Essi Ilomäki

CONDUCT DISORDER AMONG GIRLS: VIOLENT BEHAVIOUR, SUICIDALITY AND COMORBIDITY

A STUDY OF ADOLESCENT INPATIENTS IN NORTHERN FINLAND
ESSI ILOMÄKI

CONDUCT DISORDER AMONG GIRLS: VIOLENT BEHAVIOUR, SUICIDALITY AND COMORBIDITY
A study of adolescent inpatients in Northern Finland

Academic Dissertation to be presented with the assent of the Doctoral Training Committee of Health and Biosciences of the University of Oulu for public defence in Auditorium 1, Building PT1 of the Department of Psychiatry (Peltolantie 17), on 12 October 2012, at 9 a.m.

UNIVERSITY OF OULU, OULU 2012
Ilomäki, Essi, Conduct disorder among girls: violent behaviour, suicidality and comorbidity. A study of adolescent inpatients in Northern Finland
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Oulu, Finland

Abstract

Conduct disorder (CD) among girls is a common but seldom studied psychiatric disorder. The aim of this study was to examine risk factors for CD, the factor structure of CD symptoms, suicidal behaviour, comorbid disorders and nicotine dependence of adolescent girls with CD in an inpatient sample in Northern Finland.

The study subjects were 508 12- to 17-year-old inpatients treated in an acute psychiatric ward, Unit 70, at Oulu University Hospital between April 2001 and March 2006. These adolescents were interviewed using the Schedule for Affective Disorder and Schizophrenia for School-Age Children Present and Lifetime (K-SADS-PL) to obtain psychiatric diagnoses according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). In addition, the European Addiction Severity Index (EuropASI) was used to obtain information on somatic health, family situation and delinquency. From the data collected, 63 girls and 92 boys fulfilled the criteria for current DSM-IV-diagnosed conduct disorder.

It was observed that, although the number of symptoms and severity of CD was lower among girls compared to boys, the level of functioning was lowered to the same degree. Physical abuse increased the risk for violent CD, and living apart from at least one biological parent increased the risk for both violent and non-violent CD among girls. The results of this study also suggest a gender difference in the factor structure and developmental model of CD. Alcohol dependence increased the risk for suicide attempt and self-mutilation almost fourfold among girls with CD. Girls with CD had more comorbid affective and anxiety disorders than boys. Girls with CD also had more self-reported allergies. Finally, the number of CD symptoms was positively correlated with the level of nicotine dependence (ND) among both girls and boys, and a gender difference was found in the correlation between symptom subscales and the level of ND.

The findings suggest that gender differences exist in conduct disorder. Special attention should be paid to the prevention, identification and treatment of CD among girls. It seems that, among girls with CD, the well-being of primary family is important in prevention. Alcohol dependence and depression in girls with CD should be treated with special care. DSM-IV might not always be sensitive enough to diagnose CD among girls, and this should be considered when behavioural symptoms are evaluated in girls.

Keywords: adolescence, adolescent psychiatry, aggression, comorbidity, conduct disorder, gender difference, hospitalisation, impulse control, suicidality
Ilomäki, Essi, Tyttöjen käytöshäiriön erityispiirteet: väkivaltaisuus, itsetuhoisuus ja liitännässäsaistavuus. Tutkimus osastohoidossa olevista nuorista Pohjois-Suomessa

Oulun yliopiston tutkijakoulu; Oulun yliopisto, Lääketieteellinen tiedekunta, Kliinisen lääketieteet, Psyykiatria, PL 5000, 90014 Oulun yliopisto; Psyykiatrian klinikka, Oulun yliopistollinen sairaala, PL 26, 90029 OYS; Psyykiatrian tulonyskikko, Nuorisopsyykiatran klinikkarhmä, HYKS, PL 590, 00029 HUS


Tiivistelmä

Tytöjen käytöshäiriö on vähän tutkittu mutta yleinen psykiatrinen häiriö. Tässä tutkimuksessa analysoitiin tyttöjen käytöshäiriön riskitekijöitä, oireiden fa ktorirakennetta, käytöshäiriöisten itsehuhoisuutta, samanaikaisesta psykiatrista ja somaattista sairastavuutta sekä nikotiiniriippuvuutta psykiatrissa osastohoidossa olleiden alaikäisten nuorten keskuudessa.


Asiasanat: aggressiivisuus, impulssikontrolli, itsetuhoisuus, komorbiditeetti, käytöshäiriö, nuorisopsyykiatnia, nuoruusikä, sairaalahoito, sukupuoliero
To my family
Acknowledgements

This work was carried out at the Department of Psychiatry at the University of Oulu and at the Psychiatry Clinic of Oulu University Hospital. I am most grateful to the following co-workers and friends without whom this work would not have been completed.

I wish to express my gratitude to Professor Matti Isohanni, and to the current and former head of the Psychiatric Clinic, Docent Outi Saarento and Docent Juha Moring, for providing me with good facilities to work in and for their support during my work.

I am deeply grateful to my supervisors;

Professor Pirkko Räsänen has walked beside from the beginning, and has made this journey one to remember. Pirkko, you are undoubtedly among the most inspiring and most brilliant supervisors and superiors that I have ever met. In its simplicity: I consider you one of my biggest idols.

Docent Kaisa Riala has helped me markedly by sharing her extensive clinical experience in adolescent psychiatry and helping me to construct my train of thoughts in my dissertation. Thank you Kaisa.

My sincere appreciation for the comprehensive work and very important new points of view belong to the official referees of this dissertation, Dr Outi Mantere and Docent Olli Kampman. I appreciate their advice and constructive criticism.

I must especially thank Dr Helinä Hakko for her tireless help and for putting up with me, since I am truly no wizard on statistics, which she is, luckily for me. I also owe my warmest thanks to Kaisa Karvonen, who, like Helinä, helped me with statistics and cheered my days with her good attitude. Special thanks belong also to Anna Vuolteenaho and David Cowling for their careful revision of the language of this dissertation and original papers. It is my pleasure to thank Dr Taru Ollinen (Mäkikyrö) for her great input in the design of STUDY-70 in unit 70. I also appreciate the encouragement received from Professor Markku Timonen and Professor Sari Lindeman as official members of my follow-up group.

I share the credit of my work with my co-authors Professor Pirkko Räsänen, Docent Kaisa Riala, Dr Helinä Hakko, Dr Taru Ollinen, Professor Mauri Marttunen, Risto Ilomäki, Tanja Nordström and Kaisa Karvonen, acknowledging their important collaboration and expert knowledge.

Many of the people at the Department of Psychiatry of Oulu University and the Psychiatric Clinic of Oulu University Hospital have supported this work. I
want to express special thanks to Pirkko Kaan, Minna Lakkapää, Anja Kylmänen and Dr Marja-Leena Kuusimäki for their kind help with practical things whenever needed.

I owe my gratitude to all of the colleagues and the staff of Unit 70 who worked in Unit 70 during the data collection for their extensive work with this study. I have loads of good memories of our co-operation during these 5 years of data collection. It is rare to meet so many nice people, such a good attitude and good sense of humour in a single workplace. It has been an honour to work with you guys. Of course, most of all, my gratitude belongs to the all the adolescents and their families participating in the study during their treatment-period in Unit 70.

I acknowledge financial support received for my work from the Eli Lilly and Company Foundation, the Finnish Cultural Foundation, the Finnish Medical Foundation, the Foundation for Psychiatric Research, the Jalmari and Rauha Ahokas Foundation, the Research Foundation of Orion Corporation and the Yrjö Jahnsson Foundation.

I must thank all my friends equally for just being there. My friends live all around Finland and have been there for me whenever needed, even when I haven’t always been there for them. I have the privilege to have beautiful, unique spirits as my friends, and I deeply appreciate all of you. My dearest hobby is at the horse-stables, where my feet are kept firmly on the dirty ground, and I enjoy every minute of it. Thank you my lovely horses Wilma and Kaija.

I owe thanks to my family of origin. My father has taught me to finish all the important things that I start and not to be afraid of obstacles on the way, but turn them into challenges. My mother has a heart of gold. She never got tired of asking when my work would be ready and always encouraged me in her own silent way, probably knowing that is the most effective way for me. My dear sister Nelli gives me and everyone else a great example in her work of what we are capable of when filled with passion and belief.

Finally, I am most grateful to my dear children, Julia and Roi, for bringing all the laughter and smile to our home and reminding me of the most important things in life. With you there is magic in every single day. I met my husband Risto in this study group in 2001, and since then we have been inseparable. During these eleven years, we have learned to work together as co-workers, as best friends, as lovers, as parents, as partners and I hope our symbiosis is for forever. Thank you Risto, you are the love of my life.
Abbreviations

5-HTTLPR  5-HydroxyTryptamine (serotonin) Transporter Linked Polymorphic Region
ADHD  Attention deficit hyperactivity disorder
APA  American Psychiatric Association
C1QTNF7  C1q and Tumor Necrosis Factor-related protein 7
CAPA  Child and Adolescent Psychiatric Assessment
CBCL  Child Behaviour Checklist
CD  Conduct disorder
CFA  Confirmatory Factor Analysis
CGAS  Children’s Global Assessment Scale
CI  Confidence interval
COMT  Catechol-O-Methyltransferase
CSI-4  Child Symptom Inventory-4
DAWBA  The Development and Well-Being Assessment
DISC-C  Diagnostic Interview Schedule for Children
DSM-III  Diagnostic and Statistical Manual of Mental Disorders, third edition
DSM-III-R  Diagnostic and Statistical Manual of Mental Disorders, third edition, revised
DSM-IV  Diagnostic and Statistical Manual of Mental Disorders, fourth edition
EFA  Exploratory Factor Analysis
EuropASI  European Addiction Severity Index
GFI  Goodness-of-Fit Index
IQR  Interquartile range
K-SADS-PL  Schedule for Affective Disorder and Schizophrenia for School-Age Children Present and Lifetime
MDD  Major depressive disorder
mFTQ  Modified Fagerström Tolerance Questionnaire
MST  Multi-Systemic Therapy
ND  Nicotine dependence
ODD  Oppositional Defiant Disorder
OR  Odds Ratio
P  Probability in statistical significance
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>Post-traumatic stress disorder</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
<tr>
<td>WHO-CIDI</td>
<td>World Health Organisation Composite International Diagnostic Interview Version 3.0</td>
</tr>
</tbody>
</table>
List of original publications

This thesis is based on the following publications, which are referred to in the text by the Roman numerals I-V.


In addition, some previously unpublished data have been included in this thesis.
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1 Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), conduct disorder (CD) involves “a repetitive and persistent pattern of behaviour in which the basic rights of others or major age-appropriate social norms or rules are violated” (APA, 1994). On the basis of burden of treatment alone, CD is a major concern in child and adolescent psychiatry. CD is found to be one of the most common reasons for treatment referral among adolescents (Nelson et al. 2006, Merikangas et al. 2011). The treatment of CD is challenged even further with the comorbid conditions and potentially serious consequences of CD, as well as adolescents’ often complicated social situation.

Research on CD has been extensive, but it has mostly been based on data limited to males, or the proportion of girls in the analyses has been too small to study gender differences. Data on girls has thus mostly been lacking until recent years, even though CD is a common psychiatric disorder among adolescent girls. The prevalence of CD in adolescent female population is thought be around 6% (Merikangas et al. 2010 and Table 1), although this may be an underestimate (Delligatti et al. 2003). Prevalence has increased markedly during the past decades (Collishaw et al. 2004). Research to date suggests that fundamental gender differences exist in the development, course and prognosis of CD, but there is a lack of large enough gender-specific data in diagnostics as well as in prevention and intervention programmes (Moffitt et al. 2008, Keenan et al. 1999). Various serious and undesirable outcomes are associated with CD in girls, and the consequences are far-reaching. CD among girls is associated with increases in comorbid psychiatric conditions (including substance use), adult antisocial personality disorder, poor physical health, early and violent death and a forty-fold increase in adult criminality. Furthermore, CD is associated with problems in future mothering behaviours that, in turn, contribute to a high rate of transmission of antisocial behaviour to next generations (Kim-Cohen et al. 2003, Pajer 1998, Rhule et al. 2004, Zoccolillo et al. 1996).

There are many reasons for the paucity of research on CD in girls (Delligatti et al. 2003). The first potential cause is that present DSM-IV criteria for CD fail to identify all girls with CD, i.e., the criteria lack sensitivity (Zoccolillo 1996). DSM-IV-criteria for CD (APA 1994) were never validated in significant female populations and the criteria were mostly derived from studies on boys (Lahey et al. 2000). Among girls, internally focused behaviours may result in different patterns of antisocial, abusive and exploitive behaviour. These covert rule
violations may be less visible than the externalizing behaviours seen in boys. A second possibility is a false perception among mental health professionals that CD among girls is relatively rare or clinically non-significant. This may explain why many outcome studies have either concentrated solely on boys or have considered all children with CD together. A third reason may be that many studies of anti-social behaviour have used data from the criminal justice system. Males have higher arrest rates and also commit more serious crimes than females. This leads to criminal data dominated by male cases (Zoccolillo 1993). All these reasons result in girls with CD being less likely to be recognised, diagnosed and treated than boys.

The present study is a part of the STUDY-70 project, which was initiated in 2001, at the University of Oulu, Department of Psychiatry. The STUDY-70 project took place in a 10-bed adolescent psychiatric acute inward unit, and its initial objective was to examine psychosocial risk factors for adolescent mental disorders and substance use disorders. Data were gathered for 5 years. The final database comprised 508 participants, 300 girls and 208 boys, their mean age being 15.5 years. The subjects were interviewed by using a well-established, semi-structured diagnostic interview: the Schedule for Affective Disorder and Schizophrenia for School-Age Children Present and Lifetime (K-SADS-PL) (Kaufman et al. 1997, Ambrosini 2000). In the final data, 63 girls and 92 boys fulfilled the criteria for DSM-IV-diagnosed conduct disorder. This database made it possible to evaluate gender differences in CD and to study CD among girls.
2 Review of the literature

2.1 Definition of conduct disorder according to DSM-IV and ICD-10

2.1.1 DSM-IV criteria

Conduct disorder (DSM-IV code 312.8), as defined in the Diagnostic and Statistical Manual for Mental Disorders, version IV (DSM-IV) published by the American Psychiatric Association (APA), is characterised by childhood or adolescent onset of pervasive and persistent patterns of aggressive, deceptive, and destructive behaviour. For an adolescent to meet the DSM-IV criteria for the diagnosis of CD, three out of fifteen symptoms are required to have occurred during the last 12-month period, one of them during the last six months, and the behaviour must cause clinically significant impairment (APA 1994). The symptoms include the following:
1) lies, 2) truant, 3) initiates physical fights, 4) bullies, threatens or intimidates others, 5) non-aggressive stealing, 6) vandalism, 7) breaking and entering, 8) aggressive stealing, 9) fire setting, 10) often stays out at night, 11) ran away overnight, 12) use of a weapon, 13) physical cruelty to people, 14) forced sexual activity, and 15) cruelty to animals. Symptoms are classified into four sub-scales: violations of rules, destruction of property, deceitfulness or theft and physical aggression. In the current diagnostic classification manual (DSM-IV) conduct disorder is further sub-categorised into childhood- versus adolescent-onset CD and into three severity indexes (APA 2000). Conduct disorder was categorised for the first time in the DSM-III (APA 1980).

