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Internalizing Symptoms in Adolescence

Familial Aggregation and Other
Psychosocial Factors

Thesis for the degree of Philosophiae Doctor

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Norwegian University of Science and Technology

Faculty of Medicine

Regional Centre for Child and Youth

Mental Health and Child Welfare



NTNU – Trondheim
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Internaliserende symptomer hos ungdom: Opphopning i familier og andre psykososiale faktorer

Denne avhandlingen handler om unges internaliserende symptomer, definert som symptomer på depresjon, generell angst og sosial angst. Flere psykososiale faktorer relatert til slike symptomer ble undersøkt, med hovedfokus på sammenhengen mellom foreldres og barns symptomer, i tillegg til enkelte individuelle og vennskapsfaktorer. Det å ha en forelder med psykiske problemer er en av de viktigste risikofaktorer for at barn utvikler symptomer selv, men eksisterende forskning er begrenset av at fedre sjelden har blitt inkludert. Psykososiale faktorer kan være viktige for både forebygging og behandling av internaliserende symptomer fordi de ofte kan påvirkes og også øke identifisering av symptomer. Studier viser at spesielt sosial angst sjelden oppdages.

I den første studien ble sammenhenger og kjønnsforskjeller mellom ulike psykiske symptomer hos foreldre og internaliserende symptomer hos ungdom undersøkt. Den andre studien så på sammenhengen mellom symptomer på angst og depresjon hos foreldre da barna var i førskolealder (ti år tidligere) og slike symptomer hos barna i ungdomsalder. I tillegg undersøkte vi hvorvidt lav selvtillit og fysisk aktivitet hos ungdom påvirket disse sammenhengene. I den tredje studien ble symptomer på sosial angst og relaterte psykososiale faktorer på individ- og vennenivå sammenlignet blant unge i ett normalutvalg og ett ungdomspsykiatrisk utvalg.

Alle de tre studiene i avhandlingen er basert på data fra Helseundersøkelsen i Nord-Trøndelag (HUNT3) gjennomført i 2006-2008. I to studier bestod utvalget av 5732 ungdommer i alderen 13-18 år som hadde én (1761 mødre og 742 fedre) eller begge (3229 mødre og fedre) foreldre med i HUNT3. I en studie ble også data fra foreldre som deltok i HUNT2 gjennomført i 1995-1997 benyttet. I den tredje studien bestod utvalget av 7669 ungdommer som deltok i HUNT3 og 694 ungdommer som deltok i Helseundersøkelsen i Barne- og ungdomspsykiatrisk klinikk ved St. Olavs Hospital.

Funnene viste at foreldres symptomer på angst og depresjon, men ikke symptomer på alkoholmisbruk og spiseproblemer, var relatert til symptomer på depresjon, generell angst og sosial angst, lavt subjektivt velvære og lav selvtillit hos ungdom. Vi fant ingen kjønnsforskjeller, noe som betyr at internaliserende symptomer hos mødre og fedre var like viktig for slike symptomer og redusert velvære hos både døtre og sønner.

Foreldres internaliserende symptomer da barna var i førskolealder var relatert til symptomer hos barna i tenårene, men denne sammenhengen var formidlet gjennom nåværende symptomer hos foreldre. Barn av foreldre med symptomer på angst og depresjon kan derfor være i vedvarende risiko for utvikle slike symptomer siden foreldree ser ut til å få symptomer flere ganger. Sammenhengen mellom foreldres og unges internaliserende symptomer ble delvis forsterket av lav selvtillit hos ungdommene. Lav selvtillit kan være en viktig forløper for symptomer på angst og depresjon og dermed et angrepspunkt i forebygging og behandling av symptomer. Ungdommenes fysiske aktivitetsnivå, definert som trening minst en gang i uka utenom skoletid, reduserte sammenhengen mellom internaliserende symptomer hos mødre og ungdom. Fysisk aktivitet ser derfor ut til å kunne beskytte mot angst og depresjon i familier med slike symptomer, og det kan være nyttig å oppmuntre til fysisk aktivitet hos ungdom i familier der spesielt mødre har symptomer.

Symptomer på sosial angst ble ofte rapportert av ungdommer både i befolkningen generelt og av pasienter i psykiatrien, men få pasienter hadde diagnose på sosial angst. Symptomer var relatert til akademiske skoleproblemer, å bli utsatt for mobbing, spiseproblemer og kviseproblemer. Disse relaterte problemene kan være lettere å

oppdage enn sosial angst og et fokus på disse kan bidra til å øke identifisering av slike symptomer.

Basert på alle tre studiene i denne avhandlingen ser det ut til at en rutinemessig bred screening av problemer hos barn, ungdom og foreldre kan være viktig for å redusere byrden forårsaket av internaliserende problemer i samfunnet. Funnene understreker et behov for økt oppmerksomhet rundt internaliserende symptomer som et familiært problem. Når helsepersonell møter foreldre med slike symptomer, er det sentralt å undersøke den mentale status i hele familien så tidlig som mulig for å kunne redusere byrden og kostnadene assosiert med slike problemer hos både rammede familier og samfunnet som helhet. Funnene tyder også på at forebyggings- og behandlingstiltak rettet mot selvtillit og fysisk aktivitet kan være nyttige for å redusere internaliserende symptomer hos ungdom.

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The hard life of a PhD-student at a conference in Paris

LIST OF PAPERS

- Paper I:** Ranøyen, I., Klöckner, C. A., Wallander, J., & Jozefiak, T. (2014). Associations between internalizing problems in adolescent daughters versus sons and mental health problems in mothers versus fathers (The HUNT Study). *Journal of Child and Family Studies*. doi: 10.1007/s10826-014-0001-x. Epub ahead of print, available online by June 18th 2014.
- Paper II:** Ranøyen, I., Stenseng, F., Klöckner, C. A., Wallander, J., & Jozefiak, T. Familial aggregation of anxiety and depression in the community: The role of adolescents' self-esteem and physical activity level (The HUNT Study). *Accepted for publication in BMC Public Health*.
- Paper III:** Ranøyen, I., Jozefiak, T., Wallander, J., Lydersen, S., & Indredavik, M. S. (2014). Self-reported social anxiety symptoms and correlates in a clinical (CAP) and a community (Young-HUNT) adolescent sample. *Social Psychiatry and Psychiatric Epidemiology*, 49(12), 1937-1949. doi: 10.1007/s00127-014-0888-y.

ACRONYMS AND ABBREVIATIONS

ADHD	Attention Deficit/Hyperactivity Disorder
BIC	Bayesian Information Criterion
CAGE	Cut down Annoyed Guilty Eye-opener scale
CAP	Child and adolescent psychiatry
CFI	Comparative Fit Index
CONOR-MHI	Cohort Norway Mental Health Index
CR	Composite reliability
EDS	Eating Dissatisfaction Scale
FIML	Full Information Maximum Likelihood
HADS	Hospital Anxiety and Depression Scale
HUNT	The Nord-Trøndelag Health Study
ICD-10	International Classification of Diseases, 10 th Revision
IQR	Interquartile range
LPA	Latent profile analysis
MI	Multiple imputation
RMSEA	Root Mean Square Error of Approximation
SCL	Symptom Checklist
SEM	Structural Equation Modeling
SES	Socioeconomic status
SPAI-C	Social Phobia and Anxiety Inventory for Children
SWB	Subjective well-being
TLI	Tucker-Lewis Index
VO ₂ peak	Maximal oxygen uptake
WHO HBSC	World Health Organization Health Behaviour in School-aged Children
WLSMV	Weighted least squares mean and variance adjusted estimator
Young-HUNT	The Nord-Trøndelag Health Study part for adolescents ages 13-19

DEFINITIONS AND DELIMITATIONS

Internalizing symptoms

Several definitions of internalizing symptoms exist. Furthermore, in research literature the terms 'internalizing' and 'emotional' symptoms often appear to be used interchangeably, whereas other researchers claim that internalizing symptoms are a broader concept than emotional symptoms. In this line of thinking, emotional symptoms (or problems) refer to symptoms of anxiety and depression (Boyle & Jones, 1985; Goodman, 2001), whereas internalizing symptoms (or problems) also include peer problems (Goodman, Lamping, & Ploubidis, 2010) and somatic complaints (Achenbach & Rescorla, 2001). In this project, the term '*internalizing symptoms*' will be used because the focus will be on symptoms of anxiety and depression, as well as symptoms of social anxiety, which are related to peer problems (McKenna, Cassidy, & Giles, 2014). Furthermore, because positive and negative affect seem to form two independent factors which should be examined separately (Diener, 2000), we will also examine two mental health factors both related to both high and low positive affect: subjective well-being (SWB) and self-esteem. These factors are also correlates of internalizing symptoms (Derdikman-Eiron et al., 2012; Derdikman-Eiron et al., 2011).

Symptom vs. problem vs. disorder

The terms 'symptom' and 'problem' are also often used interchangeably in the research literature. A symptom has been defined as a change in the body or its functions that is an indication of disease (*The New International Webster's Comprehensive Dictionary Of The English Language*, 2003). However, a symptom may be transient and not necessarily a problem. The threshold at which one or several symptoms becomes a problem depends on the symptoms' duration, intensity, and associated impairment (Boyle & Jones, 1985). In this thesis, self-reported questionnaires were used to address symptoms of depression, general anxiety, and social anxiety, which here are combined into internalizing symptoms. Higher scores on the continuum of symptoms are considered as indications of *underlying* internalizing problems, but they do not necessarily imply the presence of psychiatric disorders. The terms 'depression',

'anxiety', and 'social anxiety' are here used as indicators of internalizing problems on a continuum. Unless otherwise specified, the terms do not imply the presence of a categorical psychiatric disorder as defined in the International Classification of Diseases, 10th Revision (ICD-10) or The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) with the respective requirements regarding onset, duration, and impairment.

Depression

The term 'depression' is used to denote depressive symptoms, excluding manic and hypomanic symptoms seen in other mood disorders, such as bipolar affective disorders.

Anxiety

The term 'anxiety' in this thesis denotes predominantly symptoms of general anxiety or social anxiety, excluding symptoms of other anxiety disorders as listed in ICD-10 or DSM-5.

Social anxiety vs. social phobia

Both in the current ICD-10 and in the previous DSM-IV the label 'social phobia' was used to denote the anxiety disorder encompassing fear of social situations (although in the ICD-10 there is also a diagnosis called 'social anxiety disorder of childhood' used to denote an exaggerated and persistent form of stranger anxiety (Goodman & Scott, 2005)). More recently, researchers have argued that the term 'social anxiety disorder' better conveys the pervasiveness and the impairment associated with this disorder than 'social phobia' (Liebowitz, Heimberg, Fresco, Travers, & Stein, 2000). Hence, in the new DSM-5, social phobia has been renamed social anxiety disorder. In this thesis, the term 'social anxiety' is used.

Self-esteem

The term 'self-esteem' refers in this thesis to a person's conscious and explicit evaluation of global self-worth unless otherwise specified.

Adolescents

Adolescents are in this thesis defined as being in the age range 13.0 through 18.9 years.

Parents

In this thesis, parents are defined as biological or adoptive parents.

Familial aggregation

Familial aggregation is broadly defined as the clustering of certain traits, behaviors, or disorders within a given family. In this thesis, familial aggregation pertains to the occurrence of more symptoms or mental health problems in parents or offspring of a person with such symptoms/problems than in control families.

Psychosocial factors

Psychosocial factors are in this thesis defined broadly as psychological or social factors, excluding biological factors.

Sex

Sex is defined as biological sex, in contrast to gender, which commonly denotes the sociocultural aspects of sex, such as culturally learned social roles and personal identification of gender. In the current project, we only have information on the biological sex of the participants, not how they perceive their sex. Hence, the term 'sex' was chosen.

SUMMARY

In this thesis, several psychosocial factors associated with internalizing symptoms in adolescence were addressed, with a focus on familial aggregation. Having a parent with mental health problems is one of the most important risk factors for developing psychiatric symptoms, but existing research is limited by the fact that paternal mental health seldom has been examined. In addition, the development and maintenance of internalizing symptoms may rely on individual characteristics of the child, peer factors, socioeconomic status, and other psychosocial factors. Psychosocial correlates can have important implications for both prevention and treatment of internalizing symptoms because such variables can often be modified, in contrast to biological correlates, and may also serve to increase identification of symptoms. Previous research indicates that especially social anxiety is understudied and not easily recognized by adults, even mental health professionals working with youth.

The main objectives in this thesis were to examine several psychosocial correlates of internalizing symptoms. In study 1, associations between several mental health symptoms in *both* parents and internalizing symptoms in adolescent offspring were investigated. In addition, we examined whether parental and offspring sex moderated these associations. In study 2, the associations between recurrent internalizing symptoms in parents over a ten-year time span and internalizing symptoms in adolescent offspring were examined. In addition, we investigated whether associations between parental and offspring internalizing symptoms were mediated by offspring self-esteem and moderated by physical activity. In study 3, we focused solely on internalizing symptoms related to social anxiety and their correlates.

All three studies were based on data from the adolescent portion of The Nord-Trøndelag Health Study (Young-HUNT3). The sample in studies 1 and 2 consisted of 5732 adolescents in Young-HUNT3 (ages 13-18) who had one (N=2503) or both parents (N=3229) participating in the adult HUNT3. In study 2, the sample moreover included data from those parents who also participated in the adult HUNT2 when offspring were of a preschool age. This constituted 3198

of the mothers (78%) and 2488 of the fathers (77%). In study 3, the study sample consisted of 7669 adolescents from Young-HUNT3, in addition to comparable data from a clinical sample consisting of 694 participants (ages 13-18) in The Health Survey in the Department of Child and Adolescent Psychiatry, St. Olav's University Hospital in Sør-Trøndelag, Norway (the CAP Survey). All participants responded to questionnaires reporting on their own mental health.

The findings showed that parental symptoms of anxiety and depression, but not alcohol abuse and eating problems, were associated with low subjective well-being, low self-esteem, and more symptoms of depression, general anxiety, and social anxiety in adolescent offspring. None of the associations were dependent on parental or offspring sex, suggesting that internalizing symptoms in fathers and mothers were equally important for offspring symptoms. Parental symptoms of anxiety and depression when offspring were of a preschool age were associated with such symptoms in offspring ten years later, but these associations were fully mediated by current parental symptoms. These findings suggest that the children of parents with internalizing symptoms are at a sustained risk for such symptoms themselves due to the apparent 10-year stability of both maternal and paternal symptoms. The associations between parental and adolescent internalizing symptoms were partly mediated by low adolescent self-esteem, which may be an important precursor of symptoms and amenable to interventions.

Adolescent physical activity moderated the association between maternal and offspring internalizing symptoms, and may reduce familial aggregation of such symptoms. This suggests encouraging physical activity in the offspring of parents with such symptoms could be useful. Social anxiety symptoms were frequently reported by adolescents, and the most prominent correlates were academic school problems, bullying, eating problems, and acne problems. These correlates may be easier to detect than social anxiety symptoms, and prevention programs targeting these factors may also be useful for reducing such symptoms. Based on the combined findings, routine screening of a broad range of problems among children, adolescents, and parents may be vital to reduce the burden of internalizing problems in adolescence.

1. INTRODUCTION

"I write of melancholy by being busy to avoid melancholy"

Robert Burton, 1638

This thesis concerns internalizing symptoms. Such symptoms are sometimes referred to as intro-punitive, meaning a tendency to blame or punish the self, and are often characterized by quiet, internal distress. Such internalizing symptoms of anxiety and depression are a natural part of the human condition, and have been part of medicine since the times of Hippocrates, when he described a bodily excess of black bile to be associated with the disease melancholy. Hence, Hippocrates is considered to be the first to describe clinical depression. Robert Burton wrote the most encompassing historical treatment of melancholy in 1621, *The Anatomy of Melancholy*, a book of more than 800 pages, which he continually rewrote. Notably, he claimed music and dance to be vital in treating this disorder. 200 years later, Griesinger wrote about the relationship between anxiety and melancholy in children: "Simple melancholic states also present themselves, whose foundation is a general feeling of anxiety" (Griesinger, Robertson, & Rutherford, 1882, p. 101). Since these times, internalizing problems have also been the theme in vast amounts of fictional literature, for example Haruki Murakami's introspective treatment of depression in *"Norwegian Wood"* (1998) and Mark Haddon's amusing yet painful portrayal of anxiety in *"A Spot of Bother"* (2006). However, here the focus will be on the scientific literature.

In this thesis, several psychosocial factors associated with internalizing symptoms in adolescence will be addressed. Internalizing symptoms are extensively examined among children and adolescents; however, in some areas research findings are still limited because of methodological problems which will be reviewed below. This thesis focuses mainly on the community population, although in one study a clinical and a community sample will be compared. Thus, the thesis mostly applies a public health perspective, but also with clinical implications.

Having a parent with mental health problems is consistently shown to be one of the most important risk factors for psychiatric symptoms in offspring (Beardslee, Gladstone, & O'Connor, 2011; Connell & Goodman, 2002; Merikangas, Dierker, & Szatmari, 1998; Weissman, Leckman, Merikangas, Gammon, & Prusoff, 1984). However, existing research is considerably limited by the fact that paternal – in contrast to maternal – mental health seldom has been investigated (Phares, 1992; Phares, Fields, Kamboukos, & Lopez, 2005). This is a problem because fathers obviously contribute 50% of their offspring's genes and are increasingly more involved in child care (Stein, Ramchandani, & Murray, 2008). Thus, in this thesis the associations between several mental health symptoms in *both* parents and internalizing symptoms in offspring were examined. First, parental and offspring sex were examined as moderators in familial aggregation. Also, we examined the associations between recurrent internalizing symptoms in parents over a ten-year time span and such symptoms in adolescent offspring. In addition, mechanisms in familial aggregation were investigated by examining whether associations between parental and offspring internalizing symptoms were mediated by offspring self-esteem and moderated by physical activity. Finally, despite being the third most common mental health disorder and the most common anxiety disorder, social anxiety has been subject to a lot less research than general anxiety and depression (Stein, Torgrud, & Walker, 2000). Thus, in the final study the focus was solely on internalizing symptoms related to social anxiety and the psychosocial correlates of such symptoms. Because previous research indicates that social anxiety is not easily recognized by physicians (Den Boer & Dunner, 1999), several correlates of social anxiety were examined in the hope of increasing identification of social anxiety so that more adolescents who are struggling with this problem can be helped.

This introduction will first focus on the rationale of the thesis. Then, depression, general anxiety, and social anxiety will be described, including the epidemiology of such symptoms and disorders in children and adolescents. Subsequently, a theoretical framework for internalizing symptoms in adolescence in general will be introduced, which emphasize familial aggregation of mental health problems. Finally, findings and limitations in previous research on the specific

topics examined in this thesis will be addressed, including familial aggregation and other psychosocial correlates of internalizing symptoms.

1.1 Rationale of the thesis

By 2030, depression will be the leading cause of disease burden worldwide, according to the World Health Organization (WHO, 2011). Recent calculations show that mental health problems annually cost the Norwegian society 60-70 billion Norwegian kroner due to disability and mortality, and depression and anxiety are the most expensive disorders, because they are the most prevalent mental health problems in the community and cause significant loss of productivity (Røsjø, 2014). This shows that despite vast research efforts on such problems, we are still not able to effectively prevent and treat internalizing problems. Thus, in order to reduce the prevalence and the cost of these problems, further research is vital.

Depression, general anxiety and social anxiety are highly comorbid problems (Ranta, Kaltiala-Heino, Rantanen, & Marttunen, 2009; Wittchen, Stein, & Kessler, 1999). 25-50% of adolescents with depression also have anxiety disorders, whereas 10-15% of adolescents with anxiety disorders also have depression (Axelson & Birmaher, 2001)¹. Thus, examining these symptoms concurrently has been recommended (Zahn-Waxler, Klimes-Dougan, & Slattery, 2000). In both adolescents and adults, depression and anxiety disorders are among the most prevalent psychiatric problems and the prevalence rates of these disorders increase during adolescence, especially among girls (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). The presence of anxiety, social anxiety and/or depression in adolescence is an important risk factor for recurrent depression and general and social anxiety in adulthood (Garber & Weersing, 2010; Pine, Cohen, Gurley, Brook, & Ma, 1998; Stein et al., 2001). Nearly 60% of adolescents with anxiety and depression have further episodes in adulthood (Patton et al., 2014). Hence, adolescence is an especially high-risk period for the development of internalizing symptoms, and focusing research on this critical period is important for prevention and treatment.

¹ These numbers pertain to *any* anxiety disorder, including separation anxiety, general anxiety, social anxiety, and panic disorder.

Most studies on familial aggregation of mental health problems have been based on clinical samples with mentally ill parents. However, these samples may consist of atypical or more severe cases of illness, and hence, may not generalize to the majority of mental health problems that are experienced in community populations (Hammen, Shih, & Brennan, 2004). This is supported by the findings showing a reduced functioning associated even with problems that lie below the threshold for the diagnostic categories (Lewinsohn, Solomon, Seeley, & Zeiss, 2000; Stein et al., 2000). Thus, studies based on community samples are much needed. This will also circumvent the possible biases resulting from the higher rates of comorbidity among treatment-seeking individuals (Berkson, 1946; Merikangas & Knight, 2009).

1.2 Internalizing symptoms

Sadness and worry are natural parts of being a human. For most individuals these symptoms are transient and do not, or only briefly, interfere with daily functioning. However, for some persons, sadness and worry are more severe and persistent, and may leave them incapacitated for longer periods of time. This is when the labels 'depression' and 'anxiety' are appropriate. The seriousness of these problems is underscored by findings that anxiety and depression in adolescence are important risk factors for suicide, social and educational impairments, substance abuse, smoking, obesity, cardiovascular disease, and stroke (Jonas & Mussolino, 2000; Suls & Bunde, 2005; Thapar, Collishaw, Pine, & Thapar, 2012; Woodward & Fergusson, 2001).

