated that almost one million people die from suicide in the world each year, representing 1.3% of the global burden of disease (WHO, 2014). However, suicide rates should be interpreted cautiously, since methods for collecting and reporting data vary across countries and the reliability of suicide statistics is recognized as an issue in need of improvement in many countries (Tollefsen, Hem, & Ekeberg, 2012). Furthermore, the official suicide rates may be underestimates (Tollefsen et al., 2012), partly due

to the difficulties in differentiating suicides from accidental deaths (Nordentoft, 2007). The estimated world mortality rate from suicide of 14.5 per 100,000 people in the year 2000 was equal to one death every 40 seconds (WHO, 2002). But the rates vary substantially across nations from as high as 40-50 per 100,000 people in some Eastern European countries, to rates of less than 5 per 100,000 people in some Latin American and Asian countries (WHO, 2002). Rates also tend to vary according to age, gender, culture and ethnicity. In Norway, the five-year age- and sex-standardized rate of death from suicide has remained at around 11 per 100,000 people in the last 15 years, with men having a suicide rate of about two and half times that of women (Statistics Norway, 2014). In 2012, 515 people died from suicide in Norway: 369 men and 146 women.

Although treatments have shown an effect on some of the symptoms of schizophrenia, the lifespan of individuals with schizophrenia is shortened by up to 22.5 years (Tiihonen et al., 2009) compared to the general population. This shortened life expectancy in individuals with schizophrenia seems to be largely attributable to deaths at an early age (Tiihonen et al., 2009). Sadly, evidence suggests that this mortality gap between people with schizophrenia and the general community has not changed for the better – it may even have widened during recent decades (Saha et al., 2007). Individuals with schizophrenia have an increased mortality by most of the major causes of death compared to the general population. The median standardized mortality ratio associated with death by suicide of 12.9 is the highest among the causes of death (Saha et al., 2007). It is estimated that more than 5% of people with schizophrenia will eventually die from suicide (Nordentoft, Mortensen, & Pedersen, 2011; Palmer, Pankratz, & Bostwick, 2005). From this perspective, working towards better understanding and prevention of suicidal behaviour in individuals with schizophrenia is of paramount importance.

In a systematic review of risk factors for suicide in schizophrenia, Hawton and colleagues (Hawton et al., 2005) found seven robust factors: previous depressive disorder, previous suicide attempts, drug abuse, recent loss, agitation or motor restlessness, fear of mental disintegration, and poor adherence to treatment. The first four factors are well established risk factors for suicide in the general population as well. The risk factors for suicide in schizophrenia thus seems to be less associated with the schizophrenia symptoms or criteria per se and more with

associated symptoms such as depressive symptoms and signs of emotional dysregulation. However, all these seven factors may be partly related to the illness and are important since they are potentially responsive to intervention. One factor - hallucinations - was associated with a reduced risk of suicide in the systematic review. Men with schizophrenia are significantly more likely to die from suicide than women with schizophrenia, but the gender difference is far less than in the general population (Hawton et al., 2005). Suicides were also more likely in Caucasian, compared to non-Caucasian, individuals with schizophrenia. However, ethnicity was only addressed in three rather old studies and the association was no longer significant when the study with the lowest quality was omitted. In the systematic review by Hawton and colleagues (2005) higher levels of education were associated with suicide in some studies but the trend did not reach statistical significance in the meta-analysis. However, a more recent, large population-based cohort study of suicide among persons previously admitted to psychiatric hospital found that higher levels of education/high income may increase the risk of suicide, also in individuals with schizophrenia (Agerbo, 2007).

The suicide risk in individuals with schizophrenia seems to be highest in the first year of illness (Alaraisanen et al., 2009), the first year after admission to hospital, in the younger age groups (Nordentoft et al., 2004), and the first year after a suicide attempt (Tidemalm, Langstrom, Lichtenstein, & Runeson, 2008). The first week after admission to hospital and the first week after discharge seem to be a period of particularly high risk (Qin & Nordentoft, 2005). Suicide in schizophrenia in the period before first treatment contact is obviously hard to study and is unknown. But it is worth remembering that since the risk of suicide is high early in the course of illness, it is not unlikely that some suicides may occur in individuals with undetected acute schizophrenia or psychosis. However, suicides can occur throughout the course of illness in schizophrenia (Heila et al., 1997), both in active illness phases with low adherence or suboptimal treatment, but also in stable phases with high adherence to treatment (Heila et al., 1999).

The risk of suicide is strongly elevated in individuals with schizophrenia, but suicide is still a rare event. Given that schizophrenia is also a low-prevalence disorder, prospectively investigating clinical characteristics associated with suicide in individuals with schizophrenia would require a

very large study sample followed for a very long period of time. This is usually not feasible, either economically or practically. Whereas psychological autopsy studies have provided valuable knowledge on risk factors for suicide in individuals with schizophrenia, these studies have methodological limitations including concerns about accuracy and range of available data (Hawton et al., 1998). Given that a previous suicide attempt is a strong risk factor for suicide (Carlborg, Jokinen, Nordstrom, Jonsson, & Nordstrom, 2010; Hawton et al., 2005) and more prevalent, it has been studied as a proxy for suicide. However, by limiting the study of self-harm in individuals with schizophrenia to suicide attempt as a proxy for suicide, other important aspects of self-harm may be missed. Self-harm affects far more people than those who die from suicide, it is a strong sign of the distress and suffering the person experiences, and both suicide attempts and non-suicidal self-harm can cause considerable challenges in providing effective treatment. Self-harm in patients with schizophrenia is the subject of the studies in this thesis.

1.2.3   Self-harm in the general population

The incidence and prevalence of self-harm episodes in Norway or globally are largely unknown due to the lack of reliable systematic monitoring systems of self-harm. Crude estimates based on regional monitoring studies and other sources suggest that about 4000-6000 self-harm episodes are treated by the Norwegian health-care system annually, with higher numbers in women than men (Hjelmeland, 2004; Kopjar, Dieserud, & Wiik, 2005; Nasjonalt folkehelseinstitutt, 2009). This estimate includes only self-harm episodes requiring medical attention. One survey (Ystgaard, Reinholdt, Husby, & Mehlum, 2003) found that 6.6% of 15 and 16 year old adolescents reported self-harm during the preceding 12 months. About one in ten adolescents in Norway reports lifetime self-harm, with higher rates reported by girls than boys (Tormoen, Rossow, Larsson, & Mehlum, 2012; Ystgaard et al., 2003). Studies from the United States indicate onset of self-harm often from the start of adolescence (12 years). The risk of self-harm increases during adolescence, lasts until young adulthood, and then decreases gradually throughout adulthood (Nock et al., 2008).

Regarding suicide attempts and non-suicidal self-harm reported separately estimates vary across nations, assessment methods, and/or samples. International adult 12 month prevalence

estimates of suicide attempts vary between 0.1-3.8% and lifetime suicide attempt estimates between 1.5-12.1% (Nock et al., 2008). Non-suicidal self-harm is mainly studied in adolescents, with an average 12-month prevalence of 19.0% (SD = 11.9) and lifetime prevalence estimates of 18.0% across countries (Muehlenkamp, Claes, Havertape, & Plener, 2012). The estimates are significantly higher when self-report inventories with a range of specific behaviours are presented, compared to single item measures. Tørmoen and colleagues, using single item measures, found in their general population sample of 11,440 adolescents aged 14-17 years in Oslo that 4.3% reported lifetime non-suicidal self-harm only, 4.5 percent reported lifetime suicide attempts only and 5.0 percent reported a lifetime history of both suicide attempts and non-suicidal self-harm. A high rate of individuals with a history of both suicide attempts and non-suicidal self-harm is also found in international studies (Hamza et al., 2012). Based on the high co-occurrence of suicide attempts and non-suicidal self-harm, researchers have suggested that these behaviours - although different – are also related (Hamza et al., 2012; Stanley et al., 2001).

1.2.4   Self-harm in individuals with schizophrenia

To my knowledge, there is no recent systematic review of rates of self-harm in schizophrenia in the published literature. Thus, a literature search of studies reporting rates of self-harm was performed (see Methods, Literature search section). Forty-five studies reporting rates of lifetime episodes of self-harm were included (Table 1). Most samples were in- and/or outpatient clinical samples requiring written informed consent for participation. Thus, the rates reported may not be representative of all patients with schizophrenia or of all individuals in the population with schizophrenia. That said, the one population-based study in the review, a Finnish nationally representative sample (Suokas et al., 2010), reported rates close to the European mean rate (Table 2), indicating that the rates in the population might not be that different from clinical samples. One or more lifetime episodes of self-harm were present in 32% (n=3590) of all participants (n=11265). However, the lifetime self-harm rate varied greatly across studies from as low as 7% (Preti, Meneghelli, Pisano, Cocchi, & Team, 2009) and up to 72% (Taylor, Gooding, Wood, Johnson, et al., 2010) (Tables 1 and 2). The rate seems to vary depending on the type of self-harm measure used and world region (Table 2). Only four studies (Chatterton, 1995; Lui, 2009; Pluck et al., 2013; Simms et al., 2007) used self-harm concepts

which includes both suicide attempts and non-suicidal self-harm. Although few, the studies using self-harm as measure reported consistently higher rates of self-harm than the mean rate in the corresponding world region and a higher mean rate (43%) compared to studies measuring suicide attempts (31%). The rate also varied depending on world region, with the rates of self-harm in Europe (36%), North-America (40%) and Oceania (40%) being about double the rate of self-harm reported in Asia (20%) and the one study from Africa (20%). The Norwegian sample in the review (Barrett et al., 2011) reported a lifetime prevalence of 30.5% using suicide attempt as measure, a rate close to the rate reported in studies from other Nordic countries (Bertelsen et al., 2007; Suokas et al., 2010) and the mean rate in Europe. The rates did not seem to vary systematically according to sample characteristics such as in- versus outpatient samples, or whether the sample was a first-episode schizophrenia sample or other sample (Table 2).

Repeated episodes were reported in nine studies using suicide attempt (47% 203/430) and one using self-harm (52%, 28/54). Although the rate of repeated episodes varies somewhat (29% - 76%), it is high across the ten studies reporting repetition rate (Table 1). Six studies have reported the rate of self-harm during a specified time period. The past year rate is reported in two studies, both using suicide attempt as measure, with a rate of 8% (Gonzalez, 2008) and 20 % (Nordentoft et al., 2002) respectively. Self-harm during follow-up also varies greatly between studies, from no suicide attempts during one-year follow-up (Preti, Meneghelli, Pisano, Cocchi, et al., 2009), to 11% during one-year follow-up (Nordentoft et al., 2002), and 34% during four-year follow-up (Crumlish et al., 2005). The one study using self-harm as measure, found a 6% rate of self-harm during a three-month follow-up.

1.2.5   When is the risk of self-harm highest?

The highest prevalence of both past year (Nordentoft et al., 2002) self-harm and self-harm during follow-up (Crumlish et al., 2005) is reported from first-episode schizophrenia samples, indicating that the prevalence of self-harm in individuals with schizophrenia is highest before the first-episode or early in the course of illness. The lack of marked differences in the rate of lifetime history of self-harm between first-episode- and mixed schizophrenia samples (Table 2) seems to point in the same direction: many individuals with schizophrenia have their first self-harm episode before the onset of psychotic symptoms or before first treatment contact. This is

in line with the findings from a systematic meta-analysis of self-harm in first-episode psychosis samples. The authors found a pooled proportion self-harm prior to first treatment of 18.4% (CI95% 14.4 – 23.3), 9.8% (CI95 6.7–14.2) during the period of untreated psychosis, and 11.4% (CI95 8.3–15.5) during follow-up of up to seven years (Challis, Nielssen, Harris, & Large, 2013). In the first-episode psychosis sample study from the TOP study in Norway we found somewhat higher rates, with 26% reporting suicide attempts before first treatment contact and 14% during untreated psychosis (Barrett et al., 2010). Although first-episode psychosis samples include a broader range of diagnoses than schizophrenia, it seems that there is a similar pattern in self-harm as in suicide: self-harm is highly prevalent in early phases of illness but occurs throughout the course of illness.

1.2.6   Non-suicidal self-harm in schizophrenia

While suicide and suicide attempts have received considerable attention in the one hundred years since Kraepelin, the minor non-suicidal self-harm behaviours that occurred in the detailed descriptions by Kraepelin (1919) have received very little attention in schizophrenia research. The limited research has focused on major self-mutilation (Favazza, 1987), such as ocular, genital, or limb mutilation that may result in permanent loss of function. Major self-mutilation has dire consequences, but is extremely rare, affecting an estimated 1 in 4 million people per year (Large et al., 2009). More common forms of non-suicidal self-harm, such as repeated cutting, burning and self-hitting, are reported in mixed adult general psychiatric samples from as low as 6% in a chart review (Langbehn & Pfohl, 1993) and up to 45% in studies with self-report questionnaires asking specifically about a wide range of behaviours (Andover & Gibb, 2010; Claes, Vandereycken, & Vertommen, 2007). No studies reporting on lifetime rates or the degree of repetition of non-suicidal self-harm in schizophrenia were found in the search of the published literature. However, a few studies have confirmed that non-suicidal self-harm is present in patients with schizophrenia, especially among patients with a lifetime history of suicide attempt (Restifo, Harkavy-Friedman, & Shrout, 2009; Shoval et al., 2006).

In conclusion, the prevalence of self-harm in individuals with schizophrenia is elevated compared to the general population. However, most studies have measured suicide attempts. The few studies using the wider concept self-harm generally find higher prevalence estimates.

Although some studies indicate that non-suicidal self-harm tends to co-occur with suicide attempts in individuals with schizophrenia, the prevalence of non-suicidal self-harm and the rate of co-occurrence of suicide attempts and non-suicidal self-harm is largely unknown.

Table 1 Prevalence estimates of self-harm in individuals with schizophrenia

Authors (Year), Country	Study design	% lifetime SH (SH n/total n)	% repeated SH (n >1/SH n)	Period prevalence % SH 3 months – 4 year
Altamura et al. (2003), Italy	cross-sectional	21 % (22/103)	55 % (12/22)	-
Barrett et al. (2011), Norway	cross-sectional	30 % (53/174)	45 % (24/53)	-
Chatterton (1995), Australia	cross-sectional	54 % (54/100)	52 % (28/54)	-
Evren & Evren (2004), Turkey	cross-sectional	45 % (27/60)	41 % (11/27)	-
Harkavy-Friedman et al. (1999)/ Restifo et al. (2009), USA	cross-sectional	36 % (59/164)	60 % (33/52)	
Jones et al. (1994), USA	cross-sectional	44 % (25/57)	76 % (19/25)	-
Tarrier et al. (2004), UK	cross-sectional	46 % (26/56)	32 % (15/26)	-
Taylor et al. (2010), UK	first episode cross-sectional	72 % (56/78)	70 % (39/56)	-
Uzun et al. (2009), Turkey	cross-sectional	35 % (104/300)	30 % (31/104)	-
Yan et al. (2013), China	cross-sectional	12 % (65/540)	29 % (19/65)	-
Crumlish et al. (2005), Ireland	prospective first episode cohort	-	-	4 year follow-up: 34 % (20/58)
Gonzalez (2008), USA	prospective cohort	48 % (489/1009)		past year: 8 % 6 months follow-up: 7 %
Nordentoft et al. (2002)/ Bertelsen et al. (2007), Denmark	prospective first episode cohort	28 % (154/547)		past year: 20 % 1 year follow-up: 11 %
Pluck et al. (2013), UK	prospective cohort	68 % (59/87)	-	3 months follow-up 6 %
Preti et al. (2009), Italy	prospective first-episode cohort	7 % (6/87)	-	1 year follow-up 0 %
Radomsky et al. (1999), USA	cross-sectional	31 % (192/613)	-	past month: 6 % (36 of 613)
Acosta et al. (2013), Spain	cross-sectional	58 % (35/60)	-	-
Albayrak et al. (2012), Turkey	cross-sectional	48 % (46/94)	-	-
Alvarez et al. (2011), Spain	cross-sectional	38 % (39/102)	-	-
Aukst et al. (2012), Croatia	cross-sectional	24 % (29/120)	-	-
Bani-Fatemi et al. (2013), Canada	cross-sectional	34 % (192/566)	-	-
Bhatia et al. (2006), USA and India	cross-sectional	USA 48 % (205/424) India 23 % (107/460)	-	-
Cohen et al. (2010), USA	cross-sectional	30 % (58/196)	-	-
Darves-Bornoz et al.(1995), France	cross-sectional	61 % (39/64)	-	-
Duno et al. (2009), Spain	cross-sectional	44 % (25/57)	-	-
Goldstein et al. (2006), USA	cross-sectional	33 % (31/93)	-	-
Grunebaum et al. (2001), USA	cross-sectional	47 % (70/150)	-	-
Gupta et al. (1998), USA	cross-sectional	29 % (98/336)	-	-
Huguelet et al. (2007), Switzerland	cross-sectional	43 % (50/115)	-	-

Authors (Year), Country	Study design	% lifetime SH (SH n/total n)	% repeated SH (n >1/SH n)	Period prevalence % SH 3 months – 4 year
Iancu et al. (2006), Israel	cross-sectional	52 % (32/61)	-	-
Kao & Liu (2011), Taiwan	cross-sectional	49 % (104/51)	-	-
Kleinhaus et al. (2012), Israel	prospective cohort	26 % (150/568)	-	-
Lui (2009), China	retrospective cohort	28 % (65/234)		
Mauri et al. (2013), Italy	cross-sectional	33 % (35/106)	-	-
McLean et al. (2012), Australia	cross-sectional	39 % (315/812)	-	-
Nangle et al. (2006), Ireland	cross-sectional	36 % (28/78)	-	-
Niehaus et al. (2004), South Africa	cross-sectional	20 % (90/454)	-	-
Ran et al. (2003), China	cross-sectional	7 % (38/510)	-	-
Roy et al. (1984), USA	cross-sectional	55 % (70/127)	-	-
Shoval et al. (2006), Israel	cross-sectional (adolescents)	29 % (52/178)	-	-
Simms et al. (2007), UK	cross-sectional	52 % (17/33)	-	-
Suokas et al. (2010), Finland	cross-sectional	35 % (37/106)	-	-
Ucok & Bikmaz (2007), Turkey	first episode cross-sectional	21 % (12/57)	-	-
Zhang et al. (2013), China	cross-sectional	9 % (48/520)	-	-
Xiang et al. (2008), China	cross-sectional	27 % (135/505)	-	-

SH: self-harm

Table 2 Prevalence estimates of lifetime history of self-harm in individuals with schizophrenia according to self-harm measure, world region and sample characteristics

	Participants	Participants with lifetime SH	% SH	% Min - Max
Total (n=45)	11265	3590	32	7-72
Self-harm measure				
Parasuicide/deliberate self-harm (n=4)	454	195	43	28-68
Suicide attempt (n=41)	10811	3395	31	7-72
World region				
Europe (n=21)	2484	899	36	7-72
North-America (n=11)	3735	1489	40	28-55
Oceania (n=2)	912	369	40	38-54
Asia (n=10)	3680	743	20	7-53
Africa (n=1)	454	90	20	-
South-America (n=0)	-	-	-	-
Sample characteristics				
First-episode/adolescent sample (n=6)	1159	315	27	7-46
Other (39)	10106	3275	32	7-72
In- or outpatient samples[a]				
Inpatients (n=15)	2738	858	31	9-61
Outpatients (n=10)	1960	653	33	21-72
Both in- and outpatients (n=15)	3834	1300	34	7-68

[a] 5 studies excluded due to missing information about out or inpatient status. SH: self-harm

1.2.7   Models of suicidal behaviour and non-suicidal self-harm

A number of theoretical models to explain self-harm and/or suicidal behaviour have been proposed. The stress-diathesis model for suicidal behaviour proposed by Mann et al. (1999) provides a broad framework for understanding distal and proximal risk factors for suicidal behaviour and strongly emphasizes mental disorder as the central diathesis or vulnerability factor that can give rise to suicidal behaviour when environmental stress and other salient risk factors are added. The model has also been applied to patients with schizophrenia (Harkavy Friedman, 2007; Roy & Pompili, 2009) and suggests that proximal risk factors, such as current negative life events and an acute depressive or psychotic episode, may act as stressors or triggers for suicidal behaviour. However, whether or not the individual responds to such stressors with suicidal behaviour will, according to this model, depend on more distal risk factors such as developmental, biologic, and/or genetic factors in combination and include, for example, traits (impulsivity, aggression), childhood trauma, and hopelessness. Joiner's interpersonal theory of suicidal behaviour (Joiner, 2005; Van Orden et al., 2010) provides an interpersonal perspective with which to understand suicidal behaviour and suggests one way to understand the relationship between suicide attempts and non-suicidal self-harm. According to this theory, attempting suicide requires both a desire and a capability to attempt suicide. The suicidal desire, according to the theory, is caused by the simultaneous presence of two interpersonal constructs: thwarted belongingness ("I am alone") and perceived burdensomeness ("I am a burden") and the hopelessness these states bring about. The model predicts that suicide attempts are most likely to occur in the context of these constructs when the individual has acquired a capability to engage in suicidal behaviour (reduced fear of suicide, and elevated physical pain tolerance). Individuals with schizophrenia may very well be at risk of experiencing both thwarted belongingness and perceived burdensomeness as a consequence of their disorder although Joiner's theory was not developed for or tested on this group. Based on converging findings from four diverse clinical and non-clinical adolescent and adult samples Klonsky et al. (2013) have suggested that non-suicidal self-harm may be an especially important risk factor for suicide attempts, since its presence is associated with both increased desire and increased capability for suicide.

Although self-harm is episodic and most often occurs in the presence of acute stressors, we need models of self-harm that also incorporates the fact that some people remain vulnerable to self-harm despite no longer being exposed to acute stressors (Mann et al., 1999; Williams, Crane, Barnhofer, & Duggan, 2005). Marsha Linehan's biosocial theory (Crowell, Beauchaine, & Linehan, 2009; Linehan, 1993) has been developed for borderline personality disorder (BPD). However, it is of interest to the present thesis since it provides a model for understanding why some people may develop a pattern of repeated self-harm behaviours as a consequence of problems with emotional regulation. The theory states that BPD is primarily a disorder of the emotion regulation system that emerges from transactions between an inborn emotional vulnerability and an invalidating environment. As a consequence, individuals with such a vulnerability do not learn how to regulate emotions and will be characterized by a pattern of rapid and intense emotional responses, with a slow return to their emotional baseline (Crowell et al., 2009). Self-harm (as well as substance ingestion, purging behaviour, and other problem behaviours) may serve the purpose of providing short term relief from intense negative affect. Nock and Prinstein (2004, 2005) suggest that non-suicidal self-harm may be maintained by several mechanisms, including automatic negative reinforcement, e.g. through the reduction of negative affect, hopelessness or tension or automatic positive reinforcement, e.g. through experiencing a physiological state (feeling something/feeling pain) in response to anhedonia or numbness or similar experiences. While we are unable to study emotional dysregulation directly in this thesis, it provides a framework for understanding why the same stressor (e.g. depressive or psychotic symptoms) may lead to non-suicidal self-harm and/or suicide attempts in some individuals but not others. For example, people with schizophrenia that have developed a pattern of emotional dysregulation, could be vulnerable to self-harm also in the absence of acute stressors compared to other individuals, due to a heightened sensitivity to environmental stressors and a low threshold for intense emotional reactions. Thus, although the present thesis focuses on lifetime history of self-harm, in which the time of assessment is often remote from the time of self-harm, current symptoms or behaviours (e.g. impulsive aggression) may differ between people with and without types of self-harm. However, while these latter theories and models provide relevant perspectives, this thesis is mainly developed within the framework of the stress-diathesis model (Mann et al., 1999).