2.1.2 ICD-10 criteria

According to the other diagnostic system, the International Classification of Diseases (ICD-10), published by the World Health Organisation (WHO), Conduct disorder (ICD-10 code F91) is characterised by a repetitive and persistent pattern of dissocial, aggressive, or defiant conduct. Such behaviour, when at its most extreme for the individual, should amount to major violations of age-appropriate social expectations, and is therefore more severe than ordinary childish mischief or adolescent rebelliousness. Isolated dissocial or criminal acts are not in
themselves grounds for the diagnosis, which implies an enduring pattern of behaviour (WHO 1992).

Examples of the behaviours on which the diagnosis is based include the following: excessive levels of fighting or bullying; cruelty to animals or other people; severe destructiveness to property; fire setting; stealing; repeated lying; truancy from school and running away from home; unusually frequent and severe temper tantrums; defiant provocative behaviour; and persistent severe disobedience. Any one of these categories, if marked, is sufficient for the diagnosis, but isolated unsocial acts are not. According to ICD-10, CD is further categorised into conduct disorder confined to the family context (F91.0), unsocialised conduct disorder (F91.1) and socialised conduct disorder (F91.2)(WHO 1992).

2.1.3 Difference in structure and use of DSM-IV and ICD-10 criteria for conduct disorder

ICD-10 is an international standard in diagnostic classification, and it now exists in its tenth revision. Chapter V covers mental and behavioural disorders (WHO 1992). ICD-10 is used for all general epidemiological and many health management purposes. The classification system developed by the American Psychiatric Association (APA), DSM-IV, consists of five axes of disorders, and it is suggested that diagnosticians avoid focusing on a single clinical disorder but consider other important aspects as well. The first axis contains clinical disorders and the second covers personality disorders and intellectual disabilities. The remaining axes cover related medical, psychosocial and environmental factors. DSM-IV was designed for both epidemiological and clinical use and to meet the needs of research. Today it is the main diagnostic tool used in psychiatric research. The next (fifth) edition of the Diagnostic and Statistical Manual of Mental Disorders, DSM-V, is currently in its consultation, planning and preparation stage (Pardini et al. 2010).

The DSM-IV diagnostic criteria for CD have been criticised regarding their poor pertinence in girls, and it is uncertain whether the threshold or subtyping of CD should actually have different criteria for girls and boys (Zoccolillo et al. 1993, Zoccolillo et al. 1996, Delligatti et al. 2003). It has been suggested that diagnostic criteria should include more non-physical aggression and more covert rule violations, symptoms that are especially common among girls but which are not identified by DSM-IV (Delligatti et al. 2003).
2.2 Prevalence of conduct disorder

Prevalence rates for CD vary between different studies. Methodological differences are also notable (Lahey et al. 1999, Maughan et al. 2004). Recent estimated lifetime prevalence of CD in the U.S. is 6.8% (females 5.8%, males 7.9%) (Merikangas et al. 2010, Table 1). In Finland, comprehensive epidemiological research on the prevalence of CD among adolescents is lacking. However, Almqvist and colleagues (1999) found that, among 8- to 9-year-old Finnish children, combined prevalence of CD and oppositional defiant disorder (ODD) using DSM-III-criteria was 4.7%. The prevalence of CD in adolescence is globally relatively consistent (Canino et al. 2010), varying e.g. from 1.7% in Hong Kong (Leung et al. 2008) to 2.9 in Chile (Vicente et al. 2012) and 3.0% in Australia (Sawyer et al. 2001).

The onset age has been found to be lower among boys meeting the current DSM-IV criteria (Cohen et al. 1993, Maughan et al. 2004), and thus the sex ratio of prevalence for CD diminishes with age; from approximately 4:1 before adolescence to 2:1 in adolescence (Frick & Dickens 2006). This finding has also been criticised. It has been suggested that part of the reason why gender differences in prevalence decrease with age is that the difficult to detect non-physical aggressive symptoms, which are typical for girls, increase with age, while physical aggression decreases (Keenan et al. 1999, Delligatti et al. 2003).
Table 1. Prevalence of CD among adolescents in Western countries.

<table>
<thead>
<tr>
<th>Country, study</th>
<th>Age of adolescents</th>
<th>Prevalence of CD among both genders %</th>
<th>Prevalence of CD among girls %</th>
<th>Prevalence of CD among boys %</th>
<th>The method for DSM-IV-diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S., Merikangas et al. 2010</td>
<td>13-18</td>
<td>6.8%</td>
<td>5.8%</td>
<td>7.9%</td>
<td>WHO-CIDI</td>
</tr>
<tr>
<td>Great Britain, Keenan et al. 2010b</td>
<td>15</td>
<td>-</td>
<td>8.9%</td>
<td>-</td>
<td>CSI-4</td>
</tr>
<tr>
<td>Germany, Ravens-Sieberer et al. 2008</td>
<td>11-17</td>
<td>9.7%</td>
<td>8.4%</td>
<td>10.9</td>
<td>CBCL*</td>
</tr>
<tr>
<td>U.S., Nock et al. 2006</td>
<td>Lifetime, retrospective study for adults</td>
<td>9.5%</td>
<td>7.1%</td>
<td>12.0%</td>
<td>WHO-CIDI</td>
</tr>
<tr>
<td>Great Britain, Maughan et al. 2004</td>
<td>5-15</td>
<td>-</td>
<td>0.8%</td>
<td>2.1%</td>
<td>DAWBA</td>
</tr>
<tr>
<td>Great Britain, Ford et al. 2003</td>
<td>13-15</td>
<td>3.3%</td>
<td>-</td>
<td>-</td>
<td>DAWBA</td>
</tr>
<tr>
<td>U.S., Rowe et al. 2002</td>
<td>9-16</td>
<td>2.2%</td>
<td>1.1%</td>
<td>3.1%</td>
<td>CAPA</td>
</tr>
</tbody>
</table>

*parent-reported information
** 1999 British Child Mental Health Survey

The increase in the prevalence of CD in both genders has been a global phenomenon. Collishaw et al. (2004) found that the proportion of both adolescent girls and boys with conduct problems more than doubled between 1974 and 1999. According to a Finnish National Research Institute of Legal policy publication from 2006, physical assaults by girls have increased both absolutely and also when compared to boys from the mid-90s. (Kivivuori 2006). In 2008, 15- to 19-year-old girls used approximately twice as much psychiatric outpatient care in Finnish health care as did boys of the same age (Saukkonen 2009).
2.3 Aetiological aspects of conduct disorder

2.3.1 Risk factors for CD

Risk factors for CD and disruptive behaviour in general have been widely studied during the last two decades, but the research has not usually been gender-specific. Risk factors have been classified in many different ways in the literature according to various intrinsic and environmental factors (Holmes et al. 2001). In this study, Burke’s model of psychosocial, child functional and biological risk factors has been used for the categorisation (Burke et al. 2002). We have also modified Burke’s model using some new research findings (Figure 1).

Psychosocial risk factors for CD

The most notable social risk factors for CD include parenting, assortative mating, child abuse, peer effects, socio-economic factors and life stressors/coping skills (Burke et al. 2002, Boden et al. 2010).

Poor parenting skills, like harsh or physical punishments, are related to disruptive behaviour (Frick et al. 1992, Haapasalo and Tremblay 1994, Boden et al. 2010), while favourable parenting behaviours may be protective (McCord 1991). Parents interact differently with boys and girls, especially with regard to the development of conduct problems. Home environmental factors are believed to expose girls to CD even more markedly than boys (Keenan et al. 1999).

Research regarding extremely harsh or abusive parenting behaviours, such as sexual and physical abuse, suggests that such behaviours increase the risk of CD up to three-fold in children and adolescents (Fergusson et al. 1996, McCabe et al. 2005, Afifi et al. 2009, Boden et al. 2010). Childhood victimisation of boys and girls, including abuse and neglect, is predictive of later antisocial personality disorder (Luntz and Widom 1994), criminality and violence (Maxfield and Widom 1996).

Group relations with deviant peers seems to lead to the initiation of delinquent behaviour in adolescence (Boden et al. 2010, Elliot and Menard 1996, Keenan et al. 1995), increasing the risk for antisocial behaviour about two-fold (Hill 2002). It has been stated that, for girls, the association with deviant peers is more common with an early onset of pubertal maturation (Stattin and Magnusson 1990). Interactions with peers with behavioural problems in treatment groups of adolescents have shown to potentially result in iatrogenic effects, such as an
increase in problem behaviour and negative outcome in adulthood (Dishion et al. 1999). The composition of treatment groups should be addressed in a strategic manner to minimise exposure to and reinforcement of antisocial behaviours. Aggregation of deviant youths to same treatment groups should be avoided; maintaining group heterogeneity and employing a competent and well-trained therapist is recommended (Dishion et al. 1999, Mahoney et al. 2004).

**Child functional risk factors for CD**

Child functional risk factors for CD are classified into temperament, attachment, neuropsychological functioning, intelligence/academic performance, reading problems, impulsivity/behavioural inhibition, poor social cognition, poor socio-moral reasoning and early physical maturation (Burke et al. 2002).

The temperament research in CD has suffered from a lack of consensus regarding difficulties distinguishing between temperament and the early demonstration of disruptive behaviour symptoms (Burke et al. 2002). In their review, Sanson and Prior (1999) concluded that specific early temperament (negative emotionality, intense and reactive responding, and inflexibility) is predictive of externalising behaviour problems later in childhood, while Lahey et al. (2008) identified infant fussiness, activity level, low predictability and low positive affect as risk factors for later conduct problems.

Deficits in reading, IQ, academic performance and neuropsychological functioning have been linked to disruptive behaviour disorders, and their importance on the development of CD has been qualified in different studies by taking into account confounding factors such as comorbid ADHD, early psychosocial factors and gender differences (Burke et al. 2002). Impulsivity has been associated with early onset CD and the presence of later antisocial behaviour (Tremblay at al. 1994, White et al. 1994).

Early physical maturation has been associated with increased problem behaviours in girls (Laitinen-Krispijn et al. 1999), but not in boys (Graber et al. 1997). Williams and Dunlop (1999) suggested that being “off-time” in pubertal development, whether early or late, is associated with deviant social status and thus contributes to later antisocial behaviour. It is also suggested that puberty in girls differs from that of boys. Among girls, physical and psychological maturation occur at the same time while among boys, psychological maturation precedes physical maturation. In this way, girls may feel less prepared for physical maturity, to the extent that physical maturation is unwanted. Early
physical maturation can also lead to lower self-esteem (Silverthorn & Frick, 1999) and broken social networks, or in some cases to pressure to associate with more self-sufficient, often externalising behaving peers (Caspi et al. 1993).

**Biological risk factors for CD**

Burke *et al.* (2002) divided biological risk factors for CD into factors related to genetics, neuroanatomy, under-arousal of autonomic nervous system, pre- and perinatal problems and neurotoxins.

CD has been demonstrated to have a strong genetic heritability, at around 50% (Gelhorn *et al.* 2005, Button *et al.* 2007), and a group of candidate genes has been studied as risk factors for CD. The influence of dopaminergic and serotonergic systems in CD has also been investigated. Both of these neurotransmitter systems mediate a wide spectrum of cognitive functions, including problem-solving under stress (Luciana *et al.* 1998, Lucki 1998). The hypothesis arising from this is that dysfunction of these systems can cause aggressive behaviour (Lucki 1998). There have also been suggestions that serotonergic functioning is directly related to aggression itself (Moffitt *et al.* 1998, Sakai *et al.* 2006). Both serotonin transporter promoter polymorphism (5-HTTLPR) (Sakai *et al.* 2006) and catechol-O-methyltransferase (COMT) valine/methionine polymorphism (Caspi *et al.* 2008) have been associated with the occurrence of CD in adolescents. However, in their genome-wide association study of CD-symptoms Dick *et al.* (2011) found evidence of a specific gene associated with CD symptomatology outside of traditional candidate genes. They found four genetic markers that meet the criteria for genome-wide significance (P<5 × 10(-8)) with the CD symptom count, two of which are located in the gene C1QTNF7 (C1q and tumour necrosis factor-related protein 7) (Dick *et al.* 2011).

The connection between CD and brain structure abnormalities has been under research. Study of adolescent boys with CD showed grey matter volume reductions in the bilateral amygdale extending into the insula when compared to healthy comparison subjects (Fairchild *et al.* 2011).

Biological correlates of antisocial behaviour have usually been associated to male prominence in CD and studies of biological risks for CD among girls are few. Girls with CD, particularly aggressive CD, have been shown to have lower cortisol to dehydroepiandrosterone ratios, higher levels of free testosterone and lower levels of sex hormone binding globulin in their blood (Pajer *et al.* 2006).
Among pre- and perinatal problems, maternal smoking during pregnancy has been found to predict a higher incidence for CD in both genders (Wakschlag et al. 1997, Keenan 1999, Boden et al. 2010). Also prenatal maternal alcohol use in the first trimester is a risk factor for conduct disorder in adolescence (Larkby et al. 2011). Parental substance use during early childhood has also been linked to disruptive behaviour disorders in offspring (Frick et al. 1992, Loukas et al. 2001). Pregnancy and birth complications have also been shown to be associated with future behaviour problems in the offspring involved (Raine et al. 1997). These data have been derived from a frequency-of-birth-complications score including for example: forceps extraction, breech delivery, umbilical cord prolapse, preeclampsia at the time of delivery, and long labour (Raine et al. 1997).

Environmental toxins, such as lead, are perhaps the most preventable risk factors for disruptive behaviour. High levels of lead in the bones of children living in urban areas at the age of 11 have been linked to aggression and delinquency (Needleman et al. 1996) and high levels of lead in blood to 9-fold increased odds of meeting DSM-IV CD criteria (Braun et al. 2008). Studies of other toxins are scarce.

