# Latha Nrugham

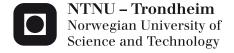
# Associates and predictors of attempted suicide among depressed adolescents

- A 6-year prospective study

Thesis for the degree of Philosophiae Doctor

Trondheim, December 2010

Norwegian University of Science and Technology Faculty of Medicine



# NTNU

Norwegian University of Science and Technology

Thesis for the degree of Philosophiae Doctor

Faculty of Medicine Department of Neuroscience

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My best friend and better half, Keshav Nrugham is the reason for my presence in Norway. As my husband, he shares the journey of my life and has supported the doctoral in countless ways.

Latha Nrugham

#### **Sacred moments**

No words here convey the pain shared via their voices and silences by my young Norwegian research participants with an Indian researcher unseen by them, unknown to them.

No words here convey the privilege I experienced at being trusted with such private moments by these young persons who questioned their entire existence.

No words here convey the sacredness with which I hold those shared moments when the universal transcended race, geography, politics and passport colors.

In trust you gave,

my young fellow-travelers,

in trust I give,

to those who open these pages,

in hope that trust thus shared,

will make life,

worth living with a smile,

despite the pain.

No words here cross the bridge between the meanings of human experience and science, as science is often a bridge away from subjective experiences. Yet, science endeavours to understand human experience and these words here are only a part of such an endeavour.

Aum

# Hellige stunder

Ingen ord her kan formidle smerten som de unge norske deltakerne i prosjektet delte med en indisk forsker som de ikke så og ikke kjente.

Ingen ord her kan formidle hvor privilegert jeg følte meg ved å bli betrodd slike private øyeblikk av disse unge som stilte spørsmål ved hele sin eksistens.

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I tillit dere gav,

mine unge reisefeller,

i tillit jeg gir,

dem som åpner disse sider, i håp om at tilliten som vi deler,

vil gjøre livet,

verdt å leve med et smil,

til tross for smerten.

Ingen ord her kan krysse broen mellom den mening som dannes av menneskelig erfaring og av vitenskap, siden vitenskap ofte er en bro bort fra subjektive erfaringer. Likevel, vitenskap prøver å forstå menneskelig erfaring og ordene her kan bare utgjøre en del av dette forsøket.

Aum

Norsk oversettelse av Prof. Lars Mehlum, Leder, Nasjonalt senter for selvmordsforskning og forebygging, Det medisinsk fakultet, Universitet i Oslo, Norge. Translated into Norwegian by Prof. Lars Mehlum, Director, National Centre for Suicide Research and Prevention, Faculty of Medicine, University of Oslo, Norway.

2. SYNOPSIS (in English): Associates and predictors of attempted suicide among depressed adolescents – A 6-year prospective study

by Latha Nrugham

In this study, the relationship of depression with attempted suicide among adolescents was examined in eight sub-studies. A representative sample of Norwegian school students (T1, N = 2464, mean age 13.7 years, participation rate = 88.3%, females = 50.8%) in grades 8 and 9 was reassessed after one year (T2) with the same questionnaire as at T1. All high scorers ( $\geq$  25) on the Mood and Feelings Questionnaire (MFQ) at T2 were matched for age-and-gender with one control from the low or middle scorers, randomly assigned on a 2:1 basis. This subset (n = 345, participation rate = 94.1%, females = 72.5%) was diagnostically assessed by face-to-face K-SADS-PL interviews (mean age = 14.9 years, SD = 0.5) within 3 weeks of the T2 questionnaires being completed. The subset was again assessed after 5 years (T3) by using the same questionnaire (n = 252) and by the same interviews on telephone (n = 242). The participation rate at T3 was 76.9% (n = 265, mean age = 20.0 years, SD = 0.6, females = 77%).

Irrespective of age and length of time, a history of attempted suicide predicted a future suicidal act. A diagnosis of any depressive disorder predicted attempted suicide among older adolescents. Not living with both biological parents predicted attempted suicide among younger adolescents. Cognitive symptoms dominated the depression profile of suicidal adolescents irrespective of age. Dysthymia by age 15 remained a predictor of suicidal acts between age 15 to 20 while major depression and a depressive episode, not otherwise specified, continued to be significant associates among younger adolescents, even when depressive symptoms were controlled for. Violent life events among older adolescents were

significant associates of suicide attempts while other traumatic events were not. Among those who had experienced violent life events, only those who had been victims of such events were likely to attempt suicide and not those who solely had been witnesses. Higher resilience protected against suicide attempts even in the context of victimization by violence and depression. Resilience, as measured in this study, is considered to be a stable, yet modifiable trait.

Risk factors of attempted suicide during adolescence were both stable and changing. Age should be an important consideration in clinical suicide risk assessments. Perhaps, it is not in the depression *per se*, but rather in the specific nature of the depression together with distinct stressors during adolescence that some of the keys to understand attempted suicide among adolescents lie.

Sammendrag (Synopsis in Norwegian): Samband mellom selvmordsforsøk og depression blant ungdom – risikofaktorer fra en forløpsstudie over 6 år av Latha Nrugham

Et representativt utvalg (T1, N = 2464, svarprosent = 88.3%, jenter = 50.8%) av norsk skoleungdom fra 8. og 9. skoleår med gjennomsnittsalder på 13.7 år ble fulgt opp ett år senere (T2) med samme spørreskjema som ved T1. Alle med høye depresjonsskårer ( $\geq$  25) målt med spørreskjemaet Mood and Feelings Questionnaire (MFQ) ved T2 ble sammenlignet med en kontrollgruppe som besto av dem som hadde lave eller middels depresjonsskårer. De i kontrollgruppen ble tilfeldig trukket ut, og hver av dem ble sammenliknet med to personer i høyskåre-gruppen med samme kjønn og alder. Delutvalget besto av 364 ungdom; totredjedeler av disse hadde altså høye depresjonsskårer. De (n = 345, svarprosent = 94.1%, gjennomsnittsalder = 14.9 år, jenter = 72.5%) ble vurdert klinisk med tanke på mulige psykiatriske diagnoser. Det ble gjennomført ansikt-til-ansikt intervjuer på skolen. K-SADS-PL var hoved instrumentet. Delutvalget ble igjen undersøkt 5 år senere (T3) med det samme spørreskjemaet (n = 252). I tillegg, ble de intervjuet over telefon (n = 242) med samme intervju. Svarprosenten ved T3 var 76.9 % (n = 265, gjennomsnittsalder = 20.0 år, standard avvik = 0.6, jenter = 77%).

Det å ha selvmordsforsøk i sin livshistorie predikerte fremtidige selvmordshandlinger uavhengig av alder. Funnet viste seg gyldig både på kortere og lengre sikt. Det å ha en diagnostisert depressiv lidelse predikerte også selvmordsforsøk blant eldre ungdom. Blant de yngre derimot, var det ikke å bo sammen med begge biologiske foreldre utslagsgivende for selvmordsforsøk. Depressive symptomer av kognitiv art dominerte depresjonsprofilen blant de suicidale ungdommene uavhengig av alder, mens forholdet mellom depressiv lidelse

(diagnose) og suicidale handlinger varierte med alder. En alvorlig depresjonslidelse og en

depresjonslidelse uten nærmere angivelse hang sammen med selvmordsforsøk blant yngre

ungdom. Dystymi predikerte selvmordsforsøk blant eldre ungdom. Voldelige livshendelser

viste seg å utgjøre en risikofaktor for selvmordsforsøk opptil tidlig voksen alder. Ingen slik

sammenheng ble funnet for andre traumatiske opplevelser. Bare de som hadde erfart å være

direkte utsatt for vold, viste økt sannsynlighet for å gjennomføre selvmordsforsøk.

Tilsvarende ble ikke observert blant de som kun var vitne til voldelige hendelser. Høyere

motstandskraft (resiliens) viste seg å beskytte mot selvmordsforsøk selv blant de som hadde

vært ofre for vold og depresjon. Høy motstandskraft (resiliens) er her betraktet som en stabil,

men modifiserbar egenskap.

I denne studien har risikofaktorne ved selvmordsforsøk i ungdomstiden vist seg å være både

stabile (for eks. selvmordsforsøk, kognitive depressive symptomer, opplevelse av voldelige

livshendelser) og varierende (for eks. diagnose av depressive lidelse og boforhold). Ved

klinisk vurdering av selvmordsrisiko er det derfor viktig å ta i betraktning personens alder.

Noe av forklaringen på at ungdom forsøker å ta livet av seg ligger antagelig i kombinasjonen

mellom spesifikke depresjon og de stressorer som ungdommene hadde vært utsatt for, mer

enn i selve depresjonen alene.

Oversatt til Norsk ved hjelp av av Henning Herrestad, Seniorkonsulent, NSSF, UiO. Translated into Norwegian with help from Henning Herrestad, Senior Consultant at NSSF, UiO.

# 3. LIST OF PAPERS

- Nrugham L, Larsson B, Sund AM. 2008. Predictors of suicidal acts across adolescence: Influences of familial, peer and individual factors. *Journal of Affective Disorders*, 109(1-2), 35-45.
- II. Nrugham L, Larsson B, Sund AM. 2008. Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. *Journal of Affective Disorders*, 111(1), 83-93.
- III. Nrugham L, Holen A, Sund AM. 2009. Associations between attempted suicide, violent life events, depressive symptoms, resilience and suicide by early adulthood. *Journal of Nervous and Mental Diseases*, 198(2), 131-136.

# 4. ACRONYMS & ABBREVIATIONS

**CD-RISC** Connor Davidson – Resilience Scale

**C-GAS** Childhood – Global Assessment of Symptoms

CI Confidence Interval

**DD-NOS** Depressive Disorder, Not Otherwise Specified

**DSM** Diagnostic Statistical Manual

**DSM-III-R** Diagnostic Statistical Manual, Third Edition, Revised

**DSM-IV-TR** Diagnostic Statistical Manual, Fourth Edition, Text Revision

**K-SADS-PL** Kiddie – Schedule for Affective Disorders and Schizophrenia – Present

and Lifetime

MDD Major Depressive Disorder

MFQ Mood and Feelings Questionnaire

**SD** Standard Deviation

SPSS Statistical Package for Social Sciences

OR Odds Ratio

T1 Time, Assessment 1 (1998-1999)

**T2** Time, Assessment 2 (1999-2000)

Time, Assessment 3 (2004-2005)

#### 5. INTRODUCTION

#### **Topic**

This dissertation examines the relationship between attempted suicide and depression by studying Norwegian high school adolescents assessed at three time-points: 1998/1999, 1999/2000 and 2004/2005. They were moving out of childhood during their first assessment and into adulthood during their last assessment.

#### Rationale

Guidelines exist for the clinical assessment of suicide risk, despite the absence of a globally accepted definition of suicide risk. The definition of attempted suicide is more complex among adolescents than adults (Shaffer & Waslick, 2002). This complexity makes the assessment of their suicide risk even more difficult. However, there is no method by which an error-free clinical suicide risk assessment may be made. Each such assessment carries with it some uncertainty. Up to 24% of the teenagers who completed suicide had made a prior attempt (Grøholt et al, 1997). Knowledge that can improve this assessment is therefore valuable. This dissertation aims at adding to such knowledge.

In community samples of adolescents, almost ten percent (9.7%) reported a suicide attempt, as estimated by a systematic review (Evans et al, 2005). There is evidence that suicide and attempted suicide are expressions of a continuum of self-harming behaviours (van Heeringen et al, 2000). This includes the strongly increased risk of suicide following attempted suicide. Among adults, more than two thirds of the suicides occur at the first attempt; a history of a suicide attempt is insufficient to predict most suicides (Mann, 2002). The scenario is similar among adolescents. Additional risk factors must therefore be considered.

Early research publications on suicidal phenomena among children and adolescents were clinical in nature, focussing on inpatients (Shaffer, 1974; Pfeffer et al, 1988; 1993). Studies on the outpatient adolescents were rare (Kovacs et al, 1993). Psychological autopsy studies (Kjelsberg et al, 1994; Shaffer et al, 1996; Grøholt et al, 1997; 1998; 1999) and epidemiological ones (Lewinsohn et al, 1994; 1996; 2001) followed these inpatient studies. In two recent reviews, several risk factors have been identified for attempted suicides among adolescents (Gould et al, 2003; Bridge et al, 2006). They were: a previous attempt and a psychiatric diagnosis (notably depression), higher age, female gender, non-intact families, a family history of suicidal behaviour, parental psychopathology, life stressors (notably interpersonal conflict or loss), childhood physical and sexual abuse, poor physical health, physical disability, functional impairment due to physical illness or injury, impulsive aggression, neuroticism, non-heterosexual orientation, exposure to suicide, and availability of lethal agents.

Although suicidality has been studied more among adolescents than among young adults, this later age group is of emerging research interest (Lewinsohn et al, 2001). Strong associations between hopelessness, other depressive symptoms and suicidality may be particularly pronounced among young adults with a vulnerability for depression (Shahar et al, 2006). Cognitive affective depressive symptoms such as sadness and a sense of failure were found by them to be more strongly associated with suicidality than physiological depressive symptoms such as appetite and sleep disturbances. Perhaps, it is not in the depression itself but rather in the specific nature of depression within the context of particular stressors that some of the key relationships of attempted suicide during adolescence may lie.

Research indicates that depression is a clinically significant risk factor in more than half of all suicides (29-88%); and also that it is a major clinical disorder (38-62%) in attempted suicides among adults (Lonnqvist, 2000). This means that only a limited proportion of the clinically depressed will eventually complete suicide. In a clinical sample, the most significant risk factor of suicide among girls was found to be major depression (Brent et al, 1994). However, the gender difference in suicide attempts disappeared when depression was controlled for in a community sample (Wichstrøm & Rossow, 2002). The identification of characteristics which can distinguish depressed suicidal individuals from the depressed yet non-suicidal ones, is therefore most important (van Heeringen et al, 2000).

Suicide is accepted as a psychiatric complication. More than 90% of those who die thus have been found to have a diagnosable psychiatric condition at the time of their death. Among psychiatric complications, mood disorders contribute substantially to the risk of both attempted and completed suicide (Bridge et al, 2006). Yet, additional risk factors are required because most psychiatric patients never attempt suicide (Mann, 2002). Inescapable life situations may influence the basic patterns of coping and the regulation of emotions from which self-destructive behaviour evolve as a maladaptive solution (Mehulm, 2005). Over a period of time, coping styles can develop to become stable traits. When under-controlled or inhibited and well-adjusted three-year olds were followed up to age 21 and compared, a suicide attempt was a common factor among those not well-adjusted at age 3 (Caspi et al, 1996). This finding from a high quality prospective study indicates psychopathology to be a stable trait from childhood into early adulthood. When adolescent suicide attempters were compared to adult suicide attempters, it was found that they had more similarities than differences, indicating the stability of characteristics related to suicidality across

developmental phases (Hjelmland & Grøholt, 2005). Although psychopathology cannot be ignored, it does not explain suicidality completely, either.

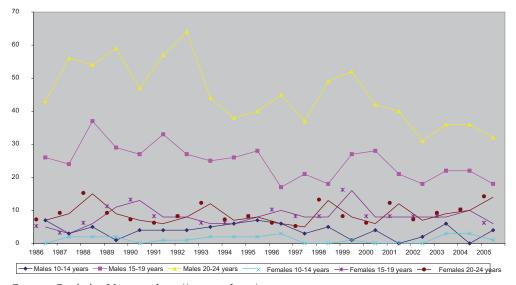
Several theoretical models have been used to explain suicidal phenomena without including or excluding children and adolescents. Some of the well-researched models of suicidal behaviour are the social integration and connectedness model (Durkheim, 1951); the cognitive model (Bedrosian & Beck, 1979); the suicidal career model (Maris, 1981); Baumeister's model of escape (1990); Shneidman's model of unendurable psychological pain (1993); the stress-diathesis model (Mann et al, 1999); the cry of pain model (Williams, 2001); and the differential activation model of cognitive reactivity (Williams et al, 2008). Empirical research on the relationship of attempted suicide to depression also relates more to adults than to adolescents. The absence of theoretical models to explain suicidal phenomena among children and adolescents imply that the developmental aspects which mark these age groups have been neglected. Age was not considered important, it seems.

Children and adolescents respond differently from adults to some pharmacological treatments of depression. Pharmacotherapy in children and adolescents under age 18 with Major Depressive Disorder (MDD) has been controversial (Lam et al, 2009). The benefits of antidepressants are less evident, and the risks include increased suicidality which is defined as worsening of suicidal thoughts and self-harm behaviours. As the management of depression and suicidal risk is not the same across these life phases, it becomes important to consider age when performing clinical suicidal risk assessments. The stress-diathesis model of suicide postulates that a predisposition or vulnerability, the diathesis, is activated during adverse or stressful interactions with the environment and may lead to psychopathology (Mann et al,

1999). Both, associates from cross-sectional studies and predictors from prospective studies provide a risk factor profile which is seen as useful for suicide risk assessments.

The rates of suicide among the young in Norway are given in Figure 1. The stable political and social environment of Norway removes speculation about the influence of major societal adversities such as war and poverty in the investigation of suicidality and depression. Accordingly, this setting is highly suitable to study the relationship between attempted suicide and depression during adolescence.

Figure 1: Suicides among Norwegian aged 10-24 years by gender between 1986-2005.



Source: Statistics Norway. http://www.ssb.no/

#### Theoretical orientation

The studies of this dissertation were based on a modification of the stress-diathesis model of suicidal behaviour among adults (Mann et al, 1999). Durkheim's analysis of suicide (1951) and the cognitive model suggested by Beck and colleagues (1971, 1974a & b, 1979a & b,

1989, 1999) were the other theoretical perspectives used to interpret the findings. As the design of this research study is prospective and covers the entire adolescence, aspects of developmental psychology (Inhelder & Piaget, 1958) were also used to place the findings in context. The choice of models was dictated by the project design and by the availability of study variables.

#### **Key concepts**

Three key concepts run through the three studies of this dissertation.

Adolescence: adolescere = (to) grow, in Latin. Piaget's formal operational stage of cognitive development and Kohlberg's conventional level of moral reasoning begin during adolescence. The transition from adolescence to adulthood is a critical period. It is the time when young people are expected to assume a number of new responsibilities which often include completing their education, obtaining a job and launching a career, becoming financially independent, developing romantic relationships, getting married, becoming a parent, developing an adult social support system, and maintaining good physical health (Rohde et al, 2007). Thus, a multidimensional and expansion-oriented reorganization of life is the hallmark of adolescence.

Attempted suicide: Most suicide researchers agree that the use of inadequate and contradictory definitions of suicidal behaviour is often a limitation in this research and communication (Silverman et al, 2007). The definition of suicide proposed by the father of suicidology, Shneidman (1985) states: "Currently, in the Western world, suicide is a conscious act of self-induced annihilation, best understood as a multidimensional malaise in a needful individual who defines an issue for which suicide is the best perceived solution."