1.2.1 The tripartite model

As mentioned above, the term internalizing symptoms will here be defined as consisting of symptoms of depression, general anxiety, and social anxiety, as factor analyses suggest that anxiety and depressive symptoms may be combined into one entity (Achenbach & Rescorla, 2001). The reasons for the high comorbidity rates between these symptoms are unknown (Rohde, 2009), but hypotheses on shared genetics (Kendler, Neale, Kessler, Heath, & Eaves, 1992), temperament and neurotransmitter abnormalities (Axelson & Birmaher, 2001), theories on helplessness and hopelessness (Alloy, Kelly, Mineka, & Clements, 1990), and attachment and

loss (Bowlby, 1982) have been proposed. An empirically supported model is the tripartite model of anxiety and depression, which posits that anxiety and depression often occur together due to shared genetic factors and a common distress factor marked by negative affect (Clark & Watson, 1991; Mineka, Watson, & Clark, 1998). This is evident in that some symptoms are common to both anxiety and depression (negative affect), whereas other symptoms are unique to either depression (low positive affect) or the different anxiety disorders as shown in Figure 1 (Mineka et al., 1998). The negative affect factor is characterized by symptoms of distress, insomnia, poor concentration, and a negative attributional style, whereas the positive affect factor is characterized by interest, well-being, energy, affiliation, social dominance, and adventurousness (Clark & Watson, 1991). Social anxiety seems to be related to the low positive affect factor of the tripartite model, possibly because impaired interpersonal engagement characterizes both depression and social anxiety (Hughes et al., 2006). This suggests that social anxiety may be a rather special anxiety disorder, emphasizing the need for more research on this disorder. The tripartite model is also related to the cognitive aspects of anxiety and depression in that some cognitions seem common to both problems, whereas others are unique to either problem (Clark, Steer, & Beck, 1994). Although initially applied to adults, the tripartite model is shown to explain comorbidity between anxiety and depression also in adolescents (Laurent & Ettelson, 2001).

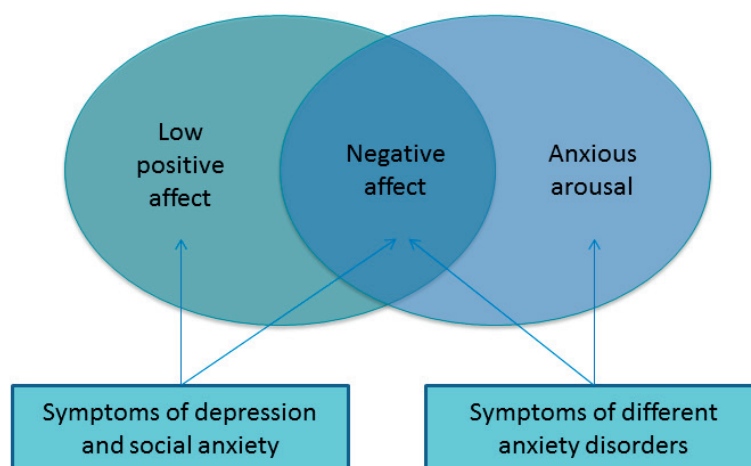


Figure 1: The tripartite model

1.2.2 Depression in children and adolescents

Even though depression has been a part of medicine since ancient times, this is not the case for children and adolescents. In the 1960s, the clinical consensus was that depression among children did not exist (Rie, 1966). Cited reasons for this were that the brains of children were too immature for the development of depression to be possible (Thompson, 2012) or that depression was masked as other behaviors (Carlson & Cantwell, 1980). Since then, however, the existence of depression in children and adolescents has been firmly established (Rao & Chen, 2009). Depression in children and adolescents is now diagnosed using mainly adult criteria due to the similar symptoms in childhood and adult depression (Zahn-Waxler et al., 2000). Symptoms include the three core categories sadness, reduced ability to experience pleasure, and loss of energy together with additional symptoms including self-blame, guilt, helplessness, hopelessness etc. (World Health Organization, 2010).

Among 4-year-olds and school-aged children, the three-month prevalence rate of depressive disorders is approximately 2.0% (Costello et al., 2003; Wichstrøm et al., 2012). In adolescence, the prevalence of depression increases, although rates vary considerably across studies, e.g. the point prevalence varies from 0.7% to 3.4% (Merikangas & Knight, 2009). In Norwegian adolescents ages 14-16, the 2-month prevalence of all diagnostic types of depression was 9.4%, and the lifetime prevalence was 23% (Sund, Larsson, & Wichstrøm, 2011a). The average age of onset is approximately 14 years of age (Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Common comorbid disorders are anxiety disorders, attention deficit/hyperactivity disorder (ADHD), substance abuse, conduct disorders, and eating disorders (Angold, Costello, & Erkanli, 1999; Brent & Weersing, 2008; Rohde, 2009).

1.2.3 Anxiety in children and adolescents

Research on anxiety in children has a longer history than research on depression, but the early focus was on specific fears rather than broader anxiety problems (Laurent & Ettelson, 2001). Hippocrates named fears as one of the illnesses among small children, but it was not until the

1860s that the first descriptions of anxiety disorders in children emerged (Treffers & Silverman, 2011). With the rise of psychoanalytic theory in the first half of the 20th century, anxiety was seen as mediating the relationship between intrapsychic conflict and all other psychopathology, whereas in the 1970s, anxiety was considered the result of dysfunctional mother-infant interactions (Zahn-Waxler et al., 2000). In the last 50 years, we have achieved a better understanding of the etiology of anxiety and the differences between anxiety disorders in children/adolescents and adults (Fonseca & Perrin, 2011), e.g. diagnostic criteria for generalized anxiety disorder require fewer somatic symptoms in children/adolescents than in adults (Goodman & Scott, 2005). Symptoms of general anxiety in adolescents include persistent worries about the future, past behavior, personal competence and appearance, accompanied by tension, inability to relax, self-consciousness, need for reassurance, headaches, and stomachaches (Goodman & Scott, 2005).

The three-month prevalence of any anxiety disorder is 1.5% among Norwegian 4-year-olds (Wichstrøm et al., 2012), and 3.8% among 8-10-year-olds (Heiervang et al., 2007). This is low compared to other countries. A meta-analysis based on findings from several countries estimated the prevalence to 12.3% for any anxiety disorder and 1.7% for generalized anxiety disorder among children aged 6 through 12, and 11% for any anxiety disorder and 1.9% for generalized anxiety disorder adolescents aged 13 through 18 (Costello, Egger, Copeland, Erkanli, & Angold, 2011). This suggests that the prevalence of general anxiety does not increase during adolescence, whereas individual studies do find an increasing prevalence with age (Beesdo, Knappe, & Pine, 2009; Costello et al., 2003). To our knowledge as of today there are no published studies on the prevalence of anxiety disorders among Norwegian adolescents, but studies based on symptom ratings indicate that the prevalence is lower in Norway than in other countries (Leikanger, Ingul, & Larsson, 2012). The average age of onset is approximately 8 years (in 50% of the cases between 6 and 12 years) (Costello et al., 2011). Common comorbid disorders are depression, conduct disorder/oppositional defiant disorder, and ADHD (Costello et al., 2011). Regarding the prevalence of comorbid anxiety and depression symptoms, 13% of adolescents in

the community self-report having such symptoms above a threshold signifying clinical relevance (Boyd, Gullone, Kostanski, Ollendick, & Shek, 2000; Skrove, Romundstad, & Indredavik, 2013).

1.2.4 Social anxiety in children and adolescents

In the 1980s, social anxiety was named “the neglected anxiety disorder” (Liebowitz, Gorman, Fyer, & Klein, 1985). Since then, research on this problem has increased, but recently both scholars and the popular press have put forward that the concept of social anxiety “medicalizes” normal human shyness (Lane, 2008; Wessely, 2008). The feeling of being insecure in social situations can be recognized by most of us. However, examinations of the relationship between shyness and social phobia show that more shy than non-shy individuals are socially anxious, yet a large proportion of shy individuals are not socially anxious, and individuals with social anxiety are more impaired and have more symptoms than non-shy individuals (Burstein, Ameli-Grillon, & Merikangas, 2011a; Chavira, Stein, & Malcarne, 2002; Heiser, Turner, & Beidel, 2003; Heiser, Turner, Beidel, & Roberson-Nay, 2009). These findings indicate that social anxiety and shyness are related but not synonymous concepts (Heiser et al., 2009). Individuals with symptoms of social anxiety fear the scrutiny of others and that they will say or do something others find embarrassing or humiliating (Stein & Stein, 2008). These fears are accompanied by emotional and physical symptoms like intense self-criticism and heart racing, dizziness, sweating, trembling, or nausea (Stein & Stein, 2008).

Among Norwegian 4-year-olds, the three-month prevalence of social anxiety disorder is 0.5% (Wichstrøm et al., 2012). A meta-analysis estimated the prevalence of social anxiety disorder to 2.2% among children aged 6 through 12, and 5.0% among adolescents aged 13 through 18 (Costello et al., 2011). In individual studies among adolescents, the lifetime prevalence of social anxiety varies considerably from 1 to 24 % (Gren-Landell et al., 2009; Ranta et al., 2009; Wittchen et al., 1999). Whereas most studies find social anxiety to increase during adolescence (Wittchen et al., 1999), some studies find a peak at around 14 years of age (Essau, Conradt, & Petermann, 1999; Ranta et al., 2007). The average age of onset is 12 years, and 80-

95% of individuals developing social anxiety do so before the age of 20 (Kessler et al., 2007; Stein & Stein, 2008). Common comorbid disorders are depressive disorders, somatoform disorders, and substance abuse (Chartier, Walker, & Stein, 2003; Essau et al., 1999; Fehm, Beesdo, Jacobi, & Fiedler, 2008).

1.3 Theoretical framework of the thesis

Several theoretical perspectives in the research literature are relevant for the theme of this thesis. Developmental psychopathology is chosen as the main theoretical framework although other relevant theories will also be mentioned.

1.3.1 Developmental psychopathology

Developmental psychopathology is a comprehensive interdisciplinary framework incorporating biological, psychological, and socio-contextual influences on both normal and abnormal development and adaptation (Cicchetti & Toth, 2009b; Masten, 2006). Hence, it is closely related to the biopsychosocial model which is based on the notion that suffering and illness should be explained by all relevant biological, psychological, and social factors that might contribute (Engel, 1977). A central feature of developmental psychopathology is sensitivity to the individual's current developmental phase in the life span and the developmental tasks that should be fulfilled for normative adaptation to occur (Masten, 2006). For example, achieving healthy attachment relationships is important for infants (Teti, Gelfand, Messinger, & Isabella, 1995), whereas developing social and emotional competence is important for preschoolers (Goodman, Brogan, Lynch, & Fielding, 1993). Adolescence is a transition period characterized by neurobiological, hormonal, psychological and social changes, and increased independence from parents is expected (Cicchetti & Toth, 2009a). These aspects should be acknowledged in studies of internalizing symptoms in adolescence. Furthermore, an important feature of developmental psychopathology is the notion of developmental cascades which emphasize the importance of examining how adaptation or maladaptation to prior developmental tasks contributes to current adaptation (Cicchetti & Toth, 2009a; Masten & Cicchetti, 2010).

The concepts of *equifinality* (different predictors leading to the same outcome) and *multifinality* (one predictor leading to different outcomes) are central tenets in this framework (Cicchetti & Toth, 2009a). Related to this is also the fact that positive and negative affect seems to be bivariate and form two independent factors, which are correlated with different variables (Cacioppo, Gardner, & Berntson, 1999; Diener, 2000). For example, individuals can feel both happy and sad at the same time (Larsen, McGraw, & Cacioppo, 2001). Also, adolescents with equal amounts of psychiatric problems may report different levels of quality of life (Bastiaansen, Koot, & Ferdinand, 2005; Jozefiak, Larsson, Wichstrøm, Wallander, & Matthejat, 2010). These findings indicate that it is possible to experience well-being even with moderate symptom levels. Depressive symptoms are in the tripartite model related to low positive affect but not high positive affect. Thus, studies examining both high and low positive affect would be informative for identifying additional targets in prevention and treatment.

Developmental psychopathology focuses on the continuum of developmental functioning and underlines that examinations of subclinical symptoms as well as mental disorders will gain useful insight into developmental events (Cicchetti & Toth, 2009a). Although epidemiology traditionally is defined as “the study of the occurrence of illness” (Rothman, 2002), more contemporary definitions highlight that the field of epidemiology is concerned with the extent and determinants of the continuum of health and disease in the general population (Merikangas & Knight, 2009). Thus, epidemiological studies may be suitable approaches to answer questions related to the field of developmental psychopathology.

1.3.2 Other relevant theories

Developmental psychopathology builds on several prevailing theories of development, among which several are relevant for this thesis. Systems theories are a basic fundament of developmental psychopathology (Masten, 2006). Bronfenbrenner’s *ecological systems theory* postulates that individuals are living systems and their world is organized in a set of systems ordered along proximal to distal dimensions called the micro-, meso-, exo-, and macrosystem

(Bronfenbrenner, 1979). Especially relevant in the current context is the microsystem, which reflects how the individual interacts with his or her family, peers or school. This is also evident in *the transactional model*, in which development is seen as an interplay between the individual and his or her biological and social context (Sameroff & MacKenzie, 2003). This model emphasizes the bidirectional effects of the individual and the environment (Sameroff & MacKenzie, 2003). In the present setting, a child's behavior is seen to influence the behavior of parents and peers and vice versa, resulting in positive or negative feedback, and ultimately affecting development. Relating this to the development of psychopathology, theories of *diathesis-stress* and *differential susceptibility* postulate that children with genetic, physiological, or temperamental vulnerabilities may be more strongly influenced by either positive or negative environmental stressors (Belsky & Pluess, 2009). *The model of bidirectional influences* includes genetic and neural activity into the systems perspective and sees development as a hierarchy of four components (genetic activity, neural activity, behavior, and environment) that influence each other bidirectionally (Gottlieb, 1991). Hence, experiences are seen to affect the genetic expression. Thus, the developmental psychopathology framework is also related to epigenetics.

1.3.3 Familial aggregation of mental health problems

Based on developmental psychopathology, an encompassing model detailing the mechanisms involved in the familial aggregation of mental health problems has been proposed (Connell & Goodman, 2002; Goodman & Gotlib, 1999). This model describes four mechanisms (genetics, innate dysfunctional neuroregulation, transaction and social modeling, and stress) proposed to explain the transmission of risk from parents with psychopathology to offspring. The mediating mechanisms reflect the complex interplay between genetic and environmental factors in familial aggregation of mental health problems. Some "natural experiments" examining children who are adopted at birth, adopted at conception, and children of twins contribute to disentangle genetic and environmental risks. Most of these studies show that the pathways involved in the transmission of risk are both genetic and environmental (Natsuaki et al., 2014). Although initially developed to explain the transmission of risk from depressed mothers to children, the

authors claim the model with some adjustments also can explain transmission of risk from both mothers and fathers and account for a broader range of psychopathology than just depression (Connell & Goodman, 2002).

1.3.3.1 Genetics

The first mechanism of the model explains how children of mentally unhealthy parents may inherit genetic predispositions towards psychopathology (Goodman & Gotlib, 1999). For example, the genetic polymorphisms 5-HTTLPR, BDNF Val66Met, and COMT Val158Met may create vulnerabilities to anxiety and depression (Gatt et al., 2009; Olsson et al., 2005; Oppenheimer, Hankin, Young, & Smolen, 2013; Rabl et al., 2014). Genes may also be related to personal characteristics such as heightened stress reactivity or temperamental features, which increase the risk for depression (Joormann, Eugene, & Gotlib, 2009). In community studies, the heritability of general anxiety and depression symptoms in parents and offspring is estimated between 0.12 and 0.17 (Czajkowski, Røysamb, Reichborn-Kjennerud, & Tambs, 2010; Tambs & Moum, 1993b). In twin studies, the heritability is estimated to be higher but the precise number varies (Czajkowski et al., 2010; Kendler, Gardner, Gatz, & Pedersen, 2007; Rapee & Spence, 2004), and may be influenced by sex or age-specific effects (Kendler, Gardner, & Lichtenstein, 2008), or possibly sibling specific environmental variability (Czajkowski et al., 2010).

Genetic and environmental factors may also correlate and interact (Manuck & McCaffery, 2014; Rutter, Moffitt, & Caspi, 2006). Gene-environment correlations are evident when individuals with certain genetic dispositions are passively exposed to or actively seek out certain environments (Jaffee & Price, 2007). An example of a gene-environment interaction is that individuals with shorter alleles of the 5-HTT genetic polymorphism exhibit a higher risk for depression when experiencing negative life events (Caspi et al., 2003). Furthermore, epigenetic animal studies have found that maternal behavior may change the genetic expression in offspring (Weaver et al., 2004).

Also related to genetics is *assortative mating*, which reflects the tendency for individuals with similar phenotypes to mate more frequently than what is randomly expected (Crow & Felsenstein, 1968). Spouses of psychiatric patients have an increased risk of psychiatric disorders themselves, and assortative mating is established for anxiety, depression, and alcoholism (Maes et al., 1998; Mathews & Reus, 2001; Merikangas, 1982; Merikangas, Prusoff, & Weissman, 1988). This phenomenon may result in an increased likelihood for psychiatric problems in offspring through both genetic and environmental mechanisms.

1.3.3.2 Prenatal development and neuroendocrinology

The second mechanism of the model posits that genetics or adverse experiences in utero, e.g. increased cortisol levels, reduced blood flow, risky health behaviors, or the use of psychopharmaceuticals during pregnancy, may result in complications such as preterm delivery, low birth weight, or dysfunctional neuroregulations which interfere with emotion regulation (Connell & Goodman, 2002; Goodman & Gotlib, 1999). These complications may result in an increased risk of psychopathology in children. For example, prenatal exposure to maternal anxiety and depression is shown (partly through epigenetic processes) to affect the offspring's functioning and reactivity of the hypothalamic-pituitary-adrenocortical (HPA) system and result in abnormal production and secretion of the hormone cortisol, which is considered the core of the human stress response (Gutteling, Weerth, & Buitelaar, 2005; Joormann et al., 2009; O'Connor et al., 2005; O'Donnell et al., 2013; Oberlander et al., 2008). Furthermore, exposure to abnormal maternal cortisol levels during pregnancy is shown to be related to negative reactivity in infant temperament (Davis et al., 2007), and thus increase the vulnerability to internalizing symptoms in offspring (Lupien, McEwen, Gunnar, & Heim, 2009). Recent research also suggests that parental psychopathology may promote the formation of a neural-immune pipeline with amplified inflammatory cytokine signaling between the brain and the periphery suggesting that inflammation may increase the risk of depression in offspring (Miller & Cole, 2012).

1.3.3.3 Transaction and social modeling in parenting

The third mechanism focuses on the social mechanisms of risk, and postulates that parents with mental health problems may not be able to meet their children's developmental needs resulting in insecure attachment relationships (Armsden, McCauley, Greenberg, Burke, & Mitchell, 1990; Teti et al., 1995). Parents may also expose their offspring to a stressful family environment and negative cognitions, behaviors, and/or affects. The family environment can be characterized by parent-child discord (including intrusive, angry, and hostile interactions), low family cohesion, and a high degree of parental control (Berg-Nielsen, Vikan, & Dahl, 2002; Joormann et al., 2009). For example, depressed mothers are shown to magnify, punish, or neglect negative emotions in their children, and thereby model ineffective emotion management (Silk et al., 2011; Silk, Shaw, Skuban, Oland, & Kovacs, 2006). Children can also imitate their parents' negative coping styles through mechanisms of social learning (Bandura, 1986; Gelfand & Teti, 1990; Goodman & Gotlib, 1999). Indeed, children of depressed mothers show high emotional reactivity, deficits in emotion understanding, and primitive coping mechanisms in response to stress (e.g. less flexible in disengaging, shifting, and refocusing attention), and these indicators of emotion regulation are tied to internalizing problems (Kovacs, Joormann, & Gotlib, 2008; Repetti, Taylor, & Seeman, 2002; Silk et al., 2006). Of course, such factors may also influence the stress response of the offspring resulting in a chronic activation of the HPA axis and thus affecting emotion regulation (Joormann et al., 2009).

Another vulnerability resulting from such processes may be low self-esteem in children, which can increase the risk of internalizing symptoms (Goodman & Gotlib, 1999). Three specific theories are proposed to explain the relationship between low self-esteem and internalizing problems. In *the vulnerability model*, low self-esteem acts as a risk factor for internalizing problems, in *the scar model*, low self-esteem is a consequence of internalizing problems, whereas in *the reciprocal relation model*, the relationship between low self-esteem and internalizing problems is considered reciprocal (Orth & Robins, 2013). There is now strong evidence supporting *the vulnerability model* indicating that low global self-esteem predicts depressive

symptoms, while depressive symptoms do not predict low self-esteem (Orth & Robins, 2013; Orth, Robins, & Roberts, 2008; Sowislo & Orth, 2013). These findings seem valid for females and males (Orth et al., 2008; Sowislo & Orth, 2013), for age groups from childhood to old age (Orth et al., 2008; Orth, Robins, Trzesniewski, Maes, & Schmitt, 2009; Sowislo & Orth, 2013), after adjusting for content overlap between measures of self-esteem and depression (Orth et al., 2008; Orth et al., 2009), and across different time lags between assessments (Sowislo & Orth, 2013). In contrast, the relationship between self-esteem and anxiety seems more bidirectional (McCarty, Stoep, & McCauley, 2007; Sowislo & Orth, 2013).