**Gender-specific risk factors for girls**

Most studies of the risk factors for CD only use data on boys or include such a limited amount of data on girls that measures of gender differences or risk calculations specific for girls have not been possible to perform. It has been suggested that home environmental factors, in particular, are a greater risk factor for CD in girls than in boys (Keenan et al. 1999). To date, the acknowledged risk factors for CD in girls include: low resting heart rate, mother’s heavy smoking during pregnancy, early maturation, low verbal ability, low general intelligence, early school failure, familial psychopathology, physical and sexual abuse, poor marital adjustment and disagreements over child-rearing issues, poverty, association of deviant peers and neighbourhood violence (Webster-Stratton,1996, Keenan et al. 1999, Hipwell & Loeber, 2006, Pajer et al. 2008, Keenan et al. 2010b). However, it seems that girls are not as sensitive to genetic risk factors as boys in the development of CD (Cadoret et al. 2003).
Protective factors for CD

Protective factors for CD are not always simply the opposite of risk factors, although this is sometimes the case. Not all adolescents exposed to known risk factors get CD, even in cases of exposure to multiple risk factors (Bassarath 2001). Female sex is itself a protective factor for CD. Other protective factors for CD include high intelligence, resilient temperament, competence at a specific skill, favourable parenting and warm/supportive relationships with adults, commitment to social values, involvement in positive extracurricular activities, strong and stable community institutions (like church, neighbourhood organisations, and extended families) (Bassarath 2001, McCord 1991).
Fig. 1. Risk factors for conduct disorder.
2.3.2 Development and subclassification of CD

Onset age and subclassification of CD

In general, CD does not appear suddenly in childhood or in adolescence, and it is not related to a single event in a child’s life (Loeber 1990). Onset age of CD is defined to be the age at which the first symptom(s) of CD appear, most often at late childhood or early adolescence (Lahey et al. 1998, Lahey et al. 2000, Nock et al. 2006). According to the DSM-IV criteria, CD is subclassified into childhood-onset type, where at least one symptom appears prior to the age of ten, and adolescent-onset type, where none of the symptoms of CD are present before the age on ten. The onset age of CD has been found to be higher among girls according to present diagnostic criteria, but there is wide variation in age distributions between different studies (Cohen et al. 1993, Lahey et al. 2000, Maughan et al. 2004, McCabe et al. 2004, Keenan et al. 2010b).

Adolescents with childhood-onset CD are more likely to show aggressive behaviour. They also continue aggressive and criminal behaviour into adulthood more often than those with adolescent-onset CD (Frick & Loney 1999). The presence of differing outcomes and risk factors in these two subtypes has led to theoretical models of the development of CD. Moffitt (Moffitt 1993, Moffitt 2003) reports that subjects in the childhood-onset group are particularly vulnerable children and grow up in an inadequate rearing environment. This process disrupts the child’s socialisation. In contrast, adolescents in the adolescent-onset group seem to show an exaggeration of normative rebellion in puberty. An adolescent in the adolescent-onset CD group participates in antisocial behaviour in a misguided attempt to obtain a subjective sense of maturity (Moffitt 1993, Moffitt 2003). Frick et al. (2005) have divided CD on basis of presence or absence of callous-unemotional traits, which markedly correlate with the existence of childhood-onset CD. The callous-unemotional subtype of CD has been studied to distinguish the adolescents with CD and more severe antisocial behaviour from those with CD but less severe symptoms, also among girls (Essau et al. 2006, Pardini et al. 2012).
Oppositional defiant disorder and conduct disorder

Many studies suggest that ODD is a precursor for CD (Lahey et al. 2000, Rowe et al. 2002, Maughan et al. 2004). DSM-IV classifies ODD and CD (and antisocial personality disorder) hierarchically and developmentally, so that concurrent comorbidity among these disorders is not possible according to the diagnostic criteria (APA 1994). The symptoms of ODD are somewhat less severe than those of CD and include features of opposing and resistance (APA 1994). However, some studies suggest that the development of symptoms of ODD and CD are also concurrent (Maughan et al. 2004, Diamantopoulou et al. 2011). The assumption of development of CD through ODD has been criticised to be not representative among girls and being more common among boys (Keenan et al. 1999, Rowe et al. 2010). Also gender difference in prevalence of CD has been studied to be larger than in ODD (Maughan et al. 2004). Merikangas et al. (2010) have studied the lifetime prevalence of ODD in adolescence to be 12.6%, which is approximately twice the prevalence of CD in their study (6.8%).

Attention deficit hyperactivity disorder and conduct disorder

ADHD and CD are often diagnosed concurrently - among children with ADHD the risk for subsequent CD is increased (Angold 1999, Monuteaux et al. 2007, Connor, 2010). In comorbidity studies, CD has been reported to appear after the onset of ADHD (Taurines et al. 2010). Hyperactivity is a risk for types of later development problems, also without the occurrence of CD (Taylor et al. 1996). It has also been suggested that progression to CD from attention-deficit/hyperactivity disorder (ADHD) is not as unambiguous among girls as it is among boys (Keenan et al. 1999). However, Monuteaux et al. (2007) found that future risk for CD in girls with ADHD was increased.

Overt, covert and authority conflict pathway

Loeber et al. (1993) developed a pathway theory of three developmental models for disruptive child behaviour: overt, covert and authority conflict pathways (Loeber et al. 1993, Loeber & Hay 1997). Loeber has found evidence for these developmental pathways in behaviour problems, with symptoms accumulating around overt (violent), covert (delinquent) and authority conflict problem
behaviours. In Loeber’s theory an early authority conflict pathway involves stubborn behaviour, defiance and avoidance of authority. A covert pathway consists of minor covert behaviours, property damage, and moderate to severe forms of delinquency while an overt pathway includes aggression, fighting, and violence. Overlap among these three pathways exists (Loeber et al. 1993). The theory was originally developed for boys. Later, its applicability for girls has also been established, but with a notion that some general consistency exists in the patterns of boys and girls, with some differences in frequency and predictors of risk for disruptive behaviours (Gorman-Smithe & Loeber 2005).

2.4 Conduct disorder and violence

WHO defines violence as follows: “The intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation” (WHO 1996). Direct violence as an intent to injure another person or destroy the property of others is not ubiquitous among adolescents with CD, but is certainly prevalent among that population. Among girls, the symptoms of CD are suggested to be less violent than among boys, at least physically. It is also mentioned in the DSM-IV that girls tend to favour nonconfrontational aggression (APA 1994). In contrast, Maughan et al. (2004) reported that gender differences between symptom subscales concerning violent symptoms are minor. Among children with CD, violent symptoms are more common in childhood than in adolescence (Maughan et al. 2004). Earlier in DSM-III (APA 1980), CD was sub-classified on the grounds of aggressive behaviour into aggressive and non-aggressive conduct disorders.

2.5 Conduct disorder and suicidal behaviour

2.5.1 Prevalence and trends in suicides among adolescents

Suicide attempts and completed suicides of adolescents have both increased in parallel (Apter et al. 1995, Rutz et al. 2004) until the last few years (Steele & Doey 2007). In the US, suicide is the third most common cause of death in 10- to 14-year-olds and in Canada, suicide is the second most common cause of death in teenagers among both genders, the suicide rate being 13/100,000 in the age group
of 15 to 19 years (Steele & Doey 2007). In Finland, the suicide rates for boys aged 12–17 have been 5–10/100,000 during the last decade, and the trend has been decreasing. For girls, the rates have been 2–4/100,000 and this trend has been increasing (Lahti et al. 2011). In childhood, completed suicide is an uncommon and not a gender-specific phenomenon. Later, usually after the age of 16, the suicide rate increases rapidly among males (Shaffer et al. 1996), while suicide attempts are more common among females (Lewinsohn et al. 2001). Suicide attempts among adolescent girls are more typically performed using a non-violent method, such as poisoning (Hepp et al. 2011), although the use of violent methods to complete suicide has also increased among girls (Lahti et al. 2011). It seems that availability has an important effect on the methods of suicide chosen by adolescents (Hepp et al. 2011). The prevalence of suicidal ideation in adolescence has been reported to be 11–14% (Granero et al. 2008, Wilcox et al. 2010, Toprak et al. 2011), being more common among girls (Granero et al. 2008), and also being a risk factor for later suicide attempt (Wichstrom 2009).

2.5.2 Risk factors for suicidal behaviour in adolescence

The risk factors for suicide attempts and completed suicides in youth are multifactorial and complex. Most empirical studies have shown no fundamental gender differences in risk factors for suicide attempts (Brent et al. 1999, Steele & Doey 2007). An increased risk for suicide attempts and suicides among youth has been found to be linked with many familial and external factors, such as parental psychopathology (Brent et al. 1999), disrupted family background (Shaffer et al. 1996), and physical or sexual abuse (Brent et al. 1999, Glowinski et al. 2001, Haavisto et al. 2003). It has also been reported that violent behaviour toward others is a risk factor for suicidal behaviour (Apter et al. 1995, Haavisto et al. 2003). Clinical depression in known to be serious risk factor for suicide attempts (Marttunen et al. 1991, Glowinski et al. 2001, Haavisto et al. 2003, Renaud et al. 2008), especially among adolescent girls (Marttunen et al. 1995, Brent et al. 1999, Lewinsohn et al. 2001), but depression is not essential prior to attempted suicide (Apter 1995). Other psychiatric disorders than affective disorders have also been connected to a risk of suicide attempts among adolescents, in particular CD (Apter 1995, Glowinski et al. 2001, Renaud et al. 2008) and alcohol abuse and dependence (Glowinski et al. 2001, Renaud et al. 2008). Adolescents with
multiple comorbid psychiatric disorders have an increased risk for suicide attempts (Marttunen et al. 1991, Wagner et al. 1996, Kelly et al. 2001).

2.5.3 Self-mutilative behaviour

Self-mutilation is a widespread yet often hidden problem in adolescents, and it has become more prevalent (Klonsky et al. 2003). Various types of self-mutilation exist, and not all of them precede a high risk for suicide (Greydanus 2009). Lifetime prevalence of self-mutilation is around 10% in adolescence, being higher among girls (Morey et al. 2008, Laukkanen et al. 2009). Self-mutilation has been connected to major depressive disorder, anxiety disorders and eating disorders in adolescence (Tuisku et al. 2006, Hintikka et al. 2009), and also to alcohol abuse (Hintikka et al. 2009). Impulsivity (Herpertz et al. 1997) and aggression (Herpertz et al. 1995) have been connected to self-mutilative behaviour.

2.5.4 Suicidality and conduct disorder

CD has been found to independently elevate the risk of attempted suicide among both genders (Brent et al. 1993, Glowinski et al. 2001). Furthermore, multiple comorbid psychiatric conditions increase the risk of suicidal behaviour (Kelly et al. 2001). In Finnish inpatient and reform school data, suicide attempt rates for girls with CD were as high as 38% (Lehto-Salo et al. 2009). Among depressive girls, comorbid CD and alcohol dependence increases the risk for suicidal behaviour (Wannan and Fombonne 1998).

2.6 Conduct disorder and nicotine dependence

The prevalence of regular smoking among adolescents with CD is high, being around 50–80% (Costello et al. 1999, Burke et al. 2001, Rohde et al. 2004). In comparison, in Finnish general population 16% of both 14- to 18-year-old girls and boys are regular smokers (Raisamo et al. 2011). CD is an independent risk factor for the early initiation of smoking (Costello et al. 1999, Bagot et al. 2001) and progression to regular daily smoking (Burke et al. 2001, Galéra et al. 2005), or heavy smoking (Cornelius et al. 2001). The association between nicotine dependence (ND) and CD in adolescence is, however, less well studied. Hakko et al. (2006) found that the likelihood of a high level of ND as compared with being a non-smoker or having a moderate level of ND was over two-fold among
psychiatric inpatient adolescents with CD or ODD. Elkins et al. (2007) investigated prospectively various dimensional or categorical measures of CD and ADHD in relation to subsequent initiation of smoking and the development of a DSM-IV diagnosis of ND among twin pairs in an adolescent sample. They found that a diagnosis of CD by the age of 14 years was independently associated with an increased risk of ND (OR 4.27) by 18 years of age, even after adjustment for comorbid ADHD (Elkins et al. 2007).

2.7 Comorbidity of conduct disorder

Comorbidity of other psychiatric disorders in adolescents with CD is very common among both genders. Moffitt et al. (2001) found psychiatric comorbidity in girls with CD to be as high as 93%, and in boys up to 88%. Internalising comorbid psychiatric conditions (such as depression, anxiety disorders, eating disorders) are especially common among girls with CD. Adolescents with CD also have an increased risk for comorbid alcohol and substance use disorders among both genders (Costello et al. 1999, Crowley & Riggs 1995, Lehto-Salo et al. 2009). Adolescents with comorbid internalising or externalising disorders are more prone to have continuing problems than those with only a single disorder (Nottelmann & Jensen 1995), and more than twice as likely to be users of psychiatric services (Costello et al. 1996).

The research on comorbid psychiatric diagnoses of CD has mostly been based on data not gender-specific, or data limited to males only, or study samples with a small proportion of girls (Angold et al. 1999). The prevalence of depression among adolescents with CD varies widely, from studies with no comorbidity found to levels of comorbidity being as high as 46% (Angold et al. 1999, Maughan et al. 2004, Romano et al. 2005). Anxiety disorders are also common comorbid conditions in CD. The prevalence of anxiety disorders varies between 5% and 55% (Angold et al. 1999, Ollendick et al. 1999). In clinical populations of adolescent substance users, the comorbidity of substance use disorders and behavioural disorders is as high as 95%, and this comorbidity appears to be more pronounced among girls (Clark et al. 1997, Weinberg et al. 1998). In Finnish data, about one third of inpatient girls with CD had either current anxiety disorder or MDD as a comorbid disorder (Lehto-Salo et al. 2009). Attention deficit hyperactivity disorder (ADHD) is suggested to be connected
with the development of CD and comorbidity exists among both genders, varying from 3% to 41% (Angold et al. 1999, Loeber et al. 2000) (Table 2).

Even though it is known that somatic conditions and general health problems are connected with antisocial personality disorder in adulthood (Frankenburg & Zanarini 2006), there are only a few studies on the connection between somatic disorders and CD among adolescents (Hanssen-Bauer et al. 2007, Dunn et al. 2009), the focus being mainly on neurological conditions. In a Finnish follow-up study of adolescents, regular headache at the age of 14 was associated with preceding externalising problem behaviours at the age of 11 (Virtanen et al. 2004). It has been documented that there is a connection between allergies and depression, especially among females (Timonen et al. 2002), but there are no studies on allergies and CD.

Table 2. Psychiatric comorbidities in conduct disorder by gender in youth.