There is an almost inextricable net of similarities and differences between adolescent suicide attempters and completers (Shaffer & Waslick, 2002). This is due to the absence of clear differences between adolescent attempters and completers apart from the gender differences in the choice of method. Adolescent males choose irreversible methods such as guns; while females choose reversible ones such as poisoning, just as adult males and females do. Adult completers have higher suicidal intent than adult attempters. It is pertinent to note that in a nationally representative sample, two-thirds of the Norwegian adolescents who responded positively to deliberately harming themselves also stated that one of the motives of the act was to die (Ystgaard, et al, 2003).

The recently developed suicidal risk analysis among children and adolescents, the Columbia Classification Algorithm of Suicide Assessment (6-17 years of age) defines a suicide attempt as: 'A potentially self-injurious behaviour, associated with at least some intent to die, as a result of the act. Evidence that the individual intended to kill him/herself, at least to some degree, can be explicit or inferred from the behaviour or circumstance. A suicide attempt may or may not result in actual injury.' (Posner et al, 2007). These acts are differentiated from preparatory acts towards imminent suicidal behaviour, which may be either aborted or interrupted. This definition was used as a guideline in the studies of this dissertation.

<u>Depression</u>: In mental health, depression is defined as 'a mental state characterized by feelings of sadness, loneliness, despair, low self-esteem, and self-reproach; accompanying signs include psychomotor retardation or, at times, agitation, withdrawal from interpersonal contact and vegetative symptoms such as insomnia and anorexia. The term refers to a mood that is so characterized or a mood disorder.' (Sadock & Sadock, 2004).

Over the years, the Diagnostic and Statistical Manual of Mental Disorders (DSM, American Psychiatric Association, 1952-2000) operationalized the criteria required for the Depressive Disorders. A set of five among nine criteria forms a Major Depressive Episode, while two are enough to form a Depressive Disorder (Not Otherwise Specified). A set of three among eight criteria, excluding suicidality, forms a Dysthymic Disorder. A psychiatric diagnostic interview by clinicians can lead to a qualitative assessment of depressive symptoms resulting in a diagnosis of depression, which is a categorical variable. However, depression can also be measured quantitatively by a self-report questionnaire with items about depressive symptoms in an ordinal scale to become a dimensional variable with a sum score. This dissertation uses both, categorical diagnostic assessments and dimensional measurements of depression. In the description of the data used in this dissertation, depression refers to questionnaire scores while depressive symptoms refer to interview data. Depressive disorders were sourced only from the interviews. However, the general usage of 'depression' as a term including both dimensional and categorical measurements is also used, especially when referring to the works of others.

Categorical assessments identify individuals suffering from the disorder so that management may be started. However, symptoms must either be at or below the clinical threshold in order to reach a diagnosis. The severity of the symptom profile is lost due to the categorisation. This loss has implications for the management and prognosis of the disorder. In a dimensional measurement, information is most uncertain around the cut-off score. Hence, the cut-off score maybe best used as a relative indicator of severity. In research, experts have suggested that the dimensional measurement of depression is a valid alternative to a categorical diagnosis (Goldberg, 2000). The use of both, categorical assessments and dimensional measurements of depression in the studies of this dissertation ensured that both, the presence and the severity of depression were examined.

#### Depression and attempted suicide up to early adulthood

Adolescents who are depressed and those who attempt suicide share many psychosocial risk factors (Lewinsohn et al, 1994). Suicidal ideation during childhood and adolescence is a well-known predictor of attempted suicide in clinical and non-clinical studies (Pfeffer et al, 1986; 1988; Lewinsohn et al, 1994; Fergusson et al, 2005). Suicidal ideation also predicted longer episodes of major depression in non-clinical samples (Lewinsohn et al, 1994). Depression before adulthood, including sub-threshold depression, is known to increase the risk of suicide attempts by early adulthood (Harrington et al, 1994; Weissman et al, 1999; Lewinsohn et al, 2001; Fergusson et al, 2005; Giaconia et al, 2001). Lower age of onset for depression has also been associated with higher levels of suicidal intent (Thompson, 2008).

On the other hand, a suicide attempt is a known risk factor for the later development of a major depression (Pfeffer et al, 1993; Lewinsohn et al, 1994; 1995) and other psychiatric diagnoses (Lewinsohn et al, 1996, 2001; Fergusson et al, 2003, 2005). Pre-adolescent suicidal risk has predicted substance abuse, depressive and anxiety disorders in young adulthood (Steinhausen et al, 2006). Co-morbidity of unipolar depression with other mental disorders in adolescents has been associated with higher frequencies of suicidal behaviours (Rohde et al, 1991). Suicide attempts have also been found to occur in conjunction with substance use, depressive and disruptive disorders (Andrews & Lewinsohn, 1992; Kovacs et al, 1993).

Cognitive vulnerabilities such as rumination, negative cognitive styles and dysfunctional attitudes have been theorised to be predictors of depression among adolescents. Negative environments including victimization may contribute to the vulnerability (Hankin et al, 2009). It has been hypothesized that stressful events may precipitate suicide among the youth already

at risk of attempting suicide (Shaffer et al, 2001). This explanation is based on the stress-diathesis model. Experiences of violence leading to post-traumatic stress diagnoses may be one such event (Wilcox et al, 2009).

Cognitive flexibility makes both reappraisal and acceptance of a problem possible. These lead to a different explanation of the situation and may also elicit a different response from the environment. The ability to find meaning, purpose and opportunity in negative situations leads to more optimistic emotional responses which can also attract social support. This in turn buffers the negative impact of stress. Such individuals are more likely to fare better, even in adversity. Resilience is one of the terms used to cover the various qualities of such persons. Although a stable trait, it is dynamic and therefore modifiable. As such, resilience can be preventive in relation to depression and suicidality, particularly among the young (Campbell-Sills et al, 2006).

Although studies of clinical and non-clinical samples using rigorous methods have provided salient information about the complex relationships between depression and attempted suicide, several clinically clinically important questions remain unanswered. 'Youth and Mental Health' is a prospective research project on adolescent depression among high school students. The data set is able to address some questions such as: Do the risk factors of suicidal acts during adolescence change with age and time? Do risk factors change due to the presence and severity of external variables such as violence and internal variables such as depression? Do specific depressive symptoms or disorders relate to attempted suicide across adolescence? What is the role of traumatic life events, especially, violence? What are the relationships between violence, depression, resilience and suicide attempts at this formative phase of life?

These broad questions were narrowed down to form the research questions of this study, comprising of three papers which include eight sub-studies.

#### Research questions

#### Study I

- What familial, peer and individual factors predict suicidal acts during the middle (ages 14-15) and the late adolescence (ages 15-20) years?
- How strong are the predictors when adjusted to each other and to two well-established predictors: a depressive disorder, and a previous suicidal act?

#### Study II

- Are specific depressive symptoms and disorders related to suicidal acts during adolescence?
- If such relationships exist, what is the nature and magnitude of such relationships,
   cross-sectionally, longitudinally and when adjusted to each other?

#### Study III

- What is the relationship between attempted suicide and violent life events?
- How does resilience at early adulthood relate to antecedent depression, violent life events and attempted suicide?

# 6. METHOD

#### Design

The three main studies (eight sub-studies) of this dissertation were conducted within the longitudinal, prospective, epidemiological research project 'Youth and Mental Health'. It investigates depression among school adolescents. A subset of the adolescents was interviewed for depressive disorders and comorbidity; they were followed up into early

adulthood. A self-report questionnaire battery including a screening measure for depressive mood and feelings was used. A clinical interview was subsequently employed to explore for psychiatric diagnoses.

The study was approved by the Regional Committee for Medical Research Ethics, Central Norway and by the local school authorities in the two counties and their school boards. Informed consent, as prescribed by The Norwegian Data Inspectorate, was obtained from the participants.

#### Sampling and participants

Participants were selected from a high school sample of adolescents from two counties in Central Norway: North and South Trøndelag. Cluster sampling resulted in a representative sample of 2813 students from 22 schools from a population of 9292. A total of 2792 adolescents were eligible while 21 adolescents were non-eligible for different reasons: they stayed abroad or they had long-term stays in hospitals or they could communicate only in foreign languages due to their recent arrival in Norway or they attended special schools.

The sample was stratified according to urbaneness: (a) City of Trondheim (n = 484, 19.5%, (b) Suburbs of Trondheim (n = 432, 17.5%), (c) Coastal area (n = 405, 16.4%) and, (d) Inland (n = 1144, 46.4%). These percentages were maintained almost intact at follow-up. Schools were drawn according to their size by using proportional allocations within each stratum. School personnel were recruited to be in charge of the screening procedures. Their training took place during two consecutive school hours.

#### **Assessment time-points**

The sample flow is given in Figure 2 below. At the first assessment (T1= fall 1998, 2464 adolescents, 50.8% females), the mean age was 13.7 (SD = 0.5) years. A questionnaire, which included the screening measure for depressive symptoms [Mood and Feelings Questionnaire (MFQ), described below], was completed at school. The participation rate was 88.3%.

About one year later (T2 = September 1999–February 2000, 2432 adolescents, 50.3% females; mean age = 14.9 (SD = 0.5) years) the same questionnaire was completed again at school. One hundred and five students (4.3%) who participated at the baseline assessment (T1) did not participate a year later (T2). However, seventy-three new participants entered the project at T2.

The non-participants had a significantly higher mean score on the MFQ (*described below*) at T1 [17.3 vs. 10.4, t (2442) = 7.13, p<0.001]. They had a non-Norwegian parental background more often [ $\chi$  <sup>2</sup> = 13.45 (1), p<0.001]. No differences with respect to gender, grade, or socioeconomic status were found between the participants and the non-participants.

#### **Subset selection**

On the basis of the MFQ scores at T2, the participants were grouped into three levels: low (0-6), middle (7-24) and high (25 and above) scorers. All high scorers were regarded as cases of depression. One age-and-gender matched control for every two high scorers was selected at random from the low and middle scorers. Of the 364 students thus selected, 345 (72.5% females) were interviewed face-to-face at their school by six trained interviewers to check for psychiatric diagnoses. The participation rate was 94.8%. The cases of depression numbered

225 (65.2%), and the controls were 120 (34.8%) yielding a case: control ratio of 1.8:1. The discrepancy in the planned (2:1) and obtained (1.8:1) case: control ratio was due to attrition.

Figure 2: Flow chart of sample

```
9292 = population (1998) \rightarrow 2792 = sample

\begin{array}{lll}
\rightarrow & 2464 = T1Q \text{ (age = 13.7 years)} \\
\rightarrow & 2423 = T2Q \text{ (age = 14.9 years)} \\
\rightarrow & 345 = T2 \text{ I (face-to-face)}
\end{array}

\rightarrow (8 = \text{At T2, did not consent to be contacted at T3,} \\
34 = \text{no consent at T3})

\rightarrow 303 = \text{invited to participate at T3 (2004/05)}

\begin{array}{lll}
\downarrow & \downarrow \\
252 = T3Q & 242 = T3I \\
\hline
76.8\% T3 \text{ participation (N = 265, age = 20.0 yrs)}
\end{array}
```

Q = Questionnaire. I = Interview.

At T2, all parents were invited to be interviewed separately, making at least one additional informant available for 79.8% of the adolescents. The clinical assessment of psychiatric symptoms and diagnoses was based on information obtained from both, adolescents and their parents. At this assessment, past and current depressive disorders among the adolescents along with their co-morbidity were investigated up to age 15.

### Subset follow-up after 5 years

According to the Norwegian Population Register, all adolescents who had consented at T2 to be contacted again were alive five years later. At the third assessment ( $T3 = October\ 2004 - March\ 2005$ ), a total of 265 young adults with a mean age of 20.0 (SD = 0.5) years were reassessed. They either filled out the questionnaire, or they were interviewed, or both. More

than two-thirds (76.9%) were females. From the original subset of 345 adolescents interviewed at T2, the overall participation rate at T3 was 76.8%. Two hundred and fifty two (73%) adolescents completed the questionnaires, while 242 (70.1%) were interviewed. The mean age of the participants at T3 was 20.0 (SD = 0.6). The age range was between 18.9 - 21.4 years. By or at T2, more than two-thirds (n = 84, 72.4%) had either received treatment or had been referred for treatment for mental health issues.

Interviews of the respondents at T3 were conducted over the telephone. All symptoms of psychopathology for the five-year follow-up period between ages 15 to 20 were retrospectively explored. The respondents were randomized to one of three interviewers. Age-appropriate word changes were made in the questionnaire and the interview.

Blind interviews were conducted at T3 by clinicians trained in psychopathology assessments as well as in the use of the psychiatric diagnostic interview. At T2, one (*co-author AMS who had 26 interviews*) among six interviewers was not completely blind as she was simultaneously also involved in the formation of the subset. Inter-rater reliability (IRR) obtained with co-author AMS, was adequate. During the training period before interviewing, Cohen's *kappa* was at 0.71 for all screening symptoms and affective supplements at T2. Similarly, the *kappa* was at 0.70 for all screening and supplement symptoms at T3. Interview integrity during the data collection was maintained with an average *kappa* of 0.83 at T2, and 0.80 at T3.

The T3 interviewers assessed psychopathology only for the five-year follow-up period. However, the section on traumatic life events was for the lifetime, that is, up to the age of 20. The mean time-lag between the questionnaire response and the interview was 20 days at T2,

and 21 days at T3. At T2, interviewers were allocated to the participants according to geographical proximity. One of the T2 interviewers was also a T3 interviewer. However, weighted randomization ensured that, at T3, this interviewer did not get any of her T2 interviewees, despite a violation of randomization among 29.2% of the allocations at T3. A trade-off had to be made between minimal violations of randomization and the possibility of a greater time-lag between the questionnaire and the interview. One hundred and fifty-eight of the 242 young adults interviewed at T3 were high scorers at T2. In essence, this means that the case-control ratio of 1.8:1 at T2 interviews was preserved at the T3 interviews.

#### Assessment tools and variables

Below, variables from the questionnaire will be presented first. Variables from the interview follow this list. At the end, *attempted suicide* or *suicidal act*, the core variable is presented. This variable included data from both, the questionnaire and the interview.

#### Questionnaire

The self-report questionnaire battery probed for psychosocial and somatic information. It included the screening measure for depression, apart from various measures *(described below)*. The questionnaire was identical at all the three assessments, T1, T2 and T3. The only change was at T3 by adding age-appropriate items and sections.

**Psychosocial and somatic variables** Age at menarche was computed from the T2 questionnaire. Age was computed from the three questionnaires as required. Both these ages were used as continuous variables. Besides the participant's age and gender, information was gathered about their residential status ('Living with both biological parents or not'), lifestyle habits such as frequency of smoking (''Never'' to ''Daily''), use of alcohol (''Never'' to

"More than 50 times in the last 12 months", and narcotics (marijuana, hashish or sniffing). Three types of bullying experiences at school, i.e., psychological, physical and social, were explored for frequency ("Never in the last six months" to "More often than 2-3 times a week") (Olweus, 1996). Participants were also asked if they knew a friend who had attempted suicide.

Somatic illness was probed for by asking if the participant had any of the following illnesses for more than three months: asthma, allergy, skin disease, migraine, diabetes, epilepsy, heart disorder and others. Furthermore, they were asked if they suffered from frequent physical pain ('Yes' and 'No'). Frequent physical pain was defined as the presence of pain at least once a week for more than three weeks.

**Depression - Mood and Feelings Questionnaire (MFQ)** This measure is used as a screening instrument for depression based on DSM–III-R criteria for major depression for the 8-18 year age group (Angold, 1995). The participants were asked about their feelings and behaviours within the last two weeks, revealed by 34 items rated on a 0-2 scale (0 = Not true, 1 = Sometimes true, 2 = True). The potential total score ranges from 0 to 68 with higher scores indicating the presence of severely depressed mood and feelings.

In the original sample from which the subset was selected, psychometric properties of the MFQ were satisfactory (Sund et al, 2001). The standardized alpha was 0.92; the three-week test-retest reliability was 0.84, and at three months, 0.80. The convergent validity of MFQ with the Beck Depression Inventory was 0.91. The mean total MFQ score for the original sample was 10.6 (SD = 9.5) at T1 (Sund et al., 2001). The prevalence rate for major depression at T1 was 2.6% for the total sample, and 3.3% for the girls (Sund et al., 2001).

**Self-Perception Profile for Adolescents (SPPA)** The revised version of the SPPA for adolescents has been validated in a Norwegian adolescent school population (Harter, 1988; Wichstrøm, 1995). The version has 15 items and is rated on a 1-4 scale. The total score may range from 15 to 60; higher scores indicate better self-perception.

McMaster Family Adjustment Device (FAD) Originally, the scale was validated in a school sample of American adolescents with 12 items and rated on a 1-4 scale (Epstein et al., 1983; Andrews et al., 1993). The items address subjective adjustment with regard to family members as a group. The total score may range from 12 to 48; higher scores reflect better adjustment.

**Conflict with parents** The scale was first validated in the Oregon Adolescent Depression Project (OADP) (Andrews, 1993). Participants were asked to rate the frequency of specified conflict situations with each parent. Five items were used for each parent on a 0-4 scale. Thus, the total scores may range from 0 to 20. Higher scores reflect higher levels of conflict.

**Inventory of Parent and Peer Attachment (IPPA)** This revised measure addresses attachment to each parent (25 items) and peers (6 items) (Armsden and Greenberg, 1989). The IPPA measures affectively toned expectancies to parents and friends associated with internalized representations of each of the three attachment types. Each item is rated on a 5-point Likert type scale. The total scores for each parent may range from 0 to 125; higher scores indicate better attachment.

**Resilience - Connor-Davidson Resilience Scale (CD-RISC)** This is a 25-item instrument rated on a 0-4, 5-point scale with a potential range of 0-100 (Connor & Davidson, 2003). The

time frame for the measurement is the past month. Higher scores reflect greater resilience. The scale elicits five factors: (1) personal competence, high standards and tenacity; (2) trust in one's instincts, tolerance of negative affect, and strengthening effects of stress; (3) positive acceptance of change and secure relationships; (4) control, and (5) spiritual influences. Psychometric properties reported by the authors were excellent with Cronbach's  $\alpha$  of 0.89 in a community sample and a test-retest reliability intra-class correlation coefficient of 0.87 (Connor & Davidson, 2003). The scale was used only at T3. Cronbach's standardised  $\alpha$  in the present sample was 0.91. The total score of the 25 items was used as a measure of global resilience.

The measure approaches resilience as a stable yet modifiable trait, providing it with unique advantages in clinical samples as increased resilience indicates a better mental health status (Davidson et al, 2006). In the present sample, among the 76 attempters, 27 (35.5%) had used some form of medication for mental health conditions up to age 20, including one who had used such medication by age 15. This means that if resilience had improved among the attempters between T2 and T3, it was unlikely to be due to the impact of psychotropic medication. Accordingly, any probable improvement in resilience between the assessments, T2 and T3 (covering ages 15-20) were likely to be a part of the natural strengthening of constructive coping expected as a part of growth into adulthood.