1.3.3.4 Stress

Finally, the fourth mechanism claims that children of mentally ill parents may be exposed to a range of stressors associated with mental illness. These stressors are assumed to mediate the association between parental and offspring mental illness (Goodman & Gotlib, 1999). Examples of such stressors may be marital discord (Davies & Windle, 1997), low socioeconomic status (Garber & Cole, 2010), disrupted social relationships (Smith & Lincoln, 2011), and an unhealthy diet (Jacka et al., 2013). The two final mechanisms in Goodman and Gotlib's (1999) model are also related to the *interpersonal stress model*, in which the negative effects of parental depression on offspring depression are assumed to mainly be caused by a stressful family environment, marital discord, parental social functioning, financial and occupational difficulties, and the effects of these factors on the interpersonal functioning of the offspring (Hammen, 2002). This model has been tested and supported in a community sample (Hammen et al., 2004).

1.3.3.5 Moderating variables

Having described the mechanisms through which parents are assumed to confer an increased risk of psychopathology in children, Goodman and Gotlib (1999) propose several variables that may moderate the familial aggregation of mental health problems. These will be the main focus in this thesis. Examples of such moderators are sex, the timing of symptoms, and various characteristics of the children (Beardslee, Schultz, & Selman, 1987; Goodman & Gotlib, 1999).

With regard to *sex*, not all mental health problems are equally heritable in females and males (Kendler, Gardner, Neale, & Prescott, 2001), and adolescent girls with shorter alleles of the genetic polymorphism 5-HTTLPR have a higher risk of depression when experiencing negative life events than boys (Eley et al., 2004). Hence, different base rates of maternal vs. paternal mental health problems may affect which symptoms are expressed in children depending on the sex of the offspring and whether mother or father (or both) display problems. Also, daughters and sons may have different experiences in the family. There are several environmental theories on why the sex differences in mental health problems occur. Maternal psychopathology may have a larger impact on offspring than paternal psychopathology because mothers spend more time with offspring (Craig, 2006; Ohannessian et al., 2005). Gender identification theories suggest that mental health problems in the same-sex parent may be more strongly associated with problems in children than when present in the parent of the opposite sex (Ohannessian et al., 2005). Theories focusing on gender role development suggest that boys are encouraged to be independent from others whereas social relationships are more important for girls (Bussey & Bandura, 1999), making girls more vulnerable to problems within the family than boys (Davies & Lindsay, 2004; Ohannessian et al., 2005).

With regard to the *timing* of both parental and offspring symptoms, this is related to the notion of sensitive periods in developmental psychopathology. Research indicate that offspring are more vulnerable to parental mental health problems in the postnatal period and in adolescence (Stein et al., 2008). Infants have a huge brain growth and are very sensitive to the quality of interaction with caregivers, whereas in adolescence physiological and psychosocial developmental changes occur. Thus, the timing of parental psychopathology will be related to the offspring's likelihood of mastering the developmental tasks relevant for their age (Goodman, 2007). Related to this is the issue of chronicity in psychopathology. Especially depression is considered a chronic problem, and this will probably increase the likelihood of transmission of risk to offspring (Garber & Cole, 2010).

Although not explicitly described in the model, children's *physical activity level* may also act as a moderator. Physical activity is assumed to affect anxiety, depression and self-esteem positively (Morgan & Goldston, 1987; Strong et al., 2005). This is intriguing because most individuals can engage in physical activity, and motivation for physical activity can be altered through public health interventions (Fortier, Duda, Guerin, & Teixeira, 2012). Exercise may lead to mood improvements by enhancing anxiety-inhibiting mechanisms (Schoenfeld, Rada, Pieruzzini, Hsueh, & Gould, 2013), increasing endorphin levels, changing body temperature or cerebral blood flow (Salmon, 2001), or as a "time out" from difficult thoughts (Morgan, 1985). In addition, exercise may help fulfil the basic human needs of autonomy, competence and relatedness which are shown to increase self-esteem and reduce anxiety and depression as explained in the *self-determination theory* (Kasser & Ryan, 1996; Kirkcaldy, Shephard, & Siefen, 2002; Ryan & Deci, 2000).

1.3.3.6 Other psychosocial correlates

The development and maintenance of internalizing symptoms do not only rely on personal and familial factors. Following Bronfenbrenner's *ecological systems theory*, peer factors, socioeconomic status, and other psychosocial factors are also likely involved, and may be both antecedents, mediators, moderators, and consequences of symptoms. Thus, identifying psychosocial correlates have important implications for both prevention and treatment as such variables can be modified, in contrast to biological correlates. Psychosocial correlates of internalizing symptoms may serve to increase impairment (Brunello et al., 2000) but can also be important for identification because correlates may be more easy to detect than symptoms per se. Mental health problems among adolescents are often not discovered within the health systems, but rather in schools (Burns et al., 1995). In this setting, possible important correlates such as learning difficulties or bullying may be easier to detect. In a developmental perspective, how internalizing symptoms are expressed will differ with age and cognitive maturation (Ollendick & Hirshfeld-Becker, 2002; Westenberg, Drewes, Goedhart, Siebelink, & Treffers,

2004). Thus, the psychosocial correlates of symptoms may also differ over development and should be examined in an age-appropriate manner among adolescents.

1.3.4 The studies in the thesis

Developmental psychopathology offers an encompassing framework, into which the components of this thesis may be put. Due to the mostly cross-sectional nature of the data on which this thesis is based, the main focus will be on the moderators and correlates of familial aggregation of internalizing symptoms. In addition, one mediating *mechanism* will be examined based on previous research strongly indicating that self-esteem prospectively predicts depression. Figure 2 shows a model outlining the relationships between the specific factors that will be examined in this thesis. The rationale for examining the factors identified in Figure 2 is based on limitations in previous research, which will be reviewed in the following sections.

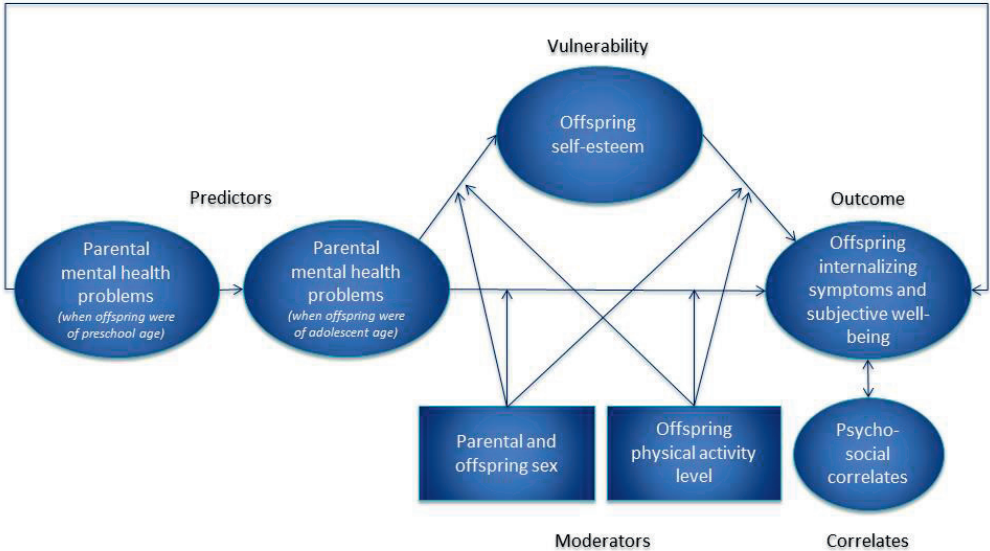


Figure 2: Model examined in this thesis

In study 1, the principal goal was to focus on Bronfenbrenner’s micro system and examine associations between different mental health problems (symptoms of anxiety and depression, alcohol abuse, and eating problems) in parents and internalizing symptoms in terms of both positive affect (subjective well-being and self-esteem) and negative affect (symptoms of

depression, general anxiety, and social anxiety), in addition to anxious arousal (symptoms of general anxiety) in offspring. This enabled a consideration of the concepts of equifinality and multifinality, which are central in developmental psychopathology. Furthermore, we focused on one of the moderators in Goodman and Gotlib's (1999) model by examining how parental and offspring sex affects the familial aggregation of these symptoms.

Based on the findings in study 1, the focus in study 2 was solely on familial aggregation of symptoms of anxiety and depression. First, the possible moderating effects of timing and recurrence of parental symptoms across a ten-year time span were examined, which may relate to sensitive periods and successful or unsuccessful achievement of relevant tasks at different points in the child's development. Second, one of the mechanisms proposed in Goodman and Gotlib's (1999) model were examined. Based on the strong findings that low self-esteem predicts depressive symptoms, we examined whether associations between parental and offspring symptoms of anxiety and depression were mediated by offspring self-esteem. Finally, we examined in this study whether one child characteristic, namely offspring physical activity level, moderated the pathways between parental and offspring anxiety and depression and offspring self-esteem.

In study 3, we focused solely on social anxiety and its psychosocial correlates in adolescents. Correlates may have important implications for both prevention and treatment as such variables can be modified. Psychosocial correlates of depressive and general anxiety symptoms have been studied previously, but this is not the case for social anxiety symptoms. Furthermore, most research on social anxiety has adult participants. Based on a developmental perspective, the correlates of social anxiety will be different among adolescents compared to adults because the developmental tasks and the associated developmental cascades of psychosocial correlates will be different. Also, the psychosocial correlates of social anxiety may be different in clinical and community samples. Thus, in study 3 correlates of social anxiety symptoms were compared in a clinical and a community sample of adolescents.

1.4 Previous research: Familial aggregation

In 1984, Sir Michael Rutter and David Quinton reported the results from one of the first studies conducted on how parental mental illness affects children. They found that two out of three children of psychiatric patients demonstrate transient or persistent emotional or behavioral problems (Rutter & Quinton, 1984). Since then, associations between mental health problems in parents and children have been documented for several types of psychiatric symptoms. As such, psychiatric problems seem to 'run in the family', and depression is now considered a familial disorder (Joormann et al., 2009). Despite the acknowledged importance of considering mental health problems in a familial perspective, research in this area still suffers from major limitations (reviewed below), hindering our understanding of such familial aggregation.

1.4.1 Specificity

Previous research has often studied familial aggregation of one specific psychiatric disorder, with most studies finding the disorder to be associated in offspring and parents. However, this makes it difficult to detect patterns of familial transmission of psychiatric symptoms across disorders, which is a problem because internalizing symptoms are highly comorbid (Clark & Watson, 1991; Hughes et al., 2006). Of the studies that do examine cross-aggregation of mental health problems in community samples, one study has found familial aggregation of psychiatric disorders to be non-specific (Bijl, Cuijpers, & Smit, 2002), whereas other studies (Kendler, Davis, & Kessler, 1997; Weissman et al., 1984) find aggregation to be specific for some disorders (e.g. major depression, generalized anxiety disorder, alcohol abuse) and more general for other disorders. For instance, drug abuse in offspring was associated with general anxiety in parents, whereas antisocial personality disorder in offspring was associated with parental drug abuse (Kendler et al., 1997). These research studies were based on diagnostic interviews, but for screening purposes in the community, symptom ratings are more practical (Tambs & Mow, 1993a).

1.4.2 High and low positive affect

Some studies find that the psychological well-being and self-esteem are reduced in offspring of depressed mothers (Goodman, Adamson, Riniti, & Cole, 1994; Goodman et al., 2011), but we are not aware of any studies examining such associations between offspring and fathers. Reduced self-esteem is also observed in adolescent offspring of parents with alcohol problems (Roosa, Sandler, Beals, & Short, 1988). Several studies indicate that adolescents and women with eating problems display reduced self-esteem (Polivy & Herman, 2002), but to the best of our knowledge no studies examine whether maternal eating problems are associated with low self-esteem or subjective well-being (SWB) in offspring.

1.4.3 The lack of attention to fathers

In 1992, Vicky Phares published a review article called “Where’s poppa? The relative lack of attention to the role of fathers in child and adolescent psychopathology” (Phares, 1992), in which she emphasized the importance of incorporating both mothers and fathers in such studies. In 2005, she and colleagues conducted an updated review (called “Still looking for Poppa”), but the conclusion was that there still was a wide gap between the inclusion of mothers and fathers in research on child and adolescent psychopathology (Phares et al., 2005). Proposed explanations of this exclusive focus on mothers include the fact that mothers used to be considered the primary caregiver, an assumption that fathers would be less willing or able to participate in research than mothers, different base rates of maternal vs. paternal mental health problems, and sexist “mother-blaming” theories (Phares & Compas, 1992; Woollett, White, & Lyon, 1982). Several studies do now indicate that paternal mental health is associated with mental health problems in offspring (Ramchandani & Psychogiou, 2009). Paternal depressive symptoms in pregnancy (Kvalevaag et al., 2013), in the postnatal period (Ramchandani, Stein, Evans, & O’Connor, 2005), and in adolescence (Connell & Goodman, 2002) are associated with emotional problems in offspring even after controlling for maternal symptoms. However, most studies do not examine *both* mothers and fathers. Some findings indicate that mental health problems in both parents result in an even higher risk for psychopathology in offspring

(Merikangas et al., 1988), whereas other researchers claim that this expression of assortative mating only has a small impact on mental health problems in offspring (Maes et al., 1998).

1.4.4 Moderator: Sex differences

In childhood, the prevalence of internalizing symptoms is approximately equal among girls and boys (Heiervang et al., 2007; Zahn-Waxler, Shirtcliff, & Marceau, 2008) or slightly higher among boys (Wichstrøm et al., 2012). In adolescence, the prevalence of depression and social anxiety increases (Essau et al., 1999; Merikangas & Knight, 2009; Sund et al., 2011a; Wittchen et al., 1999). At the same time, gender differences are emerging as the increase in prevalence is more marked among girls (Costello et al., 2011; Wichstrøm, 1999). These differences persist into adult age with a 1.9:1 female preponderance in depression, a 1.7:1 female preponderance in generalized anxiety disorder, and a 1.3:1 female preponderance in social anxiety (Seedat et al., 2009). Externalizing and substance disorders, on the other hand, show a male preponderance (Seedat et al., 2009).

Sex differences in familial aggregation of mental health problems have not been extensively examined empirically (Stein et al., 2008). In addition to the lack of attention to fathers, many studies do not distinguish between daughters and sons (Kim, Capaldi, Pears, Kerr, & Owen, 2009). One study found children of depressed mothers to have more internalizing problems than children of depressed fathers, but this was dependent on both offspring and parental depression severity (Klein, Lewinsohn, Rohde, Seeley, & Olino, 2005). Another study found maternal depression to be associated with sons' psychological distress, whereas paternal depression was related to psychological distress in daughters (Ge, Conger, Lorenz, Shanahan, & Elder, 1995). A longitudinal study found maternal internalizing symptoms equally to predict such symptoms in daughters and sons, while paternal internalizing symptoms predicted symptoms in daughters only (Kim et al., 2009). However, this study did not test whether the sex differences were significantly different. Offspring age may account for some of these inconsistent results as maternal psychopathology seem more strongly correlated with internalizing

symptoms in children below age 13, and paternal psychopathology seems more strongly correlated with symptoms in offspring above age 13 (Connell & Goodman, 2002).

Anxiety problems in mothers and fathers have been associated with anxiety in both daughters and sons, but the associations disappeared when controlling for childhood traumas and demographic variables (Bijl et al., 2002). Another study found anxiety to be associated in parents and children (Cooper, Fearn, Willetts, Seabrook, & Parkinson, 2006), but did not distinguish between daughters and sons. A third study found an especially evident association for anxiety in mothers and daughters (Merikangas et al., 1998). Also, parental anxiety was associated with offspring depression in this study. Several studies have found social anxiety, depression, general anxiety, and alcohol abuse in parents to be associated with social anxiety in offspring (Cooper et al., 2006; Lieb et al., 2000; Rapee & Spence, 2004).

Problem drinking in fathers (but not in mothers) has been associated with internalizing problems in both daughters and sons in some previous studies (Bijl et al., 2002; Cloninger, Sigvardsson, & Bohman, 1996), whereas other studies have found problem drinking in mothers (but not in fathers) to be related to offspring internalizing symptoms (Rognmo, Torvik, Ask, Røysamb, & Tambs, 2012). One longitudinal study found paternal (but not maternal) drinking problems to lead to internalizing symptoms in both daughters and sons, but only indirectly through marital conflict and decreased parental warmth (Keller, Cummings, Davies, & Mitchell, 2008). Parental alcohol problems and offspring internalizing symptoms were not directly associated. Associations between eating disorders in mothers and offspring have been documented in several studies (e.g. Watkins, Cooper, & Lask, 2012), but few studies examine the relationship between parental eating problems and adolescent internalizing symptoms, and we have not been able to find studies examining sex differences.

In summary, the findings on familial aggregation of mental health problems show inconsistent results. This may be due to methodological issues, such as employing small and/or clinical samples. Also, because some mentally ill informants ascribe their own disorder to family

members (Chapman, Mannuzza, Klein, & Fyer, 1994), studies employing one family member to report on the psychiatric symptoms of other family members are problematic.

1.4.5 Moderator: Timing, severity, and chronicity

Findings suggest that children experiencing maternal depression at any time point before the age of 10, have an increased risk of depression when they become adolescents (Hammen & Brennan, 2003). On the other hand, another study found the direction of the relationship between depressive symptoms in mothers and children at ages 5-7 years to be reciprocal (Jaffee & Poulton, 2006). In adolescence, maternal depression seems to lead to offspring depression (Kouros & Garber, 2010). However, depression is often chronic and recurrent across the life span (Patton et al., 2014), and recurrent maternal depression is associated with an even higher risk of depressive symptoms in offspring (Garber & Cole, 2010; Mars et al., 2012). Thus, the issue of timing in depression may be confounded with issues of severity and chronicity. Both maternal history of and current depression are related to offspring psychopathology and problems in functioning (Hammen et al., 1987). There are now indications that associations between maternal history of depression and offspring depression are mediated by current depression in mothers (Garber & Cole, 2010). However, to the best of our knowledge, no studies have included fathers when examining these issues, nor taken into account that anxiety and depression are highly comorbid.

1.4.6 Moderator: Physical activity

Common sense suggests that physical activity should be beneficial for mental health. However, empirical findings on the benefits of exercise on symptoms of anxiety and depression are inconsistent. Among adolescents, some studies have found a small effect of exercise on anxiety and depression (Calfas & Taylor, 1994; Motl, Birnbaum, Kubik, & Dishman, 2004; Sagatun, Sjøgaard, Bjertness, Selmer, & Heyerdahl, 2007; Sund, Larsson, & Wichstrøm, 2011b), but the clinical significance of these associations is questionable due to methodological limitations, such as diversity of participants, interventions and measurement (Larun, Nordheim, Ekeland, Hagen,

& Heian, 2006; Salmon, 2001). There are also a few studies showing that physical activity increases self-esteem in adolescents (Ekeland, Heian, Hagen, Abbott, & Nordheim, 2004; Haugen, Säfvenbom, & Ommundsen, 2011; Kirkcaldy et al., 2002). However, authors of systematic reviews claim the evidence base is currently too scarce to indicate that physical activity affects either self-esteem or anxiety and depression among adolescents (Ekeland et al., 2004; Larun et al., 2006). It has also been recommended to examine the psychosocial mechanisms explaining the links between physical activity and anxiety/depression (Rothon et al., 2010).

1.4.7 Mediator: Self-esteem

Global self-esteem refers to a person's evaluation of overall self-worth and self-knowledge (Baumeister, Campbell, Krueger, & Vohs, 2003; Rosenberg, 1965). In contrast, domain-specific self-esteem concerns a person's evaluation of his or hers competence or abilities in some specific domain (e.g. academic self-esteem, physical self-esteem) (Dutton & Brown, 1997)². Children of depressed parents have a lower global self-esteem than the children of non-depressed parents (Garber & Robinson, 1997; Goodman et al., 1994; Hirsch, Moos, & Reischl, 1985; Jaenicke et al., 1987). In contrast, a higher global self-esteem in the offspring of depressed parents is found to be the most important predictor of both the absence of a psychiatric diagnosis and high global functioning 2, 10, and 20 years later (Lewandowski et al., 2014). To the best of our knowledge, only two studies have examined self-esteem as a mediator in relation to depression in a family perspective. One study showed associations between psychological control in depressed mothers and depressive symptoms in offspring to be partially mediated by offspring self-esteem (Garber, Robinson, & Valentiner, 1997). Another study found maternal depression to partly predict offspring self-esteem, which in turn predicted offspring depression (Garber & Cole, 2010). However, these studies only included mothers.

² There is also a difference between explicit and implicit self-esteem; explicit self-esteem refers to an individual's conscious feelings about the self, whereas implicit self-esteem is an automatic evaluation of the self (Greenwald & Banaji, 1995).

1.5 Previous research: Social anxiety symptoms and their correlates

1.5.1 Clinical vs. community samples

Social anxiety is the most common anxiety disorder and the third most common psychiatric disorder (Stein et al., 2000). Few people with social anxiety problems seek treatment (Beidel & Turner, 2007). Furthermore, almost 25% of patients who meet diagnostic criteria for social anxiety disorder and do seek treatment are not recognized by physicians, but are instead diagnosed with other mental health disorders (Den Boer & Dunner, 1999), possibly because they have more comorbid problems than individuals with social anxiety who do not seek treatment (Schneier, Johnson, Hornig, Liebowitz, & Weissman, 1992). Hence, significant differences between clinical and community samples may exist, but few studies address this issue.