<table>
<thead>
<tr>
<th>Comorbid psychiatric disorder</th>
<th>Study and year</th>
<th>Prevalence, girls</th>
<th>Prevalence, boys</th>
<th>N</th>
<th>Diagnostic method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any psychiatric diagnosis</td>
<td>Moffitt et al. 2001</td>
<td>93%</td>
<td>88%</td>
<td>1000</td>
<td>DISC-C*</td>
</tr>
<tr>
<td></td>
<td>Maughan et al. 2004</td>
<td>39%</td>
<td>46%</td>
<td>10438</td>
<td>DAWBA**</td>
</tr>
<tr>
<td>MDD</td>
<td>Maughan et al. 2004</td>
<td>12%</td>
<td>14%</td>
<td>10438</td>
<td>DAWBA**</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>Maughan et al. 2004</td>
<td>16%</td>
<td>10%</td>
<td>10438</td>
<td>DAWBA**</td>
</tr>
<tr>
<td></td>
<td>Ollendick et al. 1999</td>
<td>23%</td>
<td>21%</td>
<td>79</td>
<td>DISC-C*</td>
</tr>
<tr>
<td>ADHD</td>
<td>Maughan et al. 2004</td>
<td>16%</td>
<td>31%</td>
<td>10438</td>
<td>DAWBA**</td>
</tr>
<tr>
<td>Substance abuse or dependence</td>
<td>Costello et al. 1999</td>
<td>26%</td>
<td>11%</td>
<td>1420</td>
<td>CAPA***</td>
</tr>
</tbody>
</table>

* Diagnostic Interview Schedule for Children
** The Development and Well-Being Assessment
*** The Child and Adolescent Psychiatric Assessment

2.8 Treatment of conduct disorder

In the US, behavioural disorders are the most common reason for psychiatric treatment for adolescents, but still only a third of adolescents with CD receive treatment. Treatment in this study included any treatment in special healthcare, general medical services, counsellor meetings, support groups, school services, or the juvenile justice system (Merikangas et al. 2011).

Multi-systemic therapy (MST) is perhaps the most widely referred psychosocial treatment for CD and behavioural problems (Kazdin 2000, Curtis et
al. 2009), although there is little evidence of the superiority of MST over other interventions (Littell et al. 2005). MST focuses on systems (both immediate and extended family members, peers, school and the neighbourhood) in which the behaviour is placed and on altering these systems in concrete ways that can influence the disruptive behaviour. Several other psychosocial treatments for CD are available, including parent management training, functional family therapy, brief strategic family therapy, parent-child interaction training, and cognitive problem-solving skills training (APA 2000, Kazdin 2000, Lochman et al. 2011). Treatment guidelines in Finland largely follow the principles of MST (Moilanen et al. 2004, Suvisaari & Manninen 2009), including interference of risk factors (support to parenting, organising activities for spare time, co-operation with school and, in necessary, child welfare), family interventions, guidance to school teachers and also individual and group therapies when applicable. Pharmacological treatment is used in complicated situations and only besides other treatment. In some cases, treatment periods in hospitals are required (Moilanen et al. 2004).

General guidelines for efficient pharmacological treatment of CD are under continuous research (Pandina et al. 2006, Tcheremissine & Lieving 2006). Mood stabilisers, such as lithium and carbamazepine, have been studied and found to be effective in the treatment of CD (Kafantaris et al. 1992, Steiner et al. 2003). Clonidine, an alpha-2-agonist, has positive effect on parent-rated, but not teacher-rated CD (Hazell & Stuart 2003). Of atypical antipsychotics, risperidone is most frequently studied and has the best results in reducing aggressive behaviour (Findling et al. 2000). Quetiapine has also shown promising results in treatment of aggressive symptoms in children with CD (Findling et al. 2006, Findling et al. 2007), as has aripiprazole (Findling et al. 2009). From antidepressants, fluoxetine has so far been studied to be ineffective in the treatment of CD (Riggs et al. 2007). Tcheremissine and Lieving (2006) suggest that several drug groups, such as antipsychotics, antidepressants, mood stabilisers, antiepileptic drugs, stimulants and adrenergic drugs, can be effective therapeutic options for individuals with CD and comorbid psychiatric conditions. As with any pharmacotherapy, adverse events (e.g. weight gain, headache, and somnolence) should be considered with these medications, especially in children and adolescents, and it is important to properly dose and monitor patients during medication therapy (Findling 2008).
Gender differences in the treatment of CD have rarely been examined (Keenan et al. 1999, Hipwell & Loeber 2006). In their review, Hipwell and Loeber (2006) suggested that treatment programmes should become increasingly gender-specific with age, and that the greatest need for treatments targeted specifically for females is during adolescence. In early childhood, parent management training is suggested to be an efficient treatment for behaviour problems among girls. For pre-adolescents, specifically designed multi-systemic therapy has been associated with moderate reductions in behavioural symptoms. In adolescence, both family-based interventions and individual therapies have showed positive effects on behavioural problems (Hipwell & Loeber 2006). Odgen & Hagen (2009) reported that although adolescent girls may present somewhat different problem profiles than boys, multi-systemic therapy seems flexible and robust enough to be an effective treatment, regardless of gender.

The treatment of CD has been the focus for a large number of controlled treatment outcome studies. Unfortunately, treatment approaches have proven to be largely ineffective (Brestan & Eyberg 1998). Henggeler & Sheidow (2012), however, suggest in their review that MST has positive effects such as reduced delinquency and criminal offences as well as out-of-home placements among adolescents with serious antisocial behaviour. The earlier the child with CD symptoms is treated, the better the prognosis (Connor et al. 2006, Ritakallio et al. 2003, Suvisaari & Manninen 2009). It has also been found that interventions targeted at risk families – some even before the birth of the child – have been effective in the prevention of conduct disorder (Hawkins et al. 1999, Olds et al. 1998).

2.9 Outcome of conduct disorder among girls

Adolescents with CD have three- to five-fold risk to develop later antisocial personality disorder in adulthood (Copeland et al. 2009, Simonoff et al. 2004). Also, of delinquent adolescent girls, as well as boys, 40 per cent are delinquent in early adulthood (Ferdinand et al. 1995).

There seem to be no fundamental differences in stability of disruptive behaviour between the genders. In their review, Keenan et al. (1999) suggest that stability tends to be as high, or even higher, in females compared to males. Zoccolillo et al. (1992) found that the risk of females with CD subsequently developing antisocial personality disorder was the same as that for males. Verhulst and Van der Ende (1991) found aggressive behaviour to be even more
persistent among girls, although Moffitt and colleagues (2008) have found the risk for later antisocial personality disorder as well as for delinquency to be smaller among girls.

CD among girls is associated with a forty-fold increase in adult criminality and heightened risks for depression and substance use, antisocial personality disorder, failure to finish high school, poor physical health and early and violent death. Furthermore, CD is associated with teenage pregnancies and significant problems in future mothering behaviours, which in term contribute to transmission of antisocial behaviour to following generations (Zoccolillo et al. 1996, Pajer 1998, Kim-Cohen et al. 2005, Rhule et al. 2004, Moffitt et al. 2008).

2.10 Summary of the reviewed literature: what is known and what should be studied?

The general picture of CD has been widely studied, but studies have mostly lacked the competence to make conclusions over gender differences in CD and special features of CD among girls. Large enough follow-up studies focusing on gender differences or girls specifically are almost entirely missing, although some new research in this field is now underway (Keenan et al. 2010a,b) and will hopefully provide useful information in the near future. However, it should be stressed that studies focusing on females only are not encouraged to be performed, as research should systematically compare findings in both genders to obtain true information on gender differences. In addition to the lack of sufficiently large data on girls, a major problem is the current diagnostic criteria used in DSM-IV, which have been criticised as not being sensitive enough to diagnose clinically significant CD among girls (Moffitt et al. 2008). This may lead to major problems in study designs, particularly when trying to identify girls with milder, perhaps early-phase CD in general populations. Modified criteria for identifying girls with CD require targeted research to include as many girls as possible with a risk for poor prognosis. More data on female-specific CD are needed in order to update the CD diagnostic criteria for DSM-V (Moffitt et al. 2008).
3 Purpose of the present study

The purpose of this study was to examine conduct disorder among girls, while paying special attention to gender differences in the risk factors, aetiology, suicidality and comorbidity of conduct disorder. The numbers I-V hereafter refer to the original publications.

The aims of this study were:

1. To examine the impact of familial risk factors on the development of conduct disorder and violent behaviour, for girls and boys separately (I).
2. To examine the factor structure of CD symptoms based on the DSM-IV criteria. The factor structure of boys and girls was also compared to the factor structure of Loeber’s tripartite model with overt, covert and authority conflict factors (II).
3. To examine the impact of alcohol dependence on suicide attempts and other types of suicidal behaviour, by gender, among adolescents with conduct disorder (III).
4. To examine gender differences in psychiatric comorbidity, somatic comorbidity and causes for admission to psychiatric hospital among adolescent with CD (IV).
5. To examine whether the number of CD symptoms, type of CD or various CD symptom subscales are associated with the level of ND. In addition, to investigate whether gender and psychiatric comorbidity among adolescents with CD affects the risk of developing ND (V).
4 Material and methods

4.1 Study population and data collection

This study is part of STUDY-70, a clinical follow-up project initiated to examine the association of various psychosocial risk factors with the outcomes of severe psychiatric and substance use disorders among hospital-treated adolescents aged 12–17 years. The study sample comprised 508 adolescents (208 boys, 300 girls, including 155 adolescents with CD) admitted for the first time to Unit 70 at Oulu University Hospital’s Department of Psychiatry, between April 2001 and March 2006. The number of participants in studies I and III was 278 and 387, respectively, because data collection was still in progress during the time. Of all the eligible adolescents (n=607), 508 (83.7%) participated in the research project (Luukkonen 2010).

Of the adolescents admitted to Unit 70 during the data collection period, those aged 18 years or older (n=1) and those with an intellectual disability (n=26) or organic brain disorder (n=3) were excluded, as were those who did not or whose parents or legal guardian did not give written informed consent to participate (n=77). Adolescents who were admitted to Unit 70 for a period too short to complete the necessary interviews were also excluded (n=22) (Luukkonen 2010).

Since the catchment area of Unit 70 covers the two northern provinces of Finland (the provinces of Oulu and Lapland), this data set represents an epidemiologically unselected sample of adolescent inpatients requiring acute psychiatric hospitalisation. The majority of adolescents (71%) were from the province of Oulu, and 22% were from the city of Oulu. A further 20% of the adolescents were from the province of Lapland and 9% from other provinces in Finland (see Figure 2). The majority of the adolescents were Caucasians (98%). The mean age of the participants in a completed sample was 15.5 years (SD 1.3 years), being 15.5 years (SD 1.3) among girls and 15.4 years (SD 1.4) among boys.
Fig. 2. Geographical distribution of the subjects of Study-70.
4.2 Research instruments (I-V)

4.2.1 K-SADS-PL (I-V)

During their hospitalisation, adolescents were interviewed either by the treating physician, a medical doctor specialised in adolescent psychiatry, or by trained medical students under the supervision of the treating physician. The Schedule for Affective Disorder and Schizophrenia for School-Age Children Present and Lifetime (K-SADS-PL) was used to obtain DSM-IV diagnoses (I-V), the symptoms, subtypes and severity level of CD (II), details of age and home environment (II, IV) and smoking status (IV). The K-SADS-PL is a semi-structured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescents according to DSM-III-R and DSM-IV criteria (Kaufmann et al. 1997). The full description of the K-SADS-PL is provided at:


Data were recorded on the basis of both the patients’ information and physician’s evaluation of the diagnostic interview (Mäkikyrö et al. 2004). Information from parents was also used when available: if data were missing or remained unreliable after interviewing the adolescent, the interview was complemented by interviewing one or both parents. The test-retest reliability of diagnoses reached for adolescents using the K-SADS-PL interview has been described as good to excellent, and its concurrent validity and inter-rater agreement have shown to be high (Ambrosini 2000, Kaufman et al. 1997). The Finnish version of K-SADS-PL has been translated into Finnish and then back to English to certify the accuracy of the translation, and it has been used in numerous studies of adolescents in Finland (e.g. Holi et al. 2008).

4.2.2 EuropASI (I-IV)

European Addiction Severity Index (EuropASI) (Kokkevi & Hartgers 1995) is a structured interview that was performed by the nurses at Unit 70. EuropASI contains questions on the following life issues or problems: physical health, employment and financial support, illegal and criminal activity, family and social relationships, psychiatric symptoms, and drug and alcohol use. EuropASI has provided very satisfactory results in terms of reliability and validity when applied to substance-abusing populations (Kokkevi & Hartgers 1995). EuropASI was used
to obtain social class (I), home environment (II), type of dwelling (IV), place of residence (IV), custody (III), special unit in school (III), delinquency of adolescent (II), repeating grades at school (IV), and prevalence of somatic conditions (IV).

### 4.2.3 Other research instruments (II, IV, V)

The modified Fagerström test questionnaire (mFTQ) for nicotine dependence (ND) in children and adolescents (Pomerleau et al. 1994) was also administered by the staff in the unit. It was used to assess current smoking habits (II, V) and the level of ND (V). The level of functioning (II) was measured using the Children’s Global Assessment Scale (CGAS) (Schorre & Vandvik 2004) at admission and discharge from hospital by the treating physician. Causes for hospitalisation (IV) were gathered from the semi-structured admission form (see Appendix 1) included in the patients’ hospital case notes. The form was completed by the treating physician, nurse and the patient and/or patient’s parents together at the beginning and the end of a treatment period in Unit 70.

### 4.3 Variables

#### 4.3.1 Conduct disorder (I-V)

The symptoms, subtypes and criteria for severity of conduct disorder (DSM-IV code: 312.8) were obtained from the K-SADS-PL interview following the DSM-IV criteria (APA 1994, Kaufman et al. 1997). Five symptoms (1) lies, 2) truant, 3) initiates physical fights, 4) bullies, threatens or intimidates others, and 5) non-aggressive stealing) were extracted from the screening interview, from the “Conduct disorder” part, and ten symptoms (1) vandalism, 2) breaking and entering, 3) aggressive stealing, 4) fire setting, 5) often stays out at night, 6) ran away overnight, 7) use of a weapon, 8) physical cruelty to persons, 9) forced sexual activity, and 10) cruelty to animals) from the diagnostic supplement entitled “Behavioural disorders”. Each of the 15 symptoms of CD was measured using a three-level scale: 1. symptom not present, 2. sub-threshold-level symptom, and 3. threshold-level symptom. A symptom of CD was defined to be present if it fulfilled the criteria for a threshold-level symptom. Furthermore, the DSM-IV-based diagnostic criteria for conduct disorder were met if a repetitive
and persistent pattern of behaviour in which the basic rights of others or major age-appropriate societal norms or rules were violated, as manifested by the presence of three (or more) of the aforementioned criteria in the past 12 months, with at least one criterion present in the past 6 months. Full diagnostic criteria for DSM-IV-based conduct disorder are presented in the DSM-IV diagnostic manual (APA 2000).

In studies I, II, IV and V only current diagnoses of CD were used in the analyses, in study III previous episodes of CD were also included in the analyses. In accordance with K-SADS-PL, a disorder was classified as “previous” if symptoms had been absent for at least two months.

The psychiatric diagnoses of the adolescents were subsequently scrutinized further by two experienced psychiatrists and carefully validated against the DSM-IV criteria (V). In validated data, 72 girls and 99 boys had CD according to DSM-IV-criteria. Luukkonen (2010) has described this process more thoroughly.