1.2.8 Risk factors for self-harm in patients with schizophrenia

In a search of published cohort or case-control studies (see Methods, Literature search section) investigating one or more risk factors for self-harm in patients with schizophrenia, 77 papers reporting from 74 samples were found (Table 3). The present thesis studies socio-demographic and clinical characteristics associated with self-harm in patients with schizophrenia. Neurocognitive and biological risk factors for self-harm are not the focus of this thesis and were thus excluded from the following review. Eleven studies were prospective or retrospective cohort studies reporting on risk factors during a defined follow-up/observation period. The remaining studies were case-control studies reporting on past self-harm. Five studies measured self-harm, while the remaining papers used suicide attempt as measure. No studies had non-suicidal self-harm as an outcome measure. In most studies, potential risk factors were assessed long before or after the most recent self-harm episode. Thus, some variables, in particular short-term precipitating factors (state-dependent risk factors), may have changed in the intervening period. The result of the examination of the 77 papers is summarized in Table 4. Findings from studies reporting on characteristics associated with lifetime history of self-harm versus risk factors for self-harm during follow-up are largely similar (see Table 4 for details). Thus, this divide is addressed only when important differences in findings between studies reporting on lifetime history of self-harm and self-harm during follow-up, are observed.

Table 4 Studies included in the review

Authors (Year), Country	Study design	Total no. of patients (No. of SH patients)
Acosta et al. (2013), Spain	case-control	60 (35)
Addington & Addington (1992), Canada	case-control	50[a]
Albayrak et al. (2012), Turkey	case-control	94 (46)
Altamura et al. (2003), Italy	case-control	103 (22)
Altamura et al. (2007), North America Europe Eastern Europe South Africa South America	case-control (high risk suicidality sample)	980/ 5 regions 414 (371) 236 (176) 199 (156) 37 (31) 93 (82)
Alvarez et al. (2011), Spain	case-control	102 (39)
Andriopoulos et al. (2011), Greece	case-control	106 (8)
Aukst et al. (2012), Croatia	case-control	120 (29)
Bai et al. (1997), Taiwan	case-control	38 (19)
Bakst et al. (2010), USA	prospective first admission follow-up study	208
Bani-Fatemi et al. (2013), Canada	case-control	566 (192)
Barak et al. (2008), Israel	case-control	2188 (1094)
Barak et al. (2004), Israel	case-control	692 (30)
Barrett et al. (2011), Norway	case-control	174 (53)
Bhatia et al. (2006), USA and India	case-control	USA 424 (205) India 460 (107)
Brugnoli et al. (2012), Europe	prospective follow-up study	8871 (384)
Chatterton (1995), Australia	case-control	100 (54)
Cohen et al. (2010), USA	case-control	196 (58)
Conus et al. (2010), Spain	prospective follow-up study	658 (93 past SH, 57 SH follow-up)
Crumlish et al. (2005), Ireland	prospective first-episode follow-up study	58 (20)
Darves-Bornoz et al.(1995), France	case-control (women only)	64 (39)
Duno et al. (2009), Spain	case-control	57 (25)
Evren & Evren (2004), Turkey	case-control	60 (27)
Goldstein et al. (2006), USA	case-control (veterans)	93 (31)
Gonzalez (2008), USA	prospective follow-up study	1009 (489 past SH, 67 SH follow-up)
Grunebaum et al. (2001), USA	case-control	150 (70)
Gupta et al. (1998), USA	case-control	336 (98)
Harkavy-Friedman et al. (1999), USA Restifo et al. (2009), USA Harkavy-Friedman et al. (2003), USA Harkavy-Friedman et al. (2004), USA	case-control	156 (52) 164 (59) 100 (33) 86 (29)
Huguelet et al. (2007), Switzerland	case-control	115 (50)
Iancu et al. (2006), Israel	case-control	61 (32)
Iancu et al. (2010), Israel	case-control	68 (24)
Jones et al. (1994), USA	case-control	57 (25)
Jovanovic et al. (2013), Croatia	case-control	509 (179)
Kao et al. (2011), Taiwan Kao et al. (2012), Taiwan Kao & Liu (2011), Taiwan	case-control	95 (53) 102 (52) 104 (51)
Kleinhaus et al. (2012), Israel	prospective follow-up study	568 (150)
Klonsky et al. (2012), USA	prospective follow-up study	155[a]
Lejoyeux et al. (2013), USA	case-control	100 (53)

Authors (Year), Country	Study design	Total no. of patients (No. of SH patients)
Levine et al. (2010), Israel	retrospective follow-up study	2293 (196 past SH, 151 SH during observation)
Lui (2009), China	retrospective follow-up study	234 (65, 29 SH follow-up)
Mata Cala et al. (1998), Spain	case-control	170 (40)
Mauri et al. (2013), Italy	case-control	106 (35)
McLean et al. (2012), Australia	case-control	812 (315)
Montross et al. (2008), USA	case-control (older patients with subsyndromal depression)	132 (65)
Nangle et al. (2006), Ireland	case-control	78 (28)
Niehaus et al. (2004), South Africa	case-control	454 (90)
Nordentoft et al. (2002), Denmark Bertelsen et al. (2007), Denmark Madsen & Nordentoft (2012), Denmark	prospective first episode follow-up study	321 (83 past SH) 275 (31 SH follow-up) 547 (154) 491 (104)
Pallanti et al. (2004), Italy	case-control	80[a]
Pettersen et al. (2010), Norway	case-control	32 (16)
Pluck et al. (2013), UK	case-control	87 (59)
Preti et al. (2009), Italy	prospective follow-up study	87 (6 past SH, 0 SH follow-up)
Radomsky et al. (1999), USA	case-control	613 (192)
Ran et al. (2003), China	case-control	510 (38)
Roy et al. (1984), USA	case-control	127 (70)
Roy (2005), USA	case-control	100 (50)
Salama (1988), USA	case-control	134 (9)
Sevincok et al. (2007), Turkey	case-control (oversampling of obsessive compulsive comorbidity)	57 (19)
Shoval et al. (2006), Israel	case-control (adolescents)	178 (52)
Simms et al. (2007), UK	case-control	33 (17)
Skodlar & Parnas (2010), Slovenia	case-control	25
Suokas et al. (2010), Finland	case-control	106 (37)
Tarrier et al. (2004), UK	case-control	56 (26)
Taylor et al. (2010), UK Taylor et al. (2010), UK	first episode case-control	78 (56) 60 (40)
Ucok & Bikmaz (2007), Turkey	first episode case-control	57 (12)
Uzun et al. (2009), Turkey	case-control	300 (104)
Wilkinson & Bacon (1984), UK	case-control	90 (45)
Xiang et al. (2007), China Xiang et al. (2008), China	case-control	273 (96) 505 (135)
Yan et al. (2013), China	case-control	540 (65)
Zhang et al. (2013), China	case-control	520 (48)

Table 4 Variables examined as potential risk factors for lifetime or prospective self-harm in schizophrenia

Characteristic	N	Association with self-harm (SH)	Conclusion
Socio-demographic			
Gender	40	Five studies identified SH as associated with female gender. One study identified SH as associated with male gender. Thirty-four studies found no association between SH and gender. One cohort study found more women with SH during follow-up. Three of the four follow-up studies found no association.	No association.
Age	40	Six studies found younger age at time of interview associated with SH. Thirty-four studies found no association with age at interview. Two cohort studies found no association between age and SH during follow-up, the third cohort study found mixed results, with younger age associated with SH at 1 year, but not at 2 year follow-up.	No association.
Ethnicity	9	No studies found an association between SH and ethnic background, including one retrospective and one prospective follow-up study.	No association.
Married or living in intimate relationship	26	Three studies found a positive association between marriage and SH. Three studies found a negative association between marriage and SH. Twenty studies found no association between marriage and SH. Two follow-up studies reported on single vs. other; both found no association. Having an intimate association was associated with SH during follow-up in one study.	No association.
Employment	15	One study found employment associated with SH. One study found unemployment protective from SH. Thirteen studies found no association between employment and SH. Three cohort-studies found no association between employment and SH during follow-up.	No association.
Education	31	Two studies found higher education associated with SH. One study found lower education associated with SH. Twenty-eight studies found no association between education and SH. Two cohort-studies found no association between education and SH during follow-up.	No association.
IQ	2	No study found an association between IQ and SH, including one prospective cohort study.	No association.
Living with parents/ being parent/having siblings	1	Each variable associated with lower rate of suicide attempts in single studies. Not measured in follow-up studies.	Inconclusive, too few studies.
Clinical variables			
Mental disorder in family	8	Three studies found mental disorder in the family associated with SH. Five studies found no association. Not measured in follow-up studies.	Inconclusive. Most studies found no association. A substantial minority found mental disorder in the family associated with self-harm.
Suicide and/or SH in family	6	Two studies found suicide or SH in family associated with SH. Four studies found no association. However, all four studies with no significant association had relatively small samples (mean n = 130) and higher but non-significant proportions of suicide or SH in the family among participants with SH (4% vs. 0%, 24% vs. 13%, 33% vs. 13% and 18% vs. 10%).	Most studies found no association. The lack of association might be due to lack of power to detect differences in the studies.
Diagnostic subtype	20	Five studies found schizoaffective disorder to be associated with SH compared to schizophrenia. Two studies found the opposite result. One study found that SH was higher in paranoid schizophrenia. Eleven studies found no association between SH and diagnostic subtype. One study found catatonic schizophrenia associated with SH in a follow-up period. The other prospective cohort study found no significant association between diagnostic subtype and SH during follow-up.	No overall association, but heterogenic results.
Illness history			
Childhood or past trauma	6	Five studies found a positive association between history of childhood trauma/past trauma and SH. One study found no association. The one cohort study found that past sexual and/or physical abuse was associated with SH during follow-up.	Childhood or past trauma is associated with SH.
No of inpatient treatment episodes	28	Nineteen studies found an association between inpatient treatment and SH. One study found that participants with inpatient treatment were less likely to have had SH episodes. Eight studies found no association between inpatient treatment and SH. Two cohort studies found that higher number of inpatient treatments was associated with SH during follow-up.	Inpatient treatment is associated with higher likelihood of SH.
Lifetime depressive episode(s)	12	Ten studies found lifetime depressive episode(s) associated with SH. Two studies found no association between SH and lifetime depressive episode. Both cohort studies found depressive episodes associated with SH during follow-up.	Lifetime depressive episode associated with higher likelihood of SH.

Characteristic	N	Association with self-harm (SH)	Conclusion
Past self-harm	8	All studies found that past self-harm was associated with current SH or SH during follow-up (four follow-up studies).	Past SH associated with risk of future SH episodes.
Age of onset of psychotic symptoms	25	Ten studies found SH associated with lower age of onset. Fifteen studies found no association between SH and age of onset. Age of onset was not reported in follow-up studies.	Heterogenic results. Most studies found no association, but 2/5 found lower age of onset associated with SH.
Duration of untreated psychosis (DUP)	7	Two studies found longer DUP associated with SH. One study found shorter DUP associated with SH. Four studies found no association between DUP and SH. Two cohort studies found no association between DUP and SH during follow-up.	No overall association, but heterogenic results.
Age at first mental health contact/first hospitalization	9	Two studies found SH associated with lower age at first mental health contact. Seven studies found no association between SH and age at first mental health contact. One cohort study measuring age at first mental health contact found no association with SH during follow-up	No association.
Duration of illness	27	Six studies found longer duration of illness associated with SH. Twenty-one studies found no association between duration of illness and SH. All three cohort studies found no association between duration of illness and SH during follow-up.	No association.
Involuntary hospital admissions	3	All three studies, including one prospective follow-up study, found no association between involuntary hospital admission and SH.	No association.
Symptoms and behaviour			
Nicotine use/daily smoking	5	Four studies found an association, one study found no association between smoking and SH. Not measured in follow-up studies.	Nicotine use (daily smoking) is associated with increased likelihood of SH.
Current suicidality	13	Ten studies found current suicidality associated with SH. Three studies found no association between current suicidality and SH. Both cohort-studies found an association between suicidality and SH during follow-up.	Current suicidality associated with likelihood of SH.
Current depressive symptoms	31	Twenty-one studies found higher current depressive symptoms associated with SH. Ten studies found no association. Two of the three cohort-studies reported higher depressive symptoms as a risk factor for SH during follow-up and the third study reported mixed results (no association and higher depression scores) in SH patients during follow-up, depending on follow-up time.	Higher current depressive symptoms associated with higher likelihood of SH.
Hopelessness	13	Eight studies found hopelessness associated with SH. Five studies found no association between hopelessness and SH. Of the two studies measuring SH during follow-up, one found that hopelessness was associated with SH and one had mixed results, but in the same direction (ns or higher hopelessness predicting later SH).	Hopelessness associated with SH in most studies. The results indicate that the association depends on time/context of assessment relative to SH.
Guilt	2	Both studies found guilt associated with higher SH. Guilt not measured in follow-up studies.	Too few studies to draw firm conclusions. Results indicate that guilt is associated with higher likelihood of lifetime SH.
Insight	11	Four studies found greater insight associated with SH. Seven studies found no association between insight and SH. Two cohort study found that greater insight was associated with SH episode(s) during follow-up. One cohort study found no significant association, although there was a trend towards greater insight in participants with SH during follow-up.	Inconclusive, but most follow-up studies found insight associated with SH during follow-up.
Positive psychotic symptoms	29	Five studies found elevated positive psychotic symptoms scales in patients with SH. Twenty-three studies found no association between positive symptoms scales and SH. Of the four follow-up samples, three found no association between positive psychotic symptoms scales and SH. Eight studies reported on hallucinations specifically, Six case control studies found no association with SH, but the two follow-up studies found a positive association between hallucinations and SH during follow-up.	No association between positive psychotic symptoms scales and SH. More research is needed regarding hallucinations and SH.
Anxiety	7	Four studies found that higher anxiety was associated with SH. Three studies found no association between anxiety and SH. One follow-up study measured anxiety, but were unclear about the time of measurement (before or after SH).	Inconclusive.
Physical illness/poor physical health	5	Three studies found a positive association between current physical illness and SH. Two studies found no association. Not measured in follow-up studies.	Inconclusive.
Violence or aggression	3	One study found higher violence in participants with SH. Two studies found no association. Not measured in follow-up studies.	Inconclusive.
Impulsivity	3	One study found higher impulsivity associated with SH. Two studies found no association between impulsivity and SH. Not measured in follow-up studies	Inconclusive.

Characteristic	N	Association with self-harm (SH)	Conclusion
Substance/drug abuse or dependence	20	Six found that substance/drug abuse or dependence were associated with SH. Fourteen studies found no association between substance/drug abuse or dependence and SH. Of the three cohort studies, 1 found that substance abuse/dependence was a risk factor for SH during follow-up, one found a trend towards increased risk and one found no association between substance abuse/dependence and SH during follow-up	Most studies, no association. There may be differences depending on characteristics of the sample studied and types of substances.
Negative psychotic symptoms	26	Three studies found lower scores on negative symptoms scales associated with SH. Twenty-four studies found no association. None of the follow-up studies found an association with SH during follow-up.	No association.
PANSS total score	10	One study found higher PANSS total score to be associated with SH. Nine studies found no association, including one study of SH during follow-up.	No association.
Global assessment of functioning	5	No study, including two prospective follow-up studies, found an association between GAF/GAS and SH.	No association.
Alcohol	21	Five studies found that alcohol abuse or dependence were associated with SH. Sixteen studies found no association between alcohol abuse/dependence and SH. None of the two studies of SH during follow-up found an association between alcohol use/dependence and SH.	No association.
Religion	4	None of the four studies found an association between religion and SH.	No association.
Other	<3	Non-compliance with follow-up treatment. One cohort study found non-compliance to be associated with SH during follow-up. Premorbid personality: one study, no association with SH. Premorbid adjustment: one study: no association with SH, one found higher childhood and early adolescent adjustment in participants with SH. Early parental loss: One study found early parental loss associated with SH, one study found no association between early parental loss and SH. Autobiographical memory: One study found SH associated with higher overgeneral memory another that SH was ass. with specific memories. Self-disorder: One study found no association with SH. Reasons for living: One study found no association with SH. Dexamethasone suppression test (DST): One study found DST ass. with SH	Inconclusive

Seven of the clinical characteristics examined have been found to be significant risk factors for self-harm in most studies: current suicidality and past self-harm, current depressive symptoms (including hopelessness and guilt feelings), lifetime depressive episode(s), a higher number of inpatient psychiatric treatment, childhood or past traumatic experiences, and nicotine use/daily smoking, although the last of these was not studied in any prospective cohort studies. The studies examining substance or drug abuse or dependence show heterogenic results indicating that there may be differences based on sample characteristics or the substances examined. None of the socio-demographic variables studied in more than a few studies has been found to be systematically associated with self-harm. A few studies have reported on the association between self-harm and aggressive/violent behaviours (Bai et al., 1997; Lejoyeux et al., 2013; Shoval et al., 2006) or impulsivity (Iancu et al., 2010; Iancu et al., 2006; Pluck et al., 2013) in patients with schizophrenia. Most studies find no association with lifetime history of self-harm on these two measures, but the samples are generally too small to draw any firm conclusions.

Regarding risk factors more specific to schizophrenia, the vast majority of studies found no association between self-harm and positive or negative psychotic symptom scales. However, in studies reporting specifically on hallucinations, the results differ depending on study design. Case-control studies find no association (Altamura et al., 2003; Mata Cala et al., 1998; Mauri et al., 2013; Zhang et al., 2013) but the prospective cohort studies (Lui, 2009; Madsen & Nordentoft, 2012) found that hallucinations were associated with self-harm during follow-up. Regarding the age of onset of psychotic symptoms findings also are inconsistent. Most studies (15) find no association, but a substantial proportion (10) find that self-harm is associated with a significantly lower age of onset of psychotic symptoms. Studies investigating the association between insight into illness and self-harm in schizophrenia have also been inconclusive. Some studies have found that greater insight during follow-up increases the risk of self-harm (Crumlish et al., 2005; Gonzalez, 2008) but not all (Bakst et al., 2010), and most studies of lifetime history of self-harm have found no association with insight into illness (Acosta et al., 2013; Nangle et al., 2006; Pluck et al., 2013; Restifo et al., 2009; Tarrier et al., 2004; Yan et al., 2013). And finally, the findings regarding duration of untreated psychosis (DUP) are also heterogeneous with some studies finding that self-harm is associated with longer DUP (Altamura et al., 2003; Mauri et al., 2013), some studies finding no association (Lui, 2009; Madsen & Nordentoft, 2012; McLean et al., 2012; Sevincok et al., 2007), and one study finding that self-harm is associated with shorter DUP (Preti, Meneghelli, Pisano, & Cocchi, 2009). The differences across studies with regard to illness insight, age of onset of psychotic symptoms and duration of untreated psychosis may have several causes. There may exist differences between the measures used for these dimensions. For example, in the eleven studies reporting on insight into illness, ten different measures of insight were used and only two studies used the same measure. Seemingly inconsistent findings may also arise if there are differences between studies in the sampling of subgroups with different clinical characteristics with respect to self-harm.

1.2.9   Risk factors for self-harm according to gender

Previous research indicates that risk factors for self-harm may vary according to gender. This is the case in studies investigating suicide in the general population (Qin, Mortensen, Agerbo, Westergard-Nielsen, & Erikson, 2000), suicide in schizophrenia (Heila et al., 1997), and self-harm in major depressive disorder (Oquendo et al., 2007). However, very few studies have addressed

gender differences in risk factors for self-harm in individuals with schizophrenia. Muller and colleagues (2005) found that women with a schizophrenia or affective disorder and a history of self-harm had a younger age of onset of the disorder and were more likely not to have had children compared to women without a history of self-harm. No such differences were found in men. However, since the study did not report data separately for individuals with schizophrenia, it is not known whether the findings apply to both groups. One early study (G. Wilkinson & Bacon, 1984) and one study published after the writing of study 1 (Kaplan, Harrow, & Faull, 2012) found some gender differences in risk factors for self-harm or suicidal behaviour (suicidal ideation, suicide attempt or suicide) among patients with schizophrenia. However, both included too few patients to be able to detect interaction effects. Furthermore, the known risk factors associated with self-harm in schizophrenia may be skewed towards risk of self-harm in men and not in women, since there are indications that non-epidemiologic schizophrenia research has a disproportionately high number of men (Longenecker et al., 2010). Thus, there is a need for studies powered to investigate the association of clinical characteristics with self-harm according to gender in individuals with schizophrenia.

1.2.10   Risk factors according to type of self-harm

In preparing the papers presented in this thesis, little was known about the relationship between non-suicidal self-harm (NSSH) and suicide attempts in patients with schizophrenia. However, common forms of non-suicidal self-harm were frequently reported in other diagnostic groups with high suicide risk (Zanarini et al., 2008). Furthermore, studies have shown that non-suicidal self-harm has predicted attempted suicide (Asarnow et al., 2011; Fedyszyn, Robinson, Harris, Paxton, & Francey, 2012; P. Wilkinson, Kelvin, Roberts, Dubicka, & Goodyer, 2011) or suicide (Cooper et al., 2005) in other clinical populations. A few studies suggest that patients with schizophrenia with suicide attempt report more non-suicidal self-harm than those without any suicide attempt. This was found during their most severe period of depression (Restifo et al., 2009) or during the most recent hospitalization (Shoval et al., 2006).