## Interview

The Kiddie – Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL) This well-established semi-structured diagnostic interview contains a screening section and five supplementary sections to assess present and past episodes of psychopathology in children and adolescents on Axis I (Kaufman et al., 1997). This

assessment is done in accordance with the DSM-III-R and IV criteria. Each individual symptom is rated on a 0-3 scale; a score of three represents the clinical threshold. A clinical threshold score in the screening indicates that the relevant supplement needs to be used. Each item is accompanied by guidelines on how to assess sub-threshold and threshold levels of clinical assessments.

**Depressive symptoms** K-SADS-PL provides a list of 30 items to probe for all DSM-IV-TR symptoms in a depressive episode, including all sub-types of major depression and dysthymia.

The screening section for a depressive episode has eight items. The first two items in the screening are on the primary requirement for a diagnosis of depressive episode: depressed mood and its equivalent among children and adolescents, irritable mood. The third item is on anhedonia, the other primary depressive symptom. Out of the eight items, four are on suicidality and the last one is on self-harm without suicidal intent. The key item for this study: *suicidal act*, will be described seperately.

The supplement section on depressive disorders has all the other depressive symptoms, including cognitive disturbances such as hopelessness and worthlessness. Somatic disturbances, that is, psychomotor, appetite and sleep disturbances are also in the supplement section. The interview has six kinds of sleep disturbances including non-restorative sleep, hypersomnia, a disturbed Circadian rhythym and the three types of insomnias: (a) initial insominia: difficulty in falling asleep; (b) middle insomnia: waking up after falling asleep and then experiencing difficulty in falling asleep again and (c) terminal insomina: waking up earlier than usual and not able to sleep again.

A clinical threshold score on any item assessing the various aspects of depressive symptoms was required for entry into the analyses. Sub-threshold items were therefore excluded from the analyses. Medical lethality of suicidal acts as a variable was excluded from the study as it is not a criterion for a depressive episode or a subtype of a depressive episode.

**Depressive Disorders** Diagnoses of depressive disorders included Major Depressive Disorder (MDD) and dysthymia based on the criteria given in the DSM-IV-TR. In the present study, a diagnosis of Depressive Disorder Not Otherwise Specified (DD-NOS) required at least three depressive symptoms lasting for at least two consecutive weeks. Probes for a diagnosis of any depressive disorder were limited to the most severe past episode. Functional impairment, as indicated by a score below 71 on the measurement of Childhood-Global Assessment of Symptoms [C-GAS, (Shaffer et al, 1983)], was a requirement for the diagnoses of MDD and dysthymia.

For analyses, current and past diagnoses were pooled together, as was done with depressive symptoms. For example, an episode of MDD present at any time by the age of 15 years was recorded as MDD, irrespective of whether it was current or past. However, if one individual had more than one diagnosis of depressive disorders, concurrent or historically, each diagnosis was included in the analyses (Helzer et al., 2006). All diagnoses by the age of 15 (T2) included current diagnoses and lifetime diagnoses. Similarly, all diagnoses between 15 to 20 years included the current diagnoses at 20 years (T3) and the past diagnoses during the follow-up period, that is, between the ages of 15 to 20. Before entering the analyses, all diagnoses were reviewed by the project leader and co-author AMS, as a measure of quality control.

**Traumatic Life Events** In the screening section, the K-SADS-PL probes for 13 traumatic life events during the lifetime - either as a witness or as a direct victim. The list includes car accidents, other accidents, fires, natural disasters, violence, sad news (usually death), physical abuse at home, sexual abuse, war events, and other traumatic events.

Each item specifies the clinical threshold required to qualify for a positive score. Example: A car accident would be scored positive only if the respondent or another person in the car was injured enough to have received medical treatment. Some events not reported during the T2 interview were reported at the T3 interview, even though they happened before T2. However, as the T3 interview only collected information on the follow-up period, it was possible that reports of traumatic events might have been limited to this 5-year period, thus reducing the number of events reported. The variable 'traumatic life events' was constructed using the interviewer's T2 and T3 scores to provide the lifetime perspective.

These events were grouped into: (a) *Bereavement* - the 'sad news' item was filtered to eliminate false positives: only news about deaths of primary family or close peer group members were accepted, (b) *Violent Life Events*, including sexual violence and, (c) *Others* - diverse events such as natural disasters, fires or accidents, that is, all traumatic events that were not covered by (a) or (b).

**Violent Life Events** Entry into the group of those who had experienced violent life events required endorsements from the interviewer at T2 or T3 on one of the following events: witnessed violence, victim of violence, witnessed physical abuse at home, victim of physical abuse, sexual abuse, rape, witness of war events, or victim of war events. The number of

*persons* reporting such events, *not* the number of events reported by each person, was accepted for the analyses.

**Victims of violence** If the interviewer's score was positive on victimization by violence, the person was included. Again, only the number of *persons* meeting the criterion was included, not the number of events.

**Suicidal act** The variable "attempted suicide" was constructed on the basis of information from the questionnaire and the interview. Acts of deliberate self-harm without suicidal intent were excluded. Based on the absence or presence of suicidal intent, these acts were differentiated either by the respondent in the questionnaire, or by the interviewer. The item used in the questionnaire was the same as in a previous national survey of school adolescents 'Young in Norway' (Wichstrøm, 2000): "Have you ever tried to commit suicide?" ("No, never"; "Yes, once"; "Yes, several times"). At T3, this last response option was changed ("Yes, 1-5 times"; "Yes, 5 + times"). If positively endorsed, the participants were asked for further details about the timing of the last suicidal act: 'How long ago was your last act of attempted suicide?" ("Years", 'Months").

Questions about attempted suicide were also parts of the screening probes for depressive disorders in the K-SADS-PL. A positive response to the question: "Have you ever tried to kill yourself or done something which could have killed you?" required further assessments by the interviewer to check for clinical threshold or sub-threshold levels. At T3, this question was modified to probe for a suicidal act since the last interview. If assessed by the interviewers to be at or above the clinical threshold (a score of 3, indicating clear and definite

suicidal intent), it was defined as a suicidal act. The interviewers probed for details of the most severe act, including the date of the attempted suicide.

About one-fourth (n = 86, 24.9%) of the T2 interview subset reported attempted suicide by 15 years of age, either in the T1 or T2 questionnaires or in the T2 interview. The T2 interviews revealed six adolescents who had not reported attempted suicide in any of the questionnaires. Forty-five adolescents reported attempted suicide in one of the questionnaires but not in the interview assessments. The analyses included all those who had attempted suicide, regardless of discordance between the two data sources. This inclusion was done to facilitate the use of all available information on attempted suicide at each assessment, and also, to optimize the power of the analyses.

## **Statistics**

The SPSS was used for data analyses; versions 15.0 and 16.0. Missing values in the questionnaires were substituted with values generated by the Expectation Maximization method for randomly missing data while the regression method was used for non-random data (Tabachnick & Fidell, 2006). An exception to this procedure to treat missing values was made in the second paper. Only one continuous variable was used in this paper: depression as measured by the MFQ. Data on MFQ did not have many missing values in the project. One person who had more missing values than the others was counted as a control, instead of a case. This paper reports the number of cases of depression as 224 and controls as 121, instead of 225 and 120 as in the other papers.

Descriptive statistics such as frequencies (proportions) and means (standard deviations) were used. Chi-squared and Fisher's Exact tests were used to examine associations between

categorical variables. Differences between group means of continuous variables were explored by the Student's *t*-test. Bivariate logistic regression analyses examined crude. estimates (Odds Ratios, ORs) of the variables.

Multivariate logistic regression analyses examined the relative strengths of variables with significant relationships in the bivariate analyses. Variables significant at the bivariate level were checked for multicollinearity before they were entered into the multivariate analyses (Field, 2005). The Enter method of inclusion was used. An alpha value < 0.05 indicated statistical significance. Moderation was tested by the method proposed by Baron & Kenny (1986), after the preliminary requirements for moderation analyses were tested and found to be fulfilled. The acceptable significance level was 0.10 for the moderation analyses, as is usual.

The eight sub-studies within the three main ones were designed to optimise the use of the available data. The number of those who had attempted suicide varied according to the data source, i.e., the questionnaire or the interview, and the nature of the variables, for example: the use of time. The details are provided below and for ease of understanding, the sub-groups as relevant to each paper are given in the next section. Paper 1 has two sub-studies, Paper 2 has three sub-studies, and Paper 3 has three sub-studies: all from the same subset. Specific information on the various statistical procedures used in the individual studies is also given below.

#### 7. OVERVIEW OF PAPERS

**Paper I:** Nrugham L, Larsson B, Sund AM. 2008. Predictors of suicidal acts across adolescence: Influences of familial, peer and individual factors. *Journal of Affective Disorders*, 109(1-2), 35-45.

## Research questions:

- 1. Which familial, peer and individual factors predicted suicidal acts during middle (age 14 to 15: one year) and late adolescence (age 15 to 20: five years)?
- 2. How strong were the predictors when compared to each other, and also, with the two most well-established risk factors; i.e., a depressive disorder and a previous suicidal act?

A list of psychosocial variables derived from the questionnaire and the diagnoses derived from the interviews were explored as possible predictors of these suicidal acts which were carried out in the short-term of one year, i.e., from age 14 to 15 and in the long-term of five years, i.e., from age 15 to 20 years respectively.

### Logistic regression analyses of data from:

- (a) Adolescents who had attempted suicide during middle adolescence between age 14 (T1) and 15 (T2), (n = 37; 27 females). A suicidal act before or at T1, i.e., by age 14 which is understood as early adolescence (n = 39; 32 females), was one of the predictors.
- (b) Adolescents who had attempted suicide during late adolescence between age 15 (T2) and 20 (T3), (n = 36; 31 females). A suicidal act reported before or at T2, i.e., by age 15 which is understood as middle adolescence (n = 67; 48 females) was one of the predictors of a suicidal act between T2 and T3, that is, between ages 15 and 20 which is understood as late adolescence.

Some participants reported attempted suicide at both assessments (n = 17), while some others (n = 8) did not provide any information regarding the timing of their suicidal acts. These eight participants were included only as having reported attempted suicide by T2 (age 15). The T3 participants (n = 265) were the data source for the two sub-groups given in (a) and (b) above.

#### Results:

<u>Sub-study 1:</u> The four significant bivariate predictors of attempted suicide in middle adolescence, i.e., between age 14 and 15 were:

- (i) by age 14:
  - not living with both biological parents by age 14 [OR (95%CI) = 3.1 (1.5 6.5)];
  - self-reported intoxication by alcohol more than 5 times in the last 12 months, or the use of narcotic drugs by age 14 [OR (95%CI) = 3.8 (1.1 - 12)];
  - self-reported frequent physical pain by age 14 [OR (95%CI) = 2.7 (1.3 5.3)];
- (ii) at age 14:
  - higher scores on self-reported depression [OR (95%CI) = 1.04 (1.02 1.07)].

<u>Sub-study 2:</u> The seven significant bivariate predictors of attempted suicide during late adolescence, i.e., between ages 15 and 20 were:

- (i) by the age of 15:
  - \* a diagnosis of any depressive disorder [OR (95%CI) = 4.2 (1.9 9)];
  - \* a suicidal act [OR (95%CI) = 6.4 (3 -13.5)];
- (ii) between age 14 and 15:
  - \* daily smoking [OR (95%CI) = 2.6(1.2 5.6)];
- (iii) at age 15:
  - \* lower self-esteem [OR (95%CI) = 0.95 (0.91 0.99)];

- \* higher levels of conflict with mother [OR (95%CI) = 1.09(1.01 1.1)];
- \* higher levels of conflict with father [OR (95%CI) = 1.10 (1.02 0.19)] and
- \* higher scores on self-reported depression [OR (95%CI) = 1.03 (1.005 1.05)].

The significant multivariate predictors of suicidal acts among younger and older adolescents were 'not living with both biological parents' [OR (95%CI) = 3.1 (1.4 - 7)], and 'a diagnosis of any depressive disorder' [OR (95%CI) = 2.9 (1.2 - 6.8)] respectively. Irrespective of the time (whether short-term or long-term) and age (by 14 or between ages 14 to 15), a history of attempted suicide [OR (95%CI) = 5.6 (2.2 - 14)] & [OR (95%CI) = 5.5 (2.1 - 13.5)] was a significant multivariate predictor of a later suicidal act.

Conclusion: A non-harmonious home situation, frequent physical pain, risky behaviours such as intoxication and daily smoking, depression and a diagnosis of a depressive disorder, and a history of attempted suicide were predictors of suicidal acts. High mean scores on depression remained constant as bivariate predictors, irrespective of time (whether short-term or long-term) and age, as did a previous suicidal act as a multivariate predictor of attempted suicide. The relationship of the diagnoses of a depressive disorder with suicidal acts changed with age and time as it became a predictor of suicidal acts only among the older adolescents, those between 15 to 20 years of age.

**Paper II:** Nrugham L, Larsson B, Sund AM. 2008. Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. *Journal of Affective Disorders*, 111(1), 83-93.

## Research questions:

- 1. Were specific depressive symptoms and disorders more related to suicidal acts during adolescence?
- 2. If such relationships exist, what was their nature and magnitude, cross-sectionally, longitudinally and when compared to each other?

In these three sub-studies, only data from the depressive symptoms in the screening section and the supplement on depressive disorders in the K-SADS-PL interview were explored as risk factors: associates and predictors of attempted suicide. The variable 'suicidal act' used data from the questionnaire and from the interview.

## Logistic regression analyses of these three sub-studies used data from:

- (a) adolescents who had attempted suicide by T2 (n = 86). Data obtained from all participants who were interviewed at T2 (n = 345).
- (a) adolescents who had attempted suicide between T2 and T3 (n = 34). Data obtained from all participants who were interviewed at T3 (n = 242).
- (b) adolescents who had attempted suicide between T2 and T3 (n = 36). Data obtained from all participants at T3, either by questionnaire or interview (n = 265).

Multicollinearity testing revealed minor problems at T3 as hypersomnia (.29) and worthlessness (.46) loaded together. Therefore, both variables were excluded from the multivariate analysis. All depressive symptoms and disorders providing significant ORs at p < 0.01 level were subsequently entered into the multivariate logistic regression analyses run separately for age and time (two cross-sectional analyses and one longitudinal analysis).

**Results:** Irrespective of age and time, cognitive depressive symptoms were related to attempted suicide.

Among these symptoms, suicidal thoughts [OR (95%CI) = 3.7 (1.6 - 8.4)], was a significant associate of attempted suicide among younger adolescents (up to age 15). Recurring thoughts of death [OR (95%CI) = 7.9 (1.4 - 43.1)], hopelessness [OR (95%CI) = 26.5 (4.1 - 168.5)], and disturbed concentration [OR (95%CI) = 56.9 (5.6 - 577.7)], were significant associates of attempted suicide among older adolescents (between ages 15 to 20). Self-harm without suicidal intent [OR (95%CI) = 4.5 (1.3 - 16.0)], although not a criterion for any diagnosis of depressive disorders, was found to be significantly associated with attempted suicide among younger adolescents. Middle insomnia [OR (95%CI) = 6.0 (1.3 - 27.8)], as a significant associate of suicidal acts among older adolescents, was the only somatic depressive symptom that emerged as a significant risk factor of a suicidal act.

Among all the depressive symptoms, only worthlessness by the age of 15 [OR (95%CI) = 3.3 (1.3 - 8.6)] could significantly predict attempted suicide between ages 15 to 20 in the multivariate analyses.

A major depressive disorder [OR (95%CI) = 2.6 (1.3 - 5.2)], and a depressive episode, not otherwise specified DD-NOS, [OR (95%CI) = 2.3(1.1 - 4.5)], continued to be significant associates for younger adolescents. Dysthymia by age 15 [OR (95%CI) = 2.4 (1.0 - 6.2)] remained a significant predictor of suicidal acts between ages 15 to 20, even when adjusted for depressive symptoms.

**Conclusions:** Cognitive depressive symptoms and depressive disorders were specifically found to be related to suicidal acts, as associates and as predictors, regardless of age and time.

The relationship of these single symptoms and the depressive disorders with a suicidal act changed with age and time.

**Paper III:** Nrugham L, Holen A, Sund AM. 2010. Associations between attempted suicide, violent life events, depression, resilience and suicide by early adulthood. *Journal of Nervous and Mental Disease*, 198 (2), 131-136.

# Research questions of the last three sub-studies:

- 1. Were lifetime traumatic life events associated with suicide attempts among adolescents?
- 2. Were violent traumatic events more strongly associated with attempted suicide as compared to other traumatic life events? These two questions form the sixth sub-study.
- 3. Were victims of violence more likely to attempt suicide as compared to witnesses of violence? This question and the next one form the seventh sub-study.
- 4. Did victimization of violence by age 15 predict a suicidal act between ages 15 to 20?
- 5. Did resilience moderate the relationship between violent life events and suicide attempts?
- 6. As a moderator, was resilience influenced by antecedent depression? This question and the preceding one form the eighth sub-study.

Traumatic life events were sourced from the PTSD (Post-traumatic stress disorder) screening section of K-SADS-PL diagnostic interview. Resilience was assessed by the CD-RISC and depression by the MFQ in the questionnaire.

A series of logistic and linear regression models examined the associations, including moderation, between suicide attempts and violent life events, victimization, resilience and depression. Continuous variables were mean-centered before entry into the moderation analyses. In order to detect moderation effects, we proceeded along the following lines: the

variable 'victims of violence' was entered into the first block of logistic regression analysis in which lifetime suicide attempt was the dependent variable. In the second block, mean-centered resilience was entered. In the third block, an interaction term: (victim of violence) X (mean-centered resilience) was entered. The fourth block contained the interaction term: (victim of violence) X (mean-centered resilience) X (mean-centered depression) at T2. Changes in the chi-square values of the model were checked for significance at each step. A significant change in the chi-square value of the model indicated a significant moderation effect.

#### Logistic regression analyses on data from:

Participants with a suicidal act in any of the assessment time-points taken together: T1, T2 or T3 (n = 76), based on information from all those who returned the questionnaire at T3 (n = 252).