1.5.2 Psychosocial correlates

The abovementioned findings suggest identification of social anxiety is not straightforward. Thus, examining psychosocial correlates of internalizing symptoms in adolescence may be important as these may be easier to identify, especially considering the fact that mental health problems among adolescents are often discovered in schools and not in the health system (Burns et al., 1995). Psychosocial correlates of general anxiety and depression are vastly examined and include stressful events, school stress, physical and sexual abuse, suicide attempts, low self-esteem, low social self-competence, low social support, low frequency of exercise, cohabitation status, parental socioeconomic status etc. (Lewinsohn, Gotlib, Lewinsohn, Seeley, & Allen, 1998; Lewinsohn et al., 1994; Schraedley, Gotlib, & Hayward, 1999; Sund, Larsson, & Wichstrøm, 2003). Studies examining correlates of social anxiety are, however, scarce, and then mainly focusing on comorbid diagnosed mental disorders. Even though nearly all individuals developing social anxiety do so before the age of 20 (Kessler et al., 2007; Stein & Stein, 2008), most studies have adult responders and do not account for the developmental tasks of adolescence. Hence, encompassing studies of psychosocial correlates of social anxiety in adolescence would give useful information for identification, prevention, and treatment.

Social anxiety in adolescence has been associated with impaired school functioning, lower grade point averages or dropping out of school (Gren-Landell et al., 2009; Ranta et al., 2009; Stein & Kean, 2000), but the way the questions are asked in these studies makes it unclear whether these school-related problems are caused by social anxiety or learning difficulties. Bullying is quite consistently associated with social anxiety in several studies (Hawker & Boulton, 2000; Ranta, Kaltiala-Heino, Frojd, & Marttunen, 2013). In a study from 1981, 58% of the respondents indicated that the source of their social anxiety was a traumatic incident (Öst & Hugdahl, 1981). Acne is perceived by adolescents to have negative social consequences (Krowchuk et al., 1991), and such perceptions may be considered a psychosocial factor. However, associations with social anxiety have not been examined. Drug use (Buckner, Bonn-Miller, Zvolensky, & Schmidt, 2007; Myers, Aarons, Tomlinson, & Stein, 2003) and alcohol problems (Buckner et al., 2008; Fröjd, Ranta, Kaltiala-Heino, & Marttunen, 2011) are inconsistently related to social anxiety. Eating problems have been associated with social anxiety (Wittchen et al., 1999), but it was unclear whether the association extends to both girls and boys. Finally, comorbid social anxiety and depression is associated with suicidal behavior among female adolescents (Nelson et al., 2000), but to the best of our knowledge this has not been examined among male adolescents.

Identifying a threshold for social anxiety symptoms at which severe coexisting problems occur would also be useful for clinical purposes. Such a study has been conducted among adults with negative results (Stein et al., 2000), but not among adolescents. Such studies can be conducted in two complimentary ways: by variable-centered (e.g. imposing various cut-off points in logistic regression analyses, as in the previous study) and person-centered methods (in which subgroups inherent in the data that differ from each other are identified, for example by trying to classify high- and low-scorers in latent profile analyses). Person-centered analyses provide “individual-specific profiles that may elucidate disease-related processes by empirically identifying relatively homogenous subpopulations from the observed sample based on observed variables” (Olino, Klein, Farmer, Seeley, & Lewinsohn, 2012, p. 324).

2. AIMS OF THE THESIS

Based on the literature reviewed above, the main aim of this thesis was to examine several aspects relating to internalizing symptoms in adolescence. Having a parent with mental health problems is consistently shown to be one of the most important risk factors for psychiatric symptoms in offspring. However, research on familial aggregation of mental health problems is considerably limited by the fact that paternal mental health seldom has been investigated, nor has the interaction with offspring sex been well delineated. Thus, the main focus was to examine familial aggregation of internalizing symptoms in mothers, fathers, daughters, and sons with each family member reporting on their own mental health. Several proposed moderators were examined: parental and offspring sex, recurrent parental internalizing symptoms, and offspring physical activity level. Also, we examined whether self-esteem mediated associations between internalizing symptoms in parents and offspring. Finally, we examined psychosocial correlates of social anxiety symptoms in a clinical and a community sample of adolescents to increase understanding of this understudied disorder and to facilitate its identification.

2.1 Study 1

As shown in Figure 3, cross-sectional associations were examined between symptoms of different mental health problems in mothers versus fathers and internalizing symptoms and well-being in adolescent daughters versus sons in a community sample. Another aim was to examine whether associations were stronger when both parents had internalizing symptoms.

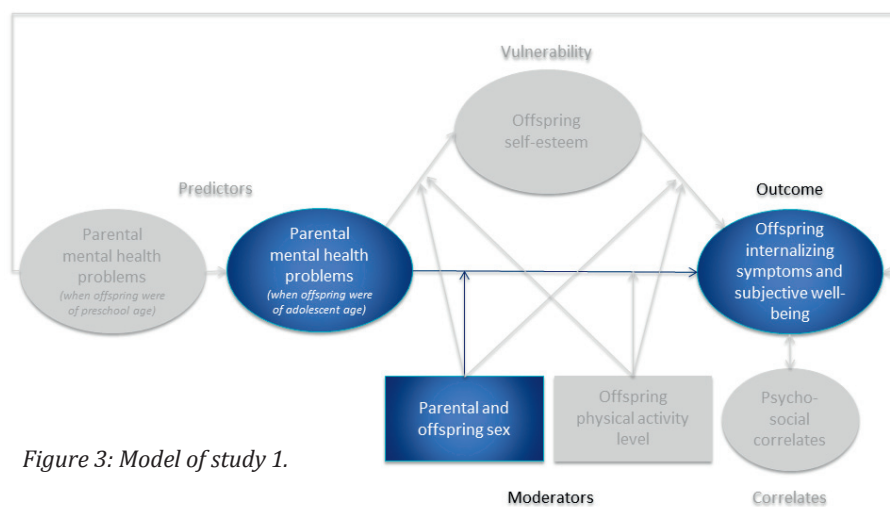


Figure 3: Model of study 1.

2.2 Study 2

As shown in Figure 4, the associations were examined between recurrent parental internalizing symptoms over a ten-year time span and offspring internalizing symptoms in adolescence in a large community sample. In addition, the possible mediating role of adolescent self-esteem and the possible moderating role of adolescent physical activity level in familial aggregation of internalizing symptoms were explored.

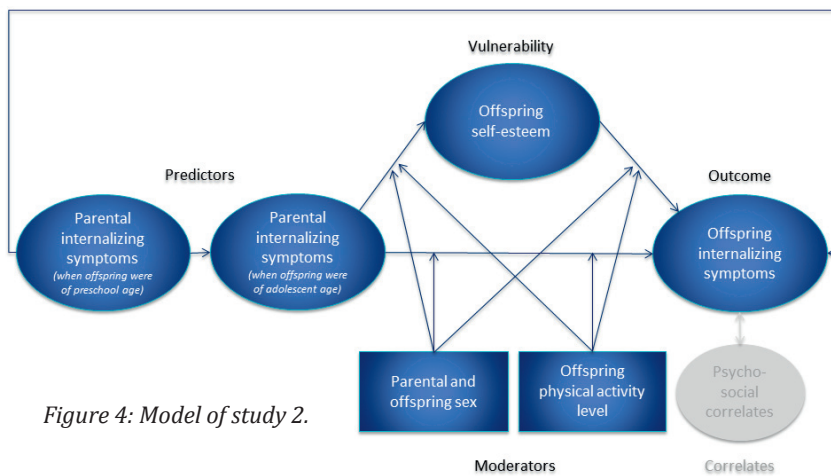


Figure 4: Model of study 2.

2.3 Study 3

As shown in Figure 5, symptoms and correlates of social anxiety were compared in a mental health clinical and a community sample of adolescents. Furthermore, a threshold for social anxiety symptoms at which severe coexisting problems occur was sought identified by employing a person-centered method.

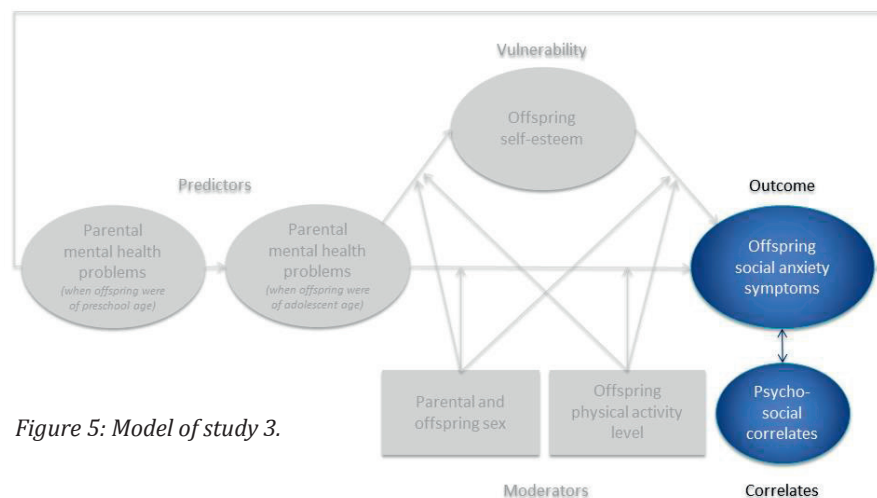


Figure 5: Model of study 3.

3. METHODS

3.1 Design and samples

The thesis was based on both cross-sectional and longitudinal data from The Nord-Trøndelag Health Study (HUNT). The HUNT study is a large, total population health survey comprised of questionnaires and clinical examinations conducted in the county of Nord-Trøndelag, Norway. All inhabitants in the county above the age of 12 were invited to participate in the study without any exclusion criteria. The county is mainly rural, and has approximately 131,000 inhabitants of primarily Norwegian descent (Holmen et al., 2014; Krokstad et al., 2013). The HUNT study is comprised of three surveys conducted approximately eleven years apart: HUNT1 was carried out in 1984-1986; HUNT2 in 1995-1997; and HUNT3 in 2006-2008. The adolescent part of the study, including participants aged 13-19 years, is called Young-HUNT, and all studies in this thesis utilize data from the Young-HUNT3 Survey, which was conducted from 2006 to 2008. In addition, study 1 is based on parental data from HUNT3, whereas study 2 examining familial aggregation longitudinally is based on parental data from both HUNT2 and HUNT3.

Finally, in the study addressing social anxiety symptoms and correlates, cross-sectional data from a clinical sample were included, in addition to data from Young-HUNT3. The clinical sample consisted of all participants between the ages of 13-18 years in The Health Survey in the Department of Child and Adolescent Psychiatry, St. Olav's University Hospital in the county of Sør-Trøndelag, Norway (the CAP Survey). This clinic provides diagnostic assessment and treatment for all psychiatric conditions in referred children and adolescents, ages 0-18. The CAP survey was specifically modeled after the community study (Young-HUNT3) to be able to compare the two samples. Thus, the clinical survey was also comprised of questionnaires and clinical examinations, and in addition, the participants' ICD-10 diagnoses were collected from their medical records. All patients between 13 and 18 years of age with at least one personal attendance at the clinic between February 2009 and February 2011 were invited to participate in the survey. Exclusion criteria were major difficulties answering the questionnaire due to

psychiatric state, cognitive function, visual impairments, or lack of sufficient language skills.

Emergency patients were invited to take part once they entered a stable phase.

3.2 Procedures

3.2.1 Adolescent community sample (Young-HUNT3)

Junior high schools and high schools were the main study sites in the Young-HUNT3 survey. An invitation letter and an information brochure were given out beforehand at school to all adolescents and their parents. The questionnaire was administered during a class at school in an exam-like situation. When the questionnaire was completed, the adolescents themselves sealed it in a blank envelope. Teachers were asked to read the questions aloud to adolescents with problems reading or answering the questionnaire. The adolescents who were temporarily absent from school on the day of survey completion received the survey approximately one month later during a health exam that was also part of HUNT3. Adolescents not attending school at all (4.2%) received the survey by mail. A more detailed description of the adolescent sample and procedures is published elsewhere (Holmen et al., 2014).

3.2.2 Adult community sample (HUNT2 and HUNT3)

Adult participants aged 20 and older received a letter, an information brochure, and a questionnaire by mail. The questionnaire (Q1) was completed at home and delivered at the time of the subsequent clinical examination. A second questionnaire (Q2) handed out at the clinical examination site was to be completed at home and returned by mail. More details on the adult sample are published elsewhere (Krokstad et al., 2013). Data from the adolescents were linked to data from their biological or adoptive parents using each citizen's unique 11-digit personal national ID number.

3.2.3 Adolescent clinical sample (CAP survey)

Newly referred patients and patients already enrolled at the clinic received verbal and written invitations during their first visit after the project started. The participants completed an electronic questionnaire about his or her mental health in conjunction with a clinic appointment,

without the presence of their parents. The questionnaire was accessed via a password-protected website. A project coordinator provided assistance if needed. The participants' psychiatric diagnoses were electronically extracted from their medical records at the clinic.

3.3 Participants

3.3.1 Community sample (Young-HUNT3, HUNT3, and HUNT2)

From a population of 10490, 8200 adolescents, ages 13-19, participated in the survey (78% response rate). In all studies, participants aged 12 (n=27), 19 (n=219), and 20 (n=41) were excluded from further analyses due to low age sample sizes.

In studies 1 and 2, the study sample consisted of those adolescents having at least one biological or adoptive parent participating in the study, excluding 2181 (28%) adolescents. Thus, in these two studies, the analysis sample was comprised of 5732 adolescents, of whom 3229 had both parents participating, 1761 had only mothers participating, and 742 had only fathers participating. The sample consisted of 4087 unique mothers and 3239 unique fathers. Twenty-seven of the adolescents in the sample were adopted. From the overall adult population of 93860 in Nord-Trøndelag, 50807 adults, ages 20-101, participated in Q1 (54%), whereas 41206 (44%) participated in Q2. In study 2, the sample also included data from those parents participating in HUNT2. This constituted 3198 of the mothers (78%) and 2488 of the fathers (77%).

In study 3, the study sample consisted of 7669 adolescents. 244 adolescents (2.3%) were excluded due to incomplete information on the study variables measuring social anxiety symptoms.

3.3.2 Clinical sample (CAP survey)

From a population of 2032 adolescent patients who visited the CAP clinic at least once in the study period, 95 were missing registration data, and hence, were not included in study recruitment. Another 289 patients were excluded according to the exclusion criteria. As a result,

1648 patients (81.1%) were eligible and invited to participate. Of these, a total of 717 (43.5%) participated in the survey. Participants aged 19 (n=9), and 20 (n=7) were excluded from further analyses due to low age sample sizes. Seven adolescents (0.4%) were excluded due to incomplete information on the study variables measuring social anxiety symptoms. Thus, the clinical sample in study 3 consists of 694 adolescents (42.1% of the eligible patients).

3.4 Measures

In study 1, symptoms of anxiety and depression, symptoms of social anxiety, SWB, and self-esteem were measured among adolescents, whereas symptoms of anxiety and depression, alcohol abuse, and maternal eating problems were measured among parents.

In study 2, symptoms of anxiety and depression, self-esteem, and physical activity level were measured among adolescents, whereas symptoms of anxiety and depression were measured among parents at two time points.

In study 3, symptoms of social anxiety, symptoms of general anxiety and depression, eating problems, academic school problems, bullying, suicidal thoughts, alcohol use, substance use, self-perceived acne problems, and sociodemographic characteristics were measured in both the clinical and the community sample of adolescents. In the clinical sample only, ICD-10 diagnoses of social phobia (World Health Organization, 2010) were set by a child and adolescent psychiatrist or a clinical psychologist.

3.4.1 Parental mental health variables

Symptoms of anxiety and depression were measured by the Cohort Norway Mental Health Index (CONOR-MHI) (Søgaard, Bjelland, Tell, & Røysamb, 2003), which consists of seven items partly based on the General Health Questionnaire (Goldberg, 1972) and the Hopkins Symptom Checklist (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974). The CONOR-MHI correlates highly with both the Symptom Check List-10 (SCL-10) ($r = .82$) and the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) ($r = .91$), but distinguishing anxiety and depressive symptoms is not possible from this reduced item set (Søgaard et al., 2003). Examples

of items include “Have you, in the course of the last two weeks, felt nervous and unsettled?” and “...happy and optimistic?”. Each item was rated on a 4-point scale (1=no, 4=very much). For descriptive analyses and examinations of the impact of the number of parents with high levels of anxiety and depression on offspring symptoms, we used the mean cut-off value of ≥ 2.15 , which was established from cut-off values of the SCL-10 and HADS that were shown to identify anxiety disorders and major depressive disorder (Søgaard et al., 2003). Composite reliability (CR) indicated good internal consistency in both studies and at both time points ($\geq .830$).

Alcohol abuse was measured by the Cut down Annoyed Guilty Eye-opener (CAGE) scale (Ewing, 1984). CAGE consists of four dichotomous questions (0=no, 1=yes) measuring four aspects of problematic drinking. For descriptive analyses we used the cutoff of ≥ 2 , which has been recommended when screening for alcohol dependency (Dhalla & Kopec, 2007). CR indicated acceptable to good internal consistency ($\geq .696$).

Maternal eating problems were measured by the Eating Dissatisfaction Scale (EDS-5) (Rosenvinge et al., 2001), which consists of five items used to screen for eating disturbances in community settings. The scale has good psychometric properties (Rosenvinge et al., 2001). Each item was rated on a 7-point scale (1=not at all/very satisfied, 7=every day/very dissatisfied). This measure was only completed by mothers in the HUNT study. For descriptive analyses, the 90th percentile was used as no cut-off value is established for this scale. CR indicated good internal consistency ($\geq .769$).

3.4.2 Adolescent mental health outcome variables

Symptoms of anxiety and depression during the previous two weeks were measured using the Symptom Checklist-5 (SCL-5), which consists of five items from the 25-item version of the Hopkins Symptom Checklist (Derogatis et al., 1974). Whereas the SCL-5 has shown very high correlations ($r = .92$) with the SCL-25 and a satisfactory reliability (Strand, Dalgard, Tambs, & Rognerud, 2003; Tambs & Moum, 1993a), distinguishing anxiety and depression symptoms is not possible from this reduced item set (Strandheim, Holmen, Coombes, & Bentzen, 2009). Each

symptom was rated on an ordinal scale (1=*not bothered*, 4=*very bothered*). In study 3, the mean across the five ratings was computed, with high scores indicating more symptoms. In all studies, CR indicated good internal consistency in both the clinical and the community sample ($\geq .868$). For additional descriptive analyses in this thesis, the mean cut-off value of > 2.00 on the SCL-5, which was established from the cut-off value of the SCL-25, was used to identify anxiety disorders and major depressive disorder (Strand et al., 2003).

Symptoms of social anxiety were measured by a short version of The Social Phobia and Anxiety Inventory for Children (SPAI-C) (Aune, Stiles, & Svarva, 2008; Beidel, Turner, & Morris, 1995) consisting of six items from the original 26-item version. SPAI-C is shown to be valid and reliable for use with adolescents ages 13 through 17 (Storch, Masia-Warner, Dent, Roberti, & Fisher, 2004). The HUNT Study adapted a shortened version of the scale comprising six items based on factor analyses of the complete SPAI-C scale (T. Aune, personal communication, April 30, 2009). A cut-off value indicating clinical problems has not been established for this shortened version of the scale. Each item was rated on an ordinal scale (1=*never*, 5=*always*). In study 3, the items were summed (range 6-30) with higher scores indicating more symptoms. In all studies, CR indicated good internal consistency in both the clinical and the community sample ($\geq .870$).

Subjective well-being (SWB) was measured with a three-item version of a SWB-scale (Moum, Næss, Sørensen, Tambs, & Holmen, 1990): (1) "When you think about the way your life is going at present, would you say that you are by and large satisfied with life or are you mostly dissatisfied?", (2) "In general, do you feel strong and in a good mood or tired and worn out?", and (3) "Are you generally happy or sad?". The questions have been validated (Røysamb, Harris, Magnus, Vittersø, & Tambs, 2002), and used in more than 20 previous publications with ample evidence for their construct validity. Each item was rated on a 7-point scale (1=*very satisfied*, 7=*very dissatisfied*). CR indicated good internal consistency ($\geq .768$).

Self-esteem was measured with a four-item version of the Rosenberg Self-Esteem Scale (Rosenberg, 1965). The items correlate highly with the original scale (0.95) (Tambs, 2004), which has demonstrated construct validity as a measure of self-esteem in a large body of literature. The items were rated on a 4-point scale (1=*totally agree*, 4=*totally disagree*). CR indicated good internal consistency ($\geq .773$).

3.4.3 Adolescent independent psychosocial variables

Physical activity level was measured with one question that was also used in the World Health Organization Health Behaviour in School-aged Children (WHO HBSC) survey (King, Wold, Tudor-Smith, & Harel, 1996): "Apart from the average school day, how many days a week do you play sports or exercise to the point where you breathe heavily and/or sweat?" The question had eight response alternatives: '*every day*', '*4–6 days a week*', '*2–3 days a week*', '*one day a week*', '*not every week, but at least once every 14th day*', '*not every 14th day, but at least once a month*', '*less than once a month*', and '*never*'. The question has shown acceptable validity demonstrated by correlations with physical fitness measured by maximal oxygen uptake (VO₂ peak), which is often considered the gold standard in assessing physical fitness (Rangul, Holmen, Kurtze, Cuypers, & Midthjell, 2008). In Norway, adolescents in this age range have at least 2-3 school lessons per week in Physical Education. Research suggests that differences in adherence, motivation, enjoyment, and genetics exist between individuals who choose to exercise regularly and those who do not (De Moor, Boomsma, Stubbe, Willemsen, & de Geus, 2008; Ryan, Frederick, Lepes, Rubio, & Sheldon, 1997; Salmon, 2001). Thus, we dichotomized the answers into regular and low physical activity based on regular exercise outside of school hours: '*regular activity*' represented '*one day a week or more*', whereas '*low activity*' represented '*less than once a week*'. Such dichotomization has also been used in other studies to detect differences between low and regularly active groups (e.g. Bjereld, Daneback, Gunnarsdóttir, & Petzold, 2014).