4.3.2 Subtypes of conduct disorder (I-V)

CD was categorised into two subtypes based on the age at onset of the disorder as in DSM-IV. CD was diagnosed as childhood-onset type if at least one of the CD symptoms appeared prior to the age of 10 years, otherwise it was classified as adolescent-onset type. The severity of CD was also assessed on a three-level scale: mild, moderate or severe, based on the number of symptoms, and the harm conduct problems caused to others (APA 2000). CD was categorised into three additional subtypes based on whether the conduct symptoms generally occurred with peers, alone or both with peers and alone (V). These three subtypes include: 1) group type, 2) solitary aggressive type, and 3) undifferentiated type as described in DSM-III-R (APA 1987).

Adolescents with CD were sub-classified further depending on their physically violent behaviour (violent CD and non-violent CD). The definition of violent behaviour was based on information obtained from the K-SADS-PL. Adolescents who had caused physical injuries to others (violence towards others that had caused moderate to severe injuries, i.e., at least bruises or cuts) were defined as violent, others as non-violent (I).

The 15 CD symptoms were further assessed in terms of four separate subscales, as categorised in DSM-IV (APA 2000): 1) aggression towards people and animals (this involves seven symptoms: initiates physical fights, bullies or threatens others, aggressive stealing, use of a weapon, physical cruelty, forced
sexual activity and cruelty to animals), 2) destruction of property (two symptoms: vandalism and fire setting), 3) deceitfulness or theft (three symptoms: telling of lies, non-aggressive stealing and breaking-in), and 4) serious violations of rules (three symptoms: truancy, frequently staying out at night and running away overnight) (V).

4.3.3 Other psychiatric disorders (I-V)

Psychiatric diagnoses were obtained from the K-SADS-PL following the DSM-IV criteria (APA 2000, Kaufman 1997). We examined DSM-IV-diagnosed MDD (296.21-36), panic disorder (300.01, 300.21), simple phobia (300.29), social phobia (300.23), agoraphobia (300.22), generalised anxiety disorder (300.02), post-traumatic stress disorder (PTSD) (309.81), attention deficient hyperactivity disorder (ADHD) (314.00-9), alcohol abuse (305.00), alcohol dependence (303.90), drug abuse (305.20-70) and drug dependence (304.00-90). In study III, both current and previous DSM-IV psychiatric diagnoses (Conduct disorder: 312.8, alcohol dependence: 303.90; MDD: 296.21-36) were used. In other studies (I, II, IV, V), only current diagnoses were used. In study V, the diagnoses were categorised into three major groups: 1) affective disorders (DSM-IV 296.2-.3, 300.4, 311), 2) anxiety disorders (300.00-.02, 300.21-.23, 300.29, 300.3, 308.3, 309.81), and 3) substance-related disorders (303.9, 304.0-.6, 304.8-.9, 305.0, 305.2-.7, 305.9).

4.3.4 Definitions of familial risk factors for CD (I)

K-SADS-PL was used to determine the occurrence of parental physical abuse. Physical abuse was defined as being present when an adolescent had experienced injury (bruises or scratches more than once or more serious injury, such as bone fracture, at least once) as a result of physical assault by a parent or a parent substitute. Presence of primary family (yes/no) was verified using K-SADS-PL anamnesis: primary family was defined as being present if the adolescent was living with both biological parents, otherwise it was recorded as absent. Both the adolescent and their parents (if available) were asked about family history of psychiatric disorder (yes/no) during the K-SADS-PL interview. If any maternal or paternal psychiatric illness (including drug or alcohol dependence) was reported, the family history of psychiatric disorder was rated as positive, otherwise it was
recorded as negative. Social class was determined using the mother’s occupational status during the last 3 years from EuropASI. If the mother’s primary occupational status had been full-time work, social class was defined as upper, while unemployment, part-time work, retirement or other social class were defined as lower social class.

4.3.5 Variables for suicidal features (III)

Information on suicidal behaviour (suicide attempt, life-threatening suicide attempt, suicidal ideation and self-mutilative behaviour) was obtained from K-SADS-PL (Kaufman et al. 1997). Suicide attempt was defined as present if an adolescent had been reported to have made at least one attempt with definite suicidal intent. Life-threatening suicide attempt was defined as positive if an attempt had potential medically lethal consequences (e.g. unconsciousness after taking drugs as a suicide method). Suicidal ideation was defined as being present when thoughts of suicide had been recurrent and the adolescent had planned the method of suicide. Self-mutilation was defined as present when non-suicidal physical self-damaging acts were repetitive (at least four times a year) or this damaging had caused serious injury to self (e.g. broken bones or burns with scarring).

4.3.6 Variables for antisocial features (III)

Information on delinquency was obtained from EuropASI and was defined as being present if the patient had been arrested for a crime at least once. Violent behaviour towards others was obtained from K-SADS-PL. Adolescents who had caused physical injuries to others (i.e., moderate to severe injuries, at least bruises or cuts) were defined as violent. Illicit drug use was obtained from K-SADS-PL and was defined as present if the adolescent had at least one experiment with any narcotics or had taken prescription medication with the intention of becoming intoxicated. Impulsiveness was obtained from K-SADS-PL and was recorded as present if the patient often behaves impulsively (acts before thinking) and their impulsiveness has a moderate to severe effect on functioning. Custody was obtained from EuropASI and was recorded as present if the adolescent was in protective custody of the Finnish child welfare authorities at the time of the interview. Special unit at school signified problems at school and was recorded as
present when the adolescent had been in a special class meant for troubled children or youths.

4.3.7 Causes for psychiatric hospital admission (IV)

Causes for hospitalisation were gathered from a semi-structured admission form (see Appendix 1) included in patients’ hospital case notes. The form was completed by the treating physician, nurse and the patient and/or patient’s parents together at the beginning and at the end of each treatment episode at Unit 70. This information was then categorised into eight alternative reasons for admission: depressive mood, suicidality (including both suicidal ideation and suicide attempts), psychotic symptoms, anxiety symptoms, substance use, behavioural problems, aggressive behaviour and sleeping disorders.

4.3.8 Definitions of comorbid somatic conditions (IV)

Information on somatic conditions was extracted from the EuropAsi. Self-reported allergy was defined as positive if the patient or his or her parents reported the patient to have any allergies (yes/no). Regular medication for somatic condition was recorded as present (yes/no), when the adolescent had daily and continual doctor-prescribed medication for a somatic condition. Chronic, life-disturbing disease was recorded as being present (yes/no) if the adolescent had a chronic, diagnosed somatic condition that subjectively disturbed everyday life.

4.3.9 Measure of Nicotine Dependence (V)

Information on current smoking habits and the level of ND was collected from the seven-item modified Fagerström Test Questionnaire (mFTQ) for adolescents (Prokhorov et al. 1996), the reliability and validity of which have been demonstrated in earlier studies (Prokhorov et al. 2000, Chen et al. 2002). The items in the mFTQ assess the subject’s smoking rate, frequency of inhalation, interval between waking up and the first cigarette, level of unwillingness to give up the first cigarette in the morning, difficulty of refraining from smoking in places where it is forbidden, smoking despite medical illness, and smoking more during the first 2 hours than during the rest of the day. The mFTQ sum score can
range from 0 to 9. Following Prokhorov et al. (1996), a sum score of 6 or higher was considered to represent a high level of ND among adolescents.

### 4.3.10 General characteristics of the data

The socio-demographic characteristics of the study subjects are presented in Table 3. The listed variables were taken into account as confounding variables.

| Table 3. The socio-demographic characteristics of the study subjects |
|-----------------|-----------------|-----------------|-----------------|
| Variables       | All adolescents (N=508) | Adolescents with present CD (n=155) |  |
|                 | (300 girls, 208 boys) | Girls with CD (n=63) | Boys with CD (n=92) |
| Mean-age        | 15.5 (SD=1.3) / 15.4 (1.4) | 15.6 (SD=1.3) | 15.4 (SD=1.5) |
| Treatment       |  |
| Duration of treatment, days | 12.2 (SD=16.2) / 11.8 (SD=9.3) | 11.8 (SD=8.4) | 10.5 (SD=7.4) |
| In involuntary treatment (%) | 125 (42%) / 104 (50%) | 28 (44%) | 40 (44%) |
| Place of residence |  |
| City (>100 000 inhabitants) | 63 (21%) / 47 (23%) | 16 (25%) | 18 (20%) |
| Town (10 000-100 000) | 71 (24%) / 62 (30%) | 16 (25%) | 33 (36%) |
| Rural area (<10 000) | 166 (55%) / 98 (47%) | 31 (50%) | 40 (44%) |
| Dwelling place  |  |
| Two-parent family (%) | 156 (51%) / 77 (38%) | 16 (25%) | 27 (30%) |
| One-parent family (%) | 53 (18%) / 45 (22%) | 11 (18%) | 17 (19%) |
| Child welfare placement (%) | 50 (17%) / 60 (29%) | 23 (36%) | 38 (42%) |
| Other family type (%) | 41 (14%) / 23 (11%) | 13 (21%) | 8 (9%) |
| Under custody (%) | 59 (20%) / 81 (29%) | 29 (46%) | 39 (42%) |
| Other           |  |
| Repeated grades  | 29 (10%) /48 (23%) | 9 (14%) | 25 (27%) |
| In special education | 165 (55%) / 141 (48%) | 41 (65%) | 73 (79%) |
| Convicted of a crime | 13 (4%) /35 (17%) | 9 (14%) | 25 (27%) |
| Delinquency     | 86 (29%) / 95 (46%) | 30 (48%) | 49 (53%) |
| Daily smoking   | 211 (70%) / 158 (76%) | 59 (94%) | 84 (92%) |
| Experience of illegal drug | 99 (30%) / 94 (45%) | 38 (60%) | 61 (66%) |
| cGAS (mean)     | 42 (SD=15) / 43 (SD=10) | 43 (SD=9) | 43 (SD=9) |

* p-value < 0.05, Statistical comparison between girls with CD and boys with CD.

### 4.4 Statistical methods (I-V)

Group differences (two independent groups) in categorical variables were analysed using Pearson’s Chi-Square test or Fisher Exact test. Student’s t-test or
Mann-Whitney U-test were used for continuous variables. All statistical tests were two-sided and the limit for statistical significance was set at 0.05. Statistical analyses were carried out using the SPSS (PASW) for Windows (version 17.0, SPSS Inc.), statistical software and SAS Version 9.1 for Windows (SAS 2007).

In addition, the following statistical analyses were used:

Study I. The association of familial risk factors to CD with violent and non-violent behaviour was assessed using a logistic regression model, after adjusting for adolescents’ age (years), for girls and boys separately.

Study II. Exploratory factor analysis (EFA) was used to investigate factor structure of the 15 symptoms of CD. A three-factor EFA for categorical data was performed using tetrachoric correlations and Varimax rotation. Confirmatory factor analysis (CFA) with structural equation modelling was used to assess the level of observed factor structure accordance with the theoretical model proposed by Loeber in the present data. Loeber suggested a factor structure of three components including overt, covert and authority conflict factors among the symptoms of CD in children and adolescents (Loeber et al. 1993).

Study III. The association of alcohol dependence with suicidal and antisocial variables was assessed using a logistic regression model after adjusting for age (years), living in the primary family at the time of admission to the unit (yes/no), and regular drug use.

Study V. Partial correlation adjusted for age was used to examine the associations between nicotine dependence and the CD subscales. A regression analysis was used to investigate the association between CD symptoms, age and affective, anxiety and substance-related disorders with the sum score of ND.

4.5 Ethical considerations and personal involvement

The research plan for the STUDY-70 project, including the present research, was reviewed and approved by the Ethics Committee of the Faculty of Medicine, University of Oulu on 11th April 2001. The topic of this doctoral thesis was approved by the Postgraduate Research Committee of the Faculty of Medicine at the University of Oulu.

The subjects were given a complete description of the research plan and were advised that declining to participate in the research would not have any affect on their treatment. For each case, a signed informed consent was obtained from both
the adolescents and at least one parent (or in some cases guardian) before enrolment.

I have personally participated in the STUDY-70 as a researcher since 2001. I have participated in data collection by interviewing approximately 100 adolescents. I also took part in designing the study, recording data and analysing and reporting the results. I had the original ideas for studies I-IV. I made a major contribution to all of the original papers and was named as the first author in papers I-IV and the second author in paper V. I wrote the first draft of manuscripts I-IV and I am responsible for the final version of each paper as submitted.
5 Results

5.1 Prevalence of conduct disorder

Of the 508 patients enrolled in this study, 300 (59.1%) were girls and 208 (40.9%) boys. On admission to the hospital, the mean age was 15.4 (SD±1.4) years for boys and 15.5 (SD±1.3) years for girls (p=0.548). A hundred and fifty-five of the subjects (31%) fulfilled the criteria for conduct disorder. Details of the patient sample are presented in Figure 3.

Fig. 3. Gender and CD distributions in the study sample.
5.2 Familial risks, conduct disorder and violence (I)

In the inpatient sample of 278 adolescents (163 girls, 115 boys), the prevalence of CD was 35.6%, being higher among boys (50.4%) than among girls (25.5%, χ²=18.8, df=1, P<0.001). The prevalence of violent CD was 19.8%, (30.4% among boys, 12.3% among girls, χ²=14.0, df=1, p<0.001). Prevalence of non-violent CD was 13.7% (boys 18.3%, girls 10.4%, χ²=3.5, df=1, p=0.061) and prevalence of parental physical abuse 28.9% (boys 29.4%, girls 28.6%, χ²=0.02, df=1, p=0.889).

In girls, parental physical abuse was associated with an increased likelihood of violent CD (OR 4.2 95% CI 1.4–12.2, p=0.01). Not living with both biological parents was also associated with an increased likelihood of both violent (OR 7.8 95% CI 1.7–36.4, p=0.01) and non-violent (OR 7.0 95% CI 1.5–33.5, p=0.01) CD among girls. Among boys, none of the familial risk factors were associated with the occurrence of violent or non-violent CD.

Table 4. The association between familial risk factors during childhood and later CD in adolescence among girls (adjusted for age).

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Violent CD (girls)</th>
<th>Non-violent CD (girls)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Physical abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 (27.5)</td>
<td>4.2 1.4-12.2</td>
</tr>
<tr>
<td>No*</td>
<td>9 (8.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>Primary family (both biological parents)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18 (21.4)</td>
<td>7.8 1.7-36.4</td>
</tr>
<tr>
<td>Yes*</td>
<td>2 (3.2)</td>
<td>1.0</td>
</tr>
<tr>
<td>Family history of psychiatric disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (13.7)</td>
<td>1.1 0.4-3.4</td>
</tr>
<tr>
<td>No*</td>
<td>13 (13.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>Social class**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>11 (15.5)</td>
<td>1.8 0.6-5.4</td>
</tr>
<tr>
<td>Upper*</td>
<td>9 (12.7)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*Reference category
**Mother’s occupational status in the last 3 years
Table 5. The association between familial risk factors during childhood and later CD in adolescence among boys (adjusted for age).