**Results:** Attempters were significantly more likely to be victims of violence, [OR (95%CI) = 5.5 (3.0 - 10.1)], not just witnesses. They were significantly more depressed both at T1 [OR (95%CI) = 1.06 (1.03 - 1.08)] and at T2, [OR (95%CI) = 1.07 (1.04 - 1.09)], and significantly less resilient [OR (95%CI) = 0.96 (0.94 - 0.98)], than the non-attempters. Resilience was a significant moderator of both, lifetime violent events and attempted suicide, even in the presence of antecedent depression at age 15. The chi-squared values of the model changed significantly (p<0.0005), with attempted suicide as the dependent variable for all the interaction model steps: victim of violent life event = 31.51, resilience = 39.87, victim of violent life event X resilience = 39.97 and victim of violent life event X resilience X depression = 40.75. The differences between the model chi-squared values of the interaction

steps from 31.51 were also significant at the p < 0.10 level, an acceptable level of significance for interaction analyses.

Conclusions: Violent life events were significant associates of suicide attempts while other traumatic events were not. Among those who had experienced violent life events, only direct victims of violence were likely to attempt suicide while witnesses were not. Resilience protected against suicide attempts. The strength of the relationship between victimization by violent life events and attempted suicide during their lifetime varied with the scores of resilience at age 20, even in the context of depression at age 15. In this study, resilience was measured at age 20. Nevertheless, it is considered to be a fairly stable, yet modifiable lifetime trait.

## 8. DISCUSSION

## **Main Findings**

The present study found both, stability and change in the risk factors of attempted suicide during the entire period of adolescence investigated. This was true for both self-reported and for clinically assessed depression as well. Therefore, age should be considered important during clinical assessments of suicide risk. A summary of the main findings in response to the research questions will now be presented.

While a diagnosis of any depressive disorder predicts attempted suicide only among older adolescents, not living with both biological parents predicts attempted suicide only among the younger adolescents. A possible explanation for the latter could be that the influence of the parents is replaced by peers as the adolescents grow older. Although the attempters reveal consistent and more severe depression on all three dimensional measurements, it is the formal

diagnosis of a depressive disorder which predicts attempted suicide among older adolescents. This may be a pointer to the severity of depression not being as important as its presence among adolescents. However, in this study, it cannot be stated that the clinical threshold is more important than the statistical cut-off as sub-threshold depressive symptoms were not used. Irrespective of age, a history of attempted suicide predicts another suicidal act. It is a predictor, both in the short-term and in the long-term, for suicidal acts. This finding, therefore, reflects the behavioural aspect of suicidality more than any other result of the present study.

Cognitive depressive symptoms dominates the depressive symptom profile of suicidal adolescents irrespective of age, while depressive disorders varies with age and time in relation to adolescent suicidal acts. Dysthymia by 15 years remains a predictor of attempted suicide between 15 to 20 years while major depression and a depressive episode, not otherwise specified, continues to be significant associates among younger adolescents, even when controlling for depressive symptoms. These findings provide more support to the presence of depression than to its severity as important with regards to suicidality among depressed adolescents. The cognitive triad consisting of rigidity, rumination and perfectionism is one of the well-known risk factors for suicidality among adults and older adolescents. The findings of the present study indicate that younger suicidal adolescents are also vulnerable to depressive cognitive processes.

Violent life events are significant associates of suicide attempts whereas other traumatic events are not. Among those who had experienced violent life events, only direct victims of violent events were likely to attempt suicide, not the witnesses. One explanation may lie in the humiliation and powerlessness experienced by the victims of violence. An alternative interpretation may lie in gender as two-thirds of the sample were females. A similar

relationship between suicidality and violence was not found in another study with an equal gender distribution (Wilcox et al, 2009). The authors found that it is post-traumatic stress psychopathology which was related to suicidality, not assaultive violence by itself. Violent events are associates, not predictors of attempted suicide in the present study. This may indicate that the peer-related violent events play a greater role in suicidality among adolescents than home-based violence.

Adolescents who had not attempted suicide had higher resilience as young adults. The cognitive flexibility implied by resilience may be one of the mechanisms in which suicidal acts are prevented or delayed despite violence and depression. Resilience appears as a moderator of the relationship between victimization by violent life events and attempted suicide, even in the context of depression. In other words, the strength of the link between attempted suicide and of being a victim of a violent event changed according to the level of resilience and depression. It may be argued that resilience at age 20 cannot protect against suicide attempts up to age 20. In the present study, resilience is understood as a stable, although modifiable trait, running throughout the individual's lifetime. Therefore, measurement of resilience at age 20 indicates its presence also prior to that age. It may be argued that psychotropic medication between the last two assessments could have improved resilience. This seems unlikely due to the small number of adolescents on medication in the sample.

Many findings are consistent with earlier empirical reports on suicidality across different samples. These consistencies are briefly reviewed here. Not living with both biological parents (Grøholt et al, 1998 & 1999; Wichstrøm, 2000; Evans et al, 2004) and a diagnosis of a depressive disorder (Kovacs et al, 1993; Lewinsohn et al, 1994, 2001; Bridge et al, 2006) are

strong predictors of suicidal acts. A previous attempt is a strong predictor, regardless of age and time (Kovacs et al, 1993; Grøholt et al, 1997 & 1999; Lewinshon et al, 1994, 2001; Fergusson et al, 2003; Bridge et al, 2006). Cognitive depressive symptoms (Arffa, 1983; Beautrais et al, 1999) overshadow other depressive symptoms as predictors and associates of attempted suicide. Violent life events are significant associates of suicide attempts (Bridge et al, 2006) while higher resilience protects against suicide attempts (Campbell-Sills et al, 2006; Campbell-Sills & Stein, 2007).

The findings which are not consistent with earlier empirical reports of suicidality are now presented and discussed. Some variables do not reach significance in more than one assessment and are therefore age or time-specific. They were: conflicts with mother or father at age 14; smoking daily, any diagnosis of a depressive disorder by age 14; low self-esteem score at age 15 and having experienced a violent life event by age 15. Other variable are insignificant in all three assessments. The quality of the adolescent's relationship with parents (Fotti et al, 2006), or that the adolescent was a victim of bullying (Klomek et al, 2007), was friends with someone who had attempted suicide (Lewinsohn et al, 1994), had chronic physical pain (Fishbain, 1999), had frequent alcohol intoxications (Wichstrøm, 2000; Evans et al, 2004), had mood worsening in the evenings, weight loss and gain (Bulik et al, 1990), had terminal insomnia and both aspects of psychomotor disturbances (Leventhal et al, 2008); non-violent life events and witnessing violent life events (Berenson et al, 2001) - all failed to reach significance.

Many of the inconsistencies with earlier empirical reports may be explained by differences in the sample composition. The present sample is neither clinical nor representative of the general population. The subset of high school adolescents with mostly high scorers on depression suggests a resemblance to adolescent outpatients most. This is an under-researched group with reference to suicidal phenomena (Bridge et al, 2006). Several of the findings are in line with prior reports of adolescent suicide and, clinical and non-clinical longitudinal studies of attempted suicide (Grøhlot et al, 1997, 1998, 1999; Lewinsohn et al, 2001, Bridge et al, 2006). This overlap of findings across samples is yet another indication of the sample composition being nearer to a clinical sample and therefore adequate for exploring the complex phenomenon of suicidality among adolescents.

Among adolescents, the main difference between completers and attempters of suicide is gender: males choose irreversible methods and die, while females chose more reversible methods such as poisoning, and they appear to have lower suicide rates (Shaffer & Waslick, 2002). This gender preference for methods is also seen among adults. However, there are other differences among adult completers and attempters of suicide such as higher impulsivity among attempters and higher intent among completers. On the other hand, such differences are absent between adolescent completers and attempters (Shaffer & Waslick, 2002). This absence of differences among adolescents is what makes their suicidality so complex. The procedure of identifying the subset of mainly depressed adolescents and the strict clinical criteria used in the study, made it possible to find a group which needs to come to the attention of mental health professionals.

## **Consistency with theory**

At the outset, it is relevant to note that the first three theoretical models discussed forthwith are suicide models, not models trying to explain or understand attempted suicide. In addition, it must be noted that the models refer primarily to adults; they do not specifically include or exclude adolescents. Accordingly, it is warranted to examine the findings in the light of

developmental psychology models. This will be done after the other theoretical models have been briefly looked at.

<u>Durkheim's model</u>: Durkheim proposed his model as explanations for suicide rates, not as motivations of individual acts; his model is sociological, not psychological. The egoistic type of suicide is explained as the rise of individualism and anomic suicide as the rise of normlessness by Durkheim, both being similar in many ways with their roots in the organic solidarity of society. Early stages of the egoistic or the anomie types of this suicide model maybe cautiously considered for some of those adolescents who attempted suicide in the present study.

The dispersal of the biological parental unit is related to attempted suicide among younger adolescents. In middle adolescence, depression was not as important as the history of a suicidal act. Both types of suicide are seen as a consequence of the loosening of bonds between the individual and the community. Yet, the relationship between attempted suicide and the family functioning, conflicts with parents among younger adolescents and attachment with parents or peers were non-significant in the present study. Therefore, enough information is not available in the present study, either to accept or reject Durkheim's model. The findings do not allow the conclusion that the parental figures were non-supportive, either.

Accordingly, we are limited to noting that both the attempters and their parental units were distressed. The findings highlight the vulnerability of childhood and adolescence in the backdrop of the absence of an intact familial unit in line with the conclusions of two comprehensive reviews on attempted suicide among adolescents (Gould et al, 2003; Bridge et al, 2006).

Cognitive model: The dominance of the cognitive depressive symptoms among adolescents who attempted suicide in the present study, regardless of age and time (short-term/long-term), is a clear indicator of the support lent to the cognitive model. However, the fit of the findings to the model needs comment. Self-harm without suicidal intent as a behavioural depressive symptom emerged as a risk factor. Increased appetite and initial insomnia are somatic symptoms which turned from being risk factors in the bivariate analyses to become protective factors for older adolescents in the multivariate analysis. The reason for this is possibly confounding. Worthlessness, a cognitive depressive symptom, is well-established as a predictor of both attempted suicide and suicide. However, worthlesssness did not enter one of the multivariate analyses due to multicollinearity with a somatic depressive symptom, hypersomnia. These indicators of an imperfect fit of our findings to the cognitive model warrant closer investigations as the support lent to the model is limited.

Stress-diathesis model: In addition to depression and a previous suicidal act, the present study reveals two stressors among adolescents with attempted suicide: not living with both biological parents by age 14, and direct victimization of violence. Belonging to a non-intact family emerged with nearly unchanged statistical values in the multivariate analyses while a previous suicidal act decreased considerably in strength in the same analysis. This indicates that non-intact families with children or adolescents may need attention and support. The finding of higher resilience being protective against attempted suicide can also be understood by this model. Adolescents with lower resilience are more likely to attempt suicide due to the diathesis being activated in the presence of stress such as violence directed against them. In the context of these specific stressors and with the specific nature of depression revealed by the present study, suicidal acts among these adolescents can be interpreted as a sign of severe distress.

<u>Developmental models:</u> According to Piaget, the construction of the meaning of existence is expected to happen during adolescence (Inhelder & Piaget, 1958). Linking together the theoretical aspects of the models above, it appears that this important process of finding meaning in existence is distressful for suicidal adolescents. The relationship between cognitive depressive symptoms and the suicidal act in the sample makes this clear. Both, the non-intact parental unit and the direct experience of direct violence among peers, have an impact on depressed adolescents.

The protective scaffolding required to navigate successfully the transitional challenges into adolescence and subsequently into adulthood, did not appear to be adequately present among the attempters. These adolescents do not seem to have the internal compensatory influences such as resilience. They also appear to lack an external environment which may prevent or delay their decision to attempt suicide as they come from non-intact families and are victims of violence directed against them. Herein lie opportunities for contemporary society to work towards reducing suicidality among adolescents. Additionally, it is seen that age is important, and theories of suicidality may consider including it.

An effort was made to understand the findings of the present study in the light shed by these models. A few clarifications on the complex relationship between depression and attempted suicide up to early adulthood are provided. However, theory building was not a specific objective in any of the sub-studies or of the overall study. Theoretical models are used only to understand the findings better.

In addition, it is important to have in mind the difficulties involved in defining attempted suicide among adolescents. The definition of a suicidal act included self-reported acts in the

questionnaires and acts assessed by a diagnostic psychiatric interview to be at or above the given clinical threshold. The three studies used only suicidal intent and did not consider medical lethality or ambivalence. Statistical power would have decreased if medical lethality also had been included while the inclusion of ambivalence would have increased the power. The number of adolescents with attempted suicide available for the analyses would have decreased or increased correspondingly. Choosing suicidal intent at or above the clinical threshold was a way to optimize power. Two-thirds of adolescents in the subset had depression scores above 25 on the MFQ. These sample characteristics makes the group resemble adolescent outpatients more than the general population.

#### Weaknesses and strengths

Due to the small proportion of males in the subset, the impact of gender was not studied. As the subset was two-thirds female, the generalization of the findings is mainly applicable to girls and young women. Semi-structured interviews were used to obtain diagnostic information. Parents were available as additional informants at T2. It is useful to note that interview information could have been subject to recall bias as it is retrospective, except for the current diagnoses. At the five-year follow-up, the attrition was almost 30% as may be expected in follow-up studies at this age. The non-participants at T3 were more likely to have been victims of violence. Information is lost when categorical definitions are used. Most of the variables used in this study were categorical. These two factors, that is: the nature and extent of attrition, and the use of categorical variables, might have led to underestimates of the relationships between suicide attempts and the explanatory variables due to loss of power.

In an effort to streamline the present sub-studies, many variables were not considered, for example: age of onset, duration of the depressive episode, timing of the depressive episode (such as pre/post pubertal, seasonal, age grouping), recurrence of depressive episodes, sub-threshold symptoms, sub-typing of depressive episodes, presence of double depression and diagnoses other than those comorbid with depressive disorders by age 15, daily hassles, stressful and traumatic life events, and coping styles. It is possible that the inclusion of such variables might have influenced the findings.

Each of the sub-studies was designed to capitalize on information across the entire age span of adolescence. Time was grouped into short and long-term. Assessments were made at different ages. A wide range of variables were probed for by using self-reports and diagnostic interviews. Accordingly, the eight sub-studies together were able to explore variations across time, age and sub-groups. However, due to space constrictions, we were not able to provide the preliminary analyses required for the moderation study.

A prospective longitudinal design was used to cover the time from early adolescence into early adulthood. The strategy of selecting, assessing and following-up depressed adolescents as cases, and non-depressed adolescents as controls in a subset with almost 2:1 ratio, led to an over-inclusion of depressed adolescents. The strategy increases statistical power. A large and representative school-based sample, the selection of a subset by screening the participants for depression; and the blind, randomized diagnostic follow-up interviews by clinicians with excellent interview integrity add to the strengths. In a comparative study, the use of telephone interviews has been found to be as reliable as face-to-face psychiatric interviews for Axis I and II psychopathology; with substantial economic and logistic advantages (Rohde et al., 1997). As the subset was formed with age and gender matching, the systematic bias which could have been present due to these two variables was reduced. In addition, the standard deviation of the mean age of the groups at each assessment was 0.6 or less, regardless of how

the groups were formed. This low standard deviation was an indicator that age by itself was not likely to be a significant variable in the analyses.

Although inferential statistical methods have been used, the generalization of the results does not apply to the ordinary high school student. The highly selected sample limits our generalization to cover only adolescent high-scorers on self-reports of depression, who possibly resemble outpatient adolescents most.

#### Conclusion and implications

As this thesis is about the relationship of depression to attempted suicide among adolescents, the main findings can be organized into 'depressive and attempted suicide' and 'non-depressive and attempted suicide'.

The *depressive* associates of attempted suicide are: recurrent thoughts about death, self-harm without suicidal intent, worthlessness, hopelessness, and initial insomnia. The *non-depressive* associate is victimization by violence. The *depressive* predictors are: worthlessness, suicidal act, dysthymia and any diagnosis of a depressive disorder. The *non-depressive* predictors are: not living with both biological parents and lower resilience. It is evident that the *non-depressive* risk factors are either stressors or poor coping. It has also been shown that the nature and magnitude of risk factors were both, stable and yet varying with age. The relationship between depression and suicidality among Norwegian school adolescents is primarily cognitive with frequent self-harm in the context of an inability to cope with non-intact parental units and violence in the environment.

The findings indicate that perhaps, it is not depression *per se*, but rather the specific nature of external stressors and internal vulnerabilities that linked together depression and suicidal acts during adolescence. This was found in a nation which is doing its best to be classless. Norway has been consistently on the top of the Human Development Index (HDI) composed and published annually by the United Nations Development Program. This setting adds meaning to the findings. Countries aiming to climb the HDI must consider the consequences of internal vulnerability among children and adolescents in the face of rapid societal transitions with unstable family units and violence among peers.

#### Implications of results

Non-intact parental units at distress must be identified and assisted to tide over such times. Age must be considered in both, theory building and clinical assessments of suicide risk. In the group of high school adolescents selected on the basis of their depression scores, a subgroup was found to have severe mental health challenges in the form of suicidality. These adolescents can receive clinical help if school personnel make timely referrals. The following list maybe helpful in such a process: cognitive depressive symptoms, acts of self-harm with or without suicidal intent, dysthymia, victims of violence and belonging to struggling, non-intact parental units. Future research on suicidality among adolescents needs to address the role of modifiable risk factors such as lower resilience and sleep disturbance; and particularly, the vulnerability of being male.

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# Research report

# Predictors of suicidal acts across adolescence: Influences of familial, peer and individual factors

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# Abstract

Objective: To examine the influences of familial, peer and individual predictors of suicidal acts in a longitudinal study with a subset of school adolescents reporting high levels of depressive symptoms.

Method: A representative sample of Norwegian school students (N=2464, mean age 13.7 years, T1) was reassessed after 1 year (T2) with the same questionnaire. All high scorers of depressive symptoms on the Mood and Feelings Questionnaire (MFQ) at T2 were defined as cases. One control from low or middle scorers, matched for age and gender, was randomly assigned to every two cases. This subset (n=345) was diagnostically assessed by face-to-face K-SADS-PL interviews (mean age=14.9 years). The same subset was reassessed after 5 years (T3) by using the same questionnaire (n=252, mean age=20.0 years) and telephone K-SADS-PL interviews (n=242). The participation rate at T3 was 76.9% (n=265). The questionnaire explored various relationships with family members, peers and individual factors such as lifestyle habits, and physical health.

Results: Irrespective of time, history of a suicidal act significantly predicted a later suicidal act. Not living with both biological parents and a diagnosis of any depressive disorder were significant predictors for younger and older adolescents, respectively. Conclusions: In line with the findings of previous clinical studies, our results underline the importance of identifying previous suicidal acts, depressive disorders, broken homes and risk behaviours such as smoking and intoxication in the assessment of suicidal risk across adolescence.

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# 1. Introduction

A recent review of community based studies comprising of 513,188 adolescents concluded that 9.7% adolescents had attempted suicide at some point in their lives (Evans et al., 2005). Although the corresponding

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rates for Norwegian adolescents ranged from 3% to 8.2% in the 1990s (Wichstrøm, 2000; Larsson & Sund, 2008), a recent study reported a 30% increase in the prevalence rate of suicidal acts among adolescent girls (Kvalen and Wichstrøm, 2007).