Academic school problems were measured by six items (e.g. comprehension, concentration problems) rated on an ordinal scale (1=*never*, 4=*very often*). Five items comprised

the “academic” factor in a scale on school functioning (Størksen, Røysamb, Holmen, & Tambs, 2006). In addition, a question on current learning problems was included. The mean across the six items was computed, with high scores indicating more problems. CR indicated good internal consistency in both samples ($\geq .734$).

Bullying was assessed by four items. Two items on name-calling and exclusion by peers were rated on an ordinal scale (0=*never*, 3=*very often*). Another two items on sexual harassment and physical threats by peers were rated on a three-point scale (0=*never*, 1=*yes, previously*, 2=*yes, in the past year*). A sum score for the four items was computed (range=0-10). CR indicated good internal consistency in both samples ($\geq .814$).

Eating problems were assessed with a seven-item-version of The Eating Attitude Test (Garner & Garfinkel, 1979) addressing oral control, bulimia and food preoccupation. Each symptom was rated on an ordinal scale (1=*never*, 4=*always*), which were summed (range=7–28) with high scores indicating more symptoms. CR indicated good internal consistency in both the clinical and the community sample ($\geq .803$).

Suicidal thoughts were measured by one dichotomous item, “Have you ever thought about ending your own life?” (0=*no*, 1=*yes*). In the community sample, only adolescents above the age of 16 answered this item.

Alcohol use was measured by one item, “Have you ever drunk so much alcohol that you felt intoxicated (drunk)?”. We recoded the original six-point scale (1=*no, never*, 2=*yes, once*, 3=*yes, 2-3 times*, 4=*yes, 4-10 times*, 5=*yes, 11-25 times*, 6=*yes, more than 25 times*) into three categories (0=*never*, 1=*1-10 times*, 2=*11 or more times*), as in previous studies (Lintonen, Ahlstrom, & Metso, 2004; Strandheim et al., 2009). Individuals who had not tried alcohol were coded as 0=*never*.

Use of illegal substances was measured by one dichotomous item, “Have you ever tried hash, marijuana or other drugs?” (0=*no*, 1=*yes*).

Subjective perception of acne problems was measured by one item, "How much has acne bothered you?", rated on an ordinal scale (1=*no impact*, 4=*a lot of impact*). Individuals reporting no acne were coded as 1=*no impact*.

3.4.4 Sociodemographic variables

Age and *sex* were in all studies calculated from the 11-digit personal national ID number unique for each Norwegian citizen.

Maternal and paternal level of education and *marital status* were included as sociodemographic variables in studies 1 and 2, in addition to age and sex. These measures were obtained from Statistics Norway. Data from 2007 were used. The highest attained level of education was coded according to the Norwegian Standard Classification of Education (NUS2000) as 0=*no education and pre-school education*, 1=*primary education*, 2=*lower secondary education*, 3=*upper secondary education, basic education*, 4=*upper secondary, final year*, 5=*post-secondary non-tertiary education*, 6=*first stage tertiary education, undergraduate level*, 7=*first stage tertiary education, graduate level*, 8=*second stage tertiary education (postgraduate education)*, 9=*unspecified*. Marital status was coded as 1=*married*, 2=*unmarried, widow(er), divorced, separated*.

Cohabitation status and *subjective perception of family economy* were included as sociodemographic variables in study 3, in addition to age and sex. Cohabitation status was coded as 0=*living alone, with friends, siblings and/or partner/spouse*, 1=*living with one parent/stepparent/grandparent(s)*, 2=*living with two parents, one parent and one stepparent, foster parents or adoptive parents*. Subjective perception of family economy was measured by one item asking whether the adolescent feels his or her family is better or worse off economically than others (0=*worse off*, 1=*the same*, 2=*better off*).

3.5 Statistical methods

Latent variable modeling was used to analyze data in all three studies in this thesis. Studies 1 and 2 were based on structural equation modeling (SEM), whereas study 3 was based on factor

analyses and multiple linear regression conducted separately, and latent profile analysis (LPA). In this paragraph, the precise details of the analyses will be presented, whereas the rationale for employing these methods will be discussed later.

3.5.1 Structural equation modeling

In all studies, composite reliability (CR) was used as measure of internal consistency. An estimated CR of .7 or higher indicates good reliability and a CR between .6 and .7 is considered acceptable (Bagozzi & Yi, 1988). Further, several fit indices for the measurement model were examined in order to validate the latent constructs being addressed. A non-significant χ^2 -statistic, CFI- and TLI-values $> .95$, and RMSEA-values $< .06$ indicate a good model fit (Hu & Bentler, 1999). The models were estimated with the weighted least squares mean and variance adjusted estimator (WLSMV) due to the categorical and non-normal nature of the indicators. In studies 1 and 2, we estimated multigroup models separating daughters and sons and tested possible sex differences with Wald tests of parameter constraints. Portions of our sample were hierarchically structured. 2062 adolescents had at least one sibling also participating, whereas 3670 adolescents did not. Standard errors and χ^2 -tests were corrected for this potential cluster effect in the analyses when possible³. Parental marital status and level of education were not related to our dependent variables, and we did not adjust for these variables.

In study 1, we examined the model fit of scalar measurement invariance (unstandardized factor loadings and thresholds were held invariant across daughters and sons) to ensure that adolescent girls and boys interpreted the measures in the same way and their scores on the latent variables could be compared. Structural coefficients were allowed to be estimated freely. An explorative saturated structural model with all adolescent latent variables regressed on all parental variables was tested because existing research was too inconsistent to suggest testing a specific theoretical path model. Thus, decomposable fit indices were not reported. Thereafter,

³ Adjustment for cluster effects is not available with bootstrapping, which was used in study 2. We examined differences between bootstrapped estimates without clustering and non-bootstrapped estimates with clustering. Not adjusting for clustering resulted in lower χ^2 -values, but no evident differences in standard errors.

we trimmed the model by constraining possible non-significant paths to zero (Kline, 2011). We also examined if adolescent problems were dependent on whether 0, 1 or 2 parents scored above the cut-off value on the anxiety/depression scales. Finally, we tested whether paths in the models for daughters and sons were significantly different. Because internalizing symptoms were influenced by adolescent age, all paths in the structural model were adjusted for age.

In study 2, measurement invariance was examined in depth prior to estimating the structural models. By applying increasingly more restrictions, configural (the same pattern of fixed and free factor loadings was specified for each group), metric (same pattern + invariant factor loadings across groups), and scalar measurement (same pattern + invariant factor loadings + invariant thresholds across groups) invariance were tested (Vandenberg & Lance, 2000). When scalar invariance is established, measurement invariance is assumed (Meredith, 1993). This indicates that sex differences in the means of observed items stem from differences in the means of the latent variables. When evaluating measurement invariance, we also examined CFI-differences and RMSEA-differences as have been recommended (Chen, 2007)⁴ because χ^2 -difference tests are sensitive to sample size and model complexity (Cheung & Rensvold, 2002). $\Delta CFI \geq .010$, and $\Delta RMSEA \geq .015$ indicate measurement noninvariance (Chen, 2007). Four structural models were tested. When estimating mediation, we followed recommended procedures with 1,000 bootstrap samples (Lau & Cheung, 2012). Multigroup mediation models were used to test moderated mediation because such analyses with latent variables often result in model non-convergence. As recommended (Lau & Cheung, 2012), the indirect effects, the difference between direct and indirect effects and between effects across groups were tested by computing new parameters and examining their statistical significance. Adolescent age was associated with symptoms of anxiety/depression but not with self-esteem. Thus, we adjusted for age in paths including adolescent anxiety/depression.

⁴ These recommendations are based on simulation studies using maximum likelihood estimations of continuous data. No standards for such evaluations of alternative fit indices exist for WLSMV estimation (Sass, 2011), although there are some indications that especially WLSMV $\Delta RMSEA$ performs well (Koziol, 2010).

3.5.2 Latent profile analysis

LPA was performed in study 3 to empirically identify a division of social anxiety symptoms into groups instead of imposing an arbitrary cut-off point. Subgroups (latent classes) of adolescents were identified based on how similar or different they scored on the six social anxiety items (e.g. high- and low-scoring adolescents). Once classes had been established, we examined whether individuals in these classes had different characteristics with regard to psychosocial and sociodemographic correlates. These variables were entered as auxiliary to prevent the correlates from changing the class memberships for respondents. Differences between latent classes on psychosocial and sociodemographic correlates were analyzed by χ^2 -tests.

3.5.3 Multiple linear regression

To further examine psychosocial and sociodemographic correlates in study 3, linear regression analyses with the sum score of social anxiety symptoms as the dependent variable were also performed. First, the associations between social anxiety and each psychosocial and sociodemographic correlate were analysed, adjusting only for age, because age was associated with social anxiety. Then multi-adjusted regression analyses were carried out with all covariates entered simultaneously in the model. Multi-adjusted analyses should be interpreted with some caution due to the difficulty of deciding whether variables are mediators, confounders, or colliders (Christenfeld, Sloan, Carroll, & Greenland, 2004). Still, if a variable remains significant in such analyses, the importance of this variable is strengthened. To obtain comparable regression coefficients in both samples, all covariates were divided by the standard deviation of that covariate in the community sample.

3.5.4 Treatment of missing data

Full information maximum likelihood (FIML) and multiple imputation (MI) are considered “gold standards” in treating missing data (Schafer & Graham, 2002). When using Mplus with categorical data, the FIML procedure may result in bias when data are not missing completely at random. Thus, MI is the recommended approach in such cases (Asparouhov & Muthén, 2010).

Here, the FIML procedure was used in study 2 because of a low rate of missing values ($\leq 4\%$), which was assumed to reduce the likelihood of bias. In studies 1 and 3, the rates of missingness were higher, and thus, MI was used except for the LPA in study 3. For LPA, results from complete case analyses are reported because tests of class differences are not readily available for MI datasets.

In study 1, all missing values were substituted through multiple imputation (MI) with 10 imputed data sets in Mplus, version 7.11 (Muthén & Muthén, 1998-2013) and were based on variables in the data set assumed to be relevant predictors of missing values. In study 3, missing values on social anxiety in the community sample ranged from 2.9 to 3.2 % across the six items, and in the clinical sample from 1.1 to 1.4 %. Following the SPAI-C-manual (Beidel, Turner, & Morris, 1998), respondents with missing on more than one of the six items were excluded from further analyses. The remaining missing values on the dependent variable and all independent variables were substituted by MI with 100 imputed datasets in IBM SPSS Statistics 21 (SPSS). All variables used in the analyses were included in the imputation models. Social anxiety, general anxiety and depression, eating problems, and academic school problems were transformed with the natural logarithm to approximate normality which is required when using MI in SPSS.

3.5.5 Levels of statistical significance

In study 1, two-sided p values $< .01$ were considered statistically significant, whereas in studies 2 and 3, two-sided p -values $< .05$ were considered statistically significant. The reasons for this will be discussed in a later section.

3.6 Ethics

All adolescents participating in the studies, and at least one parent when the adolescent was below 16 years of age, signed a written informed consent to participate. All studies were approved by the Regional Committee for Medical and Health Research Ethics and the Norwegian Social Science Data Services, and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

4. SUMMARY OF RESULTS

4.1 Characteristics of the samples

In studies 1 and 2, the sample was identical. The mean age among adolescents was 15.8 ($SD = 1.6$). The proportion of adolescent girls (50.3%) and boys (49.7%) were approximately the same. 35.5% of the adolescents reported having parents not living together. More mothers than fathers participated (56% vs. 44%). As expected, the mothers were significantly younger ($M = 44.2$; $SD = 5.2$) than the fathers ($M = 47.6$; $SD = 5.9$) ($t(7306) = 26.104, p < .001$). Consistent with the overall Norwegian population, the mothers had higher levels of education ($M = 4.43$; $SD = 1.54$) than the fathers ($M = 4.21$; $SD = 1.47$) ($t(7322) = 6.188, p < .001$). The most frequent educational level among participating parents was upper secondary education, which was somewhat higher than in the general Norwegian population (Krokstad & Knudtsen, 2011).

Regarding mental health problems, 6.6% of mothers and 5.8% of fathers scored above the cut-off value on anxiety/depression. The corresponding numbers for alcohol abuse were 3.1% of mothers and 6.5% of fathers. 10.0% of mothers had a sum score above the 90th percentile on eating problems. When the offspring were of a preschool age, 7.5% of the mothers and 4.0% of the fathers scored above the cut-off value on anxiety/depression. For additional descriptive information, the prevalence of scoring above the cut-off value on adolescent anxiety/depression in relation to the presence of parental mental health problems is shown in Table 1.

In study 3, the mean age among the participants in the clinical sample was 15.8 ($SD = 1.53$) for girls and 15.3 ($SD = 1.52$) for boys. In the community sample, the mean age was 15.8 ($SD = 1.66$) for girls and 15.7 ($SD = 1.62$) for boys. 54.6% of the participants in the clinical sample were girls, whereas 50.8% in the community sample were girls. In the clinical sample, approximately 46% reported living with two parents, whereas in the community sample, approximately 64% reported living with two parents.

Table 1 – Descriptives of mental health problems in the sample

		Adolescent anxiety/depression % (N)	
		No	Yes
Adolescents total		86.2 (4943)	11.6 (665)
Adolescent daughters		81.9 (2328)	18.1 (514)
Adolescent sons		94.5 (2615)	5.5 (151)
Number of parents in family with anxiety/depression	0	87.0 (4521)	10.8 (562)
	1	79.2 (411)	18.7 (97)
	2	64.7 (11)	35.3 (6)
Maternal anxiety/depression	No	86.7 (4695)	11.1 (603)
	Yes	78.2 (248)	19.6 (62)
Paternal anxiety/depression	No	86.6 (4758)	11.2 (618)
	Yes	78.4 (185)	19.9 (47)
Number of parents in family with alcohol abuse	0	87.9 (1371)	10.3 (161)
	1	85.5 (284)	13.3 (44)
	2	77.3 (17)	22.7 (5)
Maternal alcohol abuse	No	86.6 (3006)	11.4 (394)
	Yes	81.3 (143)	17.6 (31)
Paternal alcohol abuse	No	87.3 (2078)	10.8 (258)
	Yes	83.9 (375)	13.4 (60)
Maternal eating problems	No	86.4 (3100)	11.6 (415)
	Yes	84.9 (354)	13.4 (56)

4.2 Measurement models

In studies 1 and 2, fit indices for the measurement models indicated good model fit for all models, and scalar measurement invariance was established (study 1 $RMSEA \leq .025$; study 2 $RMSEA \leq .037$). In study 3, a measurement model where items were made to load on their assumed latent variable had an acceptable-to-good model fit in both the clinical and the community sample (e.g. $RMSEA \leq .065$). Thus, the factor structure was retained in all studies.

4.3 Study 1 – main results

Figure 6 shows a summary of the results in study 1. Maternal and paternal alcohol abuse and maternal eating problems were not associated with any of the symptoms measured in offspring. Parental symptoms of anxiety and depression were, on the other hand, associated with all symptoms measured in offspring. When examining sex differences, no paths were significantly different for daughters and sons. Also, none of the adolescent mental health indicators were more strongly associated with maternal or paternal symptoms of anxiety and depression. Thus, internalizing symptoms in parents were associated with more symptoms of anxiety and depression, more symptoms of social anxiety, reduced SWB, and reduced self-esteem in adolescent offspring. Compared to one parent scoring above the cut-off value on anxiety and depression, having two parents scoring above the cut-off value were associated with more symptoms of anxiety and depression, social anxiety, and lower SWB in daughters, and more symptoms of anxiety and depression in sons.

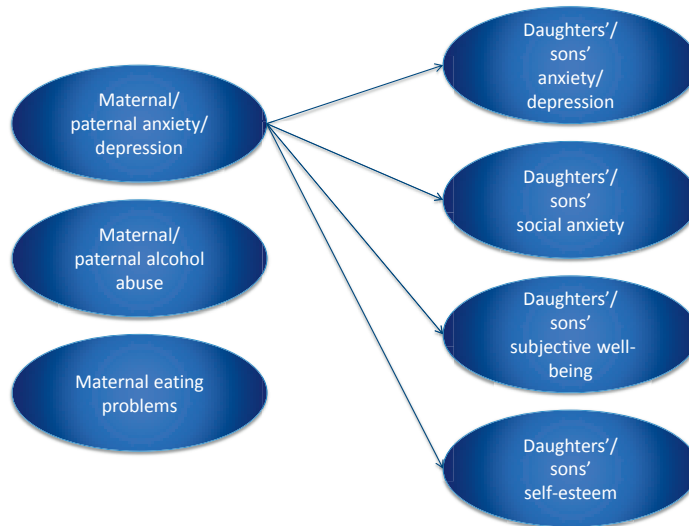


Figure 6: Results in study 1

4.4 Study 2 – main results

Figure 7 displays the results in study 2. Maternal and paternal symptoms of anxiety and depression when offspring were of a preschool age were associated with such symptoms in daughters and sons ten years later. However, these associations were fully mediated by current parental symptoms. When including offspring self-esteem in the pathway, the associations between current parental and offspring internalizing symptoms were partly mediated by offspring self-esteem (dashed lines). In addition, parental and offspring internalizing symptoms were still directly associated (solid lines). Thus, current parental and adolescent offspring internalizing symptoms were partly directly associated (solid lines) and partly mediated by low adolescent self-esteem (dashed lines).

When examining whether adolescent physical activity level moderated these paths, findings indicated that maternal and offspring internalizing symptoms were not directly associated among adolescents exercising at least once a week outside of school. Thus, regular physical activity moderated the direct path (solid) between maternal and offspring internalizing symptoms but not the indirect paths (dashed) between maternal and offspring symptoms via self-esteem. Physical activity did not moderate either the direct (solid) or the indirect (dashed) paths between paternal and adolescent internalizing symptoms. Still, the regular activity group had significantly higher self-esteem than the low activity group.

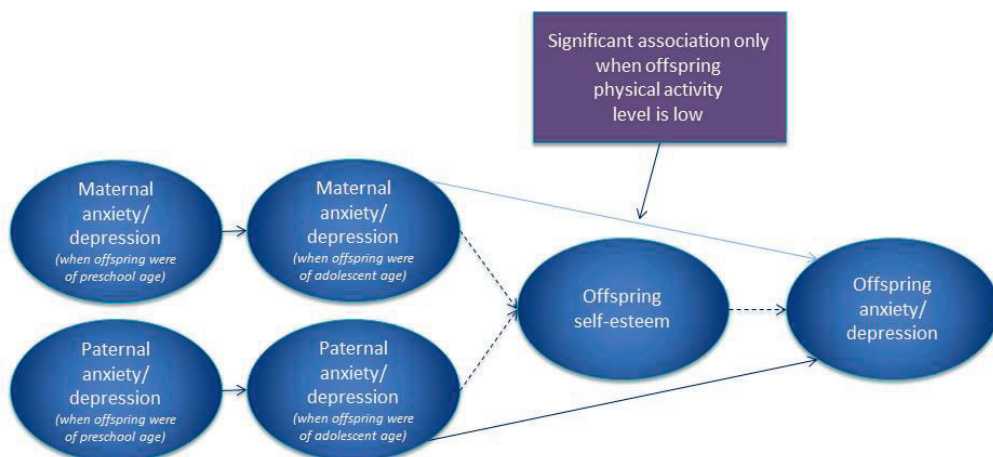


Figure 7: Results in study 2

4.5 Study 3 – main results

Social anxiety symptoms were frequently reported by adolescents, significantly more so in the clinical than in the community sample, and among girls compared to boys in both samples. In the clinical sample, 2.3% ($n=16$) received a primary ICD-10 diagnosis of social phobia. In both samples, two subgroups (latent classes) of adolescents reporting high versus low levels of social anxiety symptoms were identified. Among girls, 40.4% of the clinical and 26.5% of the community sample were identified as “high-scorers” on social anxiety symptoms. The respective numbers among boys were 26.7% in the clinical and 16.2% in the community sample. The profiles of reporting on social anxiety symptoms in the latent classes are shown in Figure 8.

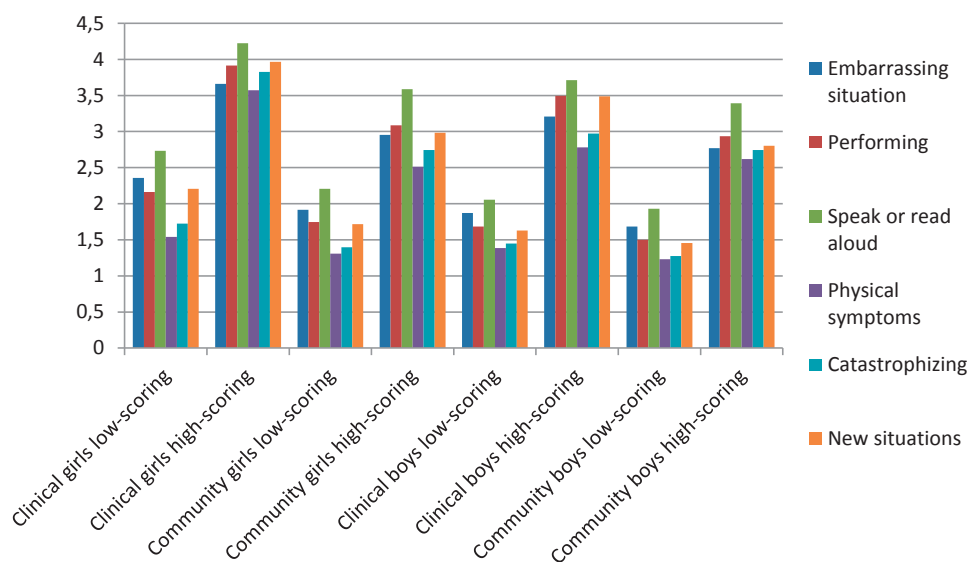


Figure 8: Mean scores on the six social anxiety items in each identified latent class

In both samples, the most prominent correlates of social anxiety symptoms were academic school problems, bullying, eating problems, acne problems, symptoms of general anxiety and depression, older age, and a negative perception of family economy. The class with “high-scorers” on social anxiety had significantly higher scores on correlates than the class with “low-scorers”. Alcohol use was inconsistently related to social anxiety; however, LPA was able to show that girls in the high-scoring class had a higher probability of alcohol intoxications.