As mentioned above, self-report, laboratory studies and clinical observations indicate that the regulation of negative affect is an important mechanism often underlying non-suicidal self-harm

(Klonsky, 2007). From this perspective, non-suicidal self-harm can be viewed as a proxy for emotion regulation difficulties. Studies from adult inpatient non-psychotic clinical samples indicate that patients with a history of both suicide attempts and non-suicidal self-harm display more severe symptoms than patients with suicide attempts only (Claes et al., 2010; Stanley et al., 2001). For example, Stanley and colleagues (2001) found that patients with cluster B personality disorders who had a history of both suicide attempts and non-suicidal self-harm tended to be more depressed, had more persistent suicidal ideation, reported childhood physical abuse, and had more symptoms of affective instability and impulsivity than patients with suicide attempts only. Such differences seem to be present from an early age: adolescents with both suicide attempts and non-suicidal self-harm were more likely to be diagnosed with major depression and had higher scores on measures of hopelessness, anger, reckless behaviour and alcohol use than adolescents with suicide attempts only (Guertin et al., 2001). These findings suggest that patients with both suicide attempts and non-suicidal self-harm may have a more severe course of illness with higher scores on both symptom and trait measures from an early age. Little is known, however, about whether the same pattern applies to self-harm in individuals with schizophrenia, where psychotic symptoms play a prominent role in the defining characteristics of the disorder. The aim of study II was to explore the hypothesis that a similar pattern as in non-psychotic clinical samples would be present in patients with schizophrenia.

1.2.11   Childhood trauma, non-suicidal self-harm and suicide attempts

Both the stress-diathesis model for suicidal behaviour (Mann et al., 1999) and Linehan's biosocial theory (Crowell et al., 2009) suggest that childhood trauma is an important predisposing factor for suicide attempts and/or non-suicidal self-harm; this assumption has been confirmed in studies of adolescent and adult samples from the general population and in non-psychotic clinical samples (Brodsky & Stanley, 2008). The mechanisms for this association could be linked to alterations in stress responsivity, developments in the biological and psychological aspects of impulsivity and aggression, and/or diagnostic comorbidity (e.g. cluster B personality disorder, depression, and post-traumatic stress disorder) (Brodsky & Stanley, 2008).

The prevalence of childhood trauma is high in people with psychosis, although estimates vary greatly (between 28% and 73%) (Bendall, Jackson, Hulbert, & McGorry, 2008; Schafer & Fisher, 2011) and childhood trauma has consistently been associated with suicide attempts also in individuals with schizophrenia (Alvarez et al., 2011; Conus et al., 2010; Darves-Bornoz et al., 1995; Roy, 2005; Ucok & Bikmaz, 2007). Whether childhood trauma is a risk factor for non-suicidal self-injury in individuals with schizophrenia is, however, unknown. Non-suicidal self-harm has been found to be associated with childhood sexual, physical and emotional abuse in other samples (Glassman, Weierich, Hooley, Deliberto, & Nock, 2007; Klonsky & Moyer, 2008; Lang & Sharma-Patel, 2011; Muehlenkamp, Kerr, Bradley, & Adams Larsen, 2010). Furthermore, a few studies which have measured both suicide attempts and non-suicidal self-harm have shown that people who report both suicide attempts and non-suicidal self-harm have a particularly high likelihood of childhood physical abuse, compared to patients with suicide attempts only (Stanley et al., 2001; Ystgaard, Hestetun, Loeb, & Mehlum, 2004), non-suicidal self-harm only or no self-harm (Asarnow et al., 2011). Whether there is a similarly higher prevalence of physical or other types of abuse or neglect among people with schizophrenia and a history of both suicide attempts and non-suicidal self-harm is unknown. Thus, the first aim of study III of this thesis was to investigate the hypothesis that childhood exposure to trauma would be elevated in schizophrenia patients with both suicide attempts and non-suicidal self-harm.

Previous findings (study II) have suggested that patients with both suicide attempts and non-suicidal self-harm could represent a distinct subgroup with the early onset of psychotic or depressive symptoms, a high rate of repeated suicidal behaviour and high levels of current depressive and impulsive aggressive symptoms. Such clinical characteristics are often reported as elevated in people with psychotic symptoms who have been exposed to childhood trauma, both in adult (Schafer & Fisher, 2011) and adolescent clinical samples (Hainsworth, Starling, Brand, Groen, & Munro, 2011). Furthermore, research from other clinical samples suggests that the presence of childhood traumatic experiences may be associated with repeated self-harm, an early age of onset of major depression, and impulsive or aggressive personality traits (Brodsky et al., 2008; Gladstone et al., 2004). With these findings taken together, we were particularly

interested in investigating whether illness history (early onset of depressive or psychotic symptoms) and symptom profile could be linking childhood trauma with a history of both suicide attempts and non-suicidal self-harm. Thus, the second aim of study II was to investigate to what extent a relationship between childhood trauma and a history of both suicide attempts and non-suicidal self-harm would diminish when adjusting for early symptom onset and current levels of symptoms.

2   Aims of this thesis

The overall aim of this thesis was to describe the prevalence and clinical characteristics of a lifetime history of self-harm in patients with schizophrenia and to investigate whether such clinical characteristics vary according to gender or the type of self-harm. More specifically, we wanted to explore the hypothesis that patients with both suicide attempts and non-suicidal self-harm constitute a specific subgroup with regard to illness history and current clinical characteristics.

The first study had three aims: (1) to report the prevalence of a lifetime history of self-harm within a large clinical sample of patients with schizophrenia; (2) to investigate the clinical characteristics associated with such a history in patients with schizophrenia; and, (3) to investigate whether the clinical characteristics associated with a lifetime history of self-harm vary according to gender.

The second study had two aims: 1) to investigate whether patients with schizophrenia with a lifetime history of both suicide attempts and non-suicidal self-harm have an earlier onset of clinical symptoms (psychotic and/or depressive); and, 2) to investigate whether these patients report more impulsive aggression, suicidal ideation and depressive symptoms than patients with a lifetime history of suicide attempts only, or patients without any history of suicide attempts.

The third study was partly based on the findings from the second study and had two aims: 1) to investigate whether a lifetime history of both suicide attempts and non-suicidal self-harm is associated with childhood trauma in people with schizophrenia; and, 2) to investigate to what extent a relationship between childhood trauma and a lifetime history of both suicide attempts and non-suicidal self-harm would diminish when adjusting for early symptom onset and current levels of symptoms.

3 Method

3.1 Setting and design

This thesis is based on data collected from patients participating in the Thematically Organized Psychosis (TOP) study. The first patients were recruited in 2002 and the TOP study was launched as a collaborative study between the University of Oslo and in- and outpatient psychiatric units at four hospitals in the Oslo region. Inclusion of patients is still on-going. It was initially funded by the University of Oslo, the Regional Health Trust, and the Research Council of Norway. The aim of the TOP study is to investigate clinical, neurocognitive and biological characteristics of psychotic disorders in order to gain more knowledge about pathophysiological mechanisms. The TOP study collects clinical, neurocognitive and neuroimaging data as well as genetic information. The three studies in this thesis are based on clinical data only. The participants in the TOP study are patients treated in standard outpatient and inpatient psychiatric units at hospitals in the Oslo area and Innlandet Hospital Trust. Together these hospitals serve people living in urban, suburban and rural areas. The clinics provide publicly funded mental health care for the entire population within the catchment area and thus the TOP study recruits patients from all socio-economic strata of the Norwegian population.

All three studies in this thesis have a naturalistic and cross-sectional design, comparing groups based on the presence or absence of a lifetime history of self-harm behaviours.

3.2 Procedure

Patients included in the TOP study were recruited consecutively from in- and outpatient psychiatric units at any of the hospitals participating in the study. Patients with a suspected or confirmed psychotic disorder were invited to participate in the study by the clinician in charge of their treatment. Patients referred to the study were interviewed at their local clinic or at TOP premises. All the TOP research interviews were conducted by clinical psychologists or medical doctors who had been trained and reliability tested in the use of the study measures.

3.3 Participants

The inclusion criteria for all three studies were:

- Meeting the DSM-IV narrow schizophrenia spectrum disorder (DSM IV 295.xx) criteria (American Psychiatric Association, 2000), i.e. schizophrenia, schizoaffective disorder or schizophreniform disorder

- Age between 18 and 65 years

- Being able to speak and understand a Scandinavian language

- Providing written informed consent to participate in the study

The exclusion criteria were the same in all three studies: a history of severe head injury, neurological disease, or having an Intelligence Coefficient (IQ) score of < 70).

A total of 432 patients participated in the three studies. The number of participants in each study and the inclusion periods are presented in Table 5. The number of participants varies, due to the ongoing nature of the TOP study and the expansion of the research protocol in 2007 to address the research questions in studies II and III. These expansions include the separate assessment of lifetime history of suicide attempts and non-suicidal self-harm (studies II and III) and inclusion of a self-report measure for history of childhood trauma (study III). The number of participants in studies II and III is thus limited to the number of participants who were assessed after the expansions of the research protocol had been implemented. The samples are partly overlap; the number of patients from study I included in studies II and III is 224 and 177 respectively. One hundred and eighty-five patients participated in both study II and study III.

Table 5. Samples included in the thesis

	Patient group	N	Inclusion period	Mean age	Women
Study I	Schizophrenia	388	September 2004 - January 2010	31	57%
Study II	Schizophrenia	251	April 2007 - November 2010	30	58%
Study III	Schizophrenia	208	January 2007 - June 2012	29	57%

3.4 Measures

3.4.1   Diagnostic assessment

Diagnoses were made using the Structural Clinical Interview for the DSM-IV-TR Axis I disorders (SCID I, modules A–E) (First, Spitzer, Gibbon, & Williams, 1995). Patients were interviewed by clinical psychologists and medical doctors trained in SCID assessment based on the programme developed at the University of California, Los Angeles (UCLA) (Ventura, Liberman, Green, Shaner, & Mintz, 1998). All TOP interviewers attended regular diagnostic consensus meetings led by an experienced clinical professor in the field of diagnostics of severe mental disorders. The mean overall kappa for SCID diagnoses made by interviewers after they had completed the training course was 0.77. To assess the reliability of diagnoses for study participants, a stratified random sample was drawn of cases from actual study interviews. Anonymous vignettes describing symptoms and the development of the illness were then rated by two experts blind to the study ratings. For the 28 vignettes the overall agreement for DSM-IV diagnoses was 82% and the overall kappa was again 0.77 (95% CI: 0.60 – 0.94).

3.4.2   Assessment of socio-demographics and clinical characteristics

The assessment of socio-demographic and clinical characteristics was based on a detailed interview. The following clinical and socio-demographic variables were chosen based on previous research on self-harm behaviour and for the purposes of this thesis, within the limitations of the research protocol. Whenever more than one measure of the same phenomenon (more specifically, suicidal behaviour and current depressive symptoms) were available, the one with the highest quality or with the most complete data for the purposes of the study was chosen. An overview of the variables used in studies I-III is provided in Table 6.

3.4.2.1   Self-harm

The information about episodes of self-harm was based on all available information, but was collected mainly by way of a semi-structured interview. Lifetime episodes of self-harm were measured in all three studies using the following question adopted from a previous European

study of self-harm (CASE–study) (Hawton et al., 2002): "Have you ever deliberately taken an overdose (e.g. of pills or other medication) or tried to harm yourself in some other way (such as cut yourself)?". The response options were "no", "yes, once" and "yes, more than once". In addition to the self-harm question, the classification of the participants' most recent episode of self-harm was based on an open description which included a description of the method(s) used (studies I and II). The information about methods used was categorized into four groups: overdoses, cutting (knife/sharp object), hanging/strangulation and other methods. The patients were asked whether they considered this behaviour a suicide attempt ("yes"/"no"/"uncertain"), and what they wanted to achieve trough the act ("I wished to die" ("yes"/"no"), "I wished to get help from someone" ("yes"/"no"), "I wished to escape an unbearable emotion" ("yes"/"no"), or "other reasons" (describe)). The patients were also asked when the most recent episode took place ("less than a month ago"/"between a month and a year ago"/"more than a year ago") (study III), and whether they had been given hospital treatment for the most recent episode of self-harm ("yes"/"no") (studies I and II). The degree of premeditation was measured using the question: "When you took the overdose or tried to harm yourself, how long had you thought about doing it?" ("less than an hour"/"more than an hour, but less than a day"/"more than a day, less than a week"/"more than a week"/"less than a month"/"a month or more") (study II). Furthermore, interviewers rated the medical lethality of the most recent self-harm episode (little or no death risk/moderate death risk/great death risk/and potentially lethal) (studies I and II).

In early 2007 the interview was extended to include information about the number of self-harm episodes and the type of self-harm; this allowed for categorization of all self-harm episodes as either suicide attempts, or non-suicidal self-harm. In this extended protocol, used in studies II and III, the response options to the self-harm question were "no", "yes" and if yes, "the specific number of times" with the follow-up question: "how many times did you try to kill yourself?" (suicide attempts) and "how many times did you harm yourself without a wish to die" (non-suicidal self-harm). The presence of at least some suicidal intent led to the classification of the behaviour as a suicide attempt, also when additional reasons were given for the behaviour (e.g. 'I wished to get help from someone'). The principal author reviewed all scores on self-harm variables and - in cases of ambiguity - case notes were checked. In the few cases where doubt

remained a consensus was reached with the senior author. Based on these data it was possible to divide the study sample into four groups relative to the presence of suicide attempt (SA) and non-suicidal self-harm (NSSH) (Figure 1): 1) NoSH (patients with no self-harm), 2) NSSH only (patients with non-suicidal self-harm and no suicide attempt), 3) SA only (patients with suicide attempt and no non-suicidal self-harm), and, 4) SA+NSSH (patients with both suicide attempts and non-suicidal self-harm). The groups with no suicide attempts (NoSH and NSSH only) were merged into one group NoSA (non-attempters) in most but not all analyses (see Figure 1).

Figure 1 Grouping of patients according to life-time prevalence of self-harm behaviours
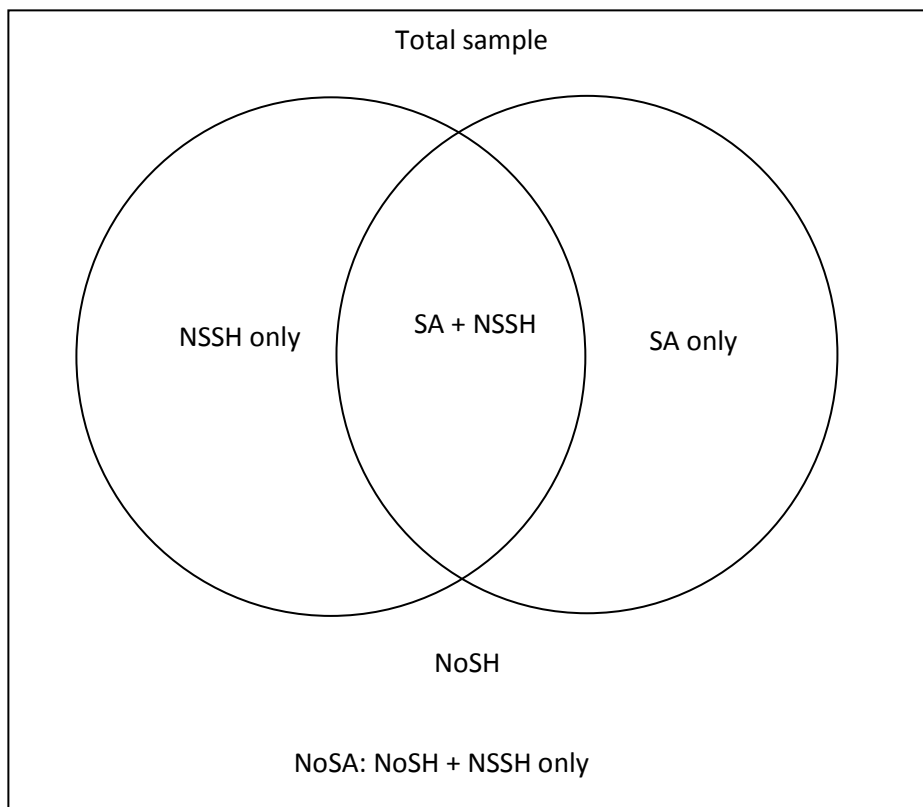
NSSH: non-suicidal self-harm SA: suicide attempt

NoSH: No self-harm, NoSA: non-attempters

3.4.2.2 Illness history

Age of onset of psychotic or depressive symptoms was defined as the age of onset of the first SCID-verified depressive or psychotic symptoms. Presence of psychosis was defined as a score of ≥ 4 on items P1 (delusions), P3 (hallucinatory behaviour), P5 (grandiosity), P6 (suspiciousness/persecution), or G9 (unusual thought content) on the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987). Duration of illness was defined as the difference between the age at the time of the clinical interview and the age at the onset of psychotic symptoms. Information about the number of psychiatric inpatient admissions, the age of first treatment for a psychiatric disorder, and age at first adequate treatment for psychosis was based on the research interview and hospital records. Duration of untreated psychosis was measured as the time from psychosis onset until the start of adequate treatment for the psychotic disorder, defined as admission to hospital due to psychosis or antipsychotic medication in adequate dosage. The number of lifetime depressive episodes was recorded based on the SCID interview (First et al., 1995). Lifetime history of hallucinations (yes/no) was also based on the diagnostic interview, hospital records and all available information.

3.4.2.2.1 Childhood trauma

Traumatic events in childhood were rated using a Norwegian version of the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1994; Larsson et al., 2013), a self-report questionnaire comprising 28 items and the following five subscales of childhood traumatic exposure: emotional abuse, physical abuse, sexual abuse, physical neglect, and emotional neglect (Bernstein et al., 1994; Bernstein et al., 2003). The reliability and validity of the CTQ have been demonstrated previously (Bernstein et al., 1994). Each subscale consists of five items scored on a 5-point Likert-type scale, from 1 (never true) through to 5 (very often true). In addition, four score-ranges were defined for each scale: none to low; low to moderate; moderate to severe; and severe to extreme exposure. The overall internal consistency of the scale was excellent with a Cronbach alpha of 0.91, and for the subscales emotional abuse 0.87, physical abuse 0.85, sexual abuse 0.89, physical neglect 0.60 and emotional neglect 0.88.

3.4.2.3   Current symptoms and behaviours

3.4.2.3.1   Psychotic symptoms and global assessment of functioning

Study participants' experiences of psychotic and related symptoms over the previous seven days was evaluated using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) based on information obtained in the Structured Interview for Positive and Negative Syndrome Scale (SCI-PANSS) (Kay, 1991). The PANSS is a 30-item rating scale where each item is rated from 1 ("Absent") to 7 ("Extreme"). Symptoms are characterized on a positive subscale, negative subscale, the general psychopathology scale and a total score. In addition, scores from two items of the positive symptoms scale were reported separately, namely delusions and hallucinatory behaviour. All interviewers participated in inter-rater reliability testing which entailed rating of patient videos. Inter-rater reliability was acceptable with intra-class correlation coefficients (Shrout & Fleiss, 1979) for PANSS subscales ranging from 0.71 to 0.73. Global level of functioning was measured with the Global Assessment of Functioning scale (GAF) (S. H. Jones, Thornicroft, Coffey, & Dunn, 1995), split version functioning scale (GAF-F) (Pedersen, Hagtvet, & Karterud, 2007). The GAF-F is scored from 0 – 100, with higher scores indicating better functioning. ICC for GAF-F was 0.85 (95% CI: 0.76 – 0.92).

3.4.2.3.2   Impulsive aggression (emotional dysregulation)

The research protocol did not include a measure of emotional dysregulation. However, PANSS general psychopathology scale, item G14 measures "disordered regulation and control of action on inner urges, resulting in sudden, unmodulated, arbitrary or misdirected discharge of tension and emotions without concern about consequences" (Kay, 1991). Preliminary analyses in a subpopulation of patients (n = 88) showed a significant correlation between the PANSS G14 item and the S1 ('anger') (r = 0.59, P < 0.01) and S3 ('emotional lability') (r = 0.31, P < 0.01) items. PANSS item G14 was thus included in all three studies as a single item proxy for problems of emotional dysregulation. In study I this construct was called emotional dysregulation, according to the explanation above. However, during the review process with study II and study III, it became clear that the specific rating criteria of PANSS item G14 (Kay, 1991) focus more on overt aggressive and impulsive behaviours than inner emotional states. Hence, it was decided to change the labelling of the PANSS G14 measure from 'emotional dysregulation' (study I), to 'impulsive aggression' in studies II and III. In this dissertation I have decided to consequently use

the term impulsive aggression to avoid confusion. However, I sometimes use the term emotional dysregulation in parenthesis when referring to study I. The important is to keep in mind that these concepts are based on the same item in PANSS general psychopathology scale, and thus are identical.

3.4.2.3.3   Depression and suicidality

In study I, the PANSS depression dimension (PANSS-D), composed of four items - G1 somatic concern, G2 anxiety, G3 guilt feeling and G6 depression - was used as a measure of depressive symptoms over the previous seven days. The PANSS-D has been shown to be highly inter-correlated with scores on the Calgary Depression Scale for Schizophrenia (CDSS) and the Hamilton rating scale for depression in patients with schizophrenia (El Yazaji et al., 2002). In studies II and III, current depression was assessed by the total score of the CDSS, excluding the suicide item. The CDSS has been shown to have satisfactory psychometric properties in assessing depression (D. Addington, Addington, & Maticka-Tyndale, 1994; D. Addington, Addington, Maticka-Tyndale, & Joyce, 1992; D. Addington, Addington, & Schissel, 1990). In study I, suicidal ideation during the preceding week was assessed using the Clinical Global Impression for Severity of Suicidality (CGI-SS) (Meltzer et al., 2003), a five-point scale that was scored based on all relevant information provided. In study II, suicidal ideation during the preceding week was measured using five items from the InterSePT scale for suicidal thinking (InterSePT 5) (Lindenmayer et al., 2003). The InterSePT 5 is based on items from the Scale for Suicidal Ideation (Beck, Kovacs, & Weissman, 1979) regarding the past week: wish to die, reasons for living versus reasons for dying, desire to make active suicide attempt, frequency of suicidal ideation and specificity/planning of contemplated attempt, each scored 0-2, with a high score indicating higher levels of suicidal ideation. The mean total score was divided into three groups: no current suicidality (0), low suicidality (0.1-1.0), and moderate to high suicidality (1.1-2.0).

3.4.2.3.4   Insight into illness, medical adherence, medication, and alcohol or drug abuse or dependence

Insight into illness was assessed using the Birchwood Insight Scale (IS), a scale that has shown satisfactory internal consistency for patients with schizophrenia in the TOP sample (Birchwood et al., 1994; Jonsdottir et al., 2008). It is a self-reported scale consisting of three subscales, each with a sum score of 0–4 (higher scores indicate greater insight): awareness of illness (two items), relabelling of symptoms (two items) and need for treatment (four items). The Medication Adherence Report Scale (MARS-5) (Horne & Weinman, 2002) was used to measure adherence to medication. The validation of MARS-5 in the TOP study sample suggests that it is a reasonably valid method for measuring adherence; see Jonsdottir et al. (2010) for details. Scores range from 5 to 25, with higher scores indicating higher adherence. Alcohol or drug abuse or dependence during the previous six months was scored with the Evaluating Substance Abuse in Persons with Severe Mental Disorders (Drake, Mueser, & McHugo, 1996) in which alcohol and drug use are rated separately as: 1 (non-use), 2 (use), 3 (abuse), 4 (dependence), and 5 (dependence with hospitalization). For alcohol and drug use, participants were collapsed into two groups according to the presence (3-5) or absence (1-2) of abuse or dependence in the previous six months. This scoring was based on all available information, including a detailed history of alcohol use (number of alcohol units) and drug/substance use (times used) during the six months prior to study entry and from information about lifetime alcohol disorders or drug disorders established in the SCID-I interview (First et al., 1995). Information on medication use at the time of assessment, daily smoking and socio-demographic information were obtained from the detailed clinical interview and hospital records.