Research has consistently shown that history of a suicidal act and a depressive episode are the most prominent predictors of completed suicide and suicidal behaviour among youth (Apter & King, 2006). However, in a review of youth suicide studies, the strongest

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Table 1 Gender, MFQ score distributions displayed as frequency (percentages) and mean scores (SD) of MFQ among school adolescents who had reported suicidal acts up to T1 and between T1 and T2 and between T2 and T3 in a subset followed up into early adulthood (n=265)

	T1		T2		T3		
	Suicidal acts	No suicidal acts Suicidal acts N	No suicidal acts	Suicidal acts	No suicidal acts		
	(n=39)	(n=226)	(n=226) $(n=37)$ $(n=228)$		(n=36)	(n=229)	
Female (%)	32 (82)	168 (74.3)	27 (72.9)	173 (75.8)	31 (86.1)	169 (73.7)	
* MFQ high scorers at T1 (%)	27 (69.2)	48 (21.2)	21 (56.7)	54 (23.6)	17 (47.2)	58 (25.3)	
* MFQ high scorers at T2 (%)	35 (89.7)	142 (62.8)	37 (100)	140 (61.4)	31 (86.1)	146 (63.7)	
MFQ mean scores at T1 (SD)	28.9 (14.3)	15.7 (10.6)	24.4 (12.9)	16.6 (11.6)	23.4 (1.9)	16.8 (12)	
MFQ mean scores at T2 (SD)	36.4 (12.4)	24.9 (14.2)	42.2 (9.2)	24.1 (13.6)	31.9 (12.7)	25.8 (14.6)	

Note: \* MFQ = Mood and Feelings Questionnaire. MFQ high scores: a total of 25 or more; T1-T2=14-15 years; T2 to T3=15-20 years.

risk factors of suicide were found to be mental disorders, particularly affective disorders, substance use disorders, antisocial behaviours and a history of psychopathology (Beautrais, 2000). In a recent review of epidemiological studies, a model of youth suicidal behaviour was presented, wherein suicidal behaviour ensues as a result of interaction between socio-cultural, developmental, psychiatric, psychological and family—environmental factors (Bridge et al., 2006).

Several psychosocial predictors of suicidal behaviour have been identified in longitudinal studies of school adolescents: female gender (Wichstrøm, 2000; Larsson & Sund, 2008), history of suicidal act (Lewinsohn et al., 1994; Wichstrøm, 2000; Borowsky et al., 2001; Fergusson et al., 2005; Larsson & Sund, 2008), major depression (Giaconia et al., 2001; Lewinsohn et al., 2001), higher levels of self-reported depressive symptoms (Larsson & Sund, 2008), attempt by a friend (Lewinsohn et al., 1994; Borowsky et al., 2001; Larsson & Sund, 2008), low self-esteem (Lewinsohn et al., 1994; Wichstrøm, 2000; Fergusson et al., 2003), not living with both parents (Fergusson et al., 2000; Wichstrøm, 2000), maladaptive parenting (Johnson et al., 2002), poor attachment to parents (Fergusson et al., 2000), somatic symptoms (Borowsky et al., 2001), smoking (Fergusson et al., 2000; Larsson & Sund, 2008), alcohol intoxication (Wichstrøm, 2000; Borowsky et al., 2001), substance use (Fergusson et al., 2000; Borowsky et al., 2001; Giaconia et al., 2001) and violence victimization (Borowsky et al., 2001).

However, none of these studies compared the relative strengths of these predictors with the most prominent predictors of suicidal acts, i.e., a suicidal act and a depressive disorder or distinguished between short- and long-term predictors. An exception is a report from the Oregon Adolescent Depression Project (OADP) which investigated for variables predicting future attempts even after controlling for variables that predict depression and after controlling for a history of past attempt

(Lewinsohn et al., 1994). They found that history of substance-use disorder (alcohol or drugs), low social self-competence, low social support from friends, having been born to a teenage mother, hopelessness, suicide attempt by friend and functional impairment due to illness/injury predicted suicide attempts. In a later study conducted by the same group, the power of the same set of predictors for two different ages: during adolescence and early adulthood, was investigated (Lewinsohn et al., 2001). Only five of the eighteen variables continued to predict suicidal acts for the female gender and four for males, during both, adolescence and early adulthood. These findings indicate that predictors of suicide attempts up to adulthood differ with age.

Given the importance of depression as a predictor of suicidal acts (Bridge et al., 2006; Lewinsohn et al., 1993) and that the prevalence of major depression in adolescents has been estimated to be between 2% to 8% (Fleming & Offord, 1990; Lewinsohn et al., 1993), statistical power in studies predicting suicidal acts in the general population is often limited. In the present study, two-thirds of the adolescent school sample reported a high mean score on self-reported depressive symptoms at the one-year follow-up, providing sufficient power to estimate effects as suicidal acts.

The aim of the present study was to examine predictors of suicidal acts among school adolescents reporting high levels of depressive symptoms in a longitudinal design with cases and controls of self-reported depressive symptoms. Three important spheres of influence were examined: family, peer and individual characteristics. Assessment of their relative importance as compared to the two most robust predictors of suicidal acts, i.e., history of a depressive disorder and suicidal act, was considered. The first objective was to examine predictors by 14 years (T1 or baseline) for suicidal acts performed in middle adolescence, between 14 to 15 years of age, i.e. across a one-year interval. The

second objective was to examine predictors by 15 years (T2 or 1-year follow-up of baseline questionnaire) for suicidal acts performed during late adolescence to early adulthood, between 15 to 20 years of age (T3 or 5-year follow-up of interview subset), i.e., across a five-year interval. The third objective was to compare the strength of the identified predictors with that of a history of a depressive disorder and a suicidal act. (Tables 1, 2 and 3).

# 2. Methods

# 2.1. Participants and design

The participants were selected from a school sample of adolescents in 8th and 9th grades in 1998 from two

counties in Central Norway. Entry into school in Norway is at 6 years of age and therefore, 8th graders would generally be 13 years old and 9th graders, 14 years old. A cluster sampling technique resulted in a representative sample of 2792 students from 22 schools. A detailed description of the sampling procedure and the original sample is provided elsewhere (Sund et al., 2001, 2003).

# 2.2. Assessment points

At the first assessment (T1 or baseline=fall 1998), 2464 adolescents ( $N^1$ ) with a mean age of 13.7 (SD=0.5) years with 50.8% females, entered the project. A questionnaire, which included a screening measure for depressive symptoms (see below), was completed at school. The participation rate was 88.3%.

Table 2
Means (SD), frequencies (percentages), crude and adjusted ORs (95% CI) for predictors of suicidal acts performed between 14 to 15 years of age (T1 to T2) in a subset of school adolescents (n=265)

	Suicidal acts	No suicidal acts		
	(n=37)	(n=228)		
Predictor (T1)	M (SD)	M (SD)	Crude OR (95%CI)	Adjusted OR (95%CI)
Age	13.6 (0.6)	13.7 0(.6)	0.8 (0.4–1.4)	
MFQ	24.3 (13.1)	16.6 (11.6)	1.04 (1.02-1.07)	1.01 (0.9–1.05)
Self-perception	38.2 (10.1)	40.6 (8.5)	0.9 (0.9–1.008)	
Family functioning	33.4 (7.8)	35.3 (5.5)	0.9 (0.8–1.006)	
Conflict with mother	16.2 (4.4)	17.6 (4.2)	0.9 (0.8–1.006)	
Conflict with father	18.6 (3.5)	19 (3.9)	0.9 (0.89-1.06)	
IPPA-mother: alienation	11.7 (3.4)	11.9 (4.1)	0.9 (0.9–1.08)	
IPPA-mother: trust	43.4 (5.5)	42.4 (6.6)	1.02 (0.9–1.08)	
IPPA-mother: communication	35.9 (6.1)	34.2 (6.3)	1.03 (0.97–1.09)	
IPPA-father: alienation	12 (3.5)	12.1 (4.1)	0.9 (0.9–1.08)	
IPPA-father: trust	42.6 (5.3)	41.8 (6.8)	1.02 (0.9–1.07)	
IPPA-father: communication	32.1 (5.9)	32 (6.5)	1.001 (0.9–1.05)	
IPPA-friends	35.4 (5.5)	34.1 (5.6)	1.04 (0.97–1.1)	
	N (%)	N (%)		
Gender (female)	27 (72.9)	173 (75.8)	1.1 (0.5–2.5)	
Not living with both	24 (64.8)	84 (36.8)	3.1 (1.5–6.5)	3.1 (1.4–7)*
biological parents				
Daily smoking	3 (8.1)	8 (3.5)	2.4 (0.6-9.5)	
Bullied in the last 6 months	10 (27)	44 (19.2)	1.5 (0.6–3.4)	
Intoxicated by alcohol more than 5 times in the last 12 months	2 (5.4)	3 (1.3)	4.2 (0.6–26.5)	
Intoxicated by alcohol more than 5 times in the last 12 months or used narcotics	5 (13.5)	9 (3.9)	3.8 (1.1–12)	3 (0.8–11)
Knew a friend who had attempted suicide	13 (35.1)	55 (24.1)	1.7 (0.8–3.5)	
Chronic somatic illness	9 (24.3)	83 (36.4)	.5 (0.2 -1.2)	
Frequent physical pain	16 (43.2)	49 (21.4)	2.7 (1.3–5.3)	1.7 (0.7-4)
Depressive disorder diagnosis	10 (27)	40 (17.5)	1.7 (.7–3.8)	
Suicidal act	17 (45.9)	22 (9.6)	7.9 (3.6–17.3)	5.6 (2.2–14)**

Significant estimators in bold.

<sup>\*</sup>*p*<0.01 \*\* *p*<0.001.

Table 3 Means (SD), frequencies (percentages), crude and adjusted ORs (95% CI) for predictors of suicidal acts performed between 15 to 20 years of age in a subset of depressed school adolescents (n=265) followed up into early adulthood

	Suicidal acts	No suicidal acts			
	(n=36)	(n=229)			
Predictor (T2)	M (SD)	M (SD)	Crude OR (95%CI)	Adjusted OR (95%CI)	
Age	14.8 (0.6)	14.9 (0.6)	0.8 (0.4–1.4)		
MFQ	31.9 (12.7)	25.8 (14.6)	1.03 (1.005–1.05)	0.9 (0.9-1.01)	
Self-perception	34.9 (10.7)	38.7 (9.0)	0.95 (0.91-0.99)	0.96 (0.92-1.01)	
Family functioning	27.7 (8.0)	25 (7.2)	1.04 (1-1.09)		
Conflict with mother	15.0 (4.8)	12.9 (4.7)	1.09 (1.01-1.1)	1.04 (0.9-1.1)	
Conflict with father	13.3 (4.7)	11.1 (4.3)	1.10 (1.02-0.19)	1.05 (0.9–1.1)	
IPPA-mother: alienation	11.9 (5.1)	12.2 (5)	0.98 (0.92–1.06)		
IPPA-mother: trust	41.6 (9.3)	41.6 (7.6)	0.99 (0.95-1.04)		
IPPA-mother: communication	33.6 (7.6)	33.6 (7.2)	1.001 (0.9–1.05)		
IPPA-father: alienation	12.9 (5.3)	12.7 (5.2)	1.007 (0.9–1.07)		
IPPA-father: trust	41.1 (8.4)	39.9 (8.7)	1.01 (0.9–1.06)		
IPPA-father: communication	29.1 (7.6)	30 (7.8)	0.98 (0.94-1.03)		
IPPA-friends	23.4 (4.8)	22.9 (4.9)	1.02 (0.9–1.1)		
	N (%)	N (%)			
Gender (female)	31 (86.1)	169 (73.7)	0.45 (0.1–1.2)		
Not living with both	16 (44.4)	78 (34.1)	1.5 (0.7–3.1)		
biological parents					
Daily smoking	15 (41.6)	48 (20.9)	2.6 (1.2–5.6)	1.2 (0.5-2.9)	
Bullied	14 (38.9)	55 (24)	2 (0.9–4.2)		
Intoxicated by alcohol more than	5 (13.8)	25 (10.9)	1.3 (0.4–3.6)		
5 times in the last 12 months					
Intoxicated by alcohol more than 5 times in the last 12 months or used narcotics	3 (8.3)	30 (13.1)	1.3 (0.5–3.4)		
Knew a friend who had attempted suicide	19 (52.7)	93 (40.6)	1.6 (0.8–3.3)		
Chronic somatic illness	17 (47.2)	105 (45.8)	1.05 (0.5-2.1)		
Frequent physical pain	14 (38.8)	74 (32.3)	1.3 (0.6–2.7)		
Depressive disorder	25 (69.4)	80 (34.9)	4.2 (1.9–9)	2.9 (1.2-6.8)*	
Suicidal act	19 (52.7)	43 (18.7)	6.4 (3–13.5)	5.4 (2.1–13.5)**	

Significant estimators in bold.

At the second assessment (T2 or 1-year follow-up of baseline questionnaire=fall 1999), 2432 adolescents, ( $N^2$ ) of whom 50.3% were females, completed the same questionnaire again at school. The participation rate was 86.7%.

# 2.2.1. Subset selection

On the basis of scores of the screening instrument for depressive symptoms (described below) at T2, the participants were grouped into three levels: low (0-6), middle (7-24) and high (25 and above) scorers. All high scorers were regarded as cases. One control for every two cases was selected at random from the low and middle scorers, matched for age and gender. Of the 364 adolescents thus selected, 345 were diagnostically interviewed, face-to-face by six trained interviewers at

school, leading to a participation rate of 94.8%. The cases numbered 225 (65.2%) and the controls, 120 (34.8%). Females constituted 72.5% of this subset. The mean age was 14.9 (SD=0.6) years.

Eight adolescents did not consent to be contacted again. The consenting adolescents from the T2 interview subset were invited to participate at T3. From this pool of 337 adolescents (97.6%) who had not refused to be contacted again, 301 young adults (89.3%) consented to receive the invitation letter to participate at T3.

At the third assessment, (T3=October 2004–March 2005), 265 young adults ( $N^3$ ) with a mean age of 20.0 (SD=0.5) years and consisting of 77% females were reassessed. The overall participation rate at T3, from the original subset of 345 adolescents interviewed at T2, was 76.9%. At T3, 252 (73% with 77% females) and 242

<sup>\*</sup>*p*<0.05 \*\**p*<0.001.

(70.1% with 76.9% females) young adults returned the questionnaire and participated in the telephone interviews, respectively. Their mean age was 20.0~(SD=0.6) years.

The *non-participants* at T3 reported significantly higher scores on depressive symptoms at T1 (M=12.8, SD=11.0) than the participants (M=10.3, SD=8.8), t (343)=-2.01, p<0.05 (effect size of r=.10). They were also significantly more likely to be male than female [ $\chi^2$ (1)=6.5, p<0.01]. However, no differences between the participants and non-participants were found for mean depressive symptom scores at T2, depressive disorders or suicidal acts at any assessment point.

# 2.3. Assessment

# 2.3.1. Questionnaire

2.3.1.1. Psychosocial variables. Besides participant age and gender, information was gathered on residential status ("Living with both biological parents or not") lifestyle habits such as frequency of smoking ("Never" to "Daily"), use of alcohol ("Never" to "More than 50 times in the last 12 months") and narcotics (marijuana, hashish or sniffing).

Three types of bullying experiences at school, i.e., psychological (I have been derided, teased badly or been the object of unpleasant/hurtful statements at school or on the way), physical (I have been harassed, beaten, shoved or kicked badly at school or on the way) and social (Sometimes, one is intentionally excluded by classmates, it being then impossible to be together. Has this happened to you?), based on single items each, were explored for frequency ("Never in the last six months" to "More often than 2–3 times a week") (Olweus, 1996).

Somatic illness was probed for by asking if the participant had any of the following illnesses for more than three months: asthma, allergy, skin disease, migraine, diabetes, epilepsy, heart disorder and others. They were further asked if they suffered from *frequent physical pain* ("Yes" and "No"). Frequent pain was defined as at least once a week for more than 3 weeks.

In line with earlier findings (Lewinsohn et al., 1994, Borowsky et al., 2001; Larsson & Sund, 2008) participants were also asked if they knew a friend who had attempted suicide. Due to low frequencies, the other options of 'knowing a family member who had attempted suicide' and 'knowing others who had attempted suicide' were dropped from the analyses. Due to low variation, socio-economic and cultural variables were also dropped from the analyses.

2.3.1.2. Mood and feelings questionnaire (MFQ) (Table1). This measure was developed for the 8–18 years age group and addresses depressive symptoms based on DSM-III-R criteria for major depression (Angold et al., 1995). The participants were asked about their feelings and behaviours in the last 2 weeks with 34 items rated on a 0–2 scale with a total score range between 0 and 68. Psychometric properties of the MFQ in the original sample from which the subset was selected, have been found to be satisfactory with a standardised alpha of 0.92; a 3-week test-retest reliability of 0.84 and for 3 months of 0.80; and a convergent validity with the Beck's Depression Inventory at 0.91. The mean score for the original sample was 10.6 (SD=9.5) at T1 (Sund et al., 2001).

2.3.1.3. The self-perception profile for adolescents (SPPA) (Harter, 1988). The revised version of the SPPA for adolescents has been validated in a Norwegian adolescent school population (Wichstrøm, 1995). This version had 15 items rated on a 1–4 scale and total score ranges from 1 to 60.

2.3.1.4. The McMaster family adjustment device (FAD) (Epstein et al., 1983). This scale was validated in a school sample of American adolescents and includes 12 items rated on a 1–4 scale (Andrews et al., 1993). The items address subject adjustment with regard to family members as a group. The total scores range from 1 to 48.

2.3.1.5. Conflict with parents. This scale has been validated in the Oregon Adolescent Depression Project (OADP) (Andrews et al., 1993). Participants were asked to rate the frequency of specified conflict situations by using 5 items for each parent on a 0–4 scale. Thus, the total scores range from 0 to 20, reflecting levels of conflict with each parent.

2.3.1.6. The inventory of parent and peer attachment (IPPA). This revised measure addresses attachment to each parent (25 items) and to peers (6 items) (Armsden and Greenberg, 1989). The IPPA measures affectively toned expectancies to parents and friends associated with internalized representations of each of the three attachment types. Each item is rated on a 5-point Likert type scale and total scores for each parent range between 0 and 125.

The items relate to three domains of attachment quality: (a) *trust* reflecting the degree of mutual understanding and respect (e.g., "My mother/father/friends respect my feelings"); (b) communication addressing the extent of spoken communication (e.g., "I tell my mother/father/

friends about my problems and troubles"); and (c) alienation rating feelings of anger and interpersonal isolation (e.g., "My mother/father/friends do not understand what I am going through these days").