5. DISCUSSION

5.1 Methodological strengths and limitations

The main strengths of this thesis include the large comparable community and clinic samples employed, and having the ability to examine sex differences without jeopardizing statistical power. Also, the inclusion of a large number of fathers (> 3000) is an important addition to previous research. Another advantage was that each family member reported on their own mental health. Furthermore, examining symptoms of several mental health problems in parents and both internalizing symptoms and well-being in offspring resulted in knowledge that may be important for prevention and treatment. Before discussing the findings related to theory and previous research, possible methodological limitations must be considered as factors influencing the reliability and validity may affect the trustworthiness of the findings.

5.1.1 Causality

With the exception of parts of study 2, most of the findings in this thesis are based on cross-sectional data. Because temporality is a necessary criterion for causality, causal inferences from this research are not possible. Although the paths in the SEM model appear to be directional, implying that parental mental health problems affect offspring symptoms, a model testing whether offspring symptoms affect parental problems would be statistically equivalent. Familial aggregation is due to both genetic and environmental factors, and whereas the genetic associations imply directionality, the environmental associations do not (with the exception of in utero experiences). The aim of this thesis is not to disentangle genetic and environmental effects, and hence, the obtained results indicate associations between parental and offspring internalizing symptoms. Also in study 3, the correlates of social anxiety symptoms cannot be considered either antecedents or consequences of social anxiety. For example, acne may be a result of the psychological stress associated with social anxiety (Yosipovitch et al., 2007). Furthermore, the correlates may interact and be associated with a range of psychiatric problems, not uniquely with social anxiety. Prospective and, if possible, experimental studies are

needed to clarify these issues. Still, the associations found in the studies in this thesis elucidate the correlates of internalizing symptoms and can be used to increase identification and point to important areas for prevention and treatment of such problems, which would then need to be evaluated empirically.

5.1.2 Random errors

5.1.2.1 Self-reports

This research was based on self-reports. Collecting information by self-reports is convenient, but several problems may be associated with such measures and lead to random error. For example, individuals' responses may be affected by temporary mood, physical illness, time pressure, or an inability to understand and report emotions (Pavot & Diener, 1993). On the other hand, internalizing symptoms are subjective perceptions of internal distress, and thus not readily observable to others (Michael & Merrell, 1998). Therefore, researchers have stressed the necessity of assessing internalizing symptoms by self-reports (Michael & Merrell, 1998). Previous research suggests that adolescents' self-reports of mental health and health-risk behavior are generally valid and reliable (Brener, Billy, & Grady, 2003; Lintonen et al., 2004; Pavot & Diener, 1993), whereas the validity of self-reported physical activity may be more questionable (Rangul et al., 2008). Thus, these problems must be recognized when evaluating our findings.

5.1.2.2 Sample size

With increasing sample sizes, the likelihood of random errors decreases leading to more precise estimates and narrower confidence intervals. In all three studies, the sample sizes were quite large. Two-sided p values $< .01$ were considered statistically significant in study 1 because small differences without practical importance may reach statistical significance in large samples. The results in study 1 indicated, however, that even though the sample size was large, the statistical magnitude of effects was small because most participants in community samples are healthy. Thus, we considered two-sided p -values $< .05$ as statistically significant in studies 2 and 3.

5.1.2.3 Measuring latent variables with few items based on item correlations

To reduce the amount of random errors due to respondent fatigue, short forms of established measurement scales were used in both the HUNT study and the CAP survey. However, the reliability and validity of the original scales may not apply to the short forms. As recommended (Widaman, Little, Preacher, & Sawalani, 2011), data were analyzed by structural equation modeling (SEM), which combines factor analysis (*the measurement model*) and multiple regression analysis (*the structural model*). In regression analyses, the predictor variables are assumed to be measured without error. In psychological and psychiatric research, not directly observable variables (often called latent constructs, latent variables or factors), such as anxiety or self-esteem, are often measured. High correlations between a set of items are assumed to reflect that an individual's response to these items in combination measure the impact of an underlying latent variable. It is, however, impossible to know that the latent construct is measured perfectly, and the paths in regression analyses may be over- or underestimated due to both random and systematic measurement error. SEM makes it possible to evaluate the fit between data and theory. For example, a good model fit results if the covariance matrix between the items assumed to load on a factor can be reproduced when making them load on that factor. Thus, the measurement model is supposed to account for possible measurement errors and give more trustworthy estimates of the regression paths. SEM was employed in all studies in this thesis to account for measurement error.

However, this method is difficult to employ when variables consist of only one item. This problem pertains especially to study 3, in which suicidal thoughts, alcohol use, drug use, and acne problems were measured by one item, and may result in low sensitivity in the analyses. On the other hand, research suggests that in some cases one question may be sufficient to obtain valuable information (Bowling, 2005). Furthermore, no questions were open-ended which, at least for the reporting of alcohol use, has been shown to provide more reliable answers (Lintonen et al., 2004). Another problem concerns the inability to distinguish anxiety and depression symptoms in the measures used in our studies. Thus, it is uncertain whether these

variables mainly measure symptoms of anxiety, depression, or both. Initially, we tried to distinguish between parental anxiety and depression symptoms by employing the HADS measure, but due to low factor loadings this scale was considered inappropriate in this sample. Although this emphasizes the utility of employing SEM in these studies, the use of shortened scales and variables measured by one or a few items represents limitations in this thesis. Confirming the findings with more sensitive and comprehensive measurements is needed.

5.1.2.4 Measuring internal consistency

Also related to measurement error is internal consistency, which measures how well a set of items relate to the same latent variable. Cronbach's coefficient alpha (Cronbach, 1951) is the most commonly used measure of internal consistency, and is routinely reported in research where multiple items are used to measure a latent construct. However, the coefficient alpha is based on several underlying assumptions, such as that the items represent one single latent construct and all items are equally good indicators of the latent construct (Schmitt, 1996), which would be evident by all items having equal factor loadings (Widaman et al., 2011). If these assumptions are not met, which may be a possibility when using short forms of scales (e.g. to reduce respondent fatigue), coefficient alpha may be underestimated and other measures of internal consistency would be more appropriate (Raykov, 1997; Widaman et al., 2011). Hence, composite reliability (CR) was used in all three studies, because this measure is based on factor loadings and does not assume that all items are equally good indicators of the latent variable measured (Fornell & Larcker, 1981).

5.1.2.5 Measuring latent variables based on respondent correlations

Ideally, the validity and reliability of survey questions should be evaluated by comparing the answers with some error-free external measure (Kreuter, Yan, & Tourangeau, 2008). However, when measuring latent variables, such objective external measures are not easily available. Thus, latent class analysis or latent profile analysis (LPA) are alternative methods of accounting for error because they do not rely on error-free measures (Kreuter et al., 2008). Instead of

grouping individuals based on high correlations between variables as in factor analysis, LPA focuses on high correlations between individuals' scores on items. Thus, LPA is a person-centered method to group individuals based on how similar or different they score on items. The goal is to identify subgroups inherent in the data that include people who respond similarly to the items, but differ from groups of other respondents. In study 3, LPA was used to identify two subgroups reporting high and low levels of social anxiety symptoms. This method was employed because no cut-off value indicating clinical levels of symptoms had been established for the shortened version of the scale. The fact that the identified subgroups consisted of high- and low-scorers on the social anxiety items, supports the validity of this analysis. Furthermore, such a method may better illustrate that symptom levels below the threshold for the diagnostic categories also are associated with reduced functioning and quality of life.

5.1.3 Systematic errors

5.1.3.1 Representativeness

The sample in studies 1 and 2 and partly in study 3 was from a total population health survey in which all inhabitants in a county above the age of 12 were invited to participate. Ideally, this should ensure the generalizability of the findings, but the county is not necessarily representative of all Norwegian counties or other countries because the county is mainly rural, with both coastal and inland municipalities. The level of education and income is somewhat lower than the national average (Langhammer, Krokstad, Romundstad, Heggland, & Holmen, 2012). Also, Norway is one of the wealthiest countries in the world with significant resources available to the whole population, including prominently universal public health insurance coverage and equal status of the sexes, which may affect the generalizability of our findings to other cultures. The county of Nord-Trøndelag is, however, quite representative of Norway as a whole with regard to sources of income, age distribution, morbidity, and mortality (Holmen et al., 2014), and the socioeconomic health inequalities are comparable to other countries in Northern Europe (Krokstad, Kunst, & Westin, 2002), suggesting that the findings at least may be

representative for other North European countries. The clinical sample was also based on a total population of adolescent patients in child and adolescent psychiatry in a county contiguous to the county where the HUNT study was performed. Nord-Trøndelag and Sør-Trøndelag are quite similar counties although there is one large city in Sør-Trøndelag, possibly increasing the representativeness of the findings in this sample. Thus, the clinical sample is probably also quite representative of adolescent patients in child and adolescent psychiatric clinics in Norway and in the north of Europe.

5.1.3.2 Selection bias

Selection bias results when the associations between exposure and disease are different for participants and non-participants (Rothman, 2002). In HUNT3, the participation rate was quite high among adolescents (78%), probably due to the fact that the survey was conducted in the schools. The highest participation rate was in junior high schools (85%), and lowest among individuals not in school (23%). Non-participants were more often older, boys, and if in school they attended vocational rather than academic classes (Holmen et al., 2014). This suggests that the findings are not representative of adolescents not attending school, but this group constituted only 4% of the total population of adolescents. Yet, this group probably has worse mental health and life style (Holmen et al., 2014). The high participation rate should reduce the likelihood of selection bias, but the low participation rate among adolescents not attending school may lead to a small underestimation of the associations in the studies.

Among adults the participation rate was lower (54%). Non-participants were more often men, unmarried, had an unhealthier lifestyle, higher prevalence of psychiatric disorders, higher alcohol consumption, lower socioeconomic status (SES), and higher mortality than participants (Langhammer et al., 2012; Torvik, Rognmo, & Tambs, 2011). These factors affect the number of adolescents with participating parents, which constitute our sample in studies 1 and 2. Thus, we tested whether adolescents with and without parents participating in the study differed on the measured variables. These tests suggested no differences on social anxiety symptoms, but the

excluded adolescents had significantly more symptoms of anxiety and depression, lower SWB, lower self-esteem, and were less physically active than adolescents with parents participating in the study. This might lead to an underestimation of the associations observed in the studies, but effect sizes for these differences were very small and should thus partially abate that concern. In HUNT2, the adult participation rate was higher (70%), and 77% of the parents in our sample from HUNT3 also participated in HUNT2.

In study 3, the participation rate among adolescents in the community sample was 73%, which should support the representativeness of the findings in that sample. In the clinical sample, however, the response rate was considerably lower (42%), and represents a limitation of the study. Comparisons of the participants and all adolescents at the clinic in the study period showed that participants were somewhat older and more often girls. However, main reason for referral, which is a variable with 16 categories coded according to a national classification system of suspected mental health problems, did not differ between participants and non-participants. This suggests that the participants were fairly representative of the clinical population with regard to presenting problems.

5.1.3.3 Information bias

Information bias arises when the information collected from the participants is erroneous (Rothman, 2002). All studies in this thesis are based on self-report questionnaires. Thus, information bias cannot be excluded. Social desirability may affect the responses given although the exam-like situation in which the adolescents completed their questionnaires may contribute to reduce this likelihood. However, the missing data on alcohol use and alcohol abuse were substantial among both adolescents (25%) and adults (28%). This may possibly be due to social desirability. Regardless, we tried correcting for this by employing multiple imputation because it results in less biased estimates than complete case analyses and the FIML procedure with categorical data (Asparouhov & Muthén, 2010; Schafer & Graham, 2002).

Recall bias is another type of information bias. With regard to familial aggregation of mental health problems, one family member is often asked to report on such problems in other family members, which may result in such bias. In this thesis, however, all family members reported on their own health, which constitutes a strength of this research. Another important factor relating to recall bias is the time frame of the questions asked as a shorter time frame reduces the likelihood of such bias. The questions on symptoms of anxiety and depression and maternal eating problems had a time frame of the previous two weeks and the previous month, respectively, whereas none of the other measures used in this thesis described any time frame. This may have contributed to some amount of recall bias in our studies.

5.1.3.4 Confounding

Confounding is a form of bias resulting from the mixing of effects (Rothman, 2002), and is the consequence of a third variable causing the observed association between the predictor and the outcome variable. Several third variables may cause the associations found in the studies in this thesis. For example, age, sex, SES, living situation, neighborhood characteristics, negative life events, low social support, externalizing symptoms, violence, physical disease, chronic pain, and inflammation may be confounding variables (Baumeister, Russell, Piarante, & Mondelli, 2014; Connell & Goodman, 2002; Dalgard, Bjørk, & Tambs, 1995; Kaasbøll, Lydersen, & Indredavik, 2012; Landolt, Ystrøm, Stene-Larsen, Holmstrøm, & Vollrath, 2014; Leventhal & Brooks-Gunn, 2000). Adjustment for confounders depends on firm knowledge that a variable in fact is a confounder as adjustment for colliders or mediating variables in the causal chain would lead to bias (Christenfeld et al., 2004; Hernán, Hernández-Díaz, Werler, & Mitchell, 2002). For example, it is conceivable that chronic pain is a consequence of internalizing symptoms rather than a cause. Ideally, experimental designs are required to disentangle such relationships, but would not be ethical within this research area. Thus, in this thesis internalizing symptoms were examined while adjusting for well-known confounders with a strong empirical foundation, such as age and sex.

In all studies, we stratified on sex because internalizing symptoms are more prevalent among women than men (Costello et al., 2011; Wichstrøm, 1999). Furthermore, all internalizing symptoms were associated with adolescent age, probably because of the increase in prevalence in adolescence (Merikangas & Knight, 2009; Wittchen et al., 1999). Thus, we adjusted for offspring age in all studies. Other sociodemographic variables in studies 1 and 2 (parental marital status and level of education) were not significantly associated with the dependent variables, and were thus not adjusted for. Controlling for these factors in supplementary analyses resulted in somewhat weaker associations between mental health symptoms in parents and offspring but these effects were very small and not statistically significant. Potential reasons for the lack of associations may be the high number of married parents (70%) and the relatively small differences in SES in Nord-Trøndelag (Krokstad et al., 2002). In study 3, the findings indicated that subjective perception of family economy was associated with social anxiety symptoms, whereas cohabitation status was not. One reason for the differences between the studies may be that SES was measured subjectively by self-report in study 3, whereas in studies 1 and 2 SES was measured objectively by official records. Such differences have also been found in previous studies (Burstein et al., 2011b; Wittchen et al., 1999).

5.2 General discussion and implications

5.2.1 Summary of main findings

This thesis contributes to an increased understanding of internalizing symptoms in adolescence. The findings showed that internalizing symptoms in parents were associated with low positive affect as well as high negative affect in adolescents, whereas parental symptoms of alcohol abuse and maternal eating problems were not. Specifically, parental symptoms of anxiety and depression were associated with low SWB, low self-esteem, and more symptoms of depression, general anxiety, and social anxiety in offspring. Examining recurrent parental internalizing symptoms, findings indicated that parental symptoms of anxiety and depression when offspring were of a preschool age were weakly associated with such symptoms in offspring ten years later.

These associations were, however, fully mediated by current parental symptoms. The associations between current parental symptoms of anxiety and depression and such symptoms in adolescents were partly directly associated and partly mediated by low adolescent self-esteem. None of the abovementioned associations were moderated by parental or offspring sex. However, the direct association between maternal and offspring symptoms of anxiety and depression was moderated by adolescent physical activity level.

Examining social anxiety symptoms in adolescence in depth, findings showed such symptoms to be frequently reported by adolescents, more so by girls than boys as well as by the clinical compared to the community sample. The most prominent correlates of social anxiety symptoms were academic school problems, bullying, eating problems, acne problems, and symptoms of general anxiety and depression. There were few differences between the clinical and the community sample with regard to correlates of social anxiety symptoms.

5.2.2 Multifinality in internalizing symptoms?

Given the developmental psychopathology perspective adopted in this thesis, the examinations were extended beyond symptoms of psychopathology to also include positive affective functioning in offspring. The findings in study 1 showed that parental internalizing symptoms were associated with several outcomes in children, whereas parental alcohol abuse and maternal eating problems were not associated with either symptoms of depression, general anxiety, social anxiety, SWB or self-esteem in offspring. These findings are consistent with the model of multifinality where one predictor is associated with different outcomes. Equifinality (different predictors being associated with the same outcome) was not apparent in our data as parental alcohol abuse and maternal eating problems were not associated with internalizing symptoms, SWB or self-esteem in adolescent offspring. Even though our findings are consistent with these interpretations, as mentioned previously, causal claims cannot be made based on cross-sectional studies. The findings from study 2 showing associations between parental symptoms when offspring were of a preschool age and internalizing symptoms in offspring

during adolescence may imply that the stability of parental internalizing symptoms over long periods of time leads to similar symptoms in offspring. Still, in a ten-year interval, other exposures may also occur, such as stressful life events. Furthermore, without measuring internalizing symptoms in preschoolers, a causal claim cannot be made based on these studies. Indeed, previous research suggests a reciprocal relationship between depressive symptoms in mothers and children ages 5-7 (Jaffee & Poulton, 2006), and may provide support for the transactional model emphasizing bidirectionality between the individual and the environment. On the other hand, there is quite strong evidence that exposure to maternal depressive symptoms by age 12 leads to depressive symptoms in adolescent offspring (Garber & Cole, 2010; Hammen & Brennan, 2003). Notably, adolescents' depressive symptoms did not predict maternal symptoms (Garber & Cole, 2010). In addition, studies show that improvement in parental depression leads to improvement in offspring psychopathology (Gunlicks & Weissman, 2008; Weissman et al., 2006), whereas continued maternal symptoms are related to fewer declines or elevations of offspring symptoms (Kouros & Garber, 2010). These findings may suggest that parental psychopathology in the early years of life may have long-term implications for offspring and trigger negative developmental cascades possibly related to not achieving developmental tasks, such as secure attachment or social and emotional competence. Thus, parental internalizing symptoms leading to symptoms in adolescent offspring seems more likely than the converse, and multifinality rather than equifinality appear to be the better matching model for familial aggregation of internalizing symptoms. This should, however, be further examined in prospective studies across different developmental phases.

The suggestion that equifinality does not appear applicable was somewhat surprising as associations between offspring internalizing symptoms and self-esteem and parental alcohol abuse have been found in several studies (Bijl et al., 2002; Cloninger et al., 1996; Rognum et al., 2012; Roosa et al., 1988). However, one other study found alcohol abuse and internalizing symptoms to be only *indirectly* associated through marital conflict and decreased parental warmth (Keller et al., 2008). Thus, the dysfunctional parenting resulting from alcohol abuse may

be more important for child outcomes than the specific psychiatric symptoms. These findings may also indicate specificity in familial aggregation of alcohol abuse as has been suggested in previous studies (Kendler et al., 1997). There was no association between maternal eating problems and offspring internalizing problems. To the best of our knowledge, no studies have examined this relationship previously. Thus, this finding should be replicated in further studies before firm conclusions can be drawn.

Our findings also show the importance of assessing factors related to both high and low positive affect. Recall that positive affect and negative affect are separable dimensions of affect. SWB and self-esteem are included in this thesis because these factors are assumed to measure the entire continuum of positive affect (Diener, 2000; Wood, Heimpel, & Michela, 2003) whereas symptoms of depression, general anxiety and social anxiety only measure the lower end of the continuum of positive affect (in addition to negative affect). Parental internalizing symptoms were associated with measures of both positive and negative affect in our study. This indicates that the impact of parental internalizing symptoms on offspring mental health is quite broad in adolescence, and not limited to mere psychiatric symptoms. High SWB and self-esteem are shown to protect against depressive symptoms (Lewandowski et al., 2014; Lewinsohn, Redner, & Seeley, 1991), whereas low SWB and self-esteem may be precursors for developing more serious psychiatric problems (Goodman et al., 2011; Sowislo & Orth, 2013). Targeting these factors in prevention may thus be important.

Multifinality may be operationalized at different levels. Parental internalizing symptoms have in previous research also been related to externalizing symptoms in offspring (Connell & Goodman, 2002; Goodman et al., 2011). Such findings are strong indications of the multifinality of parental internalizing symptoms, but we lacked in our studies the opportunity to measure externalizing symptoms. One may question whether the finding that one predictor (parental internalizing symptoms) is associated with constructs of both high and low positive and negative affect also indicate multifinality. Rather, one may argue that the various offspring

variables measured in study 1 constitute a cluster of quite similar symptoms. For example, self-esteem and depression have been claimed to be essentially one construct with global self-esteem at the positive and depression at the negative end on a continuum (Watson, Suls, & Haig, 2002). Low self-esteem is also named as a symptom of both depressive disorder and social phobia (World Health Organization, 2010). However, in our study the correlations between self-esteem and depressive and social anxiety symptoms were not as strong as expected if the factors were opposite ends of one factor ($\leq .639$). Furthermore, self-esteem is found to be a more stable trait than depression (Orth et al., 2008), and unique genetic processes are involved in self-esteem and depression (Neiss et al., 2005). We conclude from the combination of these findings that self-esteem and depressive symptoms are different constructs. Hence, in this thesis, the term multifinality is used when one predictor is associated with different but related factors of positive and negative affect. This does not preclude that the end point may be depression and/or social anxiety in adult age, yet in adolescence, parental internalizing symptoms appear to be related to both positive and negative affect.