Table 6. Variables included in the studies in the thesis

	Study I	Study II	Study III
Sociodemographic variables			
Age (years)	x	x	x
Gender	x	x	x
European ethnicity	x	x	x
Marital status (single vs. married/co-habiting)	x	x	x
Living alone	x		
Divorced	x		
Education	x		
Being a parent	x		
Employed or studying	x		
Clinical characteristics of self-harm	x	x	x
- Single vs. multiple episodes	x		
- Treated in hospital	x	x	
- Lethality of most recent episode	x	x	
- Method used in most recent episode	x	x	
- Degree of premeditation in most recent episode		x	
- Suicide attempts, number of episodes		x	x
- Non-suicidal self-harm, number of episodes		x	x
- Self-harm episode during most recent year			x
Illness history			
Childhood trauma – Childhood trauma questionnaire			x
Depressive episode, lifetime	x	x	x
Age of onset of depression		x	x
Age of onset of first psychotic symptoms	x	x	x
Age of first treatment for psychiatric disorder		x	
Age of first treatment for psychosis		x	
Duration of untreated psychosis		x	
Duration of illness	x		
Diagnoses - Structural Clinical Interview for the DSM-IV	x	x	x
Number of psychiatric inpatient admissions	x		
Lifetime hallucinations	x		
Current symptoms and behaviours			
Positive and negative symptoms – Positive and Negative Syndrome Scale (PANSS)	x	x	x
- Total score		x	x
- Negative symptoms	x	x	x
- Positive symptoms	x	x	x
- P1 Delusions		x	
- P3 Hallucinatory behaviour		x	
Impulsive aggression (emotional dysregulation) - PANSS item G14	x	x	x
Current depression - Calgary depression rating scale for schizophrenia		x	x
- PANSS-D PANSS depression dimension	x		
Current suicidality - InterSePT5		x	
- Global impression of severity of suicidality	x		
Insight into illness - Birchwood insight scale	x		
Global assessment of functioning - Global assessment of functioning scale	x	x	x
Alcohol abuse or dependence in last 6 months – Alcohol use scale	x	x	
Drug or substance abuse or dependence in last 6 months – Drug use scale	x	x	
Current medication		x	
Medication adherence - The medication adherence report scale	x		
Daily smoking	x		

3.5 Literature search

A series of searches of the relevant literature in databases (PubMed and Psychinfo) were performed from the outset of the work on this thesis of aspects relevant to the studies. These include two thorough searches of studies published in English in peer-reviewed journals from the last three decades up until November 2013 on:

a) prevalence rates of self-harm in individuals with schizophrenia. Studies reporting from consecutively or randomly recruited samples of individuals with schizophrenia were selected. Studies systematically oversampling patients with self-harm, suicidal behaviour or depressive symptoms were excluded from the review of papers on rates of self-harm.

b) follow-up cohort or case-control studies investigating one or more risk factors for self-harm in individuals with schizophrenia.

Searches for studies reporting on schizophrenia, schizoaffective and/or schizophreniform disorder were performed. Samples reporting separately or predominately on individuals with these diagnoses were included in the review. This search strategy was combined with searches for studies on self-harm using the terms self-harm, deliberate self-harm, suicide attempt, parasuicide, non-suicidal self-injury, self-mutilation, non-suicidal self-harm and self-injurious behaviour. Papers reporting separately on one or more of these terms in patients with schizophrenia were included in the review. Reference lists from important publications were hand checked for relevant references. Studies reporting primarily on neurocognitive and biological risk factors for self-harm in individuals with schizophrenia were excluded, since these factors were not examined in this thesis. It should be noted that although the search procedures employed were thorough, these are not systematic reviews and some studies may have been omitted.

3.6 Ethical considerations

The TOP study was approved by the Regional Committee for Medical and Health Research Ethics South East, Norway (ref # 493-03-01179). The collection and handling of data were approved by the Norwegian Data Protection Agency (ref # 2003/2052). The patients were invited to participate in the TOP study while in standard clinical care at their in- or outpatient treatment

units. The TOP Study was carried out in adult patients, in principle capable of giving informed consent. The clinician in charge of treatment, in co-operation with the TOP interviewer, assessed whether patients were competent to give consent depending on their current clinical state. Measures were taken to ensure that the patients were well informed about the study and their rights and to minimize potential adverse consequences of participation. These included emphasizing that participation was voluntary and that refusal would have no repercussions on their future treatment, and information was provided in both writing and orally, bearing in mind potential cognitive difficulties in the patient. The information about the study was given by the TOP interviewer (medical doctor or psychologist) and included the purpose of the study, the extent of investigations and interviews, how and for how long personal information would be stored, how confidentiality would be maintained, and when the project end. Furthermore, patients were explicitly informed about their right to see all data collected in their name and have these deleted on request at any time during or after assessment. Written informed consent was obtained prior to study participation. From the beginning of the TOP study, patients did not receive monetary compensation for participation, but compensation was given for travel expenses or transportation was provided. As of December 1st 2008 under the revised permit from the Regional Ethical Committee, all participants were given a one-off compensation of 500 NOK.

The TOP study has a thorough and time-consuming assessment protocol, including clinical interview, a general medical examination, self-report measures, neurocognitive testing, blood/urine sampling, and in some cases even neuroimaging. The assessment was adjusted to the patients' level of functioning, with shorter sessions, breaks, and over several appointments when necessary. The motivation for participation was often to give a contribution to research whereby to gain new knowledge. Many also appreciated the opportunity to have a comprehensive evaluation of their condition. If the patient agreed to it, the clinician in charge of the treatment would receive a report on clinical findings, diagnostic evaluations and neuropsychological test results. The impression was that the evaluations were experienced as highly useful by most patients and clinicians. Despite the detailed and time-consuming assessment, the burden for the patients was not considered to be substantially different from that of a thorough clinical examination.

3.7 Statistical analyses

Statistical analyses were conducted using PASW statistics 18 (studies I, II) and 20 (study III) software (SPSS Inc., Chicago, Illinois, USA), except for one power analyses using nQuery Advisor® Release 6.0 software (Statistical Solutions, Cork, Ireland). All tests were two-tailed with α < 0.05. Group comparisons of demographical and clinical variables were conducted with a range of analyses. Bivariate relationships were analysed using Chi-square tests for categorical variables, Student t-tests for continuous normally distributed variables, and Mann–Whitney U test for non-normally distributed continuous variables. Comparison of three or more groups was analysed using one-way ANOVAs (with post-hoc Scheffé's tests) for normally distributed continuous variables and Kruskal-Wallis test (with post hoc Mann–Whitney U tests) for non-normally distributed continuous variables. Exploration of interaction effects between two independent variables was conducted within the logistic regression analysis. A series of multiple logistic regression analyses (study I) were applied to search for models that best differentiated patients with and without a lifetime history of self-harm whereas multinomial logistic regression models (study II and III) were generated to search for models that best differentiated patients with suicide attempts only, both suicide attempts and non-suicidal self-harm or non-attempters. Highly skewed non-normally distributed variables were either dichotomized or log transformed in the regression analyses. Detailed descriptions of the statistical analysis used in the studies are presented in the three papers.

4 Results – summary of papers

4.1 Paper I: Self-harm in patients with schizophrenia spectrum disorders

Background: Self-harm is a strong risk factor for suicide in people with schizophrenia. The aim of this study is to describe the prevalence, clinical characteristics, and gender differences associated with self-harm in schizophrenia.

Methods: In a cross-sectional study, 388 patients with schizophrenia spectrum disorders were interviewed and assessed with respect to lifetime history of self-harm and relevant clinical variables.

Results: Overall, 49% of the patients reported self-harm. Self-harm was associated with female gender, having had a depressive episode, younger age at psychosis onset, alcohol abuse or dependence in the previous six months, current suicidality, awareness of illness and low adherence to prescribed medication in the multivariate analysis. Lifetime hallucinations, number of psychiatric inpatient admissions and daily smoking were bivariately associated with self-harm, but did not have a significant contribution in the multivariate analyses. Gender significantly modified the effect of two clinical characteristics associated with self-harm: greater awareness of having a mental disorder was associated with self-harm in men only, while impulsive aggression (emotional dysregulation) was associated with self-harm in women only.

Conclusions: While self-harm in patients with schizophrenia spectrum disorders is highly prevalent in both genders, risk factors in men and women differ in several important ways.

4.2 Paper II: Clinical characteristics in schizophrenia spectrum disorder patients with or without suicide attempts and non-suicidal self-harm - a cross-sectional study

Background: To investigate whether patients with schizophrenia with both suicide attempts and non-suicidal self-harm have an earlier age of onset of psychotic and depressive symptoms and higher levels of clinical symptoms compared to patients with only suicide attempts or without suicide attempt.

Methods: Using a cross-sectional design, 251 patients (18 - 61 years old, 58% men) with schizophrenia spectrum disorders treated at hospitals in Oslo, Norway, were assessed with a comprehensive clinical research protocol and divided into three groups based on their history of suicide attempts and non-suicidal self-harm.

Results: Seventy-five patients reported one or more lifetime episodes of non-suicidal self-harm. Patients with non-suicidal self-harm were significantly more likely to report suicide attempts than patients with no episodes of non-suicidal self-harm. Suicide attempts were present in 88 patients (35%); 52 had suicide attempts only (21%) and 36 had both suicide attempts and non-suicidal self-harm (14%). When compared with non-attempters and those with suicide attempts without non-suicidal self-harm, patients with both suicide attempts and non-suicidal self-harm were more frequently women, younger at the onset of psychotic symptoms, had longer duration of untreated psychosis, and had higher levels of current impulsivity/aggression and depression. Patients with both suicide attempts and non-suicidal self-harm were more likely to repeat suicide attempts than patients with suicide attempts only.

Conclusions: Patients with both suicide attempts and non-suicidal self-harm had different illness histories and clinical characteristics compared to patients with only suicide attempts or patients without suicide attempts. Our study suggests that patients with both suicide attempts and non-suicidal self-harm represent a distinct subgroup among patients with schizophrenia and suicidal behaviour with their early onset of psychotic symptoms, high rate of repeated suicidal behaviour and significant delay in treatment.

4.3 Paper III: The association of childhood trauma with a history of both suicide attempts and non-suicidal self-harm in patients with schizophrenia

Background: Studies have shown that childhood trauma is associated with suicide attempts in patients with schizophrenia and with suicide attempts and non-suicidal self-harm in other clinical groups. In a previous study, we found that patients with schizophrenia and both suicide attempts and non-suicidal self-harm reported an earlier onset of psychotic or depressive symptoms and more severe current symptoms compared to patients with suicide attempts only or non-attempters. The purpose of this study was to investigate whether a history of having had

both suicide attempts and non-suicidal self-harm is associated with childhood trauma in patients with schizophrenia, and whether this association would diminish when adjusting for onset of depressive or psychotic symptoms and current symptoms.

Methods: Using a cross-sectional design, 208 patients (18 - 61 years old, 57 % men, mean age 28.6 years (SD = 9.4)) with DSM-IV schizophrenia spectrum disorders treated at hospitals in Oslo, Norway, were assessed clinically and grouped based on their history of suicide attempts and non-suicidal self-harm. Traumatic events were measured using the Childhood Trauma Questionnaire (CTQ) with scores on emotional, physical and sexual abuse and physical and emotional neglect.

Results: Patients with both suicide attempts and non-suicidal self-harm had higher scores on all subtypes of childhood traumatic exposure compared with patients with no history of self-harm, and significantly higher scores on childhood sexual abuse than patients with suicide attempts only. Childhood emotional abuse was the subscale most strongly associated with both suicide attempts and non-suicidal self-harm and with suicide attempts only. The association between childhood emotional abuse and a history of both suicide attempts and non-suicidal self-harm diminished and was no longer significant when adjusting for onset of depressive and psychotic symptoms, and current depressive and impulsive aggressive symptoms. The association between childhood emotional abuse and suicide attempts only remained significant and unaffected when adjusting for these clinical characteristics.

Conclusions: This study suggests that childhood exposure to trauma is particularly high in patients with schizophrenia who report a history of both suicide attempts and non-suicidal self-harm. Our findings are consistent with a hypothesis that patients with schizophrenia with and without a history of non-suicidal self-harm may have different pathways to suicidal behaviour, and that a history of childhood trauma may play an important role.

5 Discussion

5.1 Main findings

This thesis has focused on describing the prevalence and clinical characteristics of a lifetime history of self-harm in patients with schizophrenia and on investigating whether such clinical characteristics vary according to gender or the type of self-harm. Furthermore, possible pathways to suicidal behaviour have been investigated. More specifically, a hypothesis that patients with schizophrenia with both suicide attempts and non-suicidal self-harm constitute a specific subgroup with regard to illness history and current clinical characteristics was presented and explored. The main findings of this thesis which has studied lifetime history of self-harm in patients with schizophrenia are:

1. The prevalence of a lifetime history of self-harm (49%), the frequency of repetition (58%) and the severity of the last episode of self-harm was high and comparable to that described in previous research.

2. According to multivariate analyses, self-harm was associated with female gender, having had a depressive episode, a younger age of psychosis onset, alcohol abuse or dependence in last six months, current suicidality, insight into illness (awareness of illness), and low adherence to prescribed medication.

3. Gender significantly modified the effect of two clinical characteristics associated with self-harm: greater awareness of having a mental disorder was associated with self-harm in men only, while impulsive aggression (emotional dysregulation) was associated with self-harm in women only.

4. Both non-suicidal self-harm (30%) and suicide attempt (35%) were relatively frequent. A lifetime history of both suicide attempt and non-suicidal self-harm was present in 36 patients (14%) and 52 patients (21%) had a lifetime history of suicide attempt only.

5. Patients with a history of both suicide attempts and non-suicidal self-harm were more frequently women, younger at the onset of psychotic symptoms, had a longer duration of untreated psychosis, and higher levels of current impulsive aggression and depression than patients with suicide attempts only.

6. Patients with both suicide attempts and non-suicidal self-harm had elevated scores on all subtypes of childhood trauma compared to patients with no self-harm. They also had

higher scores on childhood sexual abuse compared to patients with suicide attempts only.

7. The association of childhood emotional abuse with a history of both suicide attempts and non-suicidal self-harm was no longer significant after adjusting for onset of depressive and psychotic symptoms and current symptoms of impulsive aggression and depression.

The findings in the present thesis suggests that patients with a history of both suicide attempts and non-suicidal self-harm represent a distinct subgroup of patients with schizophrenia with elevated childhood exposure to trauma, early onset of psychotic symptoms, significant treatment delay, a high rate of repeated suicidal behaviour, and elevated levels of current depressive and impulsive aggressive symptoms compared to other patients with schizophrenia.

5.1.1   Prevalence of a lifetime history of self-harm

Forty-nine percent of the sample of 388 patients with schizophrenia in the first study in this thesis had at least one lifetime episode of self-harm. This prevalence estimate is approximately 50% higher than the rate reported in previous studies from the Nordic countries (Bertelsen et al., 2007; Suokas et al., 2010) and also substantially higher than the mean rate reported in previous studies of the lifetime history of self-harm in individuals with schizophrenia in Europe (Table 2). However, most previous studies have used the construct suicide attempt, and the rate of suicide attempts reported in this thesis (35%) is close to the mean prevalence estimates in Europe. Furthermore, two previous small European studies have used the self-harm construct and these studies reported as high (Simms et al., 2007) or higher (Pluck et al., 2013) rates of a lifetime history of self-harm than in the present thesis. Our findings of a high frequency of repetition (58%) and high severity of the most recent episodes were comparable to previous research (Bhatia et al., 2006; Harkavy-Friedman et al., 1999). We found a significant higher rate of self-harm in women than men in this thesis. This finding is in contrast to most previous studies on lifetime history of self-harm in schizophrenia who find no gender differences in rates of self-harm according to gender (Table 4). However, there are a few exceptions (D. E. Addington & Addington, 1992; Bani-Fatemi et al., 2013), including one study from Denmark (Bertelsen et al., 2007) that have also found higher rates of lifetime history of self-harm in women than men with

schizophrenia. These differences between studies are difficult to explain. However, in the present thesis the gender ratio of self-harm in patients with schizophrenia is similar to the gender ratio in the general population in Norway (Hjelmeland, 2004; Kopjar et al., 2005), in contrast to previous research from most other countries.

5.1.2 Clinical characteristics associated with a lifetime history of self-harm

Consistent with previous research, we found that a lifetime history of self-harm was associated with lifetime depressive episode(s), current suicidality and depressive symptoms, childhood trauma, the number of psychiatric inpatient admissions, and daily smoking, although for the two last characteristics only in bivariate analyses. Furthermore, low adherence to medication was significantly associated with self-harm. This is consistent with one previous study which has found that non-compliance with follow-up treatment was associated with self-harm or suicide during follow-up (Lui, 2009), and consistent with the finding that poor compliance with treatment is a robust risk factor for suicide (Hawton et al., 2005).

With respect to clinical characteristics such as hallucinations, insight into illness and, age of onset of psychotic symptoms, previous research has reported inconsistent findings, with most studies finding no association (Table 4). In our large and representative sample, however, greater insight into illness, a younger age at onset of psychotic symptoms, and the presence of lifetime hallucinations, were all significantly associated with self-harm in the bivariate analyses. Two of these characteristics, insight into illness (measured with the subscale greater awareness of illness) and age of onset of psychotic symptoms were still associated with self-harm after adjusting for other known risk factors for self-harm. Since awareness of illness was associated with a lifetime history of self-harm in the multivariate analyses, this association could not be explained by depressive episodes or current suicidal symptoms alone. In a previously published follow-up study of first-episode schizophrenia patients using the same measure of insight as in our study (Crumlish et al., 2005) the same association was found, whereas other studies have either not found such an association (Nangle et al., 2006; Pluck et al., 2013; Restifo et al., 2009; Yan et al., 2013) or the association has been mediated by, or disappeared, after adjusting for

hopelessness or depression (Evren & Evren, 2004; Kao & Liu, 2011). The participants in this thesis had a relatively short mean duration of illness (7.4 years, study I) and one potential explanation for these discrepancies may be that greater awareness of illness is primarily associated with self-harm in the early phases of schizophrenia. Studies reporting the age of onset, the duration of illness and insight into illness seem to support this explanation in that awareness of illness/insight into illness is more consistently associated with self-harm in studies with individuals with a short mean duration of illness (Crumlish et al., 2005) compared with studies including patients with a longer mean duration of illness (Nangle et al., 2006; Restifo et al., 2009; Yan et al., 2013). The difference in studies with respect to hallucinations could possibly be explained in the same way. The two studies which have reported bivariate associations between current hallucinations and future self-harm were both based on samples with short duration of illness (Lui, 2009; Nordentoft et al., 2002) whereas studies finding no bivariate association between current hallucinations and a lifetime history of self-harm all included patients with a longer mean duration of illness (12-22 years) (Altamura et al., 2003; Mauri et al., 2013; Sevincok et al., 2007; Zhang et al., 2013). Thus, it could be that hallucinations are a risk factor for self-harm early in the course of illness, but not later. The finding in the present thesis that lifetime hallucinations was bivariate, but not multivariate, associated with self-harm in a sample with a mean duration of illness 7.4 years, seems to fit well with such an interpretation.

Whether or not a younger age of onset of psychotic symptoms is found to be associated with a lifetime history of self-harm also seems to be influenced by sample characteristics. Studies finding a significant association between a younger age of onset and a lifetime history of self-harm, such as in the present thesis, have samples with a much shorter mean duration of illness (Albayrak et al., 2012; Andriopoulos et al., 2011; Aukst Margetic et al., 2012; Uzun et al., 2009) than studies finding no association (Altamura et al., 2003; Evren & Evren, 2004; Harkavy-Friedman et al., 1999; Kao & Liu, 2011; Mauri et al., 2013; McLean et al., 2012; Nangle et al., 2006; Yan et al., 2013; Zhang et al., 2013). This rather unexpected finding could, however, be spurious since any recall bias in terms of about self-harm could increase with the increasing duration of illness. However, the prognosis of schizophrenia is heterogeneous; it can take a chronic course, but it can also lead to partial or full recovery. For example, in comparison to men, women with schizophrenia express more severe affective symptoms, fewer or less intense

negative symptoms, have less severe cognitive impairment and have a better prognosis (Tandon, Nasrallah, & Keshavan, 2009). Thus, it could be that individuals with a young age of onset of schizophrenia and self-harm may have a better prognosis compared to other individuals with schizophrenia. If this holds true, some patients may improve to the extent that they may no longer satisfy criteria for a diagnosis of schizophrenia or they may no longer be in need of specialist mental health care as time goes by, and will thus no longer be part of the clinical populations targeted for recruitment into research studies. Furthermore, a small group of individuals with an increased risk of self-harm and early onset of psychotic symptoms may also die from suicide early in the course of illness, and thus there may be a selective survival bias in studies recruiting primarily chronic patients.

We found that impulsive aggression, a measure included in this thesis as a proxy for emotional dysregulation (as described in Methods, Current symptoms), was significantly associated with a lifetime history of self-harm in patients with schizophrenia. Findings from previous research into the association between a lifetime history of self-harm and impulsivity (Iancu et al., 2010; Iancu et al., 2006; Pluck et al., 2013) or aggression (Bai et al., 1997; Lejoyeux et al., 2013; Shoval et al., 2006) have been inconclusive and previous studies are difficult to compare with each other and the present thesis, since different measures have been used. That said, emotional dysregulation has been linked to self-harm in disorders that are high in negative emotions, especially BPD (Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2006). As highlighted in the introduction, there are both theoretical and empirical indications that self-harm is associated with problems with regulation of negative affect (Crowell et al., 2009; Gratz & Roemer, 2008; Klonsky, 2007). As patients with schizophrenia often have high levels of negative affect (A. S. Cohen, Minor, & Najolia, 2010), it is plausible that one pathway to self-harm in individuals with schizophrenia may involve emotional dysregulation.