Cronbach alpha coefficients for mother and father IPPA were .91/.92 for the whole IPPA, respectively, .89/.90 for Trust, .81/.84 for Communication and .73/.73 for the Alienation subscales in the larger sample of this study, while for the peer IPPA scale it was .82 (Sund & Wichstrøm, 2002). High test–retest reliabilities over 3 weeks have been reported with  $r_s$  of 0.93 and 0.86 for parent and peer attachment scores, respectively (Armsden and Greenberg, 1987).

# 2.4. Interview (Table 2)

2.4.1. The Kiddie-schedule for affective disorders and schizophrenia-present and lifetime version (K-SADS-PI)

This well established, semi-structured diagnostic interview is built to assess present and past (most severe one) episodes of psychopathology in children and adolescents on Axis I according to DSM-III-R and IV criteria (Kaufman et al., 1997). Each individual symptom is rated on a clinical threshold score of 0–3 scale with a score of 3 representing clinical threshold.

At T2, all parents were invited to be interviewed separately and 79.8% of the adolescents had at least one additional informant. Summary symptom scores and diagnostic assessments were based on information obtained from both adolescents as well as parents. Diagnoses of depressive disorders and their comorbidity were investigated for the lifetime period, i.e., up to15 years of age. All the interviews at T2 were conducted face-to-face at schools.

The interviews at T3 were conducted on telephone and explored complete psychopathology for the five-year follow-up period retrospectively, i.e., from 15 to 20 years of age. In a comparative study, the use of telephone interviews has been found to be as reliable as face-to-face psychiatric interviews for Axis I and II psychopathology with substantial economic and logistic advantages (Rohde et al., 1997). The average interval between filling out the questionnaires and interviews was 3.5 weeks at T2 and 3 weeks at T3.

Experienced clinicians trained in psychopathology and the use of K-SADS-PL conducted the interviews. The interviewers were blind to the case/control status of the participant, at both the interview assessments. At T3, the young adults were randomized to one of the three interviewers. Inter Rater Reliability (IRR), for all screening symptoms, before interviewing was good

with Cohen's kappa at 0.71 at T2 and 0.75 at T3 with the third author, an experienced child psychiatrist. Interview integrity was maintained at both the interview assessments with an average kappa of 0.83 for all screening and affective symptoms at T2 and 0.80 for all screening symptoms at T3.

# 2.5. Depressive disorders

Diagnoses of depressive disorders included Major Depressive Disorder and Dysthymia based on DSM-IV-TR criteria (American Psychiatric Association, 2000). However, the project used more stringent criteria than the DSM-IV-TR to set a diagnosis of Depressive Disorder Not Otherwise Specified (NOS) by requiring at least three depressive symptoms lasting for at least two weeks, somewhat similar to the one used in the National Comorbidity Survey (Kessler and Walters, 1998), which required between two to four symptoms, lasting for 2 weeks to fulfill the criteria for minor depression. In the present study, three or more depressive symptoms, among which at least one had to be either depressed mood or anhedonia, were required to be present for at least 2 weeks to reach diagnostic threshold. The start and end of each depressive episode was dated in the interview by the interviewer and this information was used to time the diagnoses into by T1 or by T2.

# 2.6. Suicidal acts

This variable was based on information from two data sources, i.e., questionnaires and interviews. Acts of deliberate self-harm without suicidal intent were separate items in the interview and in the questionnaire. These were differentiated either by the respondent or the interviewer and excluded from the present study.

The item used in the questionnaire was the same as in a previous national survey of school adolescents 'Young in Norway', (Wichstrøm, 2000): "Have you ever tried to commit suicide?" ("No, never"; "Yes, once"; "Yes, several times"). If positively endorsed, the participants were further asked to fill out details of the timing of the last act: 'How long ago was your last act of attempted suicide?' ("Years", 'Months").

Questions on suicidal behaviour were also parts of the screening probes for depression in the K-SADS-PL. A positive response to the question: "Have you ever (or since the last interview) tried to kill yourself or done something which could have killed you?" and assessed to be at/above the clinical threshold level (a score of 3) by the interviewers was defined as a suicidal act. The interviewer also probed for details of the most serious act, including the date.

This information regarding timing of the last act was also used, along with the timing information in the questionnaire, to group suicidal acts into the following intervals (a) up to/by T1, (b) between T1 and T2, (c) up to/by T2 and (d) between T2 and T3.

From the two information sources, i.e., questionnaires and interviews, two dependent variables were formed: (a) suicidal acts performed between 14 to 15 years of age (T1-T2), (n=37; 27 females). A suicidal act reported up to T1 i.e., by 14 years of age, (n=39; 32)females) was one of the identified predictors for the first analysis. (b) suicidal acts reported between 15 to 20 years (T2-T3) years of age (n=36; 31 females). For this analysis, suicidal acts reported up to T2, i.e., by 15 years of age (n=67; 48 females) was one of the predictors identified. The number of persons who reported suicidal acts by T2 was different from those reporting suicidal acts by T1 added to those who reported between T1 and T2 because some participants reported suicidal acts at both assessments (n=17), while others (n=8) did not provide any information regarding the timing of their suicidal acts. These eight persons were included only in the analyses as having reported suicidal acts by T2, i.e., by 15 years of age, in the predictor variable for suicidal acts performed between T2 and T3, i.e., by 20 years of age.

The project was approved by the Regional Committee for Medical Research Ethics, Central Norway and by local school authorities in the two counties and the school boards. Informed consent, as prescribed by The Norwegian Data Inspectorate, was obtained from the participants.

# 2.7. Statistical analyses

SPSS 14.0 was used for all the analyses. Missing values in the questionnaires were substituted with values generated by the Expectation Maximization method for randomly missing data and regression for non-random data as indicated by the significance of Little's Missing Completely at Random chi-squared test value (Tabachnick and Fidell, 2006).

All variables with significant Odds Ratios (ORs) in the bivariate logistic regression analyses were entered into a subsequent multivariate logistic regression analysis. Variables significant at the bivariate levels were checked for multicollinearity before they were entered into the multivariate analyses (Field, 2005). Since the analyses were exploratory in nature, the Enter method of predictor inclusion was used. Alpha value was set to p < .05 to indicate statistical significance.

#### 3. Results (Table3)

3.1. Predictors of suicidal acts in middle adolescence (T1 to T2)

High scores on depressive symptoms as rated on the MFQ, not living with both biological parents, having been intoxicated by alcohol more than five times in the last twelve months or used narcotics by 14 years, suffering from more frequent physical pain and a suicidal act by 14 years were significant predictors of suicidal acts performed between 14 to 15 years of age, in the bivariate analysis. However, when these predictors were entered into a multivariate logistic regression analysis, the model retained only two of them, i.e., not living with both biological parents and a suicidal act by 14 years.

This model's  $\chi^2$  value was 40.5 (5), p<.0005 with Nagelkerke's  $R^2$  value at .26. The Hosmer and Lemeshow test statistic was calculated to be 9.7 (8), non-significant at .28. Although this model correctly classified 86.8% of all adolescents, only 21.6% of those who had reported suicidal acts between 14 to 15 years were correctly classified

3.2. Predictors of suicidal acts from late adolescence to early adulthood (T2 to T3)

Higher scores on depressive symptoms as rated on MFQ, lower self-perception scores, more frequent conflicts with both parents at 15 years, daily smoking, a diagnosis of any depressive disorder and a suicidal act by 15 years were significant predictors of suicidal acts between 15 to 20 years of age, in the bivariate analysis. However, when these predictors were entered into a multivariate logistic regression analysis, the model retained only two of them, i.e., a diagnosis of any depressive disorder and a suicidal act by 15 years of age.

This model's  $\chi^2$  value was 36.1 (7), p < .0005 with Nagelkerke's  $R^2$  at .23. Its Hosmer and Lemeshow test statistic was calculated to be 5.5 (8), non-significant at .70. While this model correctly classified 86.4 of all subjects, only 8.3 of those who had reported suicidal acts between 15 to 20 years of age were correctly classified.

# 4. Discussion

In the present longitudinal study, predictors of suicidal acts in three important areas of adolescent life, i.e., family, peers and individual factors were examined with regard to the most prominent predictors of adolescent suicidal acts, i.e., history of a suicidal act and depressive disorders, in a selected sample of school

adolescents wherein two-thirds had reported high levels of depressive symptoms. This over-sampling of depressed adolescents lent more power to the investigation of predictors of suicidal acts than would have been possible in a study of the general population since the prevalence of depression in the general population is between 4%–8% (Sund et al., 2001). Most of our findings support earlier reports from school-based and clinical studies, however, with the added benefits of being able to differentiate between age groups, time-period and comparisons with other predictors.

In line with findings of previous longitudinal studies and reviews, history of a suicidal act was found to be a significant predictor, irrespective of age, i.e., it was a predictor across the entire period of adolescence (Lewinsohn et al., 2001, 1994; Fergusson et al., 2003; Bridge et al., 2006; Foley et al., 2006), while not living with both biological parents was a predictor relevant to middle adolescence (Wichstrøm, 2000) and a diagnosis of any depressive disorder was a predictor relevant to late adolescence/late adulthood (Lewinsohn et al., 2001; Bridge et al., 2006; Foley et al., 2006), even when adjusted for familial, peer and individual factors.

We also found that the quality of relationship with parents (Bridge et al., 2006; Fotti et al., 2006), use of stimulants (Cho et al., 2007), intoxicants (Wichstrøm, 2000; Bridge et al., 2006; Hacker et al., 2006; Cho et al., 2007) and narcotics (Rossow et al., 2005; Bridge et al., 2006; Cho et al., 2007) though significant, differed according to age and time point in their importance as significant independent predictors of suicidal acts. Early indulgence in high risk behaviours such as use of alcohol or narcotics was significant in the bivariate analysis (Lewinsohn et al., 1994) but daily smoking was significant as a bivariate predictor of suicidal acts performed up to early adulthood, indicating these as high risk factors across the entire period of adolescence. In our bivariate analyses, higher levels of depressive symptom scores were significant predictors of suicidal acts among school adolescents (Lewinsohn et al., 1994: Wichstrøm, 2000; Fotti et al., 2006; Goldston et al., 2006; Larsson & Sund, 2008), irrespective of their age and assessment time point. Although chronic pain has been found to be a risk factor for adults, for both, attempted and completed suicide, (Fishbain, 1999), no such relationship was obtained in this selected sample of depressed school adolescents.

In the present study, relationships between adolescent depression and attempted suicide emerged with finer details not previously reported. High levels of depressive symptoms *at* 14 years were a significant predictor in the bivariate analysis, while being diagnosed with a

depressive disorder by 14 years was not. Yet, high levels of depressive symptoms at 14 years were nonsignificant in the multivariate analysis for this younger age group. By contrast, high levels of depressive symptoms at 15 years and a diagnosis of any depressive disorder by 15 years predicted suicidal acts between 15 to 20 years of age in the bivariate analysis. The results of multivariate analysis for the older age group, however, retained only a diagnosis of depressive disorder by 15 years as a significant predictor of suicidal acts across the next five year follow-up period. In essence, our findings underline the importance of a formal psychiatric diagnostic procedure as compared to questionnaire screenings. A formal, psychiatric diagnosis of depressive disorder had long-term predictive strength and was a significant and powerful predictor of suicidal acts among older adolescents, even after controlling for all other predictors. Adolescents, who reported suicidal acts at any assessment point, also reported higher levels of depressive symptoms at both earlier assessment points, thus emphasizing the importance of early identification of recurrent or longstanding, severe levels of depressive symptoms among adolescents. This is consistent with a report from the OADP study which found suicidal ideation to be associated with chronic, long-lasting and recurrent major depression (Lewinsohn et al., 1996).

In contrast to findings of a previous cross-sectional study (Fotti et al., 2006), none of the parent attachment variables contributed significantly to the risk of a suicidal act performed across adolescence. While increased conflicts with mothers and fathers and low family functioning did not predict suicidal acts performed between 14 to 15 years of age, when reported at 15 years, they emerged as significant predictors of suicidal acts performed between 15 to 20 years of age in the bivariate analyses. When considering these findings and that, not living with both biological parents by 14 years emerged as a significant predictor of suicidal acts between 14 to 15 years of age, in the multivariate analysis, the following interpretations may be considered. Firstly, changes in parental residential status influenced the adolescent negatively only if these changes had occurred before 14 years of age, i.e., for younger adolescents. However, relationships with parents appeared to be affected negatively only after this age, i.e. for older adolescents. Secondly, it is possible that not living with both biological parents has time-limited influence on adolescent suicidality. This might be explained by normal developmental processes in middle adolescence when bonds with biological parents gradually loosen and relationships with peers become more important. Conflicts between adolescents and parents were not maintained as a significant predictor when controlling for depressive diagnostic status at 15 years of age. This could be understood as an indication of conflicts associated with the adolescent's depression, which is a well-known risk factor of suicidal acts in adolescence. Altogether, these findings emphasize the need for further fine-grained analyses addressing the potential impact of parental relationships on adolescent suicidal behaviour into early adulthood.

Some of the findings of this study with a substantial over-inclusion of school adolescents who had self-reported a high score on a screening instrument for depression as compared to those adolescents who had reported low or moderate scores and followed up into early adulthood, are not consistent with earlier reports of representative, schoolbased samples from longitudinal and cross-sectional studies. First, lower self-perception scores, which have been found to be a significant predictor of suicidal acts in previous epidemiological studies (Lewinsohn et al., 1994; Wichstrøm, 2000), did not emerge as a significant predictor in our bivariate analyses for suicidal acts performed during early adolescence though they were weakly significant predictors during middle adolescence. Further, being a victim of bullying which was reported to be a significant associate of suicidal behaviour in older American and younger Dutch adolescents was not a predictor in the present study (van der Wal et al., 2003; Klomek et al., 2007). In contrast with earlier reports on older American adolescents, knowing a friend who had attempted suicide was not a significant predictor (Lewinsohn et al., 1994). Similarly, poor physical health was not a significant predictor of suicidal adolescent behaviour in the present study, again in contrast to outcomes of previous research (Bridge et al., 2006). The differences in findings between previous studies of school samples and the present study are most likely to be due to differences in sample characteristics and the over-sampling of depressed school adolescents.

Most clinical studies have focussed either on completed suicides or inpatients (Groholt et al., 1998) and very few reports exist on predictors of suicidal acts in outpatient samples of adolescents (Skarbø et al., 2005). Although the original sample of adolescents of the present study was representative of a school-based population, the over-inclusion of depressed adolescents in the subset makes the sample of the present study resemble the regular outpatient adolescents. Further, in the present study, the definition of a suicidal act performed by adolescents was based on criteria commonly used in the assessment of suicidal risk in clinical adolescent outpatients.

In line with findings of previous epidemiological and clinical studies, the most important predictor of adolescent suicidal acts was a history of a suicidal act (Fergusson et al., 2005; Apter & King, 2006). In both perspectives, comparisons between familial, peer and individual influences to a history of a suicidal act and depressive disorders revealed that history of a suicidal act and a diagnosis of any depressive disorder were the most important predictors of suicide attempts for older adolescents, while not living with both biological parents, and a history of a suicidal act were the most important predictors for younger adolescents.

# 4.1. Limitations

A few limitations of the present study merit consideration. Due to the small numbers of males in the sample, the effect of gender as a predictor was not possible to investigate. Therefore, the findings of the present study can primarily be generalized to female adolescents and young adults.

Although the attrition rate from T1 to T2 was much lower, 70% of those who had been interviewed at this time point (T2) were re-interviewed 5 years later (at T3). The non-participants at T3 had higher depressive symptom scores at the first assessment, however, this difference was modest and no differences between participants and non-participants in depressive symptom levels were found for T2 assessment.

In addition, it must be taken into account that diagnostic data was also retrospective and could have been hampered by recall bias of number of depressive symptoms and timing. A note of caution needs to be added with reference to the generalization of the findings due to the limited ability displayed by the multivariate models to correctly classify adolescents who had performed suicidal acts, which could be a consequence of the small numbers of adolescents who had performed suicidal acts.

It may be possible that the variables which were only significant in the bivariate analyses and not in the multivariate analyses might have contributed to the risk of depression and in that manner, contributed to the risk of suicidal acts. Since the outlining of pathways is not the purpose of the current study, it is suggested that future research considers pathways to suicidal acts in adolescence as an objective.

This study also has substantial strengths in its use of:
(a) a longitudinal design covering the entire period from early adolescence into early adulthood, (b) a design with cases and controls of self-reported depressive symptoms, leading to an over-inclusion of depressed adolescents enabling us to control for the effects of high levels of depressive symptoms and a formal

diagnosis of depression, (c) a large school-based representative sample from which the subset was selected, and (d) blind and randomized diagnostic interviews by clinicians with excellent interview integrity.

# 4.2. Implications

In conclusion, school health personnel and clinicians assessing suicidal risk among school adolescents should be alerted to the importance of a history of a suicidal act, a diagnosis of any depressive disorder and not living with both biological parents as powerful potential predictors of suicidal acts from early adolescence to early adulthood.

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#### Conflict of interest

All authors declare that they have no conflict of interest.

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Paper II



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# Research report

# Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence

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# Abstract

Objective: To examine the role of depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. *Method:* A representative sample of Norwegian school students (N=2464, mean age 13.7 years) in grades 8 and 9 was reassessed after one year (T2) with the same questionnaire. All high scorers of depressive symptoms on the Mood and Feelings Questionnaire (MFQ) at T2 were defined as cases. One control from low or middle scorers, matched for age and gender, was randomly assigned to every two cases. This subset (n=345) was diagnostically assessed by face-to-face K-SADS-PL interviews (mean age=14.9 years). The same subset was reassessed after 5 years (T3) by using the same questionnaire (n=252, mean age=20.0 years) and telephone K-SADS-PL interviews (n=242). The participation rate was 76.9% (n=265).

Results: Cognitive symptoms dominated the depressive symptom profile among suicide attempters, irrespective of age and time. Among younger adolescents, suicidal thoughts and acts of self-harm without suicidal intent were associated with suicidal acts. Recurrent thoughts about death, hopelessness, disturbed concentration and middle insomnia were associates of suicidal acts among older adolescents.

Worthlessness by 15 years was a significant predictor of suicidal acts between 15 to 20 years. MDD and a depressive episode, not otherwise specified, continued to be significant associates among younger adolescents, while dysthymia by 15 years remained a predictor of suicidal acts between 15 to 20 years, even when controlled for depressive symptoms.

Conclusions: Self-harm without suicidal intent, middle insomnia, cognitive depressive symptoms and a formal psychiatric diagnosis of any depressive disorder should alert professionals in the risk assessment of suicidal adolescents.