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Violent CD (boys)</th>
<th>Non-violent CD (boys)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>OR</td>
</tr>
<tr>
<td>Physical abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (52.0)</td>
<td>2.0</td>
</tr>
<tr>
<td>No*</td>
<td>22 (34.9)</td>
<td>1.0</td>
</tr>
<tr>
<td>Primary family (both biological parents)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27 (40.9)</td>
<td>1.8</td>
</tr>
<tr>
<td>Yes*</td>
<td>8 (28.6)</td>
<td>1.0</td>
</tr>
<tr>
<td>Family history of psychiatric disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10 (28.6)</td>
<td>1.6</td>
</tr>
<tr>
<td>No*</td>
<td>25 (42.2)</td>
<td>1.0</td>
</tr>
<tr>
<td>Social class**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>17 (38.6)</td>
<td>1.0</td>
</tr>
<tr>
<td>Upper*</td>
<td>15 (40.5)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*Reference category

**Mother’s occupational status in the last 3 years

5.3 Factor structure of DSM-IV-based conduct disorder criteria (II)

5.3.1 The prevalence of symptoms and subtypes of CD

The median (interquartile range, IQR) number of CD symptoms was higher among boys (6, 4–8) compared with girls (4, 3–6) (p<0.001). Boys presented more commonly the following CD symptoms: initiates physical fights, vandalism, breaking and entering, use of a weapon, physical cruelty to people and cruelty to animals. Girls presented more commonly mild CD (few conduct symptoms and conduct problems causing only minor harm to others), while severe CD (many conduct symptoms or conduct problems causing considerable harm to others) was more common among boys. Early-onset CD was more common among boys and late-onset CD in girls (Table 6).
Table 6. The prevalence of subtypes and symptoms of conduct disorder.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Girls (n=63)</th>
<th>Boys (n=92)</th>
<th>Gender comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD-Symptoms</td>
<td>n (%)</td>
<td>n (%)</td>
<td>p-value</td>
</tr>
<tr>
<td>Lies</td>
<td>20 (32)</td>
<td>35 (38)</td>
<td>0.421</td>
</tr>
<tr>
<td>Truant</td>
<td>32 (51)</td>
<td>55 (60)</td>
<td>0.268</td>
</tr>
<tr>
<td>Initiates physical fights</td>
<td>31 (49)</td>
<td>65 (71)</td>
<td>0.007</td>
</tr>
<tr>
<td>Bullies or threatens others</td>
<td>32 (51)</td>
<td>46 (50)</td>
<td>0.923</td>
</tr>
<tr>
<td>Non-aggressive stealing</td>
<td>29 (46)</td>
<td>52 (57)</td>
<td>0.199</td>
</tr>
<tr>
<td>Vandalism</td>
<td>21 (33)</td>
<td>51 (55)</td>
<td>0.007</td>
</tr>
<tr>
<td>Break-ins</td>
<td>15 (24)</td>
<td>43 (47)</td>
<td>0.004</td>
</tr>
<tr>
<td>Aggressive stealing</td>
<td>3 (5)</td>
<td>13 (14)</td>
<td>0.060</td>
</tr>
<tr>
<td>Fire-setting</td>
<td>4 (6)</td>
<td>12 (13)</td>
<td>0.178</td>
</tr>
<tr>
<td>Often stays out at night</td>
<td>47 (756)</td>
<td>63 (69)</td>
<td>0.409</td>
</tr>
<tr>
<td>Ran away overnight</td>
<td>37 (59)</td>
<td>53 (58)</td>
<td>0.889</td>
</tr>
<tr>
<td>Use of a weapon</td>
<td>9 (14)</td>
<td>28 (30)</td>
<td>0.021</td>
</tr>
<tr>
<td>Physical cruelty</td>
<td>29 (46)</td>
<td>57 (62)</td>
<td>0.050</td>
</tr>
<tr>
<td>Forced sexual activity</td>
<td>1 (2)</td>
<td>2 (2)</td>
<td>0.640</td>
</tr>
<tr>
<td>Cruelty to animals</td>
<td>4 (6)</td>
<td>21 (23)</td>
<td>0.006</td>
</tr>
<tr>
<td>Number of CD symptoms, median (IQR)</td>
<td>4 (3-6)</td>
<td>6 (4-8)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Subtypes of CD

| Early-onset                                   | 13 (23)      | 51 (57)     | <0.001          |
| Late-onset                                    | 45 (75)      | 33 (38)     | <0.001          |

Severity of CD

| Mild                                           | 16 (27)      | 10 (11)     | 0.015           |
| Moderate                                       | 31 (50)      | 41 (47)     | 0.681           |
| Severe                                         | 12 (20)      | 36 (41)     | 0.008           |

Level of functioning, mean (sd)

| CGAS at the beginning of the treatment         | 42.6 (9.0)   | 43.0 (8.3)  | 0.744           |
| CGAS at the end of the treatment              | 53.9 (7.8)   | 53.9 (8.0)  | 0.979           |
| CGAS change during treatment                  | 11.2 (9.3)   | 10.8 (9.8)  | 0.774           |

5.3.2 Factor analysis of the CD symptoms

The factor structure of CD symptoms was organised according to Loeber’s tripartite factor model (Loeber et al. 1993) and is presented for both genders in Table 7. The item “forced sexual activity” in boys and girls and the items “non-aggressive stealing” and “fire-setting” in girls were omitted from exploratory
factor analysis due to the small number of cases causing violations of statistical assumptions required by this method.

Among boys, four out of five items in Loeber’s overt factor model loaded to Factor 2. Factor 1 comprised four out of six covert symptoms from Loeber’s model. Factor 3 included exactly the same items as the authority conflict factor in Loeber’s model. The results of the confirmatory factor analysis (CFA) suggested that Loeber’s model fit reasonably well with the sample data for boys (GFI=0.90, $\chi^2 = 80.5$, df=74, $p=0.535$), if the item “forced sexual activity” was removed from the model.

Among girls, Factor 1 comprised four out of five items from Loeber’s overt factor, and Factor 2 included three out of four items from Loeber’s covert factor. Factor 3 included two out of three symptoms from Loeber’s authority conflict factor. Results of the CFA also indicated adequate fit with Loeber’s model in the sample data for girls (GFI=0.88, $\chi^2=49.4$, df=51, $p=0.535$). However, three items (forced sexual activity, aggressive stealing and fire setting) had to be omitted from the model for girls due to the small number of cases identified.

Table 7. Factor structure of 15 symptoms of CD among adolescent psychiatric inpatients according to the exploratory factor analysis (EFA), using tetrachoric correlations and Varimax rotation method.

| Loebert's factor model | Symptoms for conduct disorder according to DSM-IV criteria | Adolescents with conduct disorder | | | | |
|------------------------|----------------------------------------------------------|----------------------------------|---|---|---|
|                        |                                                          | Boys (n=92)                      | Factors a | Girls (n=63) | Factors a |
|                        |                                                          | 1 | 2 | 3 | 1 | 2 | 3 |
| Overt                  | Initiates physical fights                              | - | 0.86 | 0.85 | - | - | - |
|                        | Physical cruelty                                       | - | 0.80 | 0.77 | - | - | - |
|                        | Use of a weapon                                         | - | 0.71 | 0.69 | - | - | - |
|                        | Bullies or threatens                                   | - | - | 0.46 | 0.69 | - | - |
|                        | Cruelty to animals                                     | - | 0.51 | - | - | 0.54 | - |
|                        | Forced sexual activity                                  | - | - | - | - | - | - |
| Covert                 | Aggressive stealing                                     | 0.66 | - | - | - | - | - |
|                        | Fire setting                                            | 0.60 | - | - | - | - | - |
|                        | Break-ins                                              | 0.95 | - | - | - | - | 0.65 |
|                        | Non-aggressive stealing                                 | 0.81 | - | - | - | - | 0.86 |
|                        | Vandalism                                              | - | 0.61 | - | 0.74 | - | - |
|                        | Lies                                                   | - | - | 0.77 | - | - | 0.32 |
| Authority conflict     | Stays out at night                                     | - | - | 0.79 | - | 0.70 | - |
|                        | Ran away overnight                                     | - | - | 0.61 | - | - | 0.62 |
|                        | Truant                                                 | - | - | 0.42 | - | 0.88 | - |
a) The item “forced sexual activity” in both genders and the items “non-aggressive stealing” and “fire-setting” in girls were excluded from factor analyses.

5.4 Suicidal behaviour and alcohol dependence in conduct disorder (III)

Of the 59 girls and 82 boys with diagnosed CD, 24 (40.7%) girls and 24 (29.3%) boys were diagnosed to have alcohol dependence. Twenty-one (35.6%) girls and thirteen (15.9%) boys had a history of attempted suicide. Fourteen (58.3%) girls and five (20.8%) boys with CD and comorbid alcohol dependence had attempted suicide.

In girls with CD, alcohol dependence increased the risk for suicide attempts to 3.8-fold (95% CI=1.06–13.44, \( P=0.041 \)) and the risk for self-mutilation to 3.9-fold (95% CI=1.09–13.76, \( P=0.037 \)) compared with CD-girls without alcohol dependence. Alcohol dependence was associated with increased risk for drug experimentation (OR=13.98, CI 1.60–122.07, \( P=0.017 \)). Protective custody by the child welfare authorities decreased the risk for alcohol dependence (OR 0.23, CI 0.06–0.89, \( P=0.034 \)).

Among boys with CD, alcohol dependence increased the risk for life-threatening suicide attempts to 9.8-fold (CI 1.21–80.06, \( P=0.033 \)) compared with CD-boys without alcohol dependence. The risk for self-mutilation was also elevated to 5.3-fold (CI 1.07–24.46, \( P=0.041 \)). Among boys, alcohol dependence was also associated with a high risk for drug experimentation (OR 7.98, CI 1.53–41.56, \( P=0.014 \)).

Table 8 describes clinical features of the most serious suicide attempts (attempts classified as life-threatening suicide attempts according to K-SADS-PL) of adolescents with CD and co-morbid alcohol dependence. Seventy per cent of the girls who attempted suicide used a violent suicide method and all of them were suffering from comorbid depressive disorder. Half of the boys used a violent method in suicide attempts.
Table 8. Methods of life-threatening suicide attempts among inpatient adolescents with CD and alcohol dependence.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Comorbid psychiatric DSM-IV diagnoses in addition to CD and alcohol dependence</th>
<th>Suicide methods</th>
<th>Method classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Female</td>
<td>MDD, Drug dependence, PTSD, MDD</td>
<td>Deep wrist cuts (twice), Intoxication (alcohol, drugs)</td>
<td>Violent</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>MDD, Attention deficit disorder, Simple and social phobia</td>
<td>Deep wrist cuts, Jumping a bridge, Intoxication (alcohol, drugs)</td>
<td>Violent</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>MDD, Drug dependence, PTSD, Simple and social phobia</td>
<td>Jumping a bridge, Intoxication (drugs)</td>
<td>Violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>Drug dependence, Adjustment disorder</td>
<td>Deep cuts to wrist and abdomen</td>
<td>Violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>MDD, Drug abuse</td>
<td>Deep wrist cuts</td>
<td>Violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>MDD, PTSD</td>
<td>Deep wrist cuts (twice), Intoxication (drugs)</td>
<td>Violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>MDD, Psychotic features, Panic disorder, Obsessive-compulsive disorder, Simple and anxiety disorder</td>
<td>Jumping a bridge, Deep cuts to wrist and throat, Intoxication (severe drugs)</td>
<td>Violent</td>
</tr>
<tr>
<td>14</td>
<td>Female</td>
<td>Drug abuse</td>
<td>Intoxication (alcohol and sleeping pills)</td>
<td>Non-violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>MDD, Simple phobia</td>
<td>Intoxication (drugs)</td>
<td>Non-violent</td>
</tr>
<tr>
<td>17</td>
<td>Female</td>
<td>Drug abuse, Anorexia nervosa</td>
<td>Intoxication (alcohol and drugs)</td>
<td>Non-violent</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>MDD, Panic disorder</td>
<td>Deep wrist cuts, Drowning, Drug intoxication</td>
<td>Violent</td>
</tr>
<tr>
<td>17</td>
<td>Male</td>
<td>Drug abuse</td>
<td>Jumping in front of the train</td>
<td>Violent</td>
</tr>
<tr>
<td>15</td>
<td>Male</td>
<td>MDD, Drug dependence</td>
<td>Injected detergent intravenously</td>
<td>Non-violent</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>none</td>
<td>Drinking methyl-alcohol</td>
<td>Non-violent</td>
</tr>
<tr>
<td>17</td>
<td>Male</td>
<td>Depression NOS, Social Phobia, Drug dependence</td>
<td>Data missing</td>
<td>Non-violent</td>
</tr>
</tbody>
</table>

5.5 Gender differences in comorbidity of conduct disorder (IV)

5.5.1 Causes for hospitalisation

Of the 155 adolescents with CD the most common cause for hospitalisation of girls was suicidality (girls 42.9% vs. boys 23.9%, p=0.013). Among boys, the most common reason for hospitalisation was aggressive symptoms (boys 33.7% vs. girls 22.2%, p=0.122). An equal proportion of boys (n=40, 43.5%) and girls
(n=28, 44.4%) were in involuntary treatment (p=0.905). Two or more causes for admission were observed in 73 (47.1%) adolescents; in 32 (50.8%) girls and in 41 (44.6%) boys (p=0.445).

5.5.2 Comorbid somatic conditions

Girls with CD had more often allergies than boys (60% vs. 25%, p<0.001). In girls with CD, MDD was more common among allergic girls compared to those without allergies (45.9% vs. 20.0%, χ²=4.39, p=0.036), while in boys with CD no such association was observed (21.7% vs. 23.5%, χ²=0.03, p=0.860). Gender differences were not found in the following somatic health-related variables: regular medication, chronic disease, HIV-infection or hepatitis.

5.5.3 Comorbid psychiatric disorders

Comorbidity of psychiatric disorders was common (Table 9). Seventy-nine percent of the subjects with CD were diagnosed to have at least one other psychiatric condition (including substance use disorders). The mean number of comorbid diagnoses was 1.9 (SD 1.6) for boys and 2.1 (SD 1.6) for girls (p=0.435, t-test). Girls with CD had more often post-traumatic stress disorder (12.7% vs. 3.3%, p=0.025). 35.5% of the girls with CD had MDD as a comorbid psychiatric diagnosis, compared to 22.8% of the boys (p=0.086).

Table 9. Comorbid psychiatric disorders of adolescents with conduct disorder in a clinical inpatient sample according to the K-SADS-PL interview.