5.1.3   Clinical characteristics of a lifetime history of self-harm according to gender

Study I of this thesis is to my knowledge the first to be powered to explore the clinical characteristics associated with self-harm according to gender in patients with schizophrenia. We

found that greater insight into illness (measured by the subscale awareness of having a mental disorder) was associated with self-harm in men but not in women. Thus, another explanation for the inconsistent results regarding the association between insight into illness and self-harm could be that insight into illness is associated with self-harm only in men. To my knowledge, the association between insight into illness and a lifetime history of self-harm according to gender has not been addressed in previous research on patients with schizophrenia. As most studies of self-harm in schizophrenia are based on samples with a majority of men, or since samples have been too small to analyse subgroup differences, there is a potential for bias in the research literature towards risk factors that are specific to men. That said, there is no systematic association between gender ratio and whether or not studies report a significant association between insight into illness and self-harm. Hence, this finding should be interpreted with caution. If it is replicated, it might be fruitful to explore gender differences regarding coping with the experience and consequences of developing a severe mental disorder or gender differences in the association between depression/hopelessness and an awareness of illness. For example, it could be that the fear of not getting a job, or the fear of losing one's independence may cause more hopelessness in men than women, or that awareness of illness may impact men to a greater extent if they do not confide in others about their problems as much as women do. The constructs thwarted belongingness and perceived burdensomeness developed in the context of Joiner's interpersonal theory of suicidal behaviour could be one framework within which to study these questions further.

The second finding regarding self-harm according to gender is that current impulsive aggression was associated with a lifetime history of self-harm in women, but not in men. In our sample, women with self-harm had higher mean scores on current impulsive aggression than both women without self-harm and men with or without self-harm. It should be noted that the interaction between gender and impulsive aggression was significant after all other variables had been entered in the multivariate analyses. It is thus less likely that this finding is an artefact of systematic differences in levels of other current symptoms between groups. I would instead suggest that it could be an indication of a more trait-like vulnerability for self-harm in some patients with schizophrenia. The results from study II of this thesis add to this picture by showing that it is the patients with both suicide attempts and non-suicidal self-harm who report

elevated levels of impulsive aggression, compared to patients with suicide attempts only and patients with no history of suicide attempts.

5.1.4 Prevalence of suicide attempt and non-suicidal self-harm in patients with schizophrenia

This thesis is, to my knowledge, the first to report the lifetime prevalence of a history of non-suicidal self-harm in patients with schizophrenia and the first to explore the clinical characteristics associated with a history of lifetime suicide attempts with or without non-suicidal self-harm. We found that the lifetime history of non-suicidal self-harm (30%) and suicide attempts (35%) was relatively frequent. A lifetime history of both suicide attempts and non-suicidal self-harm was present in 36 patients (14%) and 52 patients (21%) had a lifetime history of suicide attempts only. The non-suicidal self-harm usually carried little death risk, was often highly repetitive, and in most cases involved cutting. These results are consistent with findings in studies of non-psychotic psychiatric samples (Andover & Gibb, 2010; Briere & Gil, 1998; Claes et al., 2010) and suggest that non-suicidal self-harm in patients with schizophrenia is similar to that seen in non-psychotic clinical samples in terms of lethality, frequency and methods.

5.1.5 Clinical characteristics associated with a history of both suicide attempts and non-suicidal self-harm

We found that a history of both suicide attempts and non-suicidal self-harm in patients with schizophrenia is associated with an earlier onset of psychotic symptoms and a longer duration of untreated psychosis compared to patients with suicide attempts only or with no history of suicide attempts. A history of both lifetime suicide attempts and non-suicidal self-harm was more common in women, and participants with both suicide attempts and non-suicidal self-harm had higher levels of current impulsive aggression and depressive symptoms than the other groups. Furthermore, patients with both suicide attempts and non-suicidal self-harm were more likely to repeat suicide attempts than patients with suicide attempts only.

Depression/depressive symptoms, suicidal ideation, impulsivity and repeated self-harm behaviours are symptoms and behaviours which have been found to be linked to each other and to underlying problems with emotion regulation in other diagnostic groups with high suicide risk, especially BPD (Stanley et al., 2001). Furthermore, a previous study has found an association between affective variability, in particular variability in negative affect, and suicidal ideation in individuals with a high risk of developing schizophrenia (Palmier-Claus, Taylor, Gooding, Dunn, & Lewis, 2012). Thus, one possible interpretation of the findings in the present thesis is that disturbances in emotion regulation may be a underlying mechanism behind the combination of a higher degree of repeated suicide attempts, impulsive aggression and, higher current depressive symptoms in patients with schizophrenia and a history of both non-suicidal self-harm and suicide attempts.

Since we did not interview specifically for personality traits, it is possible that patients with both suicide attempts and non-suicidal self-harm would have shown signs of BPD traits in addition to schizophrenia if these had been checked for. Indeed, studies of patients with prodromal or recent onset schizophrenia have shown that such patients may experience a wide array of comorbid syndromes, including premorbid BPD traits (Hogg, Jackson, Rudd, & Edwards, 1990; Rosen, Miller, D'Andrea, McGlashan, & Woods, 2006). However, the younger age of onset of psychotic symptoms in the patients with both suicide attempts and non-suicidal self-harm could indicate that the emergence of psychotic symptoms during adolescence may increase the risk of self-harm (Kelleher et al., 2012), perhaps to regulate affect.

We did not have an a priori hypothesis regarding the role of duration of untreated psychosis, but included the measure as part of a range of potential risk indicators. It is of clinical importance that patients with both suicide attempts and non-suicidal self-harm had significantly more often longer DUPs while at the same time more than half of this group reported that they had their first treatment contact with mental health services early on, but for reasons other than their psychotic disorder. It is thus unlikely that the observed treatment delay can be explained by an unfamiliarity with mental health services. Rather, we could speculate that the early onset of depression, possibly in combination with repeated self-harm behaviours and/or

other symptoms and behaviour such as suicidal ideation and impulsive aggression, may have drawn the focus away from psychotic symptoms and caused misinterpretation of symptoms or even misdiagnoses, and thus delayed a thorough diagnostic assessment of psychotic symptoms. From this point of view, it is important to note that one-third of patients with both suicide attempts and non-suicidal self-harm did not use any antipsychotic medication at the time of assessment; a significantly higher fraction of non-users than among those with no history of suicide attempts. The higher severity of depressive symptoms and the higher current suicidality in patients with both suicide attempts and non-suicidal self-harm suggest that they are at increased risk of future suicide attempts compared to non-attempters and patients with suicide attempts only.

The younger age of onset of psychotic symptoms, the higher rate of women, and the higher levels of current impulsive aggression compared to non-attempters where specific to the group with both suicide attempts and non-suicidal self-harm. No significant differences in terms of these clinical characteristics were found between non-attempters and patients with suicide attempts only. This suggests that the differences we found in study I concerning these measures between those with or without a lifetime history of self-harm are largely attributable to patients with both suicide attempts and non-suicidal self-harm.

5.1.6 Childhood trauma in patients with both suicide attempts and non-suicidal self-harm

In line with previous research (Alvarez et al., 2011; Conus et al., 2010; Darves-Bornoz et al., 1995; Roy, 2005; Ucok & Bikmaz, 2007), we have found that elevated levels of childhood trauma were associated with a history of suicide attempts in patients with schizophrenia. Our study adds to current knowledge in that it suggests that the association between childhood trauma and suicide attempts differs depending on whether or not the patient has a history of non-suicidal self-harm. While childhood abuse was elevated across all subtypes of trauma in patients with both suicide attempts and non-suicidal self-harm, childhood trauma was elevated only on two subscales in patients with suicide attempts only: the subscales childhood emotional- and physical abuse. Childhood sexual abuse, the type of trauma most often studied in previous

research (Alvarez et al., 2011; Darves-Bornoz et al., 1995; Roy, 2005; Ucok & Bikmaz, 2007), was almost twice as prevalent in patients with a history of both suicide attempts and non-suicidal self-harm than in patients with suicide attempts only and no self-harm. Childhood emotional abuse was the type of trauma most strongly associated with a history of suicide attempts only and, with a history of both suicide attempts and non-suicidal self-harm.

5.1.7   Childhood emotional abuse and type of self-harm adjusted for illness history and current symptom

We have found that the association between childhood emotional abuse and a history of both suicide attempts and non-suicidal self-harm was reduced and no longer significant when we adjusted for onset of depressive and psychotic symptoms and higher levels of current symptoms. The underlying assumption is that the early onset of depressive or psychotic symptoms and higher levels over time of affective or impulsive aggressive symptoms may partly or fully mediate the association between childhood emotional abuse and a history of both suicide attempts and non-suicidal self-harm. However, since the main outcome variable was a lifetime history of self-harm, and since the temporal relationship between variables cannot be studied using the present design, the study should be interpreted as hypothesis-generating. There are some important reasons that this hypothesis should be further explored. Firstly, childhood trauma has been established as a risk factor for suicidal behaviour in non-psychotic samples and first-episode psychosis patients with past sexual and/or physical abuse were more likely to attempt suicide during treatment (Conus et al., 2010). Secondly, the same pattern emerged when including only patients with self-harm episodes during the last year. This finding is consistent with the assumption that childhood exposure to trauma were before the most recent self-harm episode and that self-harm is reported after onset of depressive or psychotic symptoms. However, it is not evidence for a causal relationship. Thirdly, a previous study has shown that the combination of depressive and psychotic symptoms during adolescence is a very strong risk factor for suicide attempts or suicide plans (Kelleher et al., 2012). Finally, the association between childhood emotional abuse and a history of suicide attempts only remained unaffected by adjustment for onset of symptoms and current levels of depression and impulsive aggression, suggesting specificity to patients with both suicide attempts and non-suicidal self-harm. However, other potential explanations exist. For example, an underlying

shared vulnerability, that an elevated emotional reactivity to stress may explain both the increased risk of (negative consequences of) childhood trauma, impulsive aggression, the early onset of psychotic/depressive symptoms, and self-harm (Brodsky & Stanley, 2008; Myin-Germeys & van Os, 2007). Thus, these findings are consistent with, but not evidence of, a hypothesis that childhood emotional abuse may increase the risk of a history of both suicide attempts and non-suicidal self-harm through early onset of depressive or psychotic symptoms and subsequent higher levels of affective or impulsive aggressive symptoms.

Both these interpretations are consistent with the stress diathesis model for suicidal behaviour (Mann et al., 1999). However, the finding from this thesis that patients with both non-suicidal self-harm and suicide attempts have significantly more repeated suicide attempts and higher depression scores than patients with suicide attempt only, may be better understood in light of Joiners interpersonal theory of suicidal behaviour (Joiner, 2005). His model states that attempting suicide requires both a desire and a capability. As described earlier, Klonsky et al (2013) suggested that non-suicidal self-harm may be an especially important risk factor for suicide attempts, since when present, it is associated with both an increased desire (hopelessness, depression) and increased capability for suicide. The finding from previous research that patients with schizophrenia and a lifetime history of suicide attempt are more likely to report non-suicidal self-harm than non-attempters during their most severe period of depression (Restifo et al., 2009) or during their most recent hospitalization (Shoval et al., 2006), seems compatible with this suggestion. As does the finding from this thesis that patients with a lifetime history of both non-suicidal self-harm and suicide attempts report more repeated suicide attempts and higher depression scores than patients with suicide attempt only. That said, it should be emphasized that this thesis is not designed to test the theoretical models.

However, the data presented in this thesis suggest that patients with a history of both suicide attempts and non-suicidal self-harm represent a distinct subgroup of patients with schizophrenia with their elevated childhood exposure to trauma, the early onset of psychotic symptoms, significant treatment delay, a high rate of repeated suicidal behaviour, and elevated

levels of current depressive and impulsive aggressive symptoms compared to other patients with schizophrenia.

5.2 Methods discussion

5.2.1   Design

All three studies in this thesis have a cross-sectional design. The relatively large sample limits the risk of imprecision associated with small samples in the estimation of population parameters. However, the presence of systematic bias is not affected by sample size and biases may have occurred in these studies. Systematic bias can result from a number of sources, including information bias or selection bias. The issues of validity and reliability of the measurements, the representativity of the sample, and the generalizability of the findings will be discussed later.

The most important limitation to the cross-sectional design is that the temporal sequence of variables being studied is unknown, and that the design cannot differentiate causes and effects from associations. For example, in Study III, the temporal sequence between childhood trauma, onset of depressive and psychotic symptoms and self-harm is largely unknown. As discussed above, we could only assume that childhood exposure to trauma lead to self-harm in individuals with schizophrenia and that the early onset of depressive or psychotic symptoms may be a pathway to suicide attempts and non-suicidal self-harm in individuals with childhood exposure to trauma. In hindsight, if we had collected detailed data on the age of onset and a more detailed history of the interplay between suicide attempts and non-suicidal self-harm, we may have known more about the temporal relationship between suicide attempts, non-suicidal self-harm and the age of onset of psychotic or depressive episodes.

In all three studies we measured self-harm retrospectively. Information on self-harm may thus have been affected by recall bias. Although such bias cannot be ruled out, measures were taken to reduce the influence of recall bias. Most importantly, information on the history of self-harm was gathered from multiple sources in all three studies: specific questions about the prevalence

and characteristics of self-harm episodes, responses to questions in the SCID-I interview (First et al., 1995), and hospital records. Another limitation to the cross-sectional design in the context of this thesis is that it provides a snapshot of the prevalence of, and clinical characteristics associated with, a lifetime history of self-harm. Since the time of assessment was in most cases remote from the most recent episode of self-harm, the present studies are not suited to measuring immediate stress/trigger variables for self-harm. This is a limitation shared with most previous studies of risk factors for self-harm in schizophrenia, including the prospective studies. But it is an important limitation, since the impact of environmental factors and the (changes in) proximal risk factors for self-harm remains more or less unknown. Furthermore, individuals not reporting self-harm currently, may have future episodes of self-harm. As mentioned previously, an underestimation may also result from selective survival since all three studies included patients in all phases of the disorders. Thus, some individuals with a history of self-harm may not have been included, due to suicide. Prospectively following a cohort of individuals with schizophrenia over time, would have provided better prevalence estimates and, in particular, better control over the temporal sequence of the studied variables.

That said, prospective cohort studies are demanding, both practically and economically. Studying risk factors for self-harm according to gender, and studying non-suicidal self-harm in individuals with suicide attempts and schizophrenia, are areas of suicide research where current knowledge is very limited. In a situation such as this, the cross-sectional design provides an initial first step in the efforts to describe and examine patterns of associations in order to develop better hypotheses about causal relationships.

5.2.1   Sample representativity

Patients in the TOP study were recruited consecutively from in- and outpatient psychiatric units at the hospitals participating in the study. These units provide publicly funded mental health care for the entire population within their catchment area and with a similar quality of care across districts, regardless of socio-economic and socio-cultural differences. Recruiting both in- and outpatients may have contributed to a diversified sample in terms of current symptom

levels. Thus we expected that the TOP study sample would be representative of the population of patients with schizophrenia who are treated within a publicly funded health-care system.

Patients with a suspected or confirmed psychotic disorder were invited to participate in the study by the clinician in charge of their treatment. Some patients declined this invitation, and a very small additional group of patients declined to go further after the initial assessment by the TOP interviewer. Under regulations from the Norwegian Data Inspectorate, researchers are not permitted to obtain information about patients who do not provide informed consent. Thus, no data about these patients have been registered. Furthermore, no national hospital discharge register with diagnoses was available. We were thus unable to gather data on patients who were either not invited to participate by their clinician or who declined to participate. This made it impossible to estimate the rate of participation. Accordingly, measures were taken to facilitate the inclusion of all eligible patients. The TOP interviewers were located at the various treatment units, regularly participating in meetings and maintaining close contact with the clinicians in charge of treatment. This procedure made it easier for the TOP interviewers and clinicians to discuss potential cases on a daily basis and to provide information about and strengthen clinicians' on-going awareness of the study. Nonetheless, we cannot rule out the possibility that some eligible patients may have failed to be referred for inclusion in the study. Some clinicians may have refrained from referring patients due to a lack of motivation or scepticism of the study or of clinical research in general. Our general impression, however, was that many clinicians were highly cooperative and even tended to refer more patients than those eligible, presumably because they felt the thorough assessment conducted by the TOP interviewer was useful. All in all, however, I would assume that there exists some degree of selection bias in that patients who lacked the capacity to provide informed consent and patients with severe cognitive deficits, paranoid ideation, or patients generally less adherent to treatment, would tend to decline to participate. There are indications that patients with schizophrenia in the TOP sample were relatively high-functioning with mean IQ-scores within the normal range (Jonsdottir et al., 2013). This is only natural since the study systematically excluded patients with IQ-scores below 70. Concerning other aspects of the sample characteristics, Ringen at al. (2008) found no statistically significant differences in the mean age, gender distribution, or prevalence rates of illicit drug use when comparing patients from the

TOP study sample (n=148) to all other patients with psychotic and affective disorders (ICD-10, F 20 – F 39) treated at the psychiatric units at the then called Ullevål University Hospital (n= 849) in Oslo in 2003 - 2005 (WHO, 1993).

In conclusion, although efforts were made to reduce the selection bias as much as possible, there are indications, although not systematically studied, that patients with a very low level of functioning or low adherence to treatment might be underrepresented in the TOP study sample. This is an important potential limitation: findings from study I in this thesis and studies of suicide in individuals with schizophrenia (Hawton et al., 2005) find that non-adherence to medication/treatment increases the risk of suicidal behaviour. If this is the case, the present study might have underestimated the prevalence of self-harm in patients with schizophrenia. Although this is a challenge shared with all studies of self-harm requiring informed written consent, any generalization of the findings in this thesis to this subgroup should be made with caution.

Importantly, the sample excludes some groups of individuals with schizophrenia. Firstly, the TOP study invites only patients in treatment at hospitals with psychiatric units. Thus, individuals with schizophrenia not in treatment due to undetected illness or individuals treated solely in primary health care were not included in the TOP study. However, it is likely that most individuals with schizophrenia are in contact with specialist mental health care at some point, due to the severity of the illness. Secondly, only patients able to speak and understand a Scandinavian language were included. Thus parts of the migrant population are excluded, in which the rate of individuals with schizophrenia may be higher than in the majority population (McGrath et al., 2004). It is not known how these excluded patients may differ from the included patients regarding self-harm, but generalization of the findings from this thesis to this group should be made with caution.

5.2.2 Validity and reliability of measurement

5.2.2.1 General clinical assessment

The instruments used to determine diagnoses and measure symptoms in the TOP study are all widely used and accepted within schizophrenia research. All the TOP research interviews were conducted by clinical psychologists or medical doctors who underwent a general training programme for the main clinical instruments, SCID-I, PANSS and GAF. Furthermore, all TOP interviewers were supervised at regular diagnostic consensus meetings led by an experienced clinical professor in the field of diagnostics of severe mental disorders. The inter-rater reliability of diagnoses (SCID-I), PANSS and GAF was found to be satisfactory and is detailed in the Methods section.

5.2.2.2 Assessment of self-harm

The broad concept of self-harm (previously deliberate self-harm) was chosen as an overarching term in the present thesis to describe non-fatal, intentional self-harm. Most previous research into self-harm in individuals with schizophrenia has focused solely on self-harm with suicidal intent, i.e. suicide attempts. One consequence of focusing solely on suicide attempts is that the potential role of non-suicidal self-harm as a predictor of future suicidal behaviour in people with psychosis has remained unexplored until recently (Fedyszyn et al., 2012). Furthermore, the concept of suicidal intent is not easily delineated and measured. Firstly, it is likely that both suicide attempts and non-suicidal self-harm have multiple intents and functions. While a suicide attempt is an important risk factor for suicide, most individuals with suicide attempts will die from reasons other than suicide. Individuals that make suicide attempts also report other complex and seemingly contradictory motives or reasons for their behaviour (Brown et al., 2002; Hjelmeland et al., 2002). Secondly, although motives and reasons given for suicide attempts and non-suicidal self-harm differs, they also overlap extensively (Brown et al., 2002; Maddock, Carter, Murrell, Lewin, & Conrad, 2010). In one study of women with borderline personality disorder almost all participants reported that one reason for both suicide attempts and non-suicidal self-harm was to relieve negative emotions (Brown et al., 2002). And finally, if self-harm behaviour is severe enough to require hospital treatment, self-reported suicidal intent does not predict who will later die from suicide (Cooper et al., 2005). As a substantial part of self-harm

behaviours with and without expressed suicidal intent may have overlapping or common functions, the concept of self-harm is robust since it takes into account the heterogeneity of reported motives.

On the other hand, there is substantial evidence that suicide attempts and non-suicidal self-harm can to some degree be differentiated, in terms of intention, function, frequency and lethality. For example, non-suicidal self-harm often has lower lethality than suicide attempts and tends to occur more frequently than suicide attempts in clinical samples (Andover et al., 2012; Guertin et al., 2001; Hamza et al., 2012; Klonsky, 2007; Muehlenkamp & Gutierrez, 2007). Furthermore, while there is evidence that non-suicidal self-harm may predict future suicide attempts (Fedyszyn et al., 2012; P. Wilkinson et al., 2011), there is less evidence that suicide attempts predict future non-suicidal self-harm (Wichstrom, 2009). My view is that suicide attempts and non-suicidal self-harm are partly overlapping constructs and the validity of differentiating between suicide attempts and non-suicidal self-harm depends on the degree to which they can be reliably differentiated in terms of dimensions such as intention, motives and functions, lethality, repetition, methods, and clinical characteristics across samples.

Based on experiences from a previous European multicentre survey of self-harm in which Norway participated (Hawton et al., 2002; Ystgaard et al., 2003), the self-harm questions were adopted for the purposes of this thesis. The inter-rater reliability of self-harm was not measured in the TOP study. Furthermore, given that we measured the lifetime history of self-harm, recall bias may have occurred. We know from previous research that the reporting of a lifetime history of self-harm may be volatile. A substantial proportion of individuals may report lifetime suicide attempts at one point in time but not when they are assessed years later (Christl, Wittchen, Pfister, Lieb, & Bronisch, 2006). There may be several reasons for this discrepancy, beyond memory problems. The way the individual interprets his or hers own self-harm behaviour may change as time goes by. Furthermore, the individuals' reporting of intent may be influenced by the context and the consequences of acknowledging the intent and may thus change over time (Christl et al., 2006; McKeon, 2009). Whether these factors may cause random error or create systematic bias is not clear, but this is likely to cause some degree of underestimation of prevalence rates. These are challenges shared by all studies reporting on a

lifetime history of self-harm. However, measures were taken in the TOP study to decrease the effect of such biases: firstly, the detailed questions about intention, hospital treatment, lethality, methods, degree of premeditation and the reasons given for the most recent self-harm episode may have decreased the chance of misunderstandings or misclassification of behaviours. Secondly, information from the interview was supplied with information from hospital records. Thirdly, questions about suicidal behaviour were returned to on several occasions throughout the interview, increasing the potential for capturing self-harm episodes. Finally, in cases of doubt regarding classification based on the information recorded from the interview, the TOP interviewers were asked for clarification and the information was rechecked against hospital records. The TOP study interviewers showed satisfactory inter-rater reliability on other measures in TOP, indicating that the inter-rater reliability could be acceptable also in terms of self-harm measures. The general impression from the interviews was that the patients were familiar with the differentiation between non-suicidal self-harm and suicide attempts and did not have any difficulty answering whether or not they had single or repeated episodes of lifetime suicide attempts or non-suicidal self-harm. However, patients did have difficulty reporting the actual number of episodes when the behaviour was highly repetitive, which was the case in some patients with non-suicidal self-harm. This may have led to the underreporting of self-harm episodes, although I assume that this would be limited to a few cases.