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# 1. Introduction

The assessment of suicidal youth is one of most common and demanding emergencies in adolescent mental health services (Brent, 2001). The ratio of suicide attempts to suicide completions is higher in adolescence than in any other age group (King, 1997). The prevalence of

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suicide attempts starts increasing from the age of 14 years onwards (Lewinsohn et al., 2001a). Up to 32% of clinically referred adolescents will attempt suicide at least once by early adulthood (Kovacs et al., 1993), while 20% will repeat the attempt (Harrington et al., 1994). In community settings, 70–91% of youth who attempt or think about suicide have a psychiatric disorder (Gould et al., 1998). Research on suicidal phenomena among adolescents has mainly explored for other risk factors associated with depressive disorders (Brent et al., 1994; Lewinsohn et al., 2001a; Bridge et al., 2006), since most persons with mood disorders do not commit suicide and about half of them never attempt suicide (Rihmer, 2007).

Depressed mood has been found to be the most common depressive symptom among 11 to 18 year old adolescent inpatients and outpatients who have attempted suicide (Bettes and Walker, 1986). Among adolescent emergency unit inpatients, high levels of self-reported depressive symptoms predicted suicide attempts in a 2 to 4 year follow-up (Ivarsson et al., 1998). Among 13 to 17 year olds, hopelessness, negative self-esteem and violent behaviour were more common among depressed, suicidal adolescents than among those who are depressed but non-suicidal (Csorba et al., 2003). A recent review on sleep and suicidal behaviour among youth has called for the use of longitudinal studies due to inconsistencies in findings of cross-sectional studies, wherein the associations with insomnia often disappeared when controlled for depression (Liu and Buysse, 2006).

Major depressive disorder (MDD) and dysthymia were specifically associated with higher rates of suicidal behaviours than other diagnoses among outpatients aged 8–13 years, followed up for five years (Kovacs et al., 1993). MDD has also been significantly associated with suicidal acts among older school adolescents (Lewinsohn et al., 1994).

Although current empirical research has added considerably to our knowledge on sucidality among adolescents, gaps continue to exist about specific aspects which can potentially aid the clinician in the assessment of suicide risk among adolescents, for example: are there specific depressive symptoms and disorders related to suicidal acts? Do these relationships differ with age and time? To the best of our knowledge, longitudinal studies exploring the role of specific depressive symptoms and disorders as associates and predictors of suicidal acts among adolescents have not yet been reported.

The aim of the current study was, therefore, to examine relationships between specific depressive symptoms and disorders with suicidal acts in a sample of depressed school adolescents and non-depressed controls followed for a five-year period into early adulthood. We

first studied the prevalence of depressive symptoms and disorders in adolescents with high mean scores on depressive symptoms as compared to those with low to moderate mean scores as reported in a questionnaire. The next objective was to examine the specificity of depressive symptom and diagnostic profiles as associates of suicidal acts at two developmental phases, i.e., by 15 years and for the next 5-year period as assessed retrospectively at 20 years of age. Thirdly, we explored the role of specific depressive symptoms and disorders by the age of 15 years as potential prospective predictors of suicidal acts between 15 to 20 years of age. Finally, we investigated the role of self-harm without suicidal intent as an associate and predictor of suicidal acts, across age and time, given its complex relationship with suicidal acts (Grøholt et al., 2000; Jacobson and Gould, 2007; Larsson and Sund, 2008).

#### 2. Methods

# 2.1. Participants and procedures

The participants were selected from a school sample of adolescents in 8th and 9th grades in 1998 from two counties in Central Norway. A cluster sampling technique resulted in a representative sample of 2792 students from 22 schools. Based on prevalence estimates of 5–10% of MDD among adolescents in the general population (Lewinsohn et al., 1998; DSM-IV-TR, 2000), we calculated that a sufficient number of participants with a formal diagnosis of depressive disorder would be included in the present study to provide powerful comparisons with non-depressed adolescents. A detailed description of the sampling procedure and the original sample is provided elsewhere (Sund et al., 2001, 2003).

# 2.2. Assessment points

At the first assessment, (T1), 2464 ( $N^1$ ) adolescents with a mean age of 13.7 (SD=0.5) years and a participation rate of 88.3% (50.8% females) entered the project. A questionnaire, including a screening measure for depressive symptoms, was completed at school. At the second assessment (T2), 2432 ( $N^2$ ) adolescents with a mean age of 14.9 (SD=0.5) years, with a participation rate of 86.7% (50.3% females) completed the same questionnaire again at school.

# 2.2.1. Subset selection

On the basis of the mean total scores for depressive symptoms on the Mood and Feeling Questionnaire (MFQ) (described below), at T2, the participants were grouped into three levels: low (0–6), middle (7–24) and high (25 and above) scorers. All high scorers were regarded as cases. One control for every two cases was selected at random from the low and middle scorers, matched for age and gender. Of the 364 adolescents thus selected, 345 were diagnostically interviewed face-to-face by trained interviewers at school. The cases numbered 224 (64.9%) and the controls, 121 (35%). The participation rate was 94.7% and included 72.5% females.

At the third assessment (T3), 265 young adults ( $N^3$ ) with a mean age of 20.0 (SD=0.5) years and a participation rate of 76.9% (77% females) were reassessed. Two hundred and fifty-two young adults (73%) completed the questionnaire with a mean age of 20.0 (SD=0.6) years, of whom 77% of them were females. For the interviews, the participation rate was 70.1% (n=242) with a mean age of 20.0 (SD=0.6) years, of whom 76.9% were females. Of the 224 high scorers on the MFQ at T2, 155 were reinterviewed at T3, with a participation rate of 69.1%.

The non-participants at T3 were significantly more often males,  $[\chi^2 \ (1)=6.5, \ p<0.01]$ . While the non-participants reported significantly higher depressive symptoms scores on the MFQ at T1 (M=12.8, SD=11.0) than the participants (M=10.3, SD=8.8), t (343)=-2.0, p<0.05 (effect size of r=.10), no difference between the participants and non-participants was found for mean depressive symptom scores on the MFQ, depressive disorders or suicidal acts as assessed at T2.

# 2.3. Measures

# 2.3.1. Questionnaire

2.3.1.1. Mood and Feelings Questionnaire (MFQ). This measure, which was developed for 8-18 year olds and includes all depressive symptoms based on DSM-III-R criteria for major depression (Angold, 1989), was chosen since it is adolescent-friendly in its wording. The cut-off score for grouping of high scorers as a category was chosen on the basis of the assessment of the 2464 adolescents with the MFQ one year (T1) before the interviewing study, when the 90th percentile was at 24. The participants were asked about their feelings and behaviours in the last 2 weeks for 34 items rated on a 0-2 scale with a total score range of 0-68. Psychometric properties of the MFQ in the original sample have been found to be satisfactory (Sund et al., 2001). A detailed analysis of MFQ scores and suicidal acts across adolescence revealed that respondents with suicidal acts had significantly higher mean scores at all three assessment points (Nrugham et al., 2008).

#### 2.3.2. Interview

2.3.2.1. The Kiddie – Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL). This well established semi-structured diagnostic interview is built to assess present and past episodes of psychopathology in children and adolescents on Axis I according to DSM-III-R and IV-TR criteria (Kaufman et al., 1997). Each individual symptom is rated on a 0–3 scale, with a score of 3 representing clinical threshold.

Experienced clinicians trained in psychopathology and the use of K-SADS-PL conducted the interviews. The interviewers were blind to the case/control status of the participant, at both interview assessments, i.e., T2 and T3. The average interval between filling out the questionnaires and interviews was 20 days at T2 and 21 days at T3. Inter Rater Reliability (IRR) for all K-SADS symptoms at the end of training and before initiation of real interviews, was good, with Cohen's kappa of 0.71 at T2 and 0.70 at T3 with the third author, an experienced child psychiatrist. Interview integrity was maintained at T2 and T3 with average kappas of 0.83 and 0.80, respectively, for all screening symptoms and affective supplement symptoms.

At T2, 79.8% of the adolescents had at least one parent as a separate informant. Summary symptom scores and diagnostic assessments were based on information obtained from both informants. A diagnosis of depressive disorder and its co-morbidity was investigated for the lifetime period, i.e., up to 15 years of age. At T3, the young adults were randomly allocated to interviewers.

The interviews at T3 were conducted on telephone and explored psychopathology for the five-year follow-up period retrospectively, i.e., from 15 to 20 years of age. In a comparative study of follow-up interviews of young adults, the use of telephone interviews as follow-ups of face-to-face interviews has been found to be as reliable as face-to-face psychiatric interviews for Axis I and II psychopathology with substantial economic and logistic advantages (Rohde et al., 1997). The K-SADS PL interviews also provide information regarding functioning levels in three areas: family, school/work and friends.

# 2.3.3. Key variables

2.3.3.1. Depressive symptoms. K-SADS-PL provides a list of 30 items, with guidelines to assess sub-clinical

and clinical thresholds, to probe for all DSM-IV-TR symptoms in a depressive episode, including all subtypes of major depression and dysthymia. The screening section for a depressive episode has eight items and a threshold score in the screening indicates the use of supplement items. A clinical threshold score on items assessing various aspects of depressive symptoms was required for entry into analysis. Medical lethality of suicidal acts was excluded from the present study since it is not a DSM-IV-TR criterion for a depressive episode or a subtype of depressive episode.

2.3.3.2. Depressive disorders. Diagnoses of depressive disorders included Major Depressive Disorder (MDD) and dysthymia based on DSM-IV-TR criteria. However, in the present study, a diagnosis of Depressive Disorder Not Otherwise Specified (DD-NOS) required at least three depressive symptoms lasting for at least two weeks. Probes for a diagnosis of any depressive disorder were limited to the most serious past episode. Functional impairment, as measured by Childhood-Global Assessment of Symptoms (C-GAS), was a requirement for a diagnosis of MDD or dysthymia during the diagnostic assessments (Shaffer et al., 1983). All respondents with a formal diagnosis of MDD had either reduced functioning or a CGAS score below 71. However, two young adults had a diagnosis of MDD at T3, with a C-GAS score above 71, in spite of reduced functioning. For the purpose of analysis, current and past diagnoses were pooled together, as was done with depressive symptoms. For example, an episode of MDD present at anytime up to the age of 15 years was recorded as MDD, irrespective of whether it was current or past. However, if, one individual had more than one diagnosis of depressive disorder, each such diagnosis was considered (Helzer et al., 2006).

2.3.3.3. Suicidal acts. Positive responses to items on suicidal acts, either in the questionnaire or the interview were used. Suicidal acts and acts of self-harm without suicidal intent were assessed on separate items, both in the interview and questionnaire. Acts of self-harm without suicidal intent were differentiated from suicidal acts, either by the respondent in the questionnaire or the interviewer using either seriousness of suicidal intent or lethality or both. Ambiguous instances were defined as sub-threshold levels of suicidal acts. Acts of self-harm without suicidal intent and sub-threshold levels of suicidal acts were excluded from the definition of suicidal acts.

The item used in the questionnaire was the same as in a previous, national survey of youth, 'Young in Norway' (Wichstrøm, 2000): "Have you ever tried to commit suicide?". The response options were: "No, never"; "Yes, once"; "Yes, several times". All respondents who answered positive to this item were defined as atempters. Questions on suicidal behaviour were parts of the screening probes for depression in the K-SADS. A positive response to the question: "Have you ever (or since the last interview) tried to kill yourself or done something which could have killed you?" and assessed to have reached the clinical threshold level by the interviewer was defined as a suicidal act. Thus, two groups were formed: those who reported never to have attempted a suicidal act at any one assessment (T1, T2, or T3), as attempters.

The assessments were approved by the local school authorities, the school boards and the Regional Committee for Medical Research Ethics, Central Norway. Based on standards prescribed by The Norwegian Data Inspectorate, informed consent was obtained from the participants at all assessment points.

# 2.4. Statistics

Descriptive methods were used to examine frequencies of depressive symptoms and disorders. A series of bivariate logistic regression models were conducted to examine crude estimates for potential associates and predictors. All depressive symptoms and disorders providing significant Odds Ratios (ORs) at p<.01 level were subsequently entered into multivariate logistic regression analyses run separately for age and time. Multicollinearity diagnostics revealed minor problems for data at T3 with hypersomnia (.29) and hopelessness (.46) loading together leading to both being excluded from analyses (Field, 2005). The multivariate analyses used the standard method of entry and significance level was set to p<.05.

# 3. Results

3.1. Frequency of depressive symptoms and disorders by 15 years of age and between 15 to 20 years of age

Depressed mood was found to be the most frequent symptom at both assessment points (T2 and T3), (see Table 1), while the next highest frequencies changed according to age and time. The frequency and distribution of depressive diagnoses also differed with age. In the younger age group, MDD and DD-NOS constituted 76.1% of the depressive diagnoses with a roughly equal distribution between them, while among older subjects, these two diagnoses accounted for 86.6% of the

Table 1
Percentages of depressive symptoms and diagnoses in a subset of non-depressed and depressed school adolescents as assessed by K-SADS interviews at two assessments, T2 (at 15 years) and T3 (at 20 years) and grouped into high and low scorers on the Mood and Feelings Questionnaire (MFQ)

	T2 $(n=345)$			T3 $(n=242)$		_
Depressive symptoms/diagnoses	MFQ low scorers (n=121)	MFQ high scorers (n=224)	All	MFQ low scorers (n=87)	MFQ high scorers (n=155)	All
Depressed mood	24	58	46.1	32.2	57.4	48.3
Irritable mood	14.9	32.6	26.4	13.8	28.4	23.1
Anhedonia	9.1	18.8	15.4	13.8	25.8	21.5
Initial insomnia	3.3	24.1	16.8	14.9	32.9	26.4
Middle insomnia	1.7	8.9	6.4	6.9	19.4	14.9
Terminal insomnia	2.5	7.1	5.5	6.9	9.7	8.7
Circadian reversal	1.7	11.6	8.1	9.2	21.3	16.9
Non-restorative sleep	6.6	22.8	17.1	20.7	31	27.3
Hypersomnia	0.8	10.3	7	12.6	26.5	21.5
Decreased appetite	2.5	13.8	9.9	12.6	19.4	16.9
Weight loss	0	5.4	3.5	3.4	5.8	5
Increased appetite	0.8	5.8	4.1	2.3	7.7	5.8
Weight gain	0	1.8	1.2	0	2.6	1.7
Psychomotor agitation	5.8	5.8	5.8	3.4	9	7
Psychomotor retardation	1.7	9.4	6.7	8	12.3	10.7
Fatigue	11.6	34.8	25.5	25.3	40.6	35.1
Disturbed concentration	8.3	34.8	26.7	16.1	31.0	25.6
Indecisiveness	3.3	14.3	10.4	6.9	11.6	9.9
Worthlessness	15.7	26.3	22.6	20.7	31.6	27.7
Excessive guilt	3.3	13.8	10.1	11.5	18.7	16.1
Hopelessness	9.1	21.9	17.4	11.5	27.1	21.5
Recurrent thoughts about death	10.7	38.4	28.7	11.5	27.1	21.5
Suicidal thoughts	5.8	21.4	15.9	12.6	21.3	18.2
Suicidal acts	3.3	24.1	8.1	1.1	10.3	7
Self-harm without suicidal intent	0.8	7.1	4.9	4.6	12.3	9.5
Non-reactive mood	11.6	25	20.3	19.5	32.9	28.1
Depressed mood qualitatively different from grief	13.2	33.0	26.1	11.5	24.5	19.8
Diurnal variation — morning	1.7	9.8	7	1.1	3.9	2.9
Diurnal variation — evening	13.2	26.8	22	11.5	21.9	18.2
Increased sensitivity to rejection	9.1	18.3	15.1	5.7	7.7	7
MDD	5.7	25.9	18.8	19.5	38.7	31.8
Dysthymia	5.7	15.1	11.9	3.4	6.4	5.4
DD-NOS	10.7	23.6	19.1	4.5	5.8	5.4

depressive diagnoses and MDD dominated the picture. However, higher mean scores of depressive symptoms on the MFQ at 15 years were more strongly associated with suicidal acts by 15 years [OR (95% CI)=6.5(3.1–13.5)] than with any depressive disorders by 15 years [OR (95% CI)=4.4(2.7–7.4)].

# 3.2. Associates of suicidal acts performed by 15 years of age

The results of the first set of bivariate logistic regression analyses which examined depressive symptoms

and disorders assessed at 15 years (T2), retrospectively for lifetime, (see Table 2), showed that suicidal thoughts, self-harm without suicidal intent, Circadian reversals and hopelessness were most strongly associated with suicidal acts. Among diagnoses, MDD and DD-NOS were significant and strong associates of suicidal acts.