<table>
<thead>
<tr>
<th>Comorbid psychiatric disorder</th>
<th>Total (n=155) n (%)</th>
<th>Girls (n=63) n (%)</th>
<th>Boys (n=92) n (%)</th>
<th>Gender comparison p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD</td>
<td>43 (27.9)</td>
<td>22 (35.5)</td>
<td>21 (22.8)</td>
<td>0.086</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>5 (3.2)</td>
<td>3 (4.8)</td>
<td>2 (2.2)</td>
<td>0.397</td>
</tr>
<tr>
<td>Simple Phobia</td>
<td>4 (2.6)</td>
<td>2 (3.2)</td>
<td>2 (2.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>10 (6.5)</td>
<td>4 (6.3)</td>
<td>6 (6.5)</td>
<td>1.000</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>8 (5.2)</td>
<td>5 (7.9)</td>
<td>3 (3.3)</td>
<td>0.271</td>
</tr>
<tr>
<td>Generalised anxiety disorder</td>
<td>3 (1.9)</td>
<td>1 (1.6)</td>
<td>2 (2.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>PTSD</td>
<td>11 (7.1)</td>
<td>8 (12.7)</td>
<td>3 (3.3)</td>
<td>0.025</td>
</tr>
<tr>
<td>ADHD</td>
<td>16 (10.3)</td>
<td>6 (9.5)</td>
<td>10 (10.9)</td>
<td>0.787</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>51 (32.9)</td>
<td>21 (33.3)</td>
<td>30 (32.6)</td>
<td>0.925</td>
</tr>
</tbody>
</table>
Comorbid psychiatric disorder | Total (n=155) | Girls (n=63) | Boys (n=92) | Gender comparison
---|---|---|---|---
Alcohol dependence | 40 (25.8) | 18 (28.6) | 22 (23.9) | 0.515
Drug abuse | 22 (14.2) | 8 (12.7) | 14 (15.2) | 0.659
Drug dependence | 33 (21.3) | 13 (20.6) | 20 (21.7) | 0.869
Any comorbid psychiatric disorder | 121 (78.1) | 52 (82.5) | 69 (75.0) | 0.265

* Pearson χ²-test or Fisher’s Exact test, two-tailed significance

5.6 Association between severity of conduct disorder and level of nicotine dependence (V)

5.6.1 Smoking, comorbid psychiatric diagnoses and ND

A total of 86.1% of the girls and 85.9% of the boys with CD smoked regularly (at least one cigarette daily), and 41.7% of the girls and 40.4% of the boys reported a high level of ND (mFQT sum score of 6 or higher). The mean ages for the onset of smoking were 12.3 years (SD 1.6) for girls and 11.9 (SD 1.9) for boys (t-test = -1.33, df=145, p=0.187). The most common comorbid psychiatric diagnosis among both girls (66.7%) and boys (59.6%) was substance-related disorders. Gender differences in comorbidity among adolescents with CD were observed with comorbid affective disorders (48.6% in girls vs. 30.3% in boys, p=0.015) and anxiety disorders (29.2% vs. 11.1%, p=0.003).

5.6.2 Subtypes of CD and ND

There were no differences in sum scores of ND between the subtypes of CD (group, solitary aggressive and undifferentiated type/childhood-onset and adolescent-onset type) in girls or boys. Comorbid substance use disorder was associated with a higher level of ND among both girls (p=0.019) and boys (p< 0.001). The level of ND did not differ between those with or without affective or anxiety disorders.

5.6.3 The severity of CD and ND

The mean number of lifetime CD symptoms was 5.3 (SD 2.2) in girls and 6.9 (SD 2.8) in boys (F=4.48, df=169, p < 0.001). The total number of CD symptoms was
positively correlated with the level of ND in both girls and boys. Furthermore, the number of CD symptoms correlated with the level of ND in boys in all subscales except the aggression subscale, whereas in girls only the subscale of deceitfulness or theft correlated with the number of CD symptoms (Table 10).

Table 10. Correlation between the number of symptoms on each CD subscale and the sum score on the Fagerström Tolerance Questionnaire (mFTQ).

<table>
<thead>
<tr>
<th>Number of CD symptoms</th>
<th>r</th>
<th>p-value</th>
<th>adj r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIRLS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of symptoms</td>
<td>0.406</td>
<td>&lt;0.001</td>
<td>0.324</td>
<td>0.006</td>
</tr>
<tr>
<td>Aggression</td>
<td>0.169</td>
<td>0.156</td>
<td>0.143</td>
<td>0.235</td>
</tr>
<tr>
<td>Destruction of property</td>
<td>0.097</td>
<td>0.419</td>
<td>0.037</td>
<td>0.760</td>
</tr>
<tr>
<td>Deceitfulness or theft</td>
<td>0.362</td>
<td>0.002</td>
<td>0.328</td>
<td>0.005</td>
</tr>
<tr>
<td>Serious violations or rules</td>
<td>0.244</td>
<td>0.039</td>
<td>0.191</td>
<td>0.110</td>
</tr>
<tr>
<td>BOYS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of symptoms</td>
<td>0.358</td>
<td>&lt;0.001</td>
<td>0.310</td>
<td>0.002</td>
</tr>
<tr>
<td>Aggression</td>
<td>0.140</td>
<td>0.167</td>
<td>0.067</td>
<td>0.514</td>
</tr>
<tr>
<td>Destruction of property</td>
<td>0.231</td>
<td>0.022</td>
<td>0.224</td>
<td>0.026</td>
</tr>
<tr>
<td>Deceitfulness or theft</td>
<td>0.256</td>
<td>0.011</td>
<td>0.214</td>
<td>0.035</td>
</tr>
<tr>
<td>Serious violations or rules</td>
<td>0.297</td>
<td>0.003</td>
<td>0.334</td>
<td>0.001</td>
</tr>
</tbody>
</table>

adj r = partial correlation, age-adjusted

5.6.4 Predictors of ND

A linear regression analysis was used to study the associations between symptoms of CD, age, affective disorder, anxiety disorder and substance-related disorder with the sum score of ND. The model showed results for both girls (F=4.53, p=0.001) and boys (F=5.51, p<0.001). An increased sum score of ND was predicted by higher symptoms of CD (p=0.040) and the presence of a substance-related disorder (p=0.002) in adolescent boys, and higher symptoms of CD in adolescent girls (p=0.010) (Table 11).
Table 11. Predictors for ND in linear regression analysis with Fagerström sum score as the dependent variable.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>β</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GIRLS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms of CD</td>
<td>0.30</td>
<td>2.66</td>
<td>0.010</td>
</tr>
<tr>
<td>Age at admission</td>
<td>0.17</td>
<td>1.41</td>
<td>0.163</td>
</tr>
<tr>
<td>Affective disorder</td>
<td>0.14</td>
<td>1.27</td>
<td>0.208</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>0.01</td>
<td>0.06</td>
<td>0.955</td>
</tr>
<tr>
<td>Substance-related disorder</td>
<td>0.18</td>
<td>1.59</td>
<td>0.117</td>
</tr>
<tr>
<td><strong>BOYS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms of CD</td>
<td>0.22</td>
<td>2.09</td>
<td>0.040</td>
</tr>
<tr>
<td>Age at admission</td>
<td>-0.05</td>
<td>-0.43</td>
<td>0.672</td>
</tr>
<tr>
<td>Affective disorder</td>
<td>-0.09</td>
<td>-0.96</td>
<td>0.337</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>0.03</td>
<td>0.32</td>
<td>0.748</td>
</tr>
<tr>
<td>Substance-related disorder</td>
<td>0.35</td>
<td>3.23</td>
<td>0.002</td>
</tr>
</tbody>
</table>
6 Discussion

6.1 Main findings

In study I, parental physical abuse during childhood increased the risk for violent CD over four-fold in girls. The lack of a primary family increased the risk for both violent and non-violent CD approximately seven-fold in girls. No association between familial risk factors and CD was found among boys.

In study II, the results suggest a gender difference in the factor structure and developmental model of CD. The factor structure of CD symptoms for boys was rather solid and corresponds strongly to the overt, covert and authority conflict developmental model suggested by Loeber et al. (1993). Although the factor structure for girls also followed Loeber’s model, it was not as coherent as in boys. Measured with both negative consequences and the number of symptoms, the severity of CD among girls was milder than among boys. The level of functioning was reduced to equally low levels in both genders, though.

In study III, alcohol dependence increased, independently from illicit drug use, the risk for suicide attempts four-fold among girls with CD and the risk of life-threatening suicide attempts over nine-fold among boys with CD. Girls with both CD and alcohol dependence also had a four-fold risk of self-mutilative behaviour when compared to girls with CD only; the risk was over five-fold among boys.

In study IV, adolescents with CD had a very high (up to 80%) rate of comorbidity of any psychiatric disorder. Girls with CD had more PTSD than had boys. Girls with CD were more likely than boys to be admitted to psychiatric hospital due to suicidality. An interesting and novel finding was the very high self-reported rate of allergies among girls with CD.

In study V, an increased number of CD symptoms was associated with higher levels of ND. This association was related to substance use disorders, but not to any other psychiatric disorders among boys; among girls psychiatric disorders did not explain the ND-CD association. The number of CD symptoms among boys correlated with the level of ND on all the subscales except aggression, whereas the only correlation for girls was found with deceitfulness or theft.
6.2 Discussion of the results

6.2.1 Familial risk-factors for conduct disorder and violence (I)

Parental physical abuse increased the risk for violent CD over four-fold among girls. It has previously been proposed that CD in girls might be more due to domestic risk factors compared to boys (Keenan et al. 1997). Also, in a Finnish study female homicide offenders had witnessed or experienced more family violence in their primary families than the corresponding group of males (Putkonen et al. 2011). The lack of both parents at home also markedly increased the risk for both violent and non-violent CD among girls, but not among boys. Even in earlier studies, it has been suggested that parental psychological status has more of an influence on girls than on boys because of girls’ greater need for socialisation in the family (Webster-Stratton 1996). This finding should be considered when treating CD in girls. Guidance on parenting skills and addressing family problems could be particularly effective elements in the treatment of girls with CD. In CD prevention, special attention could be paid to girls in families with a current high risk or recently actualised marital divorce.

One observation in this study was that CD was not associated with the social class of the adolescent. This differs from the results in most previous studies (Fergusson & Lynskey 1997, McLoyd 1998). Social class differences in Finland are smaller than in most of Europe and the USA (Kivelä et al. 2001), which probably explains this finding.

6.2.2 Developmental model for CD (II)

The results of our study suggest a gender difference in the factor structure of CD and for the developmental model. This finding presents important implications regarding the validity of current diagnostic criteria for CD in females. It has been proposed that ODD is not as strong a precursor for CD among girls as among boys (Rowe et al. 2002, Rowe et al. 2010). Since Loeber’s authority conflict pathway largely resembles the pathway from ODD to CD, our findings support the different findings by Rowe and colleagues. It should be noted that Loeber and co-authors developed their model on the basis of their findings concerning boys. Conclusions according to the Loeber model and focusing on the structure of this disorder in girls should therefore be made with caution. Callous-unemotional
traits have been studied as one alternative developmental pathway theory for CD (Frick & White 2008), and its suitability for girls has yielded some promising results (Essau et al. 2006).

6.2.3 Symptom threshold for CD (II)

The prevalence of the more severe symptoms of CD (aggressive stealing, fire-setting, forced sexual activity) was very low (0–5%) among girls even in our clinical sample of adolescents suffering from severe psychiatric disorders. The severity of CD was also shown to be milder among girls than in boys. This is in line with the previous literature (APA 2000). However, we found no gender differences in the level of functioning. This raises questions about whether girls’ level of functioning is more sensitive to conduct problems, or whether girls with more severe conduct problems and lowered levels of functioning are not currently being detected with the DSM-IV-criteria. It is also possible that comorbid psychiatric disorders in girls also have an impact on the level of functioning. It has been proposed that symptom thresholds for girls should differ from those for boys. This suggests that diagnostic criteria should include more non-physical, non-aggressive symptoms in order to identify girls with CD with better sensitivity (Zoccolillo et al. 1996, Crick & Zahn-Waxler 2003). However, there are no empirical data available to evaluate whether the inclusion of sex-specific symptoms improves the prediction of prognosis in CD (Moffitt et al. 2008).

6.2.4 CD and suicidal behaviour (III, IV)

Suicidality as a cause for hospitalisation was found to be more common among girls. This is in line with previous literature on the subject (Lewinsohn et al. 2001). The risk for suicidal behaviour must always be taken into consideration in CD, especially when comorbid MDD is suspected. The prevalence of suicidality in our study was even greater than that of comorbid depression. Earlier studies have shown that CD is an independent risk factor for suicidal behaviour (Apter et al. 1995, Glowinski et al. 2001), and that multiple co-morbid psychiatric conditions cause an increased risk of suicidal behaviour (Kelly et al. 2001). This finding explains the high rates of suicidality among adolescent girls with CD, even in the absence of clinical depression. As stated by Apter and colleagues (1995): “It seems that there are hypothetically at least two types of suicidal
behaviours during adolescence: a wish to die (depression) and a wish not to be here for a time (impulse control)”. Alcohol use increases suicidal behaviour by diminishing impulse control (Lejoyeux et al. 1999). In this study, alcohol dependence did not specifically associate with impulsivity in CD, even if it was associated with suicidality. Impulsivity was obtained from single K-SADS-PL, possibly lacking sensitivity in identifying impulsivity.

The methods of suicide used by boys have previously been reported to be violent and more irreversible, whereas among girls, suicide methods are typically non-violent (Brent et al. 1999). A worrying finding in this study was the use of violent and irreversible methods of suicide in both genders. The fact that both conduct disorder and alcohol dependence are growing problems among girls (Keenan et al. 1999, Karam et al. 2004) could be one contributing factor to this finding.

When the methods used in life-threatening suicide attempts were explored, the majority of the girls with CD who had a history of suicide attempts had used violent methods. This finding differs from earlier studies, where non-violent methods were reported to be the most prevalent in suicide attempts among girls (Brent et al. 1999). A combination of alcohol dependence and CD seemed to be a factor leading to the use of more violent methods of suicide attempts, at least among girls. Violent suicide attempts should never be underestimated, since they have a higher tendency to succeed. Given that all the girls who had used violent methods were also found to have depression implies that effective screening and treatment of depression in girls with CD and alcohol dependence is essential in clinical practice.

When studying the impact of alcohol dependence on suicidal behaviour, the focus was on alcohol dependence, rather than on all alcohol-related disorders (including alcohol abuse), because minor alcohol problems like alcohol abuse were very common in the study sample. This finding is in line with the high levels of binge drinking recorded among adolescents in Finland’s general population (Hibell et al. 2009). Binge drinking has also been found to have increased over three-fold among Finnish adolescent (14–18 year old) girls between 1981 and 1999 (Lintonen et al. 2000).

When discussing the findings on suicidality in this data, it should be noted that these findings are from data of hospitalised adolescents, where the prevalence
of suicidality is increased. This limits the generalisation of these findings to the general population.