5.2.2.3   Assessment of traumatic events in childhood

Traumatic events in childhood were rated using a Norwegian version of the CTQ. The reliability and validity of the CTQ have been demonstrated previously (Bernstein et al., 1994; Larsson et al., 2013). The internal consistency of the total score and subscales was generally good in the present study (III), with one exception: the physical neglect scale had low alpha (0.60) in line with findings from previous studies (Gerdner & Allgulander, 2009). Although low, it could be argued to be within the limit for acceptable alpha values for group comparisons (Streiner & Normann, 1989). Regardless, this finding has limited consequences for the interpretation of findings in study III, since the primary analyses were performed on other subscales with good to excellent internal consistency. However, some other limitations to the assessment of childhood trauma should be addressed: firstly, as in all studies of childhood trauma in adult populations, data on childhood trauma were obtained retrospectively, a weakness that is inherent in the

retrospective design. Psychotic patients' ability to reliably report a history of abuse and neglect has been questioned, for example due to possible difficulties in differentiating delusions from traumatic experiences in childhood. However, the reliability and validity of the retrospective collection of data on childhood traumatic events in patients with psychosis have repeatedly been supported in previous studies (Fisher et al., 2011; Goodman et al., 1999). Furthermore, conducting prospective studies of clinical characteristics of the relationship between childhood trauma and suicidal behaviour in individuals with schizophrenia would be extremely challenging considering the low base rate of schizophrenia and the long follow-up period needed. Secondly, current mood or psychotic symptoms may have led to recall biases as patients may under- or over-report traumatic events depending on their mood. Although this effect cannot be entirely ruled out, a previous study found no association between the current severity of psychotic symptoms or depressed mood and reports of childhood abuse (Fisher et al., 2011). In Study III, childhood emotional abuse was still significantly associated with suicide attempts only and a history of both suicide attempts and non-suicidal self-harm after adjusting for current symptoms: this suggests that such biases do not fully explain the observed associations.

5.2.2.4   Assessment of current symptoms and illness history

Measures of current symptoms, such as depression, insight into illness, and suicidal behaviour were based on widely used and accepted measures in schizophrenia research with one exception: the use of the PANSS item G14 impulsive aggression. The inter-rater reliability of PANSS single items was not measured in the TOP study. Although the variable exhibited a significant correlation with PANSS items on anger and emotional lability, indicating that it measured aspects related to emotional dysregulation, this measure should be considered a crude proxy for emotional dysregulation. The assessment of illness history variables, such as the age of onset, age at first treatment, depressive episodes, and the duration of illness is retrospectively gathered and vulnerable to recall bias. As was the case with the self-harm, these variables were based on all available information and interview data was cross-checked with hospital records, thereby decreasing the likelihood of inaccurate data. Furthermore, studies indicate that persons with schizophrenia report with the same level of consistency as persons without schizophrenia about premorbid functioning (Brill et al., 2007).

5.3 Strengths, limitations and future research

The major limitations of the three studies in this thesis is the cross-sectional design which inhibits the inference of causal relationships and the use of retrospectively collected data with the potential for recall bias. The time of most recent episode of self-harm was in many cases remote from the time of assessment, prohibiting the study of risk factors more proximal to self-harm behaviour. The lack of data on the patients age at the time of suicide attempts and non-suicidal self-harm strongly limits the available knowledge of the temporal sequence of self-harm relative to other clinical characteristics. Furthermore, we cannot rule out the possibility that our findings of an association between childhood abuse, time of onset of psychotic or depressive symptoms, and type of self-harm history could be better explained by biological or other characteristics underlying all of the salient variables associated with a life-time history of both suicide attempt and non-suicidal self-harm. Thus, the proposed relationships should be viewed as hypothesis generating and have to be supported or rejected through testing in prospective longitudinal designs. Lastly, the relatively small size of the groups of interests in some analyses increases the risk of Type II error. Findings must thus be interpreted with some caution.

The studies presented in this thesis have several strengths. The naturalistic multi-site cross-sectional design with participants consecutively recruited from the publically funded catchment area based mental health service systems serving all socioeconomic classes makes the sample reasonably representative of all patients treated in mental health care in Norway. The study variables were not scored solely on the basis of medical charts, as in many previous studies, but based on thorough and detailed face-to-face interviews with all participants performed by qualified clinical interviewers, trained in the use of measures with good psychometric properties. A substantial proportion of previous research in this area has been based on small samples. Thus, the relatively large samples, in particular in Study I, should be considered a strength bearing in mind the detailed information collected on a wide range of clinical characteristics that allowed for multivariate testing and exploration of subgroup relationships.

5.3.1 Future research

The hypothesis that there are different pathways into suicidal behaviour depending on the presence or absence of non-suicidal self-harm should be further investigated. One important question in this regard will be to investigate whether failure to regulate emotions is mediating the development of suicidal behaviour among patients with schizophrenia and non-suicidal self-harm. The translational research design of the TOP study may provide a valuable platform for further investigations of the interplay between clinical-, neurocognitive-, and biological characteristics in this regard. Research into the complex interplay between factors that contribute to self-harm in individuals with schizophrenia has been hampered by methodological limitations, most notably by the problems concerning ecological validity and accuracy of retrospective self-report and interview measures. To further explore the hypotheses presented in this thesis, prospective studies are warranted where the concurrent development of thoughts, feelings, psychotic/affective symptoms and behaviours in daily life are studied in relation to self-harm and in light of precipitating factors. Ecological Momentary Assessment (EMA) is a promising method to reach this goal. EMA has been shown to be a feasible and valid approach to data collection in people with schizophrenia (Granholm, Ben-Zeev, Fulford, & Swendsen, 2013; Granholm, Loh, & Swendsen, 2008) and people with psychosis and suicidal behaviour (Palmier-Claus, Shryane, Taylor, Lewis, & Drake, 2013; Palmier-Claus et al., 2012). EMA may contribute with information that is inaccessible in studies using retrospective self-report and interview data as well as in laboratory studies since the method permits real-time assessment and is thus well suited to address some of the limitations of previous research. Better and more direct measures of daily life-events, emotional dysregulation, suicidal behaviour, and self-harm are needed to better understand the complex interplay between these variables. EMA could prove especially well-suited to measure fluctuations in such clinical characteristics over short periods of time in relation to the urges to attempt suicide or engage in non-suicidal self-harm behaviour. Developing a better understanding of the interplay between environmental factors, patient characteristics and self-harm behaviours in patients with schizophrenia may provide a valuable foundation for the development of better interventions for this group at high risk for suicide.

5.4 Implications

The findings presented in this thesis suggest that the assessment and treatment of depression alone are likely to be insufficient to understand and prevent suicidal behaviour and self-harm in patients with schizophrenia. Several other potentially modifiable clinical characteristics were associated with self-harm in the multivariate analyses. The findings suggest that efforts to prevent episodes of self-harm in patients with schizophrenia should also focus on adherence to treatment of the primary disorder and close monitoring and counteracting of the discouragement that can arise from the awareness of having a mental disorder, especially in men and early in the course of illness. Furthermore, the higher levels of childhood exposure to trauma, the early onset of psychotic symptoms, the high rate of repeated suicide attempts, and elevated levels of current depressive and impulsive aggressive symptoms in patients with a history of both suicide attempts and non-suicidal self-harm suggest that these patients may have longstanding problems with emotion regulation and be at high risk of suicidal behaviours also in the future. Given the challenges these behaviours constitute for the patient as well as for treatment providers, it may be necessary to develop adjunctive treatment interventions that specifically target repeated self-harm behaviours. The adaptation of elements from effective psychosocial treatments for repeated self-harm behaviours in people with BPD (Linehan, 1993) for patients with schizophrenia with a similar pattern of repeated self-harm and emotional dysregulation, may be one option to pursue.

6 Conclusions

This thesis has presented a study using a large clinical sample to report on a wide range of characteristics of self-harm in patients with schizophrenia according to gender. The prevalence of a lifetime history of self-harm and the frequency of repetition were high and the severity of the last episode of self-harm was strong. Men and women shared important clinical characteristics associated with a lifetime history of self-harm in patients with schizophrenia, such as having had a depressive episode, a younger age at psychosis onset, alcohol abuse or dependence in the last six months, current suicidal and depressive symptoms, and low adherence to prescribed medication. However, specific differences according to gender were also found. Gender significantly modified the effect of two clinical characteristics associated with self-harm: a greater awareness of having a mental disorder was associated with self-harm in men only, and impulsive aggression was associated with self-harm in women only.

The findings presented in this thesis suggest that patients with both suicide attempts and non-suicidal self-harm represent a distinct subgroup of patients with schizophrenia by way of their elevated childhood exposure to trauma, the early onset of psychotic symptoms, a significant treatment delay, the high rate of repeated suicide attempts, and higher levels of current depressive and impulsive aggressive symptoms compared to patients with suicide attempts only or non-attempters. We hypothesize that childhood trauma may be linked to suicide attempts in patients with non-suicidal self-harm through the early onset of depressive or psychotic symptoms and current depressive or impulsive aggressive symptoms. The findings in this thesis lend support to the further testing of the hypothesis that schizophrenia patients with suicide attempts with and without non-suicidal self-harm have different pathways to suicidal behaviour.

7 References

Acosta, F. J., Aguilar, E. J., Cejas, M. R., & Gracia, R. (2013). Beliefs about illness and their relationship with hopelessness, depression, insight and suicide attempts in schizophrenia. *Psychiatr Danub, 25*(1), 49-54.

Addington, D., Addington, J., & Maticka-Tyndale, E. (1994). Specificity of the Calgary Depression Scale for schizophrenics. *Schizophrenia Research, 11*(3), 239-244.

Addington, D., Addington, J., Maticka-Tyndale, E., & Joyce, J. (1992). Reliability and validity of a depression rating scale for schizophrenics. *Schizophrenia Research, 6*(3), 201-208. doi: http://dx.doi.org/10.1016/0920-9964(92)90003-N

Addington, D., Addington, J., & Schissel, B. (1990). A depression rating scale for schizophrenics. *Schizophrenia Research, 3*(4), 247-251. doi: 0920-9964(90)90005-R [pii]

Addington, D. E., & Addington, J. M. (1992). Attempted suicide and depression in schizophrenia. *Acta Psychiatrica Scandinavica, 85*(4), 288-291.

Agerbo, E. (2007). High income, employment, postgraduate education, and marriage: a suicidal cocktail among psychiatric patients.[erratum appears in Arch Gen Psychiatry. 2008 Feb;65(2):144]. *Archives of General Psychiatry.64(12):1377-84,*.

Alaraisanen, A., Miettunen, J., Rasanen, P., Fenton, W., Koivumaa-Honkanen, H. T., & Isohanni, M. (2009). Suicide rate in schizophrenia in the Northern Finland 1966 Birth Cohort. *Social Psychiatry and Psychiatric Epidemiology, 44*(12), 1107-1110. doi: 10.1007/s00127-009-0033-5

Albayrak, Y., Ekinci, O., & Caykoylu, A. (2012). Temperament and character personality profile in relation to suicide attempts in patients with schizophrenia. *Comprehensive Psychiatry, 53*(8), 1130-1136. doi: 10.1016/j.comppsych.2012.04.007

Aleman, A., Kahn, R. S., & Selten, J. P. (2003). Sex differences in the risk of schizophrenia: evidence from meta-analysis. *Archives of General Psychiatry, 60*(6), 565-571. doi: 10.1001/archpsyc.60.6.565

Altamura, A. C., Bassetti, R., Bignotti, S., Pioli, R., & Mundo, E. (2003). Clinical variables related to suicide attempts in schizophrenia patients: A retrospective study. [References]. *Schizophrenia Research, 60*(1), 55.

Altamura, A. C., Mundo, E., Bassetti, R., Green, A., Lindenmayer, J. P., Alphs, L., & Meltzer, H. Y. (2007). Transcultural differences in suicide attempters: Analysis on a high-risk population of patients with schizophrenia or schizoaffective disorder. [References]. *Schizophrenia Research, 89*(1-3), 146.

Alvarez, M. J., Roura, P., Oses, A., Foguet, Q., Sola, J., & Arrufat, F. X. (2011). Prevalence and clinical impact of childhood trauma in patients with severe mental disorders. *The Journal of Nervous and Mental Disease, 199*(3), 156-161. doi: 10.1097/NMD.0b013e31820c751c

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders DSM-IV-TR* (4th. ed.). Washington DC: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders DSM-V* (5th ed.). Washington DC: American Psychiatric Publishing.

Andover, M. S., & Gibb, B. E. (2010). Non-suicidal self-injury, attempted suicide, and suicidal intent among psychiatric inpatients. *Psychiatry Research, 178*(1), 101-105. doi: S0165-1781(10)00158-7 [pii];10.1016/j.psychres.2010.03.019 [doi]

Andover, M. S., Morris, B. W., Wren, A., & Bruzzese, M. E. (2012). The co-occurrence of non-suicidal self-injury and attempted suicide among adolescents: distinguishing risk factors and psychosocial correlates. *Child Adolesc Psychiatry Ment Health, 6*, 11. doi: 10.1186/1753-2000-6-11

Andreassen, O. A., & Steen, V. M. (2011). Schizofreni og genetikk. In B. R. Rund (Ed.), *Schizofreni* (4th. ed., pp. 192-204). Stavanger: Hertevig Akademisk.

Andriopoulos, I., Ellul, J., Skokou, M., & Beratis, S. (2011). Suicidality in the "prodromal" phase of schizophrenia. *Comprehensive Psychiatry, 52*(5), 479-485. doi: 10.1016/j.comppsych.2010.10.011

Asarnow, J. R., Porta, G., Spirito, A., Emslie, G., Clarke, G., Wagner, K. D., . . . Brent, D. A. (2011). Suicide attempts and nonsuicidal self-injury in the treatment of resistant depression in adolescents: findings from the TORDIA study. *Journal of the American Academy of Child and Adolescent Psychiatry, 50*(8), 772-781. doi: 10.1016/j.jaac.2011.04.003

Aukst Margetic, B., Jakovljevic, M., Ivanec, D., Marcinko, D., Margetic, B., & Jaksic, N. (2012). Current suicidality and previous suicidal attempts in patients with schizophrenia are associated with different dimensions of temperament and character. *Psychiatry Research, 200*(2-3), 120-125. doi: 10.1016/j.psychres.2012.04.016

Bai, Y. M., Liu, C. Y., & Lin, C. C. (1997). Risk factors for parasuicide among psychiatric inpatients. *Psychiatric Services.48(9):1201-3,.*

Bakst, S., Rabinowitz, J., & Bromet, E. J. (2010). Antecedents and patterns of suicide behavior in first-admission psychosis. *Schizophrenia Bulletin, 36*(4), 880-889. doi: 10.1093/schbul/sbp001

Bani-Fatemi, A., Polsinelli, G., Kennedy, J. L., & De Luca, V. (2013). Ethnicity and suicide attempt: analysis in bipolar disorder and schizophrenia. *BMC Psychiatry, 13*, 252. doi: 10.1186/1471-244x-13-252

Barak, Y., Baruch, Y., Achiron, A., & Aizenberg, D. (2008). Suicide attempts of schizophrenia patients: a case-controlled study in tertiary care. *Journal of Psychiatric Research, 42*(10), 822-826.

Barak, Y., Knobler, C. Y., & Aizenberg, D. (2004). Suicide attempts amongst elderly schizophrenia patients: A 10-year case-control study. *Schizophrenia Research, 71*(1), 77-81.

Barrett, E. A., Sundet, K., Faerden, A., Nesvag, R., Agartz, I., Fosse, R., . . . Melle, I. (2010). Suicidality before and in the early phases of first episode psychosis. *Schizophrenia Research, 119*(1-3), 11-17. doi: 10.1016/j.schres.2010.03.022

Barrett, E. A., Sundet, K., Simonsen, C., Agartz, I., Lorentzen, S., Mehlum, L., . . . Melle, I. (2011). Neurocognitive functioning and suicidality in schizophrenia spectrum disorders. *Compr.Psychiatry, 52*(2), 156-163. doi: S0010-440X(10)00071-4 [pii];10.1016/j.comppsych.2010.06.001 [doi]

Beck, A. T., Kovacs, M., & Weissman, A. (1979). Assessment of suicidal intention: The Scale for Suicide Ideation. *J.Consult.Clin.Psychol, 47*(2), 343-352. doi: doi: DOI: 10.1037/0022-006X.47.2.343

Bendall, S., Jackson, H. J., Hulbert, C. A., & McGorry, P. D. (2008). Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. *Schizophrenia Bulletin, 34*(3), 568-579. doi: 10.1093/schbul/sbm121

Bernstein, D. P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., . . . Ruggiero, J. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American Journal of Psychiatry, 151*(8), 1132-1136.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., . . . Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse and Neglect, 27*(2), 169-190.

Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., Ohlenschlaeger, J., Le, Q. P., . . . Nordentoft, M. (2007). Suicidal behaviour and mortality in first-episode psychosis: the OPUS trial. *British Journal of Psychiatry - Supplementum.51:s140-6,.*

Bhatia, T., Thomas, P., Semwal, P., Thelma, B. K., Nimgaonkar, V. L., & Deshpande, S. N. (2006). Differing correlates for suicide attempts among patients with schizophrenia or schizoaffective disorder in India and USA. *Schizophrenia Research, 86*(1-3), 208-214. doi: 10.1016/j.schres.2006.04.015

Birchwood, M., Smith, J., Drury, V., Healy, J., Macmillan, F., & Slade, M. (1994). A self-report Insight Scale for psychosis: reliability, validity and sensitivity to change. *Acta Psychiatrica Scandinavica, 89*(1), 62-67.

Briere, J., & Gil, E. (1998). Self-mutilation in clinical and general population samples: prevalence, correlates, and functions. *American Journal of Orthopsychiatry, 68*(4), 609-620.

Brill, N., Reichenberg, A., Rabinowitz, J., Harary, E., Lubin, G., Davidson, M., & Weiser, M. (2007). Accuracy of self-reported premorbid functioning in schizophrenia. *Schizophrenia Research, 97*(1-3), 103-108. doi: 10.1016/j.schres.2007.05.026

Brodsky, B. S., Mann, J. J., Stanley, B., Tin, A., Oquendo, M., Birmaher, B., . . . Brent, D. (2008). Familial transmission of suicidal behavior: factors mediating the relationship between childhood abuse and offspring suicide attempts. *Journal of Clinical Psychiatry, 69*(4), 584-596.

Brodsky, B. S., & Stanley, B. (2008). Adverse childhood experiences and suicidal behavior. *Psychiatric Clinics of North America, 31*(2), 223-235. doi: 10.1016/j.psc.2008.02.002

Brown, M. Z., Comtois, K. A., & Linehan, M. M. (2002). Reasons for suicide attempts and nonsuicidal self-injury in women with borderline personality disorder. *Journal of Abnormal Psychology, 111*(1), 198-202.

Brugnoli, R., Novick, D., Haro, J. M., Rossi, A., Bortolomasi, M., Frediani, S., & Borgherini, G. (2012). Risk factors for suicide behaviors in the observational schizophrenia outpatient health outcomes (SOHO) study. *BMC Psychiatry, 12*, 83. doi: 10.1186/1471-244x-12-83

Carlborg, A., Jokinen, J., Nordstrom, A. L., Jonsson, E. G., & Nordstrom, P. (2010). Attempted suicide predicts suicide risk in schizophrenia spectrum psychosis. *Nordic Journal of Psychiatry, 64*(1), 68-72.

Carter, G., Reith, D. M., Whyte, I. M., & McPherson, M. (2005). Repeated self-poisoning: increasing severity of self-harm as a predictor of subsequent suicide. *The British Journal of Psychiatry, 186*(3), 253-257.

Challis, S., Nielssen, O., Harris, A., & Large, M. (2013). Systematic meta-analysis of the risk factors for deliberate self-harm before and after treatment for first-episode psychosis. *Acta Psychiatrica Scandinavica, 127*(6), 442-454. doi: 10.1111/acps.12074

Chatterton, R. (1995). Parasuicide in people with schizophrenia. *Australian New Zealand Journal of Mental Health Nursing.4(2):83-6,*.

Christl, B., Wittchen, H. U., Pfister, H., Lieb, R., & Bronisch, T. (2006). The Accuracy of Prevalence Estimations for Suicide Attempts. How Reliably Do Adolescents and Young Adults Report Their Suicide Attempts? *Archives of Suicide Research, 10*(3), 253-263.

Claes, L., Muehlenkamp, J., Vandereycken, W., Hamelinck, L., Martens, H., & Claes, S. (2010). Comparison of non-suicidal self-injurious behavior and suicide attempts in patients admitted to a psychiatric crisis unit. *Personality and Individual Differences, 48*(1), 83-87. doi: doi: DOI: 10.1016/j.paid.2009.09.001

Claes, L., Vandereycken, W., & Vertommen, H. (2007). Self-injury in female versus male psychiatric patients: A comparison of characteristics, psychopathology and aggression regulation. *Personality and Individual Differences, 42*(4), 611-621. doi: doi: DOI: 10.1016/j.paid.2006.07.021

Cohen, A. S., Minor, K. S., & Najolia, G. M. (2010). A framework for understanding experiential deficits in schizophrenia. *Psychiatry Research, 178*(1), 10-16. doi: doi: DOI: 10.1016/j.psychres.2009.11.016

Cohen, C. I., Abdallah, C. G., & Diwan, S. (2010). Suicide attempts and associated factors in older adults with schizophrenia. *Schizophrenia Research, 119*(1-3), 253-257. doi: 10.1016/j.schres.2010.03.010

Conus, P., Cotton, S., Schimmelmann, B. G., McGorry, P. D., & Lambert, M. (2010). Pretreatment and outcome correlates of sexual and physical trauma in an epidemiological cohort of first-episode psychosis patients. *Schizophrenia Bulletin, 36*(6), 1105-1114. doi: 10.1093/schbul/sbp009

Cooper, J., Kapur, N., Webb, R., Lawlor, M., Guthrie, E., Mackway-Jones, K., & Appleby, L. (2005). Suicide after deliberate self-harm: a 4-year cohort study. *American Journal of Psychiatry, 162*(2), 297-303.