# 3.3. Associates of suicidal acts performed between 15 to 20 years of age

The results of the next set of bivariate logistic regression analyses which focussed on the role of depressive

Table 2
Results of bivariate logistic regression of depressive symptoms and diagnoses as associates and predictors of suicidal acts (SA) across adolescence

	_	by 15 years as of suicidal acts	Depressive symptoms/diagnoses between 15–20 years as associates of suicidal acts between 15–20 years (n=242) (SA=34)		Depressive symptoms/ diagnoses by 15 years as predictors of suicidal acts between 15–20 years (n=265) (SA=36)	
Depressive symptoms	$\chi^2$	OR (95% CI)	$\chi^2$	OR (95% CI)	$\chi^2$	OR (95% CI)
Depressed mood	22.3**	3.3(1.9-5.5)	32.8***	14.6(4.3-49.4)	20.1***	5.7(2.4–13.4)
Irritable mood	9.1**	2.2(1.3-3.8)	11.1**	3.7(1.7-7.9)	6.1*	2.4(1.2-5)
Anhedonia	6.3*	2.2(1.2-4.1)	23.2***	6.7(3.1–14.5)	10.7**	3.8(1.7-8.1)
↓ Appetite	16.3***	4.5(2.1-9.3)	5.7*	2.8(1.2-6.4)	1.8	2(.7-5.2)
Weight loss	3.6	3.1(.9-10)	1	2.1(.5-8.3)	2.7	3.8(.8-16.6)
↑ Appetite	6.7**	4.2(1.4–12.6)	7.4**	5.3(1.7–16.5)	3.7*	3.7(1.1–12.6)
Weight gain	1.1	3(.4–22)	2.9	6.4(.8-47.3)	.6	2.9(.2 - 28.1)
Initial insomnia	26.2***	4.7(2.6-8.5)	10.1**	3.4(1.6-7.2)	8.8**	3.3(1.5-7)
Middle insomnia	4.5	2.6(1.1-6.4)	17***	5.9(2.6-13.3)	.04	.8(.1-3.7)
Terminal insomnia	4.6	2.8(1.1-7.2)	5.6	3.5(1.3-9.6)	.6	.4(.06-3.5)
Circadian reversal	17.4***	5.4(2.4-12.1)	16.8***	5.5(2.5-12.2)	3.2	2.6(.9 - 6.9)
Non-restorative sleep	25.1***	4.5(2.5-8.1)	14.6***	4.3(2-9.1)	2.8	2(.9-4.4)
Hypersomnia	2	1.9(.8–4.5)	10.4**	3.6(1.6–7.8)	7.1**	4.1(1.5–10.8)
Agitation	3.9	2.5(1.03-6.4)	5.3	3.8(1.3-11.1)	.05	1.2(.2-5.7)
Retardation	5.8	2.9(1.2-6.9)	5.5	3.2(1.2-8.2)	.08	.8(.1-3.5)
Fatigue	7.4**	2(1.2-3.5)	20.8***	5.7(2.6-12.8)	5*	2.3(1.1-4.7)
Disturbed concentration	20.7***	3.3(2.0-5.6)	36.4***	10.7(4.7-24.3)	10**	3.1(1.5-6.4)
Indecisiveness	1.4	1.5(.7–3.3)	12.6***	5.7(2.3-14.4)	2.9	2.3(.9-5.7)
Worthlessness	29.9***	4.5(2.6-7.8)	28***	7.7(3.5–17.2)	20.9***	5.4(2.6-11)
Excessive guilt	12.4***	3.6(1.8-7.5)	14.8***	5.1(2.3-11.4)	13.4***	5.2(2.2-11.8)
Hopelessness	30.3***	5.2(2.9-9.4)	46.3***	15.4(6.6-35.6)	6*	2.7(1.2-5.8)
Death thoughts	31.2***	4.3(2.5-7.2)	58***	22.7(9.3-55.5)	6.2*	2.4(1.2-4.9)
Suicidal thoughts	49.0***	8.8(4.7–16.7)	56***	22.5(9.4-53.8)	3.6*	2.2(1-4.9)
Suicidal acts		,		` ,	14.4***	6.2(2.6-14.8)
Self-harm — no suicidal intent	16.3***	8(2.7-23.7)	31.8***	15.4(5.9-40.2)	.4	.5(.06-4)
Non-reactive mood	23.0***	3.9(2.2-6.9)	23.4***	6.4(2.9–14)	3.7*	2.1(1-4.5)
Mood different from grief	9.6**	2.3(1.3-3.9)	5.2*	2.6(1.1-5.7)	6.3*	2.5(1.2-5.1)
Diurnal variation — morning	7.3**	3.2(1.4-7.6)	1	2.5(.4-13.6)	.9	1.8(.5-5.6)
Diurnal variation — evening	5.2*	1.9(1.1-3.3)	3	2.1(.9-4.8)	2.7	1.9(.9-4)
↑ Sensitivity to rejection	8.6**	2.5(1.3-4.7)	2.9	2.8(.9-8.5)	1.4	1.7(.7-4)
Depressive diagnoses						
MDD	20***	3.7(2.1-6.9)	29.4***	8.2 (3.6-18.4)	14.1***	4.2(2-8.7)
Dysthymia	4.5*	2.1(1.05-4.2)	5.1*	4.3 (1.3–14)	13.3***	4.8(2.1-10.6)
DD-NOS	12.2***	2.8(1.5-4.9)	.02	1.1(.2-5.2)	.8	1.4(.6-3.3)

Model Chi-square, p-values and odds ratios (95% confidence intervals).

Bold=variables entered into multivariate analyses. \*p < .05, \*\*p < 0.01, \*\*\*p < 0.001.

symptoms and disorders as assessed retrospectively at 20 years of age (T3) (Table 2), showed that recurrent thoughts about death, suicidal thoughts, hopelessness and self-harm without suicidal intent were the strongest associates of suicidal acts. All sleep disturbances, except terminal insomnia, were significantly associated with suicide attempts. Although only MDD was a significant associate with suicidal acts, the Odds Ratio (OR) for MDD in the older age group was twice as high for those in the younger age group.

3.4. Predictors of suicidal acts performed between 15 to 20 years of age

The results of the last set of bivariate logistic regression analyses which investigated depressive symptoms and disorders reported by 15 years (T2) (Table 2), showed that suicidal acts, depressed mood, worthlessness and excessive guilt were the strongest prospective predictors. However, the number of significant depressive symptoms was fewer than those obtained in the

cross-sectional analyses. MDD and dysthymia were both, strong and significant predictors of suicidal acts.

3.5. Depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence: results of multivariate analysis

# 3.5.1. Associates of suicidal acts performed by 15 years of age

The multivariate logistic regression model for associations between suicidal acts and statistically significant depressive symptoms by 15 (T2), had two depressive symptoms, i.e., suicidal thoughts and self-harm without suicidal intent (Table 3). This cross-sectional model had a  $\chi^2$  value of 82.4(df=19), p<.0005 and the Nagelkerke's  $R^2$  value was at .31. The Hosmer and Lemeshow statistic of 3.4 (df=5) was non-significant at .63. This model correctly classified 82% of all respondents, and 43% of the attempters.

When these depressive symptoms were compared with the two depressive diagnoses which had emerged as significant associates of suicidal acts by 15 years in the bivariate analyses, a significant multivariate model was obtained, with a  $\chi^2$  value of 63.5 (df=4), p < .0005and the Nagelkerke's  $R^2$  value was at .24. The Hosmer and Lemeshow statistic of 0.6 (df=3) was non-significant at .89. This model correctly classified 79.9% of all respondents, and 40.7% of the attempters. This final model of associates of suicidal acts by 15 years (T2) had four significant variables, two depressive diagnoses: MDD, OR (95%CI)=2.6 (1.3-5.2), p<.01; DD-NOS, OR (95%CI)=2.3 (1.1-4.5), p<.05; and two depressive symptoms: self-harm without suicidal intent, OR(95% CI)=3.5 (1.1–11.5), p < .05; and suicidal thoughts, OR (95%CI)=4.3 (2.1-8.8), p<.0005.

3.5.2. Associates of suicidal acts performed between 15 to 20 years of age

The multivariate logistic regression for associations between suicidal acts and depressive symptoms between 15 to 20 years, as assessed at 20 years of age (T3), had six depressive symptoms, three cognitive and three somatic (Table 3). However, two of the significant symptoms, i.e., increased appetite and initial insomnia, were protective in nature. This cross-sectional model had a  $\chi^2$  value of 102.8 (df=19), p<.0005 and the Nagelkerke's  $R^2$  value was .62. The Hosmer and Lemeshow statistic of 17.1 (df=4) was significant at .002. This model correctly classified 93% of all respondents and 67.6% of the attempters.

When these significant depressive symptoms were compared with MDD, the depressive diagnosis which had emerged as significant associates of suicidal acts between 15 to 20 years of age in the bivariate analyses, a significant multivariate model was obtained, with a  $\chi^2$  value of 90.7 (df=7), p<.0005 and the Nagelkerke's  $R^2$  value was at .56. The Hosmer and Lemeshow statistic of 2.4 (df=4) was non-significant at .65. Overall, this model correctly classified 85.8% of all respondents, and 89.7% of the attempters. Although this final model did not retain MDD, it included the following significant depressive symptoms: recurring thoughts of death, OR (95%CI)=14.6 (4.3–49.1), p<.0005; disturbed concentration, OR (95%CI)=16.3 (3.8–70.1), p<.0005; hopelessness, OR (95%CI)=8.3 (2.6–26.6), p<.0005 and initial insomnia, OR(95% CI)=0.16 (0.0–0.6), p<.01.

# 3.5.3. Predictors of suicidal acts performed between 15 to 20 years of age

In the third multivariate logistic regression analysis, depressive symptoms by 15 years as prospective

Table 3
Results of multivariate logistic regression as given by Odds Ratios (95% Confidence Intervals) of depressive symptoms as associates and predictors of suicidal acts (SA) across adolescence

Depressive symptoms	Depressive symptoms by 15 years as associates of suicidal acts by 15 years (n=345) (SA=86)	Depressive symptoms between 15–20 years as associates of suicidal acts between 15–20 years (n=242) (SA=34)	Depressive symptoms by 15 years as predictors of suicidal acts between $15-20$ years $(n=265)$ (SA=36)
Recurrent thoughts about death		7.9 (1.4–43.1)*	
Suicidal thoughts	3.7 (1.6-8.4)**		
Self-harm without suicidal intent	4.5 (1.3–16.0)*		
Worthlessness			3.3 (1.3–8.6)*
Hopelessness		26.5 (4.1–168.5)***	
Disturbed concentration		56.9 (5.6-577.7)***	
Increased appetite		0.05 (0.0-0.6)*	
Initial insomnia		0.04 (0.0-0.4)**	
Middle insomnia		6.0 (1.3–27.8)*	

Note. \*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001.

predictors of suicidal acts performed between 15 to 20 years were examined. This predictive model had only one depressive symptom: worthlessness (Table 3). It had a  $\chi^2$  value of 37.4 (df=7), p<.0005. The Nagelkerke's  $R^2$  value was .24. The Hosmer and Lemeshow statistic of 38.9(df=4) was significant at .0005, revealing poor calibration of the model. This model correctly classified 86.4% of all respondents and 13.9% of the attempters.

When the significant predictors which had emerged in the bivariate analyses, that is worthlessness, MDD and dysthymia were contrasted with each other, a significant multivariate model was obtained, with a  $\chi^2$  value of 28.1 (df=3), p<.0005 and Nagelkerke's  $R^2$  value at .18. The Hosmer and Lemeshow statistic of 11.1 (df=3) was significant at .01. This model correctly classified 86.8% of all respondents and 16.7% of the attempters. This final model included dysthymia, OR (95%CI)=2.4 (1.0–6.2), p<.05; and worthlessness, OR (95%CI)=3.3 (1.3–8.2), p<.01 as significant predictors of suicidal acts between 15 to 20 years.

# 4. Discussion

In the present study, the role of depressive symptoms and disorders as associates and predictors of suicidal acts across was examined in a subset of depressed and non-depressed adolescents recruited from a representative sample of Norwegian high school students, followed-up for a five year period. The main findings were: (a) cognitive symptoms dominated the depressive psychopathology profile of adolescents with suicidal acts, regardless of age and time (b) their roles differed with age, and (c) the role of a formal psychiatric diagnosis of depressive disorders changed according to time and age.

Among older adolescents, a decline in the frequency of depressive symptoms was observed, with the exception of anhedonia, self-harm without suicidal intent, and somatic symptoms of fatigue, eating, sleeping and psychomotor disturbances. The frequencies of dysthymia and DD-NOS also declined, while a slight increase was seen in the frequency of MDD in the older age group.

Depressed mood, initial insomnia, disturbed concentration, worthlessness and excessive guilt were all significantly related to suicidal acts in all the three bivariate profiles. In contrast, mood worsening in the evenings, terminal insomnia, weight loss and gain and both aspects of psychomotor disturbances were conspicuously absent from the three bivariate profiles.

Depressed mood has been found to be linked to suicidality among adolescents in earlier studies (Bettes and Walker, 1986; Ivarsson et al., 1998). To date, initial

insomnia has been related to suicidal acts only among adults (Bulik et al., 1990). Our findings extend this knowledge to a sparsely explored but important area, i.e., relationships between suicidal acts and initial insomnia among adolescents. The cross-sectional model of the older adolescents revealed a clear trend in sleep disturbances, with five out of the six possible sleep disturbances (except for terminal insomia) highly significantly associated with suicidal acts. This finding could be considered important in the light of recent findings on the close association between insomnia and completed suicides among adults (McGirr et al., 2007). However, similar to other reports among adults, further analysis (not presented here) showed that these sleep disturbances were primarily explained by the presence of depressive disorders (Bernert et al., 2005). Although decreased appetite and weight loss have been reported among suicidal adults (Bulik et al., 1990), this finding was not supported by our study.

In the multivariate models, core cognitive depressive symptoms known to be associates or predictors of suicidal acts among adults, i.e., recurring thoughts of death, suicidal thoughts, worthlessness, hopelessness and disturbed concentration, were found to be associates or predictors of suicidal acts among adolescents. However, these relationships were not similar or uniform in their impact, i.e., they were time-limited and age-specific in their relationship to suicidal acts. Somewhat surprisingly, increased appetite and initial insomnia between the ages of 15 to 20 years were found to be protecting against suicidal acts, with unclear interpretation.

Two longitudinal studies have reported hopelessness to be an associate, but not a predictor of suicidal phenomena (Pfeffer et al., 1988; Shahar et al., 2006), as found in the present study. Although higher levels of hopelessness have predicted suicide among adult inpatients and outpatients (Beck et al., 1990; Grøholt et al., 2006), a similar trend was not found in the present study of attempted suicide among depressed school adolescents. The role of hopelessness, diagnostically assessed by interviews, among suicidal adolescents appears to be different from its role among adults, as measured by a questionnaire for the preceding week, in that it was an associate but not a predictor, in the present study. Hopelessness has also been found to be an even stronger predictor of suicidal behaviour than depression and the best predictor of completed suicide in adult populations (Beck et al., 1974). A study on whether Beck's cognitive theory of depression and hopelessness also applied to adolescent community populations found support for his theory of depression but not for hopelessness (Lewinsohn et al., 2001b). Exploratory research into whether there are three distinct negative thoughts in the cognitive triad among adults has reported that there was only a singular one-dimensional negative view of the self (McIntosh and Fischer, 2000).

Worthlessness, a part of the cognitive triad, by the age of 15 years, was a significant multivariate predictor of suicidal acts in the present study. In a study of children and adolescents with various forms of suicidality, worthlessness has been related to all forms of suicidal behaviours, after adjustment for other depressive symptoms, comorbid disorders and demographics (Liu et al., 2006). In the present study, a cross-check revealed that suicidal acts by 15 years as predictor was not retained in the model, while worthlessness continued to be a significant predictor. In the same sample, that adolescents with suicidal acts had significantly lower mean scores on self-esteem than participants without suicidal acts, though the differences were small and age-dependent (Nrugham et al., 2008). Selfcriticism has been reported to be the cognitive variable most strongly associated with hopelessness among adolescent suicide attempters than other depressive cognitions and perfectionism (Donaldson et al., 2000).

Apart from self-harm without suicidal intent and initial insomnia, the other depressive symptoms retained in the final multivariate analyses were all cognitive in nature, across age and time. These findings underline the importance of cognitive depressive symptoms as indicators of suicidal acts from adolescence to early adulthood. Cognitive rigidity is accepted as patently implicated in suicidal phenomena among adolescents (Beautrais et al., 1999) and in adults (Arffa, 1983). Although we did not find suicidal thoughts to be a significant predictor of suicidal acts, it has been reported that 15-year olds with suicidal thoughts were 12 times more likely to have attempted suicide between 15 to 30 years of age than those without suicidal thoughts (Reinherz et al., 2006).

Our finding of self-harm without suicidal intent as a significant bivariate associate for both age groups and multivariate associate in the younger age group but not a bivariate predictor in the older group indicates that acts of self-harm without suicidal intent decreased with increased age or that acts of self-harm without suicidal intent had a limited role vis-à-vis suicidal acts in this sample. Here, it was both, age-specific and time-limited in its effects. A history of suicidal acts by 15 years, although an important bivariate predictor, was not retained in the multivariate model.

While the relationships between dysthymia, DD-NOS and suicidal acts across adolescence differed with age and time, MDD was both, a significant associate, irrespective of age and a significant predictor of suicidal

acts, in the bivariate analyses. However, MDD did not continue to be significant, neither as an associate nor as a predictor when compared with depressive symptoms in the final multivariate analyses of the older adolescents. Dysthymia by 15 years remained a significant predictor of suicidal acts performed between 15 to 20 years. This is in line with findings among adult outpatients (Klein et al., 2000). Since cognitive symptoms dominated the bivariate and multivariate models it seems that it is not depressive disorders but specific types of depressive symptoms, i.e., cognitive depressive symptoms, which are primarily related to suicidal acts across adolescence. The continuity of percentages of depressive symptoms and changes in the distribution of diagnoses as assessed at T3 among the T2 high scorers on the MFQ provide support for the conceptualization of depression as a continuous variable and calls to add dimensional criteria to categorical definitions of diagnosis (Helzer et al., 2006; Pickles and Angold, 2003; Regier, 2007).

#### 4.1. Limitations

Due to the small number of males in the subset, the present findings can primarily be generalized to female adolescents and young adults. At the five-year follow-up, 30% of the high school adolescents who had been interviewed at T2 could not be re-interviewed, which might be an indicator of bias. The analysis of differences between the participants and non-participants at T3, and the use of categorical definitions also point to possible underestimation of the relationships between suicide attempts and the explanatory variables.

Even though semi-structured diagnostic interviews were used to obtain information leading to diagnoses and parents were available as additional informants at T2, such information is subject to recall bias since it was retrospective in nature, except for current diagnoses. It should be noted that information on past and current symptoms/disorders among school adolescents were pooled, and was restricted to the most serious episode. Information regarding other psychiatric symptoms and disorders at the first interview, T2, was also limited to symptoms and disorders comorbid with depressive disorders.

The multivariate models derived in the present study need to be interpreted with caution. The Hosmer and Lemeshow statistic was significant for both the multivariate predictor models and the final model for older adolescents indicating poor model calibration. Two of the associates for the older adolescents had wide confidence intervals for ORs indicative of low sample

size. Overall, the associative models were seen to be better than the predictive models.

However, this study has substantial strengths in its use of a longitudinal design covering most of the adolescent period into early adulthood. The present subset of adolescents was selected from a school-based representative sample using a case-control design with an overinclusion of depressed adolescents, thus enabling us to assess the effects of various diagnoses of depression on suicidality with increased power, in addition to the use of blind and randomized diagnostic interviews by clinicians with excellent interview integrity. Together, the oversampling of depressed adolescents at 15 years of age and the inclusion of only clinically significant symptoms, makes the adolescents in the present study resemble the adolescent outpatient population.

#### 4.2. Conclusions

Future research should aim to replicate the findings of the present study, with special focus on cognitive depressive symptoms in adolescence and integrating categorical and dimensional approaches. Any depressive disorder, self-harm without suicidal intent in younger adolescents, middle insomnia in older adolescents and cognitive depressive symptoms irrespective of age, should alert school mental health professionals and clinicians in their assessment of suicidality among adolescents.

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# Conflict of interest

All authors declare that they have no conflict of interest.

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- 65. Kåre Bergh: APPLICATIONS OF ANTI-C5a SPECIFIC MONOCLONAL ANTIBODIES FOR THE ASSESSMENT OF COMPLEMENT ACTIVATION
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- 160.Christina Vogt Isaksen: PRENATAL ULTRASOUND AND POSTMORTEM FINDINGS A TEN YEAR CORRELATIVE STUDY OF FETUSES AND INFANTS WITH DEVELOPMENTAL ANOMALIES.

- 161.Holger Seidel: HIGH-DOSE METHOTREXATE THERAPY IN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA: DOSE, CONCENTRATION, AND EFFECT CONSIDERATIONS.
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