6.2.5 Comorbidity of CD (III, IV, V)

Both girls and boys with CD had very high rates of comorbidity with psychiatric disorders. Girls with CD had more PTSD than boys. When diagnoses were combined, gender differences, with predominance in girls, were found in both affective and anxiety disorders. High prevalence of psychiatric comorbidity is not only typical for CD but also for clinical data of hospitalised adolescents, and this limits the generalisation of these findings.

As noted in earlier studies (Angold et al. 1999), also in this study the affective disorders were more common in girls. From a clinical point of view, the higher levels of comorbid depression seen in girls with CD should lead to change in the treatment practices of these adolescent girls. A common problem for clinicians treating adolescents with CD is that the patients are often non-adherent with the treatment programmes. The treatment of comorbid internalising psychiatric disorders, such as affective disorders, for example with the use of antidepressive medication and individual psychotherapy, could lead to stronger collaboration and more effective doctor-patient relationships in the treatment of CD.

It is known that PTSD commonly co-occurs with other psychiatric disorders (Brady et al. 2000). Our finding that girls with CD are more likely than boys to have comorbid PTSD is somewhat alarming. It is possible that girls with CD fall into traumatic situations. It is also possible that some cases of conduct disorder arise secondary to PTSD. However, conclusions on causality cannot be made using our cross-sectional data.

Another interesting finding of this study was the fact that girls with CD and comorbid alcohol dependence were less commonly in protective custody than those without serious alcohol problems. It is possible that among patients with CD, a sufficiently early placement into a protective environment prevents from developing serious alcohol problems. Such an environment more likely cuts down continuous alcohol use and thus also prevents the consequences of alcohol dependence.

The relatively low comorbidity of ADHD (10%) is below the prevalence of comorbid ADHD in earlier studies (Maughan et al. 2004). Adolescents with ADHD are not generally treated in an acute inpatient setting. In addition, the
interview methods used might not recognise the symptoms of ADHD as sensitively as other diagnostic groups. We did not interview adolescents’ parents systematically; also, when diagnosing ADHD, it would be useful to interview other significant parties, such as teachers.

The prevalence of allergic diseases (asthma, allergic rhinitis, atopic dermatitis) in general population samples from different countries ranges from 14% to 32% (Fagan et al. 2001, Romano-Zelekha et al. 2007), being higher and increasing in Western countries (Dunder et al. 2001). A recent study of Finnish adolescents aged 15–16 years reported a 25% prevalence of allergic diseases (Varjonen et al. 2007). Gender differences in the prevalence of allergies are reported to be minor. In data on Finnish adolescents, boys have more asthma than girls, while no significant gender difference was found in the prevalence of allergic rhinitis (Huurre et al. 2004). Our finding of girls with CD having more self-reported allergies than boys is novel and extremely interesting. It has earlier been suspected that certain combinations of asthma medication can cause behavioural symptoms (Saricoban et al. 2011), but it does not explain the gender difference. Our finding can be partly explained by the predominance of comorbid MDD among girls, since it has been documented that there is a connection between allergies and depression, especially among females (Timonen et al. 2002). In this study, allergies were more common among girls with CD and depression than among girls with CD only. However, the fact that even half of the girls with CD but without MDD had self-reported allergy supports the need for further research into the connection between CD and atopic disorders, especially among females. Whether the gender difference actually exists, or whether boys neglect to report their allergic disorders, requires further research using valid and objective measures of atopic disorders.

6.2.6 CD and Nicotine dependence (V)

Regular smoking (at least one cigarette daily) was alarmingly a rule in adolescents with CD in this clinical data. Strong ND was also very common both in girls and boys.

Smoking has been shown to have a strong genetic heritability of around 50%, as has CD (Li 2003, Gelhorn et al. 2005, Button et al. 2007). Specific candidate genes have been studied to explain both conditions (Li 2003, Sakai et al. 2006, Malmberg et al. 2008) and ND and CD have been linked to the same genetic
background (Malmberg et al. 2008, Raine 2002). Although in this study a correlation between the number of CD symptoms and the severity of ND was found in both genders, the results suggest that neither aggressive symptoms nor childhood-onset CD and ND are related, at least in adolescence. These subtypes are thought to predict later life-long antisocial behaviour (Söderström et al. 2004), which has a strong biological background (Ferguson 2010). On the contrary, the occurrence of ND was found to be related to non-aggressive CD-symptoms that are often manifested in adolescent peer groups and constitute a less aberrant form of behaviour, characteristic of a certain stage in adolescent development. It is possible that frequent smoking and ND among adolescents with CD may be related to familiar factors and peer influences rather than any single shared genetic factor. A high level of novelty-seeking and low harm avoidance are temperament features that are commonly found to lead to the violation of rules and other disruptive activities in adolescents with CD (Schmeck & Poutska 2001). This type of behaviour often takes place in peer groups, where both the initiation and continuation of smoking are also more likely to be reinforced. It is also possible that the genetic factor explaining the connection between CD and ND is not associated with aggressive behaviour but rather with other symptoms of CD.

From another point of view, CD is associated with ND in adolescence (Hakko et al. 2006) and with maternal smoking during pregnancy (Boden et al. 2010). ND has been associated with depression (Picciotto et al. 2002); furthermore, both depression (Krishnadasm & Cavanagh 2012) and ND (Cardinale et al. 2012) have been associated with inflammatory processes. The connection observed between CD and allergies in this study makes possible inflammatory factors mediating CD an interesting issue. The potential connection between inflammation and CD and the role of depression as a possible mediator in this trajectory should be an object of interest in the research on the aetiology of CD.

6.3 Methodological considerations, strengths and limitations

6.3.1 Strengths of the study

The strengths of the study included a reasonable sample size of CD adolescents, at least in analyses conducted using completed data. Even in large general population studies the number of cases identified can be very limited when a
single disorder, such as CD in adolescent girls, is examined. A good example of this is the 1999 British Child Mental Health Survey of over 10,000 children (aged 5–15 years), where only 42 girls (0.8%) met the criteria for CD (Maughan et al. 2004).

The results of the studies in this thesis are based on well-established semi-structured diagnostic interviews (Kokkevi & Hartgens 1995, Kaufman et al. 1997, Ambrosini 2000). All the interviews were conducted by medical professionals during the inpatient treatment periods, and the patients were evaluated at several stages during their treatment at the unit. The sample comprised all hospitalised psychiatric adolescent patients in a large geographical area of northern Finland, within a specified space and period of time. This design enabled sampling a reasonably large number of girls with CD for the study. The final series of inpatients is an unselected sample of patients admitted to Unit 70 with a high participation rate.

This study represents an important additional contribution to the previous literature, particularly given the small number of studies addressing CD among girls.

6.3.2 Limitations

The main limitation of the study is that the sample comprised the most severe, hospitalised patients with the psychiatric disorders studied, presumably with increased rates of co-morbidity when compared to the general population. This limits the generalisation of our findings to adolescents with less severe problems.

Since analyses were carried out using cross-sectional data, we cannot make conclusions about the possible causal relationships between different factors. In earlier analyses (I, III), the number of adolescents with CD was lower than in the final sample.

Data on domestic violence (I) were gathered retrospectively and they were largely based on patients’ self-reports. However, where information remained ambiguous, it was complemented with information from parents, whenever possible. Nevertheless, the number of domestic violence incidents is probably an underestimation of its prevalence. There were also many known risk factors for CD, e.g., most of the biological risk factors (Burke et al. 2002) not taken into account in the study design, which may have affected the results.
The use of K-SADS-PL is undoubtedly a strength in this study, but the lack of inter-rater reliability assessment should be considered as a limitation (I-V). The test-retest reliability of diagnoses reached for adolescents using the K-SADS-PL interview has been described as good to excellent, and its concurrent validity and inter-rater agreement have shown to be high (Ambrosini 2000, Kaufman et al. 1997).

The prevalence of allergies was based of self-reports, which might differ from true prevalence, and these numbers may also be underestimates (IV).

Genetic determinants of smoking were not studied in this research setting, nor did we have any laboratory tests available to verify the presence of ND. Similarly, no information on parental smoking or substance abuse was gathered (V).

6.3.3 Ethical considerations

Many adolescents in this study were under custody. In these cases, we obtained consents to participate in the study from both the adolescents and their social welfare workers. The social workers were not always familiar with the situation regarding the adolescents or their families. Adolescents’ biological parents were not approached for consent in such cases.

The participation rate in this study was remarkably high. Interviews were extensive, especially for those who had many symptoms and therefore many supplements of K-SADS-PL had to be completed. The adolescents’ energy and willingness to participate in the study despite the clinical impairment was remarkable. The subjects had the possibility to decline an interview at any point without giving any reason for this. In cases where the adolescents had concentration problems or aggressive behaviour, tiredness, symptoms of withdrawal, anxiety or depressive symptoms, interviews were conducted over shorter periods. It was decided that video-recording interviews to double-rate interviews was not ethical, given the nature of the study population. It was also considered unethical to repeat interviews to obtain better reliability.

Interviews were conducted either by the treating physicians or by trained medical students, who interviewed patients under the surveillance of the treating physicians. The study criteria for CD were discussed with the treating physician whenever necessary. In some cases, the interview process may have inadvertently accelerated the identification, diagnosis and treatment of the patients’ psychiatric problems. On the other hand, psychiatric diagnosis can stigmatise an adolescent,
and defining a psychiatric diagnosis may not be solely favourable, especially if effective treatment is not available.
7 Conclusions and implications

The symptoms and background of girls CD diverge noticeably from boys. Family violence, parental divorce and sole custody are significant risk factors for CD among girls. Even though girls with CD may present with less severe manifestations of CD symptoms, the risk for psychiatric comorbidity is significantly elevated: girls with CD have high rates of mood and substance use disorders and an elevated risk for suicidality. Also, allergic disorders are associated with CD among girls, but the mechanism behind this comorbidity is yet unclear. Comorbid nicotine dependence is more a rule than an exception among girls with CD – as also among boys with CD. The present diagnostic classification, based mainly on observations made on male subjects, reflects a distorted image of the severity and impairment of functionality among girls with CD.

The results of this thesis are applicable only to clinical population samples; further studies and possible replication of these findings in general population samples are thus encouraged.

7.1 Research implications

There is a need for more focus on girls in research into CD. The prevalence of clinically significant CD is presumably underestimated among girls. Revising diagnostic criteria of CD and general population studies of girls CD using revised criteria as well as an indicator of impairment of functionality are recommended. In that way, it is possible to achieve higher sensitivity and correlation with clinical features and more accurate figures of the true prevalence of CD among girls. Revised criteria that could be used in future could contain e.g. symptoms of indirect aggression and lack of empathy. In defining the severity of CD, comorbid psychiatric disorders should be one aspect to consider.

As this thesis indicates, girls with CD are a group with high comorbidity and complicated background: it is possible that CD is one manifestation of traumas and undertreatment of these girls. Temporality of the onset of CD and comorbid psychiatric disorders among girls should be one target for research, with the aim of shedding more light on the specific background of girls with CD. As well, future follow-up studies on treatment efficiency and outcome of CD should focus on controlled studies between CD and other adolescent psychiatric disorders and suicidality.
7.2 Clinical implications

The clinical implications of this study are divided as follows:

1. It seems that girls with CD are more sensitive to familial risk factors. Interventions for the prevention and early detection of CD should be designed separately for girls. Therefore, providing enhanced support to risk families in prenatal clinics, healthcare centres and school healthcare could form key elements in the prevention of CD among girls.

2. The diagnosis and subtyping of CD, according to DSM-IV criteria, may underestimate the true prevalence of clinically significant CD. When meeting a girl even with low severity CD, it should be noticed that clinical impairment can be significant.

3. The risk for suicidal behaviour must always be taken into consideration when meeting girls with CD. It should also be noted, as this study implicates, that even in the absence of depression, CD is an independent risk factor for suicidal behaviour. Nevertheless, effective screening and treatment of depressive symptoms should be available for all girls with CD, especially those with comorbid alcohol dependence.

4. Reduction of binge drinking among adolescents in general can result in decreased suicide rates and psychiatric hospitalisation. Meaningful spare time activities should be organised for youths in order to reduce alcohol consumption, and more resources should be targeted to supervised youth work.

5. Smoking and nicotine dependence are very common among adolescents with CD, girls included. This should be noted in the treatment of CD with both adolescents and their families, preferably before first smoking experiments. The significant role of peer influence in smoking among adolescents with CD should be understood in treatment units, schools and homes.
References


## Appendix 1. Admission Form translated to English

Oulu University Hospital
Department of Psychiatry, unit 70

Patient's name and social security number

<table>
<thead>
<tr>
<th>Address</th>
<th>Phone</th>
<th>Age</th>
<th>County</th>
</tr>
</thead>
</table>

Medical conditions

Allergies

Period of psychiatric evaluation: from ___.___.____ to ___.___.____

Apprehended in psychiatric treatment until ___.___.____.

In voluntary treatment from ___.___.____

Patient's psychiatric nurse ___________________________ date ___.___.____

Patient's reserve psychiatric nurse ___________________________ date ___.___.____

Patient's treating physician ___________________________ date ___.___.____

Leader of family/network meetings ___________________________ date ___.___.____

Previous psychiatric evaluations / treatment periods: ___________________________ date ___.___.____

(History of previous treatment: ___________________________ date ___.___.____)

### Evaluation period:

<table>
<thead>
<tr>
<th>Family meeting</th>
<th>date</th>
<th>person responsible</th>
<th>GARF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Network meeting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation of functionality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Team/summary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other examinations</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Treatment period:

Date of admission: ___________________________ Reason for admission: ___________________________ GAS

Treatment plan date ___________________________

Date of departure ___________________________ Diagnoses ___________________________ GAS
Problems presented by adolescent:
- Date: date
- Date: date
- Date: date
- Date: date

Problems presented by others
- Date: date
- Date: date
- Date: date
- Date: date

Problems evaluated by working group:
- Date: date
- Date: date
- Date: date
- Date: date

Strengths of the adolescent:
- Date: date
- Date: date
- Date: date
- Date: date

Aims of the treatment:
- Date: date
- Date: date
- Date: date
- Date: date

Treatment received:
- Date: date
- Date: date
- Date: date
- Date: date

Involuntary treatment:
- Date: date
- Date: date
- Date: date
- Date: date

Treatment plan:
- Treatment ended: date
- Treatment interrupted: date, reason:

Opinion of the adolescent at the end of the treatment:
-
Original Publications


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The original articles are not included in the electronic version of the thesis.


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1160. Lastio, Liisa (2012) In search of new prognostic molecular markers in ovarian cancer

1161. Klintrup, Kai (2012) Inflammation and invasive margin in colorectal cancer


1170. Virtanen, Katri (2012) “Äiti, täällä on toisia samanlaisia, kumpi mää?”: Voimisteluseura ja kouluterveydenhuolto perheiden tukema lasten painonhallinnassa

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