Crowell, S. E., Beauchaine, T. P., & Linehan, M. M. (2009). A biosocial developmental model of borderline personality: Elaborating and extending Linehan's theory. *Psychological Bulletin, 135*(3), 495-510. doi: 10.1037/a0015616

Crumlish, N., Whitty, P., Kamali, M., Clarke, M., Browne, S., McTigue, O., . . . O'Callaghan, E. (2005). Early insight predicts depression and attempted suicide after 4 years in first-episode schizophrenia and schizophreniform disorder. *Acta Psychiatrica Scandinavica, 112*(6), 449-455.

Darves-Bornoz, J. M., Lemperiere, T., Degiovanni, A., & Gaillard, P. (1995). Sexual victimization in women with schizophrenia and bipolar disorder. *Social Psychiatry and Psychiatric Epidemiology, 30*(2), 78-84.

Drake, R. E., Mueser, K. T., & McHugo, G. J. (1996). Clinician rating scales. In L. I. Sederer & B. Dickey (Eds.), *Outcomes assessment in clinical practice.* (pp. 113-116). Baltimore, Md: Willians & Wilkins.

Duno, R., Pousa, E., Miguelez, M., Montalvo, I., Suarez, D., & Tobena, A. (2009). Suicidality connected with mentalizing anomalies in schizophrenia: a study with stabilized outpatients. *Annals of the New York Academy of Sciences, 1167*, 207-211. doi: 10.1111/j.1749-6632.2009.04602.x

El Yazaji, M., Battas, O., Agoub, M., Moussaoui, D., Gutknecht, C., Dalery, J., . . . Saoud, M. (2002). Validity of the depressive dimension extracted from principal component analysis of the PANSS in drug-free patients with schizophrenia. *Schizophrenia Research, 56*(1-2), 121-127. doi: doi: DOI: 10.1016/S0920-9964(01)00247-X

Evren, C., & Evren, B. (2004). Characteristics of schizophrenic patients with a history of suicide attempt. [References]. *International Journal of Psychiatry in Clinical Practice, 8*(4), 227-234.

Favazza, A. R. (1987). *Bodies under siege: Self-mutilation in culture and psychiatry.* Baltimore: The Johns Hopkins University Press.

Fedyszyn, I. E., Robinson, J., Harris, M. G., Paxton, S. J., & Francey, S. (2012). Predictors of suicide-related behaviors during treatment following a first episode of psychosis: the contribution of baseline, past, and recent factors. *Schizophrenia Research, 140*(1-3), 17-24. doi: 10.1016/j.schres.2012.06.022

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, B. W. J. (1995) Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-P), version 2. New York: New York State Psychiatric Institute, Biometrics Research.

Fisher, H. L., Craig, T. K., Fearon, P., Morgan, K., Dazzan, P., Lappin, J., . . . Morgan, C. (2011). Reliability and comparability of psychosis patients' retrospective reports of childhood abuse. *Schizophrenia Bulletin, 37*(3), 546-553. doi: 10.1093/schbul/sbp103

Gerdner, A., & Allgulander, C. (2009). Psychometric properties of the Swedish version of the Childhood Trauma Questionnaire-Short Form (CTQ-SF). *Nordic Journal of Psychiatry, 63*(2), 160-170.

Gladstone, G. L., Parker, G. B., Mitchell, P. B., Malhi, G. S., Wilhelm, K., & Austin, M. P. (2004). Implications of childhood trauma for depressed women: an analysis of pathways from childhood sexual abuse to deliberate self-harm and revictimization. *American Journal of Psychiatry, 161*(8), 1417-1425. doi: 10.1176/appi.ajp.161.8.1417

Glassman, L. H., Weierich, M. R., Hooley, J. M., Deliberto, T. L., & Nock, M. K. (2007). Child maltreatment, non-suicidal self-injury, and the mediating role of self-criticism. *Behav.Res.Ther., 45*(10), 2483-2490. doi: S0005-7967(07)00082-4 [pii];10.1016/j.brat.2007.04.002 [doi]

Goldstein, G., Haas, G. L., Pakrashi, M., Novero, A. M., & Luther, J. F. (2006). The Cycle of Schizoaffective Disorder, Cognitive Ability, Alcoholism, and Suicidality. [References]. *Suicide Life.Threat.Behav., 36*(1), 43.

Gonzalez, V. M. (2008). Recognition of mental illness and suicidality among individuals with serious mental illness. *Journal of Nervous and Mental Disease, 196*(10), 727-734.

Goodman, L. A., Thompson, K. M., Weinfurt, K., Corl, S., Acker, P., Mueser, K. T., & Rosenberg, S. D. (1999). Reliability of reports of violent victimization and posttraumatic stress disorder among men and women with serious mental illness. *J Trauma Stress, 12*(4), 587-599. doi: 10.1023/A:1024708916143

Granholm, E., Ben-Zeev, D., Fulford, D., & Swendsen, J. (2013). Ecological Momentary Assessment of social functioning in schizophrenia: impact of performance appraisals and affect on social interactions. *Schizophrenia Research, 145*(1-3), 120-124. doi: 10.1016/j.schres.2013.01.005

Granholm, E., Loh, C., & Swendsen, J. (2008). Feasibility and validity of computerized ecological momentary assessment in schizophrenia. *Schizophrenia Bulletin, 34*(3), 507-514. doi: 10.1093/schbul/sbm113

Gratz, K. L., & Roemer, L. (2008). The Relationship Between Emotion Dysregulation and Deliberate Self-Harm Among Female Undergraduate Students at an Urban Commuter University. *Cognitive Behaviour Therapy, 37*(1), 14-25.

Gratz, K. L., Rosenthal, M. Z., Tull, M. T., Lejuez, C. W., & Gunderson, J. G. (2006). An Experimental Investigation of Emotion Dysregulation in Borderline Personality Disorder. *J.Abnorm.Psychol., 115*(4), 850-855. doi: doi: DOI: 10.1037/0021-843X.115.4.850

Grunebaum, M. F., Oquendo, M. A., Harkavy-Friedman, J. M., Ellis, S. P., Li, S., Haas, G. L., . . . Mann, J. J. (2001). Delusions and suicidality. *American Journal of Psychiatry, 158*, 742-747. doi: 10.1176/appi.ajp.158.5.742

Guertin, T., Lloyd-Richardson, E., Spirito, A., Donaldson, D., & Boergers, J. (2001). Self-mutilative behavior in adolescents who attempt suicide by overdose. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*(9), 1062-1069. doi: S0890-8567(09)60448-2 [pii];10.1097/00004583-200109000-00015 [doi]

Gupta, S., Black, D. W., Arndt, S., Hubbard, W. C., & Andreasen, N. C. (1998). Factors associated with suicide attempts among patients with schizophrenia. *Psychiatric Services, 49*(10), 1353-1355.

Hainsworth, C., Starling, J., Brand, F., Groen, K., & Munro, K. (2011). Trauma and psychotic symptoms: Data from a pediatric mental health inpatient unit. *Journal of Traumatic Stress, 24*(4), 491-494. doi: 10.1002/jts.20666

Hamza, C. A., Stewart, S. L., & Willoughby, T. (2012). Examining the link between nonsuicidal self-injury and suicidal behavior: a review of the literature and an integrated model. *Clinical Psychology Review, 32*(6), 482-495. doi: 10.1016/j.cpr.2012.05.003

Harkavy-Friedman, J. M., Kimhy, D., Nelson, E. A., Venarde, D. F., Malaspina, D., & Mann, J. J. (2003). Suicide Attempts in Schizophrenia: The Role of Command Auditory Hallucinations for Suicide. *Journal of Clinical Psychiatry, 64*(8), 874.

Harkavy-Friedman, J. M., Nelson, E. A., Venarde, D. F., & Mann, J. J. (2004). Suicidal behavior in schizophrenia and schizoaffective disorder: Examining the Role of Depression. *Suicide and Life-Threatening Behavior, 34*, 66-76. doi: 10.1521/suli.34.1.66.27770

Harkavy-Friedman, J. M., Restifo, K., Malaspina, D., Kaufmann, C. A., Amador, X. F., Yale, S. A., & Gorman, J. M. (1999). Suicidal behavior in schizophrenia: characteristics of individuals who had and had not attempted suicide. *American Journal of Psychiatry.156(8):1276-8,*.

Harkavy Friedman, J. M. (2007). Depression and suicidal behavior in schizohrenia. In R. Tatarelli, M. Pompili & P. Girardi (Eds.), *Suicide in schizophrenia* (pp. 99-112). New York: Nova Science Publishers.

Haw, C., Hawton, K., Sutton, L., Sinclair, J., & Deeks, J. J. (2005). Schizophrenia and deliberate self-harm: a systematic review of risk factors. *Suicide and Life-Threatening Behavior, 35*, 50-62. doi: 10.1521/suli.35.1.50.59260

Hawton, K., Appleby, L., Platt, S., Foster, T., Cooper, J., Malmberg, A., & Simkin, S. (1998). The psychological autopsy approach to studying suicide: a review of methodological issues. *Journal of Affective Disorders, 50*(2-3), 269-276.

Hawton, K., Rodham, K., Evans, E., & Weatherall, R. (2002). Deliberate self harm in adolescents: self report survey in schools in England. *British Medical Journal, 325*(7374), 1207-1211.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Deeks, J. J. (2005). Schizophrenia and suicide: systematic review of risk factors. *The British Journal of Psychiatry, 187*(1), 9-20.

Heila, H., Isometsa, E. T., Henriksson, M. M., Heikkinen, M. E., Marttunen, M. J., & Lonnqvist, J. K. (1997). Suicide and schizophrenia: a nationwide psychological autopsy study on age- and sex-specific clinical characteristics of 92 suicide victims with schizophrenia. *American Journal of Psychiatry, 154*, 1235-1242.

Heila, H., Isometsa, E. T., Henriksson, M. M., Heikkinen, M. E., Marttunen, M. J., & Lonnqvist, J. K. (1999). Suicide victims with schizophrenia in different treatment phases and adequacy of antipsychotic medication. *Journal of Clinical Psychiatry, 60*, 200-208.

Hjelmeland, H. (2004). Suicidal behaviour in Norway. In A. Schmidtke, U. Bille-Brahe, A. Kerkhof & D. De Leo (Eds.), *Suicidal behaviour in Europe*. Göttingen, Germany: Hogrefe & Huber.

Hjelmeland, H., Hawton, K., Nordvik, H., Bille-Brahe, U., De, L. D., Fekete, S., . . . Wasserman, D. (2002). Why people engage in parasuicide: a cross-cultural study of intentions. *Suicide & Life-Threatening Behavior.32(4):380-93,.*

Hogg, B., Jackson, H. J., Rudd, R. P., & Edwards, J. (1990). Diagnosing personality disorders in recent-onset schizophrenia. *The Journal of Nervous and Mental Disease, 178*(3), 194-199.

Hooley, J. (2008). Self-harming behavior: Introduction to the special series on non-suicidal self-injury and suicide. *Applied & Preventive Psychology, 12*(4), 155-158.

Horne, R., & Weinman, J. (2002). Self-regulation and Self-management in Asthma: Exploring The Role of Illness Perceptions and Treatment Beliefs in Explaining Non-adherence to Preventer Medication. *Psychology & Health, 17*(1), 17-32.

Huguelet, P., Mohr, S., Jung, V., Gillieron, C., Brandt, P. Y., & Borras, L. (2007). Effect of religion on suicide attempts in outpatients with schizophrenia or schizo-affective disorders compared with inpatients with non-psychotic disorders. *European Psychiatry, 22*(3), 188-194. doi: 10.1016/j.eurpsy.2006.08.001

Häfner, H., & an der Heiden, W. (1999). The course of schizophrenia in the light of modern follow-up studies: the ABC and WHO studies. *European Archives of Psychiatry and Clinical Neuroscience, 249*(4), S14-S26. doi: 10.1007/PL00014180

Iancu, I., Bodner, E., Roitman, S., Piccone Sapir, A., Poreh, A., & Kotler, M. (2010). Impulsivity, aggression and suicide risk among male schizophrenia patients. *Psychopathology, 43*(4), 223-229. doi: 10.1159/000313520

Iancu, I., Sapir, A. P., Shaked, G., Poreh, A., Dannon, P. N., Chelben, J., & Kotler, M. (2006). Increased suicidal risk among smoking schizophrenia patients. *Clinical Neuropharmacology, 29*(4), 230-237. doi: 10.1097/01.wnf.0000228178.75711.eb

Johannessen, J. O. (2011). Schizofreni - klinisk bilde og utbredelse. In B. R. Rund (Ed.), *Schizofreni* (4th. ed., pp. 28-42). Stavanger: Hertevig Akademisk.

Johannessen, J. O., McGlashan, T. H., Larsen, T. K., Horneland, M., Joa, I., Mardal, S., . . . Vaglum, P. (2001). Early detection strategies for untreated first-episode psychosis. *Schizophrenia Research, 51*(1), 39-46.

Joiner, T. E. (2005). *Why people die by suicide*. Cambridge, MA: Harvard University Press.

Jones, J. S., Stein, D. J., Stanley, B., Guido, J. R., Winchel, R., & Stanley, M. (1994). Negative and depressive symptoms in suicidal schizophrenics. *Acta Psychiatrica Scandinavica.89(2):81-7,.*

Jones, S. H., Thornicroft, G., Coffey, M., & Dunn, G. (1995). A brief mental health outcome scale-reliability and validity of the Global Assessment of Functioning (GAF). *The British Journal of Psychiatry, 166*(5), 654-659.

Jonsdottir, H., Engh, J. A. M., Friis, S. M., Ph.D., Birkenaes, A. M., Ringen, P. A. M., Vaskinn, A. P., . . . Andreassen, O. A. M. (2008). Measurement of Insight in Patients With Bipolar Disorder: Are Self-Rated Scales Developed for Patients With Schizophrenia Applicable? [Report]. *Journal of Nervous and Mental Disease, 196*(4), 333-335.

Jonsdottir, H., Opjordsmoen, S., Birkenaes, A. B., Engh, J. A., Ringen, P. A., Vaskinn, A., . . . Andreassen, O. A. (2010). Medication adherence in outpatients with severe mental disorders: relation between self-reports and serum level. *Journal of Clinical Psychopharmacology, 30*(2), 169-175. doi: 10.1097/JCP.0b013e3181d2191e [doi];00004714-201004000-00010 [pii]

Jonsdottir, H., Opjordsmoen, S., Birkenaes, A. B., Simonsen, C., Engh, J. A., Ringen, P. A., . . . Andreassen, O. A. (2013). Predictors of medication adherence in patients with schizophrenia and bipolar disorder. *Acta Psychiatrica Scandinavica, 127*(1), 23-33. doi: 10.1111/j.1600-0447.2012.01911.x

Jovanovic, N., Podlesek, A., Medved, V., Grubisin, J., Mihaljevic-Peles, A., Goran, T., & Lovretic, V. (2013). Association between psychopathology and suicidal behavior in schizophrenia. *Crisis, 34*(6), 374-381. doi: 10.1027/0227-5910/a000211

Kao, Y. C., & Liu, Y. P. (2011). Suicidal behavior and insight into illness among patients with schizophrenia spectrum disorders. *Psychiatric Quarterly, 82*(3), 207-220. doi: 10.1007/s11126-010-9161-z

Kao, Y. C., Liu, Y. P., Cheng, T. H., & Chou, M. K. (2011). Cigarette smoking in outpatients with chronic schizophrenia in Taiwan: relationships to socio-demographic and clinical characteristics. *Psychiatry Research, 190*(2-3), 193-199. doi: 10.1016/j.psychres.2011.05.016

Kao, Y. C., Liu, Y. P., Cheng, T. H., & Chou, M. K. (2012). Subjective quality of life and suicidal behavior among Taiwanese schizophrenia patients. *Social Psychiatry and Psychiatric Epidemiology, 47*(4), 523-532. doi: 10.1007/s00127-011-0361-0

Kaplan, K. J., Harrow, M., & Faull, R. N. (2012). Are there gender-specific risk factors for suicidal activity among patients with schizophrenia and depression? *Suicide and Life-Threatening Behavior, 42*(6), 614-627. doi: 10.1111/j.1943-278X.2012.00116.x

Kay, S. R. (1991). *Positive and negative syndromes in schizophrenia. Assessment and research. Clinical and Experimental Research.* New York: Brunner/Mazel Inc.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull., 13*(2), 261-276.

Kelleher, I., Lynch, F., Harley, M., Molloy, C., Roddy, S., Fitzpatrick, C., & Cannon, M. (2012). Psychotic symptoms in adolescence index risk for suicidal behavior: findings from 2 population-based case-control clinical interview studies. *Archives of General Psychiatry, 69*(12), 1277-1283. doi: 10.1001/archgenpsychiatry.2012.164

Kleinhaus, K., Harlap, S., Perrin, M. C., Manor, O., Weiser, M., Harkavy-Friedman, J. M., . . . Malaspina, D. (2012). Catatonic schizophrenia: a cohort prospective study. *Schizophrenia Bulletin, 38*(2), 331-337. doi: 10.1093/schbul/sbq087

Klonsky, E. D. (2007). The functions of deliberate self-injury: A review of the evidence. *Clinical Psychology Review, 27*(2), 226-239. doi: doi: DOI: 10.1016/j.cpr.2006.08.002

Klonsky, E. D., Kotov, R., Bakst, S., Rabinowitz, J., & Bromet, E. J. (2012). Hopelessness as a predictor of attempted suicide among first admission patients with psychosis: a 10-year cohort study. *Suicide and Life-Threatening Behavior, 42*(1), 1-10. doi: 10.1111/j.1943-278X.2011.00066.x

Klonsky, E. D., May, A. M., & Glenn, C. R. (2013). The relationship between nonsuicidal self-injury and attempted suicide: Converging evidence from four samples. *Journal of Abnormal Psychology, 122*(1), 231-237. doi: 10.1037/a0030278

Klonsky, E. D., & Moyer, A. (2008). Childhood sexual abuse and non-suicidal self-injury: meta-analysis. *Br.J.Psychiatry, 192*(3), 166-170. doi: 192/3/166 [pii];10.1192/bjp.bp.106.030650 [doi]

Kopjar, B., Dieserud, G., & Wiik, J. (2005). Selvpåførte forgiftninger behandlet i sykehus. *Tidsskrift for den Norske Laegeforening, 125*, 1798-1800.

Kraepelin, E. (1919). *Dementia praecox and paraphrenia*. Edimburgh: Livingstone.

Lang, C. M., & Sharma-Patel, K. (2011). The relation between childhood maltreatment and self-injury: a review of the literature on conceptualization and intervention. *Trauma Violence Abuse, 12*(1), 23-37. doi: 10.1177/1524838010386975

Langbehn, D. R., & Pfohl, B. (1993). Clinical correlates of self-mutilation among psychiatric inpatients. *Annals of Clinical Psychiatry, 5*(1), 45-51.

Large, M., Babidge, N., Andrews, D., Storey, P., & Nielssen, O. (2009). Major self-mutilation in the first episode of psychosis. *Schizophrenia Bulletin, 35*(5), 1012-1021. doi: 10.1093/schbul/sbn040

Larsen, T. K., McGlashan, T. H., Johannessen, J. O., Friis, S., Guldberg, C., Haahr, U., . . . Vaglum, P. (2001). Shortened duration of untreated first episode of psychosis: changes in patient characteristics at treatment. *American Journal of Psychiatry, 158*(11), 1917-1919.

Larsson, S., Andreassen, O. A., Aas, M., Rossberg, J. I., Mork, E., Steen, N. E., . . . Lorentzen, S. (2013). High prevalence of childhood trauma in patients with schizophrenia spectrum and affective disorder. *Comprehensive Psychiatry, 54*(2), 123-127. doi: 10.1016/j.comppsych.2012.06.009

Lejoyeux, M., Nivoli, F., Basquin, A., Petit, A., Chalvin, F., & Embouazza, H. (2013). An Investigation of Factors Increasing the Risk of Aggressive Behavior among Schizophrenic Inpatients. *Front Psychiatry, 4*, 97. doi: 10.3389/fpsyt.2013.00097

Levine, S. Z., Bakst, S., & Rabinowitz, J. (2010). Suicide attempts at the time of first admission and during early course schizophrenia: a population based study. *Psychiatry Research, 177*(1-2), 55-59.

Lindenmayer, J. P., Czobor, P., Alphs, L., Nathan, A. M., Anand, R., Islam, Z., & Chou, J. C. (2003). The InterSePT scale for suicidal thinking reliability and validity. *Schizophrenia Research, 63*(1-2), 161-170. doi: S0920996402003353 [pii]

Linehan, M. M. (1993). *Cognitive-behavioral treatment of borderline personality disorder*. New York: Guilford Press.

Longenecker, J., Genderson, J., Dickinson, D., Malley, J., Elvevag, B., Weinberger, D. R., & Gold, J. (2010). Where have all the women gone?: participant gender in epidemiological and non-epidemiological research of schizophrenia. *Schizophrenia Research, 119*(1-3), 240-245. doi: 10.1016/j.schres.2010.03.023

Lui, S. Y. (2009). Risk factors for deliberate self-harm and completed suicide in young Chinese people with schizophrenia. *Australian and New Zealand Journal of Psychiatry, 43*(3), 252-259. doi: 10.1080/00048670802653265

MacDonald, A. W., & Schulz, S. C. (2009). What we know: findings that every theory of schizophrenia should explain. *Schizophrenia Bulletin, 35*(3), 493-508. doi: 10.1093/schbul/sbp017

Maddock, G. R., Carter, G. L., Murrell, E. R., Lewin, T. J., & Conrad, A. M. (2010). Distinguishing suicidal from non-suicidal deliberate self-harm events in women with Borderline Personality Disorder. *Australian and New Zealand Journal of Psychiatry, 44*(6), 574-582. doi: 10.1080/00048671003610104

Madge, N., Hewitt, A., Hawton, K., de Wilde, E. J., Corcoran, P., Fekete, S., . . . Ystgaard, M. (2008). Deliberate self-harm within an international community sample of young people: comparative findings from the Child & Adolescent Self-harm in Europe (CASE) Study. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 49*(6), 667-677. doi: JCPP1879 [pii];10.1111/j.1469-7610.2008.01879.x [doi]

Madsen, T., & Nordentoft, M. (2012). Suicidal changes in patients with first episode psychosis: clinical predictors of increasing suicidal tendency in the early treatment phase. *Early Interv Psychiatry, 6*(3), 292-299. doi: 10.1111/j.1751-7893.2011.00284.x

Mann, J. J., Waternaux, C., Haas, G. L., & Malone, K. M. (1999). Toward a clinical model of suicidal behavior in psychiatric patients. *American Journal of Psychiatry, 256*, 181-189.

Mata Cala, F., Bango Suarez, J., Portugal Fernandez del Ribero, E., Sanchez Cabezudo, A., Ponze Lopez, M., & Santo-Domingo Carrasco, J. (1998). Tentativas de suicidio en pacientes esquizofrenicos. *Anales de Psiquiatria, 14*, 416-419.