5.2.3 Sex differences

According to Table 1 and the findings from study 3, more adolescent girls than boys have internalizing symptoms. Surprisingly, there does not seem to be a large sex difference with regard to the proportion of mothers versus fathers who score above the cut-off on anxiety and depression although this does not preclude sex differences with regard to subthreshold symptoms. Also, no sex differences were observed in familial aggregation of internalizing symptoms in our studies. The severity of parental problems may affect offspring differentially and explain the lack of sex differences in this research and the observed differences in previous research (Klein et al., 2005). It is also possible that sex interacts with important environmental factors which were not examined in our studies. Furthermore, our findings may be culture-specific, being conducted in a Scandinavian country where equal status of the sexes is a well-established value. The majority of mothers have a job outside of home, good quality child care is generally available, and fathers participate actively in child care. Hence, more opportunities for

transaction between both parents and children may occur. Our findings may therefore not be generalizable to countries with more unequal status between the sexes.

The timing of internalizing symptoms in both parents and offspring and sensitivity to offspring's developmental phase may also contribute to these findings. Offspring may be differentially sensitive for parental problems at different ages (Garber & Cole, 2010; Jaffee & Poulton, 2006; Kouros & Garber, 2010). However, both maternal and paternal internalizing symptoms were found to be quite stable across ten years, which may reflect the chronic nature of anxiety and depression in both sexes. Also, fathers may be more active in caring for older offspring, and studies suggest that paternal mental health problems are a stronger correlate of internalizing symptoms in adolescents above age 13, whereas maternal problems were more strongly associated with symptoms in offspring below age 13 (Connell & Goodman, 2002). Our findings may partially support this finding as we observed a non-significant trend towards stronger associations between paternal anxiety/depression and internalizing symptoms in daughters than in sons. Also, this may support theories stating that adolescent girls are more vulnerable for problems within the family because girls' gender development is more connected to social relationships (Bussey & Bandura, 1999), and findings showing paternal depression to be associated with psychological distress in daughters (Ge et al., 1995).

Regardless, our results emphasize the importance of incorporating both mothers and fathers in research because the findings clearly demonstrated that internalizing symptoms in both parents are associated with such symptoms in both daughters and sons. Also, internalizing symptoms in both parents were associated with more symptoms of anxiety and depression in offspring compared to when none or one parent had such symptoms. This is consistent with several previous studies (Foley et al., 2001; Merikangas et al., 1988; Pape, Bjørngaard, Holmen, & Krokstad, 2012), and may reflect a tendency of assortative mating in parents with anxiety and depression. Taken together, our results indicate that the number of parents with internalizing symptoms may be more important than the sex of the parent or offspring.

5.2.4 Psychosocial mechanisms in internalizing symptoms

Genetic mechanisms involved in familial aggregation of internalizing symptoms are difficult to modify through interventions, whereas environmental mechanisms are more modifiable (Natsuaki et al., 2014). Identifying psychosocial factors in the pathways between parental and offspring internalizing symptoms is therefore important for developing prevention and treatment interventions aimed at reducing familial aggregation. Furthermore, identifying easily accessible moderators is equally important. Studying mediating and moderating mechanisms in cross-sectional data is usually not recommended as this violates the causal temporal order. However, when solid theory and previous research indicate directionality of associations, mediation analyses on cross-sectional data can be performed as the interpretation of findings regardless rely on rational explanations rather than statistical procedures (Hayes, 2013).

Based on previous findings that low self-esteem predicts depressive symptoms (Orth et al., 2008; Sowislo & Orth, 2013), we examined and found associations between parental and offspring symptoms of anxiety and depression to be partially mediated by offspring self-esteem. This is in accordance with Goodman and Gotlib's model detailing that children of depressed parents are exposed to risks that may eventually create vulnerability for low self-esteem, which over time increases the risk of depression, especially in adolescence (Goodman & Gotlib, 1999, 2002). Our results support previous findings that offspring self-worth partly mediates the associations between maternal and offspring depression (Garber & Cole, 2010), with the important addition of demonstrating that self-esteem also partly mediates associations between paternal and offspring internalizing symptoms.

Furthermore, our findings suggested that offspring's physical activity level moderates the direct associations between maternal and offspring symptoms of anxiety and depression but not between paternal and offspring anxiety and depression. Additionally, physical activity did not moderate the indirect paths associating parental and offspring anxiety and depression via self-esteem although it has been proposed that physical activity reduces internalizing symptoms

by increasing self-esteem (Kirkcaldy et al., 2002). Our findings support studies showing an inverse association between physical activity and internalizing symptoms (Calfas & Taylor, 1994; Motl et al., 2004; Sund et al., 2011b) because maternal and adolescent internalizing symptoms were not associated when adolescents reported self-initiated physical activity beyond that prescribed in school. This indicates that physical activity can act as an important protective factor in familial aggregation of anxiety and depression. Physical activity did not moderate the associations between paternal and offspring internalizing symptoms. One reason for this may be that physical activity in fathers is shown to strongly predict physical activity in adolescents, whereas physical activity in mothers appears less important (Edwardson & Gorely, 2010; Ferreira et al., 2007; Shropshire & Carroll, 1997). Fathers with internalizing symptoms in our sample were significantly less physically active than healthy fathers. Thus, the offspring of these fathers may also be less physically active, whereas in families with a healthy and physically active father, adolescents most likely exercise more.

There is ambiguity with regard to the effect of physical activity on anxiety and depression in previous research (Larun et al., 2006). This study expands on previous research by suggesting that adolescents exercising at least once a week outside of school may be protected against symptoms of anxiety and depression when having a mother with such symptoms. We speculate that the differential susceptibility hypothesis may be relevant for these findings. According to this hypothesis, children at risk may also be more strongly influenced by positive environmental experiences (Belsky & Pluess, 2009). Children of parents with internalizing symptoms are undoubtedly at risk due to both genetic and environmental factors. Physical activity may be a positive experience affecting these children more strongly than children of healthy parents, and thus partly account for previous ambiguous findings in this research area.

In summary, our findings suggest that self-esteem and physical activity may be target points in prevention and treatment of internalizing symptoms among adolescents in addition to established interventions. Furthermore, a range of psychosocial correlates of social anxiety were

identified. Academic school problems were strongly associated with social anxiety symptoms. However, as in previous research, the scale used to measure academic school problems in our study also included items on comprehension and concentration problems, which makes it unclear whether the scale reflects actual learning difficulties leading to social anxiety or vice versa. Bullying was also highly associated with social anxiety. This is consistent with previous studies, with explanations including deficits in social skills, poorer feedback from peers, and traumatization from bullying (Gren-Landell, Aho, Andersson, & Svedin, 2011; Ranta et al., 2013). Eating problems have been associated with social anxiety previously, but most studies have had only adult female respondents (Godart, Flament, Lecrubier, & Jeammet, 2000). The present study extends this association to adolescents of both sexes. The reasons why social anxiety and eating problems are related are unclear, although low self-esteem, bullying and a critical family environment may be possible explanations. Acne was consistently associated with social anxiety. Thus, it seems that the negative psychological effects of acne extend beyond general anxiety (Aktan, Özmen, & Sanli, 2000) to social anxiety. Suicidal thoughts were associated with social anxiety in all groups. Consistent with previous research (Nelson et al., 2000), this association disappeared when controlling for anxiety/depression, except among girls in the community sample. As girls tend to be more socially oriented than boys (Connellan, Baron-Cohen, Wheelwright, Batki, & Ahluwalia, 2000), girls with social anxiety may experience their anxiety as more burdensome. Combined these findings suggest that interventions targeting bullying, academic school problems and symptoms of eating problems in addition to self-esteem and physical activity may also have potential for preventing or relieving internalizing symptoms.

5.3 Implications for further research

The results presented in this thesis emphasize the importance of including both mothers and fathers in future research on familial aggregation because our findings clearly demonstrate that mental distress in *both* parents are associated with internalizing symptoms and reduced well-being in both daughters and sons. Thus, our findings point to the importance of including both parents when examining risk factors and mechanisms of familial aggregation. Prospective

studies are needed to advance knowledge about the direction of the associations with sensitivity to possible different effects due to sex, age, and mental health domains. Further examinations of factors related to both high and low positive and negative affect would be informative. The lack of sex differences found in our studies may not be generalizable to countries with more unequal status between the sexes. Thus, our findings should be tested in other cultures.

Our findings indicated that self-esteem partly mediates associations between parental and offspring symptoms of both anxiety and depression, as suggested in the tripartite model, and not only symptoms of depression. Future research should examine whether self-esteem also mediates parental and offspring anxiety. Because different anxiety disorders seem differently related to the factors of the tripartite model, it will also be important to distinguish among anxiety disorders when further examining the etiological role of self-esteem.

To the best of our knowledge, the present study was the first to suggest that physical activity may protect against familial aggregation of anxiety and depressive symptoms. Thus, these findings should serve as the basis for further research on this subject, and possibly examine differential susceptibility and thresholds for positive consequences of physical activity. Should the findings be replicated, interventions with the aim to increase physical activity could be developed and evaluated in randomized controlled trials. Examining the hypotheses that the offspring of fathers with mental health problems may be less physically active is also necessary. The assumption that self-esteem leads to depression was based on previous research findings and was not examined in our study. Further longitudinal studies can advance inferences about the direction of associations between these variables. Other relevant mediators and moderators were also not examined; thus, future research should include more variables to broaden the understanding of familial aggregation of internalizing symptoms by examining prospectively the mechanisms proposed in Goodman and Gotlib's (1999) model with both mothers and fathers as participants. Examples of possible mediators are genetic vulnerabilities, neurobiological dysregulation, child temperament, exposure to stressors, dysfunctional parenting, or deficits in

cognitive, affective, or social skills, whereas possible moderators may be parental comorbidity, cognitive maturity, intellectual skills, or social support (Goodman & Gotlib, 1999). The role of these variables in explaining and affecting familial aggregation should be examined further.

We did not find an association between parental alcohol abuse or maternal eating problems and offspring internalizing symptoms. These negative findings may indicate specificity in familial aggregation of alcohol abuse and eating problems. We did not have the opportunity to measure externalizing symptoms, offspring alcohol use, parental social anxiety, nor paternal eating problems. Thus, these symptoms should be examined in further research to clarify equifinality and multifinality in familial aggregation of mental health problems. More studies sensitive to detecting familial aggregation in different problem areas will be important as previous research in most cases has been limited by focusing on one clinical diagnosis at a time.

There is also a need to examine longitudinally additional correlates of social anxiety and whether these are antecedents or consequences of social anxiety (e.g. by examining academic school problems in a manner that do not confound the direction of effects). Especially, alcohol and drug use and suicidality need to be further examined in relation to social anxiety because of the inconsistent findings in our studies as well as in existing research. Also, investigations explaining why social anxiety and eating problems are related should be conducted. The psychosocial correlates examined here may also be associated with a range of psychiatric problems, and not uniquely with social anxiety. Furthermore, social anxiety and its correlates may interact and mutually influence each other. More research is needed to clarify these issues. Finally, future studies should employ person-centered methods to confirm our findings suggesting that a threshold between individuals scoring high and low on social anxiety symptoms may exist.

5.4 Clinical implications

Our findings highlight that paternal anxiety and depression is just as important for the mental well-being of adolescents as maternal symptoms, and point to the need for increased awareness

of the associations between internalizing symptoms in adolescents and both mothers and fathers. Thus, when health personnel meet parents displaying mental distress, assessing the mental status of the entire family is vital to effectively mitigate familial aggregation and societal costs. Our findings suggest that the children of parents with internalizing symptoms are at a sustained risk for problems due to the chronic nature of the symptoms, as shown by the apparent 10-year stability of both maternal and paternal anxiety and depressive symptoms. Thus, preventing familial aggregation of these problems as early as possible seems vital. For children, having a parent with internalizing symptoms may also entail extra caregiver responsibilities within the family. This may contribute to increase the risk of such symptoms in children, but research also suggests that such 'parentification' may have positive effects by providing children with a constructive family role and possibly increase their social competence (Beardslee, 1989; Gladstone, Boydell, & McKeever, 2006). Thus, it is important to acknowledge that parental mental illness may create opportunities for growth for some children. However, our results suggested that internalizing symptoms in parents are related to reduced SWB and self-esteem in addition to internalizing symptoms in offspring. Thus, adults working with adolescents should be aware of the possible negative consequences of reduced SWB and self-esteem in adolescents. Furthermore, assessing such variables appears important for community and specialist health services to mitigate familial aggregation. It should, however, be noted that the clinical significance of these findings, which were obtained in a large community sample, should be examined in longitudinal clinical studies.

Our findings may also be important for both prevention and treatment of internalizing problems. Because the associations between parental and offspring internalizing symptoms were found to be partially mediated by offspring self-esteem, efforts could be aimed at increasing self-esteem in vulnerable children as early as possible in life. Engaging in activities that fulfill the developing child's basic needs of autonomy, competence, and relatedness has been shown to increase self-esteem (Ryan & Deci, 2000; Ryan, Stiller, & Lynch, 1994); thus, encouraging such activities may also serve to mitigate familial aggregation of internalizing

symptoms. Furthermore, because physical activity might reduce familial aggregation of such symptoms, this could also be an important focus for future prevention and treatment efforts. From a public health perspective, it seems important to encourage and increase motivation for physical activity in families with internalizing symptoms, possibly from early in life.

Regarding other psychosocial correlates than parental mental health problems, academic school problems, bullying, eating problems, subjective perception of acne problems, and general anxiety and depression were important correlates of social anxiety symptoms in both the clinical and the community sample. This indicates that the pattern of correlates of social anxiety was not different in the two types of samples. These correlates may be easier to detect in adolescents than social anxiety symptoms, and can therefore be used to identify burdening symptoms. This is important as only 2.3% of the clinical sample had a primary diagnosis of social phobia, confirming that the identification of social anxiety appears to be suboptimal. We were able to identify a group of adolescents scoring high on social anxiety symptoms who also had a broad spectrum of additional difficulties and may be at high risk for mental health problems. The findings provide a rough profile on the mean score for each item on the SPAI-C instrument measuring social anxiety, which can be useful for separating high- and low-risk groups. In addition, based on the findings in this thesis, a suggestion may be for mental health professionals to screen for a broad range of mental health problems including internalizing symptoms, low self-esteem, low SWB, bullying, academic school problems, and eating problems, to increase the probability that all relevant problems can be identified when young people appear in a clinic. Furthermore, the findings from our studies should be communicated to parents, teachers, health personnel, and especially mental health professionals so that adolescents who are struggling with internalizing symptoms will be identified and helped. In light of our findings, prevention programs targeting bullying, school problems, eating problems, self-esteem, and physical activity could also be useful for reducing internalizing symptoms in adolescents.

6. CONCLUSIONS

This thesis contributed important knowledge on internalizing symptoms in adolescence by examining large comparable community and clinical samples. The most notable findings were that internalizing symptoms in fathers and mothers were equally important for such symptoms in adolescent offspring. By including a large number of fathers, our findings revealed that research on familial aggregation of internalizing symptoms is not complete without including *both* parents. Furthermore, our findings suggest that the children of parents with internalizing symptoms are at a sustained risk for such symptoms themselves due to the observed 10-year stability of both maternal and paternal internalizing symptoms. On the other hand, symptoms of alcohol abuse and eating problems in parents were not associated with internalizing symptoms in offspring, disconfirming the notion of equifinality in this study (several parental mental health problems predicting internalizing symptoms in offspring).

The results also showed that symptoms of anxiety and depression in parents were associated with internalizing symptoms as well as low self-esteem and SWB in offspring, consistent with the notion of multifinality. These latter factors may be important precursors of psychiatric symptoms and thus amenable to prevention and treatment interventions. In fact, low self-esteem was found to mediate associations between internalizing symptoms in parents and offspring, further emphasizing the important role of self-esteem. Moreover, our study is to the best of our knowledge the first to suggest that the physical activity of adolescent offspring may moderate associations between maternal and offspring symptoms of anxiety and depression, and thus possibly reduce familial aggregation of such symptoms. These findings need to be confirmed in future research, but physical activity may have potential for prevention and treatment efforts. Thus, from a public health perspective, it could be important to encourage physical activity in the offspring of parents with internalizing symptoms, possibly from early in life.

The findings from this thesis may also contribute to improve identification of social anxiety symptoms. Such symptoms were frequently reported among adolescents in both the clinical and the community samples, and were associated with academic school problems, bullying, eating problems, acne, and symptoms of general anxiety and depression. The associated problems may be easier to detect than social anxiety symptoms as such, and hence, can be used to identify burdening symptoms. Furthermore, in light of these associations, prevention programs targeting bullying, school problems, and eating problems could also be useful for reducing internalizing symptoms. Based on the combined findings from all three studies, it would appear that instead of assessing individual mental health problems in isolation, as is typical in mental health clinics, a screening of a broad range of problems among children and adolescents, including internalizing symptoms, bullying, academic school problems, eating problems, and parental internalizing symptoms, as well as self-esteem and SWB, may be vital to reduce the burden of internalizing problems in adolescence.

ERRATUM

In paper 1, the following reference is wrong:

Keller, P. S., Cummings, M. E., Peterson, K. M., & Davies, P. T. (2009). Marital conflict in the context of parental depressive symptoms: Implications for the development of children's adjustment problems. Social Development, 18, 536-555.

The correct reference is:

Keller, P. S., Cummings, M. E., Davies, P. T., & Mitchell, P. M. (2008). Longitudinal relations between parental drinking problems, family functioning, and child adjustment. Development and Psychopathology, 20(1), 195-212.

This is corrected in the thesis.

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PAPERS 1-3

Paper I

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Paper II

1 **Familial aggregation of anxiety and depression in the**
2 **community: the role of adolescents' self-esteem and**
3 **physical activity level (the HUNT Study)**

4

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26 **Abstract**

27 **Background**

28 Symptoms of anxiety and depression are significantly associated in parents and children, but
29 few studies have examined associations between recurrent parental problems and offspring
30 symptoms, and fathers have rarely been included in these studies. Additionally, few have
31 investigated factors that may protect against familial aggregation of anxiety and depression.
32 The aims of the present study are to examine the associations between recurrent parental
33 anxiety/depression over a ten-year time span and offspring anxiety/depression in adolescence
34 and to test whether two factors proposed to be inversely related to anxiety and depression,
35 namely, adolescent self-esteem and physical activity, may moderate and mediate the
36 transmission of anxiety/depression.

37 **Methods**

38 This study used data from two waves of a Norwegian community study (the HUNT study)
39 consisting of 5,732 adolescents, ages 13–18, (mean age = 15.8, 50.3% girls) who had one
40 (N = 1,761 mothers; N = 742 fathers) or both parents (N = 3,229) participating in the second
41 wave. In the first wave, 78% of the parents also participated. The adolescents completed self-
42 reported questionnaires on self-esteem, physical activity, and symptoms of
43 anxiety/depression, whereas parents reported on their own anxiety/depressive symptoms. The
44 data were analysed with structural equation modelling.

45 **Results**

46 The presence of parental anxiety/depression when offspring were of a preschool age
47 predicted offspring anxiety/depression when they reached adolescence, but these associations
48 were entirely mediated by current parental symptoms. Self-esteem partly mediated the
49 associations between anxiety/depression in parents and offspring. No sex differences were

50 found. Physical activity moderated the direct associations between anxiety/depression in
51 mothers and offspring, whereas no moderating effect was evident with regard to paternal
52 anxiety/depression.

53 **Conclusions**

54 These findings suggest that children of parents with anxiety/depression problems are at a
55 sustained risk for mental health problems due to the apparent 10-year stability of both
56 maternal and paternal anxiety/depression. Thus, preventing familial aggregation of these
57 problems as early as possible seems vital. The associations between parental and offspring
58 anxiety/depression were partially mediated by offspring self-esteem and were moderated by
59 physical activity. Hence, prevention and treatment efforts could be aimed at increasing self-
60 esteem and encouraging physical activity in vulnerable children of parents with
61 anxiety/depression.

62

63 **Keywords**

64 Intergenerational transmission, internalising problems, adolescence, self-esteem, exercise,
65 structural equation modelling

66 **Background**

67 Mental health problems, such as anxiety and depression, are significantly associated in
68 parents and children [1-4]. These problems “run in the family”, so to speak. The mechanisms
69 of such familial aggregations are most likely very complex and include genetic,
70 environmental and epigenetic processes [5-7]. Most studies have focused on the mechanisms
71 that enforce these processes [8], but few have investigated factors that may protect against
72 such aggregation [1,4]. According to the Roadmap for Mental Health Research in Europe
73 (ROAMER), such factors are important in preventing mental disorders but have too seldom
74 been considered in health sciences [9]. Although associations between positive psychological
75 factors and an adolescent’s mental health have been established (e.g., [10,11]), longitudinal
76 studies that include data on both parents’ and adolescents’ mental health are lacking.
77 Therefore, in the present study, we investigated the relevance of two factors proposed to be
78 inversely related to anxiety and depression [12-14] that may protect against familial
79 aggregation of these problems: self-esteem and physical activity. Specifically, we tested how
80 these factors may moderate and mediate the transmission of mental health problems. We took
81 advantage of the material from a large community study (the HUNT Study), including
82 maternal and paternal mental health data from two measurement points in addition to their
83 offspring’s mental health data at the second measure point.