Mauri, M. C., Paletta, S., Maffini, M., Moliterno, D., & Altamura, A. C. (2013). Suicide attempts in schizophrenic patients: clinical variables. *Asian Journal of Psychiatry, 6*(5), 421-427. doi: 10.1016/j.ajp.2013.07.001

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiologic Reviews, 30*, 67-76. doi: 10.1093/epirev/mxn001

McGrath, J., Saha, S., Welham, J., El Saadi, O., MacCauley, C., & Chant, D. (2004). A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Medicine, 2*, 13. doi: 10.1186/1741-7015-2-13

McKeon, R. (2009). *Suicidal behavior*. Cambridge, Massachusetts: Hogrefe & Huber Publishers.

McLean, D., Gladman, B., & Mowry, B. (2012). Significant relationship between lifetime alcohol use disorders and suicide attempts in an Australian schizophrenia sample. *Australian and New Zealand Journal of Psychiatry, 46*(2), 132-140. doi: 10.1177/0004867411433211

Meltzer, H. Y., Alphs, L., Green, A. I., Altamura, A. C., Anand, R., Bertoldi, A., . . . Potkin, S. (2003). Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (intersept). *Archives of General Psychiatry, 60*(1), 82-91.

Montross, L. P., Kasckow, J., Golshan, S., Solorzano, E., Lehman, D., & Zisook, S. (2008). Suicidal ideation and suicide attempts among middle-aged and older patients with schizophrenia spectrum disorders and concurrent subsyndromal depression. *The Journal of Nervous and Mental Disease, 196*(12), 884-890. doi: 10.1097/NMD.0b013e31818ec823

Muehlenkamp, J. J., Claes, L., Havertape, L., & Plener, P. L. (2012). International prevalence of adolescent non-suicidal self-injury and deliberate self-harm. *Child Adolesc Psychiatry Ment Health, 6*, 10. doi: 10.1186/1753-2000-6-10

Muehlenkamp, J. J., & Gutierrez, P. M. (2007). Risk for suicide attempts among adolescents who engage in non-suicidal self-injury. *Archives of Suicide Research, 11*(1), 69-82. doi: 10.1080/13811110600992902

Muehlenkamp, J. J., Kerr, P. L., Bradley, A. R., & Adams Larsen, M. (2010). Abuse subtypes and nonsuicidal self-injury: preliminary evidence of complex emotion regulation patterns. *The Journal of Nervous and Mental Disease, 198*(4), 258-263. doi: 10.1097/NMD.0b013e3181d612ab

Muller, D. J., Barkow, K., Kovalenko, S., Ohlraun, S., Fangerau, H., Kolsch, H., . . . Rietschel, M. (2005). Suicide attempts in schizophrenia and affective disorders with relation to some specific demographical and clinical characteristics. *European Psychiatry, 20*, 65-69. doi: 10.1016/j.eurpsy.2004.06.024

Myin-Germeys, I., & van Os, J. (2007). Stress-reactivity in psychosis: evidence for an affective pathway to psychosis. *Clinical Psychology Review, 27*(4), 409-424. doi: 10.1016/j.cpr.2006.09.005

Nangle, J. M., Clarke, S., Morris, D. W., Schwaiger, S., McGhee, K. A., Kenny, N., . . . Donohoe, G. (2006). Neurocognition and suicidal behaviour in an Irish population with major psychotic disorders. *Schizophrenia Research, 85*(1-3), 196-200. doi: 10.1016/j.schres.2006.03.035

Nasjonalt folkehelseinstitutt. (2009). Psykiske lidelser i Norge: Et folkehelseperspektiv. Oslo: Nasjonalt folkehelseinstitutt.

National Institute for Clinical Excellence. (2004). Self-harm. The short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care. *National Clinical Practice Guideline* (16 ed.): The British Psychological Society & The Royal College of Psychiatrists. (Reprinted from: Not in File).

Niehaus, D. J., Laurent, C., Jordaan, E., Koen, L., Oosthuizen, P., Keyter, N., . . . Emsley, R. (2004). Suicide attempts in an African schizophrenia population: an assessment of demographic risk factors. *Suicide and Life-Threatening Behavior, 34*(3), 320-327. doi: 10.1521/suli.34.3.320.42778

Nock, M. K., Borges, G., Bromet, E. J., Cha, C. B., Kessler, R. C., & Lee, S. (2008). Suicide and suicidal behavior. *Epidemiologic Reviews, 30*, 133-154. doi: 10.1093/epirev/mxn002

Nock, M. K., Borges, G., Bromet, E. J., Cha, C. B., Kessler, R. C., & Lee, S. (2012). The epidemiology of suicide and suicidal behavior. In M. K. Nock, G. Borges & Y. Ono (Eds.), *Suicde. Global perspectives from the WHO World Mental health Surveys*. Cambridge: Cambridge University Press.

Nock, M. K., Joiner, T. E., Jr., Gordon, K. H., Lloyd-Richardson, E., & Prinstein, M. J. (2006). Non-suicidal self-injury among adolescents: diagnostic correlates and relation to suicide attempts. *Psychiatry Research, 144*(1), 65-72. doi: 10.1016/j.psychres.2006.05.010

Nock, M. K., & Prinstein, M. J. (2004). A functional approach to the assessment of self-mutilative behavior. *J Consult Clin.Psychol., 72*(5), 885-890. doi: 2004-19094-016 [pii];10.1037/0022-006X.72.5.885 [doi]

Nock, M. K., & Prinstein, M. J. (2005). Contextual features and behavioral functions of self-mutilation among adolescents. *J Abnorm.Psychol., 114*(1), 140-146. doi: 2005-01472-014 [pii];10.1037/0021-843X.114.1.140 [doi]

Nordentoft, M. (2007). Prevention of suicide and attempted suicide in Denmark. Epidemiological studies of suicide and intervention studies in selected risk groups. *Danish Medical Bulletin.54(4):306-69,*.

Nordentoft, M., Jeppesen, P., Abel, M., Kassow, P., Petersen, L., Thorup, A., . . . Jorgensen, P. (2002). OPUS study: suicidal behaviour, suicidal ideation and hopelessness among patients with first-episode psychosis: One-year follow-up of a randomised controlled trial*. *British Journal of Psychiatry, 181 Supplement 43*, s98-s106.

Nordentoft, M., Laursen, T. M., Agerbo, E., Qin, P., Hoyer, E. H., & Mortensen, P. B. (2004). [Change in suicide rates for patients with schizophrenia from 1981 to 1997. A nested case-control study]. [Danish]. *Ugeskrift for Laeger.166(50):4602-6,*.

Nordentoft, M., Mortensen, P., & Pedersen, C. (2011). Absolute risk of suicide after first hospital contact in mental disorder. *Archives of General Psychiatry, 68*(10), 1058-1064. doi: 10.1001/archgenpsychiatry.2011.113

O'Carroll, P. W., Berman, A. L., Maris, R. W., Moscicki, E. K., Tanney, BL, & Silverman, M. M. (1996). Beyond the Tower of Babel: a nomenclature for suicidology [see comments]. *Suicide and Life-Threatening Behavior, 26*(3), 237-252.

Oquendo, M. A., Bongiovi-Garcia, M. E., Galfalvy, H., Goldberg, P. H., Grunebaum, M. F., Burke, A. K., & Mann, J. J. (2007). Sex differences in clinical predictors of suicidal acts after major depression: a prospective study. *American Journal of Psychiatry, 164*(1), 134-141. doi: 164/1/134 [pii];10.1176/appi.ajp.164.1.134 [doi]

Pallanti, S., Quercioli, L., & Hollander, E. (2004). Social anxiety in outpatients with schizophrenia: a relevant cause of disability.[see comment]. *American Journal of Psychiatry.161(1):53-8,*.

Palmer, B. A., Pankratz, V. S., & Bostwick, J. M. (2005). The lifetime risk of suicide in schizophrenia: a reexamination. *Archives of General Psychiatry, 62*, 247-253. doi: 10.1001/archpsyc.62.3.247

Palmier-Claus, J. E., Shryane, N., Taylor, P. J., Lewis, S. W., & Drake, R. (2013). Mood variability predicts the course of suicidal ideation in individuals with first and second episode psychosis. *Psychiatry Research, 206*(2-3), 240-245. doi: 10.1016/j.psychres.2012.11.014

Palmier-Claus, J. E., Taylor, P. J., Gooding, P., Dunn, G., & Lewis, S. W. (2012). Affective variability predicts suicidal ideation in individuals at ultra-high risk of developing psychosis: an experience sampling study. *British Journal of Clinical Psychology, 51*(1), 72-83. doi: 10.1111/j.2044-8260.2011.02013.x [doi]

Pedersen, G., Hagtvet, K. A., & Karterud, S. (2007). Generalizability studies of the Global Assessment of Functioning-Split version. *Comprehensive Psychiatry, 48*(1), 88-94. doi: 10.1016/j.comppsych.2006.03.008

Perala, J., Suvisaari, J., Saarni, S. I., Kuoppasalmi, K., Isometsa, E., Pirkola, S., . . . Lonnqvist, J. (2007). Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Archives of General Psychiatry, 64*(1), 19-28. doi: 10.1001/archpsyc.64.1.19

Pettersen, K., Rydningen, N. N., Christensen, T. B., & Walby, F. A. (2010). Autobiographical memory and suicide attempts in schizophrenia. *Suicide and Life-Threatening Behavior, 40*(4), 369-375. doi: 10.1521/suli.2010.40.4.369

Platt, S., Bille-Brahe, U., Kerkhof, A., Schmidtke, A., Bjerke, T., Crepet, P., . . . et al. (1992). Parasuicide in Europe: the WHO/EURO multicentre study on parasuicide. I. Introduction and preliminary analysis for 1989. *Acta Psychiatrica Scandinavica, 85*(2), 97-104.

Pluck, G., Lekka, N. P., Sarkar, S., Lee, K. H., Bath, P. A., Sharif, O., & Woodruff, P. W. (2013). Clinical and neuropsychological aspects of non-fatal self-harm in schizophrenia. *European Psychiatry, 28*(6), 344-348. doi: 10.1016/j.eurpsy.2012.08.003

Preti, A., Meneghelli, A., Pisano, A., & Cocchi, A. (2009). Risk of suicide and suicidal ideation in psychosis: results from an Italian multi-modal pilot program on early intervention in psychosis. *Schizophrenia Research, 113*(2-3), 145-150. doi: 10.1016/j.schres.2009.06.007

Preti, A., Meneghelli, A., Pisano, A., Cocchi, A., & Team, P. (2009). Risk of suicide and suicidal ideation in psychosis: results from an Italian multi-modal pilot program on early intervention in psychosis. *Schizophrenia Research, 113*(2-3), 145-150.

Qin, P., Mortensen, P. B., Agerbo, E., Westergard-Nielsen, N., & Erikson, T. (2000). Gender differences in risk factors for suicide in Denmark. *The British Journal of Psychiatry, 177*(6), 546-550.

Qin, P., & Nordentoft, M. (2005). Suicide risk in relation to psychiatric hospitalization: evidence based on longitudinal registers.[see comment]. *Archives of General Psychiatry.62(4):427-32,*.

Radomsky, E. D., Haas, G. L., Mann, J. J., & Sweeney, J. A. (1999). Suicidal behavior in patients with schizophrenia and other psychotic disorders. *American Journal of Psychiatry, 156*(10), 1595.

Ran, M. S., Chan, C. L., Xiang, M. Z., & Wu, Q. H. (2003). Suicide attempts among patients with psychosis in a Chinese rural community. *Acta Psychiatrica Scandinavica, 107*(6), 430-435.

Restifo, K., Harkavy-Friedman, J. M., & Shrout, P. E. (2009). Suicidal behavior in schizophrenia: a test of the demoralization hypothesis. *Journal of Nervous and Mental Disease, 197*(3), 147-153.

Retterstøl, N., Ekeberg, Ø., & Mehlum, L. (2002). *Selvmord - et personlig og samfunnsmessig problem*. Oslo: Gyldendal akademisk.

Ringen, P. A., Melle, I., Birkenaes, A. B., Engh, J. A., Faerden, A., Jonsdottir, H., . . . Andreassen, O. A. (2008). Illicit drug use in patients with psychotic disorders compared with that in the general population: a cross-sectional study. *Acta Psychiatrica Scandinavica, 117*(2), 133-138.

Rosen, J. L., Miller, T. J., D'Andrea, J. T., McGlashan, T. H., & Woods, S. W. (2006). Comorbid diagnoses in patients meeting criteria for the schizophrenia prodrome. *Schizophrenia Research, 85*(1-3), 124-131. doi: S0920-9964(06)00159-9 [pii];10.1016/j.schres.2006.03.034 [doi]

Roy, A. (2005). Reported childhood trauma and suicide attempts in schizophrenic patients. *Suicide and Life-Threatening Behavior, 35*(6), 690-693.

Roy, A., Mazonson, A., & Pickar, D. (1984). Attempted suicide in chronic schizophrenia. *British Journal of Psychiatry.144:303-6,.*

Roy, A., & Pompili, M. (2009). Management of schizophrenia with suicide risk. *Psychiatric Clinics of North America, 32*(4), 863-883. doi: 10.1016/j.psc.2009.08.005

Saha, S., Chant, D., & McGrath, J. (2007). A systematic review of mortality in schizophrenia: Is the differential mortality gap worsening over time? *Archives of General Psychiatry, 64*(10), 1123-1131. doi: 10.1001/archpsyc.64.10.1123

Saha, S., Chant, D., Welham, J., & McGrath, J. (2005). A systematic review of the prevalence of schizophrenia. *PLoS Medicine, 2*(5), e141. doi: 10.1371/journal.pmed.0020141

Salama, A. A. (1988). Depression and suicide in schizophrenic patients. *Suicide & Life-Threatening Behavior.18(4):379-84,.*

Schafer, I., & Fisher, H. L. (2011). Childhood trauma and psychosis - what is the evidence? *Dialogues in Clinical Neuroscience, 13*(3), 360-365.

Sevincok, L., Akoglu, A., & Kokcu, F. (2007). Suicidality in schizophrenic patients with and without obsessive-compulsive disorder. *Schizophrenia Research, 90*(1-3), 198-202. doi: 10.1016/j.schres.2006.09.023

Shoval, G., Sever, J., Sher, L., Diller, R., Apter, A., Weizman, A., & Zalsman, G. (2006). Substance Use, Suicidality, and Adolescent-Onset Schizophrenia: An Israeli 10-Year Retrospective Study. [References]. *Journal of Child and Adolescent Psychopharmacology, 16*(6), 775.

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: uses in assessing rater reliability. *Psychological Bulletin, 86*(2), 420-428.

Silverman, M. M., Berman, A. L., Sanddal, N. D., O'Carroll, P. W., & Joiner, T. E. (2007). Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 1: Background, rationale, and methodology. *Suicide Life.Threat.Behav., 37*(3), 248-263.

Simms, J., McCormack, V., Anderson, R., & Mulholland, C. (2007). Correlates of self-harm behaviour in acutely ill patients with schizophrenia. *Psychology & Psychotherapy: Theory, Research & Practice, 80*(1), 39-49.

Skodlar, B., & Parnas, J. (2010). Self-disorder and subjective dimensions of suicidality in schizophrenia. *Comprehensive Psychiatry, 51*(4), 363-366. doi: http://dx.doi.org/10.1016/j.comppsych.2009.11.004

Stanley, B., Gameroff, M. J., Michalsen, V., & Mann, J. J. (2001). Are Suicide Attempters Who Self-Mutilate a Unique Population? *American Journal of Psychiatry, 158*(3), 427-432.

Statistics Norway. (2014). Statbank, Causes of death. Retrieved 04.01.2014, from Statistics Norway https://www.ssb.no/statistikkbanken/selecttable/hovedtabellHjem.asp?KortNavnWeb=dodsarsak&CMSSubjectArea=helse&PLanguage=1&checked=true

Streiner, D. L., & Normann, G. R. (1989). *Health measurement scales: A practical guide to their development and use*. Oxford: Oxford university press.

Suokas, J. T., Perala, J., Suominen, K., Saarni, S., Lonnqvist, J., & Suvisaari, J. M. (2010). Epidemiology of suicide attempts among persons with psychotic disorder in the general population. *Schizophrenia Research, 124*(1-3), 22-28. doi: 10.1016/j.schres.2010.09.009

Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2009). Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophrenia Research, 110*(1-3), 1-23. doi: 10.1016/j.schres.2009.03.005

Tarrier, N., Barrowclough, C., Andrews, B., & Gregg, L. (2004). Risk of non-fatal suicide ideation and behaviour in recent onset schizophrenia--the influence of clinical, social, self-esteem and demographic factors. *Social Psychiatry and Psychiatric Epidemiology, 39*(11), 927-937. doi: 10.1007/s00127-004-0828-3

Taylor, P. J., Gooding, P. A., Wood, A. M., Johnson, J., Pratt, D., & Tarrier, N. (2010). Defeat and entrapment in schizophrenia: the relationship with suicidal ideation and positive psychotic symptoms. *Psychiatry Research, 178*(2), 244-248. doi: 10.1016/j.psychres.2009.10.015

Taylor, P. J., Gooding, P. A., Wood, A. M., & Tarrier, N. (2010). Memory specificity as a risk factor for suicidality in non-affective psychosis: the ability to recall specific autobiographical memories is related to greater suicidality. *Behaviour Research and Therapy, 48*(10), 1047-1052. doi: 10.1016/j.brat.2010.06.001

Tidemalm, D., Langstrom, N., Lichtenstein, P., & Runeson, B. (2008). Risk of suicide after suicide attempt according to coexisting psychiatric disorder: Swedish cohort study with long term follow-up. *BMJ.337:a2205,*.

Tiihonen, J., Lonnqvist, J., Wahlbeck, K., Klaukka, T., Niskanen, L., Tanskanen, A., & Haukka, J. (2009). 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet, 374*(9690), 620-627. doi: 10.1016/s0140-6736(09)60742-x

Tollefsen, I. M., Hem, E., & Ekeberg, O. (2012). The reliability of suicide statistics: a systematic review. *BMC Psychiatry, 12*, 9. doi: 10.1186/1471-244x-12-9

Tormoen, A. J., Rossow, I., Larsson, B., & Mehlum, L. (2012). Nonsuicidal self-harm and suicide attempts in adolescents: differences in kind or in degree? *Social Psychiatry and Psychiatric Epidemiology*. doi: 10.1007/s00127-012-0646-y

Ucok, A., & Bikmaz, S. (2007). The effects of childhood trauma in patients with first-episode schizophrenia. *Acta Psychiatrica Scandinavica, 116*(5), 371-377.

Uzun, O., Tamam, L., Ozculer, T., Doruk, A., & Unal, M. (2009). Specific characteristics of suicide attempts in patients with schizophrenia in Turkey. *Israel Journal of Psychiatry and Related Sciences, 46*(3), 189-194.

Van Orden, K. A., Witte, T. K., Cukrowicz, K. C., Braithwaite, S. R., Selby, E. A., & Joiner, T. E., Jr. (2010). The interpersonal theory of suicide. *Psychological Review, 117*(2), 575-600. doi: 10.1037/a0018697

Ventura, J., Liberman, R. P., Green, M. F., Shaner, A., & Mintz, J. (1998). Training and quality assurance with the Structured Clinical Interview for DSM-IV (SCID-I/P). *Psychiatry Research, 79*(2), 163-173.

WHO. (1993). *The ICD-10 Classification of mental and behavioural disorders. Diagnostic criteria for research.* Geneva: World health organization.

WHO. (2002). World report on violence and health. Geneva: World health organization.

WHO. (2014). Suicide prevention (SUPRE). Retrieved from Suicide prevention (SUPRE) website: http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/index.html

Wichstrom, L. (2009). Predictors of non-suicidal self-injury versus attempted suicide: similar or different? *Archives of Suicide Research, 13*(2), 105-122. doi: 10.1080/13811110902834992

Wilkinson, G., & Bacon, N. A. (1984). A clinical and epidemiological survey of parasuicide and suicide in Edinburgh schizophrenics. *Psychological Medicine, 14*(4), 899-912.

Wilkinson, P., Kelvin, R., Roberts, C., Dubicka, B., & Goodyer, I. (2011). Clinical and Psychosocial Predictors of Suicide Attempts and Nonsuicidal Self-Injury in the Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT). *American Journal of Psychiatry, 168*(5), 495-501. doi: appi.ajp.2010.10050718 [pii];10.1176/appi.ajp.2010.10050718 [doi]

Williams, J. M. G., Crane, C., Barnhofer, T., & Duggan, D. (2005). Psychology and suicidal behaviour: Elaborating the entrapment model. In K. Hawton (Ed.), *Prevention and treatment of suicidal behaviour: From science to practice* (pp. 71–89). Oxford: Oxford University Press.

Xiang, Y. T., Weng, Y. Z., Leung, C. M., Tang, W. K., & Ungvari, G. S. (2007). Quality of life of Chinese schizophrenia outpatients in Hong Kong: relationship to sociodemographic factors and symptomatology. *Australian & New Zealand Journal of Psychiatry.41(5):442-9,*.

Xiang, Y. T., Weng, Y. Z., Leung, C. M., Tang, W. K., & Ungvari, G. S. (2008). Socio-demographic and clinical correlates of lifetime suicide attempts and their impact on quality of life in Chinese schizophrenia patients. [References]. *Journal of Psychiatric Research, 42*(6), 502.

Yan, F., Xiang, Y. T., Hou, Y. Z., Ungvari, G. S., Dixon, L. B., Chan, S. S., . . . Chiu, H. F. (2013). Suicide attempt and suicidal ideation and their associations with demographic and clinical correlates and quality of life in Chinese schizophrenia patients. *Social Psychiatry and Psychiatric Epidemiology, 48*(3), 447-454. doi: 10.1007/s00127-012-0555-0

Ystgaard, M., Hestetun, I., Loeb, M., & Mehlum, L. (2004). Is there a specific relationship between childhood sexual and physical abuse and repeated suicidal behavior? *Child Abuse and Neglect, 28*(8), 863-875.

Ystgaard, M., Reinholdt, N. P., Husby, J., & Mehlum, L. (2003). Villet egenskade blant ungdom. *Tidsskrift for den Norske Laegeforening, 123*, 2241-2245.

Zanarini, M. C., Frankenburg, F. R., Reich, D. B., Fitzmaurice, G., Weinberg, I., & Gunderson, J. G. (2008). The 10-year course of physically self-destructive acts reported by borderline patients and axis II comparison subjects. *Acta Psychiatrica Scandinavica, 117*(3), 177-184.

Zhang, X. Y., Al Jurdi, R. K., Zoghbi, A. W., Chen da, C., Xiu, M. H., Tan, Y. L., . . . Kosten, T. R. (2013). Prevalence, demographic and clinical correlates of suicide attempts in Chinese medicated chronic inpatients with schizophrenia. *Journal of Psychiatric Research, 47*(10), 1370-1375. doi: 10.1016/j.jpsychires.2013.05.024