84 **Familial aggregation of anxiety and depression**

85 Having a parent with mental health problems, such as anxiety or depression, is one of the
86 most important risk factors for developing such problems [1,8,15-17]. The timing of these
87 problems in both parents and offspring seems to affect the risk for problems in other family
88 members. Children experiencing maternal depression at any time point before the age of 10
89 have an elevated risk for depression as an adolescent [18]. However, the results from one

90 study indicated that the direction of the relationship between depressive symptoms in mothers
91 and offspring at ages 5-7 may be reciprocal [19], whereas in adolescence, maternal
92 depression most likely leads to offspring depression [20]. Recurrent problems may be
93 indications of the severity and chronicity of a disorder [18,21], and recurrent maternal
94 depression is related to an even higher risk of mental health problems in offspring [21,22],
95 but fathers have rarely been included in such studies. In general, fathers are underrepresented
96 in studies on familial aggregation of anxiety and depression [1,23]. This is a problem because
97 fathers obviously contribute 50% of their offspring's genes and are increasingly more
98 involved in child care [4]. Furthermore, few studies have taken into account the fact that
99 anxiety and depression are highly comorbid. Thus, we lack information on whether current
100 symptoms in both parents mediate the relationship between a parental history of anxiety and
101 depression and offspring anxiety and depression [22].

102 **Self-esteem among adolescents**

103 Global self-esteem refers to a person's evaluation of overall self-worth and self-knowledge
104 [12,24]. Empirical research has indicated that a low global self-esteem predicts depression,
105 while depression does not predict low self-esteem [25-28]. For anxiety, the findings are
106 mixed, although the associations appear to be more bidirectional [25,28]. Several studies
107 have shown that the children of depressed parents have a lower self-esteem than the children
108 of non-depressed parents [2,29-31]. Another study showed that depressed mothers expressing
109 negative affectivity about their children have children with a lower global self-worth and
110 more psychopathology than the children of non-depressed mothers [32]. In contrast, a higher
111 self-esteem in the offspring of depressed parents is found to be the most important predictor
112 of both the absence of a psychiatric diagnosis and high global functioning 2, 10, and 20 years
113 later [33].

114 The role of self-esteem in a family perspective can be explained by an encompassing
115 developmental model detailing the mechanisms involved in the intergenerational
116 transmission of depression [34,35]. According to this theory, the children of depressed
117 mothers may inherit genetic predispositions towards depression and be born with
118 dysfunctional neuroregulations. In addition, these children may be exposed to a stressful
119 family environment and the negative cognitions, behaviours, and/or affects of the depressed
120 parent. These factors are assumed to create certain vulnerabilities in children - including low
121 self-esteem - which can contribute to depression. Whereas studies have examined a
122 straightforward relationship between parental depression and child self-esteem, to our
123 knowledge, only two studies have examined self-esteem as a mediator in relation to
124 depression in a family perspective. One study showed that psychological control in depressed
125 mothers was associated with depressive symptoms in offspring, and these relations were
126 partially mediated by offspring self-esteem [36]. Another study found that maternal
127 depression partly predicted offspring self-esteem, which in turn predicted offspring
128 depression [22]. However, these studies were limited by only including mothers. Thus, we
129 lack studies examining whether self-esteem mediates the associations between maternal,
130 paternal and offspring anxiety/depression.

131 **Physical activity level and mental health**

132 Physical activity, here defined as aerobic activity of at least moderate intensity resulting in
133 noticeably increased heart rate or rapid breathing [37], is assumed to protect against anxiety,
134 depression and low self-esteem [38,39]. For example, physical activity may be protective by
135 enhancing an individual's autonomy, competence, and social interaction, as proposed by the
136 self-determination theory [40,41]. This is intriguing because compared to many other
137 protective factors, most individuals can engage in physical activity, and motivation for
138 physical activity can be altered with public health interventions [40]. Empirical findings on

139 the benefits of exercise on anxiety and depression are, however, inconsistent. Some studies
140 have found a small effect of exercise on anxiety and depression among adolescents [42-45],
141 but the clinical significance of these associations is questionable due to numerous
142 methodological limitations [14,46]. There are also a few studies showing that physical
143 activity increases self-esteem in adolescents [47-49]. However, systematic reviews have
144 concluded that the evidence base is currently too scarce to indicate that physical activity
145 affects either self-esteem or anxiety/depression among adolescents [46,47]. Furthermore, the
146 psychosocial mechanisms explaining the links between physical activity and
147 anxiety/depression need to be examined [50]. To our knowledge, this is the first study to
148 examine whether adolescents' physical activity moderates the associations between parental
149 and adolescent anxiety/depression and self-esteem.

150 **Aims and research questions**

151 Based on the reviewed literature, the aims of the present study were to examine the
152 associations between recurrent parental anxiety/depression over a ten-year time span and
153 offspring anxiety/depression in adolescence and to explore the role of adolescent self-esteem
154 and physical activity in familial aggregation of anxiety/depression in a large community
155 sample. The following research questions were addressed: (1) Are maternal and paternal
156 anxiety/depression when offspring are of a preschool age associated with offspring
157 anxiety/depression when they reach adolescence; (2) are the associations between maternal
158 and paternal anxiety/depression when offspring are of a preschool age and offspring's
159 anxiety/depression in adolescence mediated by (current) maternal and paternal symptoms in
160 adolescence; (3) are the associations between parental and adolescent anxiety/depression
161 mediated by offspring self-esteem; and (4) are the associations between parental and
162 adolescent anxiety/depression and self-esteem moderated by offspring physical activity

163 levels? We will also explore sex differences in these relationships, and the model depicted in
164 Figure 1 will guide our research.

165 **Methods**

166 **Design and Procedures**

167 Our study is based on parental data from the questionnaire portion of the second and third
168 Nord-Trøndelag Health Study (termed HUNT2 and HUNT3, respectively) and offspring data
169 from the questionnaire portion of HUNT3 only. The HUNT study is a large, total population
170 health survey comprised of questionnaires and clinical examinations conducted in the county
171 of Nord-Trøndelag, Norway. HUNT2 was conducted from 1995 - 1997, and HUNT3 was
172 conducted from 2006 - 2008. In both waves, all the inhabitants in the county above the age of
173 12 were invited to participate in the study without any exclusion criteria. There are 131,000
174 inhabitants of primarily Norwegian descent in the county. In both HUNT2 and HUNT3, the
175 adult participants aged 20 and older received a letter, information brochure, and questionnaire
176 by mail. They completed the questionnaire at home and delivered it at the time of the
177 subsequent clinical examination. More details on the adult sample are published elsewhere
178 [51].

179 For adolescent participants ages 13-18, the questionnaire was administered during a class in
180 all junior high and high schools in the county. Teachers were asked to read the questions
181 aloud to adolescents with problems reading or answering the questionnaire. The adolescents
182 who were temporarily away from school on the day of survey completion received the survey
183 approximately one month later during a health exam that was also part of HUNT3.
184 Adolescents not attending school at all (4.2%) received the survey by mail. A detailed
185 description of the adolescent sample is published elsewhere [52]. Data from the adolescents

186 were linked to data from their biological or adoptive parents using each citizen's unique
187 personal national ID number.

188 **Participants**

189 HUNT3 included 8200 adolescents in lower and upper secondary school (78% response rate).
190 Most of the non-responders were not in school and were older, more often boys, and if they
191 were in school, they attended vocational rather than academic classes [52]. The participants
192 aged 12 (n=27), 19 (n=219), and 20 (n=41) were excluded from further analyses due to low
193 age sample sizes. HUNT3 included 50,827 adult participants ages 19 through 101.

194 The sample for the present study was formed by identifying those adolescents having at least
195 one biological or adoptive parent participating in the study, which excluded 2181 (28%)
196 adolescents. Thus, our analysis sample consisted of 5732 adolescents, of whom 3229 had
197 both parents, 1761 had only their mother, and 742 had only their father participating. Twenty-
198 seven of these adolescents were adopted. 3198 of the mothers (78%) and 2488 of the fathers
199 (77%) participated in HUNT2. The participant flow chart is shown in Figure 2.

200 **Measures**

201 **Adolescent variables.**

202 *Anxiety/depression symptoms* were measured using the Symptom Check List-5 (SCL-5),
203 which consists of five items from the 25-item version [53]. Whereas the SCL-5 has shown
204 very high correlations ($r = .92$) with the SCL-25 and a satisfactory reliability [54,55], a
205 distinction between anxiety and depressive symptoms is not possible from this reduced item
206 set [56]. However, the odds ratio for comorbidity between these problems is estimated to be
207 28 [57]. The tripartite model of anxiety and depression, which has received much empirical
208 support, posits that anxiety and depression often occur together due to shared genetic factors

209 and a common distress factor marked by negative affect [58]. This is evident in that some
210 symptoms are common to both anxiety and depression, whereas other symptoms are unique
211 to either anxiety or depression. Each symptom was rated on a 4-point scale (1=*not bothered*,
212 4=*very bothered*). The composite reliability (CR) was .886 and .879 for daughters and sons,
213 respectively.

214 *Self-esteem* was measured with a four-item version of the Rosenberg Self-Esteem Scale [24].
215 The items correlate highly with the original scale (0.95) [59], which has demonstrated
216 construct validity as a measure of self-esteem in a large body of literature. The items were
217 rated on a 4-point scale (1=*totally agree*, 4=*totally disagree*). The CR was .851 and .792 for
218 daughters and sons, respectively.

219 *Physical activity* was measured with one question that was also used in the World Health
220 Organization Health Behaviour in School-aged Children (WHO HBSC) survey [60]: “Apart
221 from the average school day, how many days a week do you play sports or exercise to the
222 point where you breathe heavily and/or sweat?” The question had eight response alternatives:
223 “every day”, “4–6 days a week”, “2–3 days a week”, “one day a week”, “not every week, but
224 at least once every 14th day”, “not every 14th day, but at least once a month”, “less than once a
225 month” and “never”. The question has shown acceptable validity demonstrated by
226 correlations with physical fitness measured by maximal oxygen uptake (VO₂ peak), which is
227 often considered the gold standard in assessing physical fitness [61]. In Norway, adolescents
228 in this age range also have at least 2-3 school lessons per week in Physical Education.
229 Research suggests that differences in adherence, motivation, enjoyment, and genetics exist
230 between individuals who choose to exercise regularly and those who do not [14,62,63]. Thus,
231 we dichotomised the answers into regular and low physical activity based on regular exercise
232 outside of school hours: “regular activity” represented “one day a week” or more, whereas

233 “low activity” represented “less than once a week”. Such dichotomisation has been used in
234 other studies to detect differences between low and regularly active groups (e.g., [64]).

235 **Parental variables.**

236 *Symptoms of anxiety/depression* were measured by the Cohort Norway Mental Health Index
237 (CONOR-MHI) [65], which consists of seven items based on the General Health
238 Questionnaire [66] and the Hopkins Symptom Check List [53]. The CONOR-MHI correlates
239 highly with both the Symptom Check List-10 (SCL-10) ($r = .82$) and the Hospital Anxiety
240 and Depression Scale (HADS) [67] ($r = .91$), but separating anxiety and depressive
241 symptoms is not possible [65]. Examples of items include “Have you, in the course of the last
242 two weeks, felt nervous and unsettled?” and “...happy and optimistic?” Each item was rated
243 on a 4-point scale (1=*no*, 4=*very much*). To be able to describe a group with high
244 anxiety/depression, we used the mean cut-off value of ≥ 2.15 , which was established from
245 cut-off values of the SCL-10 and HADS that were shown to identify anxiety disorders and
246 major depressive disorder [65]. For daughters and sons, respectively, the CR for maternal
247 anxiety/depression when offspring were adolescents was .932 and .915, while at preschool
248 age the CR was .920 and .908; for paternal anxiety/depression, the CR when offspring were
249 adolescents was .923 and .914, and at preschool age the CR was .898 and .909.

250 For descriptive purposes, *Physical activity* in parents was measured by one question: “How
251 often do you exercise?” The question had five response alternatives: “never”, “less than once
252 a week”, “once a week”, “2–3 times a week”, and “approximately every day”.

253 **Ethics**

254 All participants in the study, and at least one parent when the adolescent was under 16 years
255 of age, signed a written informed consent to participate. This study was approved by the

256 Regional Committee for Medical and Health Research Ethics (reference number
257 4.2007.2416).

258 **Statistics**

259 To reduce the likelihood of respondent fatigue, short forms of established measurement
260 scales were used in this survey. To ensure the validity of the short forms, we analysed the
261 data by structural equation modelling, as recommended [68]. The models were estimated with
262 the weighted least squares mean and variance adjusted estimator (WLSMV) due to the
263 categorical and non-normal nature of the indicators. To explore sex differences, we estimated
264 multi-group models separating daughters and sons and tested possible differences with Wald
265 tests of parameter constraints.

266 Prior to examining the aims of the study by estimating the path models, measurement
267 invariance was explored. By including increasingly more restrictions, configural, metric, and
268 scalar measurement invariance were tested [69]. When scalar invariance is established,
269 measurement invariance is assumed [70]. This indicates that the sex differences in the means
270 of the observed items stem from differences in the means of the latent variables. Within the
271 latent variable modelling framework, several fit indices are usually examined. A non-
272 significant χ^2 - statistic, CFI- and TLI-values $> .95$, and RMSEA-values $< .06$ indicate a good
273 model fit [71]. When evaluating measurement invariance, we also examined CFI-differences
274 and RMSEA-differences, as has been recommended [72]^a, because χ^2 -difference tests are
275 sensitive to sample size and model complexity [73]. $\Delta\text{CFI} \geq .010$ and $\Delta\text{RMSEA} \geq .015$
276 indicate measurement noninvariance [72]. We used composite reliability (CR) to evaluate
277 internal consistency because unlike the coefficient alpha, CR does not assume that all items
278 are equally good indicators of the latent variable measured [74]. An estimated $\text{CR} \geq .7$
279 indicates a good reliability, and a CR of $.6 - .7$ is considered acceptable.

280 Four structural models were tested (see Figures 3-6). When estimating indirect paths in the
281 mediation models, we followed the recommended procedures with 1,000 bootstrap samples
282 [75]. Multi-group mediation models were used to test moderated mediation because such
283 analyses with latent variables often result in model non-convergence. As recommended [75],
284 the indirect effects, the difference between the direct and indirect effects and between the
285 effects across groups were tested by computing new parameters and examining their
286 statistical significance. Portions of our sample were hierarchically structured. A total of 2062
287 adolescents had at least one sibling also participating, whereas 3670 adolescents did not have
288 a participating sibling. Standard errors and χ^2 -tests were corrected for this potential cluster
289 effect in the analyses when possible^b. Adolescent age was associated with symptoms of
290 anxiety/depression but not with self-esteem. Thus, we adjusted for age in the paths including
291 adolescent anxiety/depression. Parental marital status was not related to our dependent
292 variables, and we did not adjust for this variable.

293 The sample size was large; however, the magnitude of effects was small because most
294 participants in community samples were healthy. Thus, we considered two-sided p-values <
295 .05 as statistically significant. We used IBM SPSS Statistics 19 for the descriptive statistics.
296 The main analyses were performed using Mplus, version 7.11 [76]. There was a low rate of
297 missing values in the data set ($\leq 4\%$). Thus, all missing values were handled by the full
298 information maximum likelihood procedure (FIML) in Mplus.

299 **Results**

300 **Demographic and sample characteristics**

301 Characteristics of the sample have been reported in a previous publication [2]. The
302 proportions of adolescent daughters (50.3%) and sons (49.7%) were approximately the same.

303 There was no difference in the mean age for daughters ($M = 15.8$; $SD = 1.7$) and sons ($M =$
304 15.8 ; $SD = 1.6$). One-third of the adolescents reported having parents not living together.
305 There were more mothers than fathers participating (56% vs. 44%). As expected, the mothers
306 were significantly younger ($M = 44.2$; $SD = 5.2$) than the fathers ($M = 47.6$; $SD = 5.9$) (t
307 $(7306) = 26.104$, $p < .001$). Consistent with the overall Norwegian population, the mothers
308 had higher levels of education ($M = 4.43$; $SD = 1.54$) than the fathers ($M = 4.21$; $SD = 1.47$)
309 ($t(7322) = 6.188$, $p < .001$). The most frequent educational level was upper secondary
310 education, which was somewhat higher than in the general Norwegian population [77]. When
311 the offspring were of a preschool age, 7.5% of the mothers and 4.0% of the fathers were
312 identified with anxiety/depression by scoring above the cut-off value, whereas when the
313 offspring were adolescents, the corresponding proportions were 6.8% for the mothers and
314 5.9% for the fathers. 14.5% ($N=591$) of mothers and 27.4% ($N=889$) of fathers reported
315 exercising less than once a week (low physical activity), whereas 84.8% ($N=3466$) of
316 mothers and 71.3% ($N=2310$) of fathers reported exercising once a week or more (regular
317 physical activity). Parental anxiety/depression was negatively associated with parental
318 physical activity for both the mothers ($\beta (SE) = -.108 (.018)$, $p < .001$) and the fathers ($\beta (SE)$
319 $= -.071 (.021)$, $p = .001$). A total of 87.6% of the adolescents were in the regular physical
320 activity group ($N=5023$), whereas 12.4% were in the low physical activity group ($N=709$).
321 There were no sex differences in the regular (50.2% daughters) and low (50.9% daughters)
322 activity groups. In a previous study, we found that adolescents who were excluded due to not
323 having parents participating in the study had significantly more symptoms of
324 anxiety/depression and a lower self-esteem than those with participating parents, but the
325 effect sizes for these differences were very small (Cohen's $d < .14$) [2]. Adolescents without
326 participating parents were also significantly less physically active than adolescents with

327 participating parents ($t(7787) = 3.319, p < .01$), but the effect size for this difference was also
 328 very small ($d = .08; r = .04$).

329 **Measurement models**

330 Most fit indices for the measurement models indicated a good fit of all the models, but the χ^2 -
 331 statistic was significant, as expected for the large sample size and the complex model
 332 ([*configural* model: $\chi^2(1228, N=5732) = 6333, p < .001$; CFI = .951; TLI = .947; RMSEA =
 333 .038]; [*metric* model: $\chi^2(1259, N=5732) = 6435, p < .001$; CFI = .951; TLI = .948; RMSEA
 334 = .038]; [*scalar* model: $\chi^2(1326, N=5732) = 6450, p < .001$; CFI = .951; TLI = .951;
 335 RMSEA = .037]). Neither ΔCFI nor $\Delta RMSEA$ indicated a worse fit to the data when more
 336 restrictions were added ($\Delta CFI = .000$; $\Delta RMSEA = .001$). Thus, scalar measurement
 337 invariance was established. Also indicating a good model fit, the unstandardised factor
 338 loadings in the scalar model were satisfactory and statistically significant ($p < .001$) for all
 339 indicators: self-esteem ($.890 \leq b \leq 1.000$); offspring anxiety/depression ($.985 \leq b \leq 1.083$);
 340 maternal anxiety/depression when offspring were adolescents ($.632 \leq b \leq 1.000$); paternal
 341 anxiety/depression when offspring were adolescents ($.715 \leq b \leq 1.000$); maternal
 342 anxiety/depression when offspring were of a preschool age ($.720 \leq b \leq 1.000$); paternal
 343 anxiety/depression when offspring were of a preschool age ($.705 \leq b \leq 1.000$). Further details
 344 of the measurement models are available from the authors. Table 1 displays the correlations
 345 among the variables.

346 **Is parental anxiety/ depression when offspring were of a preschool age associated with** 347 **offspring anxiety/depression in adolescence?**

348 Both maternal and paternal symptoms of anxiety/depression when offspring were of a
 349 preschool age were weakly but significantly associated with such symptoms in adolescent
 350 offspring approximately ten years later (see Figure 3). Except for a significant χ^2 -test, which

351 was expected due to the large sample size, the fit indices for the model were good, (χ^2 (348,
352 $N = 5707) = 1787, p < .001$; CFI = .968; TLI = .969; RMSEA = .038). Although the path
353 from paternal symptoms to sons' symptoms was not significant, this path was not
354 significantly different for daughters and sons (Wald test of parameter constraints (1) = 0.159,
355 $p = .69$). When constraining the parameters to be equal for daughters and sons, the model fit
356 was even better, and all the paths were significant. This indicates that both maternal and
357 paternal anxiety/depression when offspring were of a preschool age were associated with
358 such symptoms in both daughters and sons ten years later.

359 **Are the associations between parental anxiety/depression when offspring were of a**
360 **preschool age and offspring anxiety/depression in adolescence mediated by current**
361 **parental symptoms?**

362 When including current parental anxiety/depression, the associations between an adolescent
363 offspring's symptoms of anxiety and depression and such symptoms in parents when
364 offspring were of a preschool age were fully mediated by parental anxiety/depression in
365 adolescence (see Figure 4). Additionally, the fit indices were good for this model (χ^2 (1124, N
366 $= 5732) = 5819, p < .001$; CFI = .950; TLI = .951; RMSEA = .038). There were no
367 significant sex differences, indicating that the associations between both maternal and
368 paternal anxiety/depression when offspring were at a preschool age and daughters' and sons'
369 anxiety/depression in adolescence were mediated by current maternal and paternal
370 anxiety/depression.

371 **Are familial associations of anxiety/depression mediated by adolescent self-esteem?**

372 An initial model showed that parental anxiety/depression when offspring was of a preschool
373 age was not associated with later adolescent self-esteem for either sex. Thus, we analysed a
374 new model excluding these paths and only including current parental anxiety/depression,

375 shown in Figure 5. The fit indices for this model were good (χ^2 (1408, N=5732) = 6397, $p <$
376 .001; CFI = .953; TLI = .953; RMSEA = .035). The results from this model (see Figure 5)
377 showed that adolescent self-esteem was significantly associated with adolescent
378 anxiety/depression for both sexes. For both daughters and sons, the indirect paths from both
379 maternal (daughters: β (SE) = -.064 (.016), $p < .001$; sons: β (SE) = -.035 (.016), $p = .028$)
380 and paternal anxiety/depression (daughters: β (SE) = -.069 (.018), $p < .001$; sons: β (SE) = -
381 .059 (.016), $p = .001$) to offspring anxiety/depression via offspring self-esteem were also
382 significant. For sons, the direct paths from both maternal and parental anxiety/depression to
383 son anxiety/depression were still significant. For daughters, the direct path from paternal
384 anxiety/depression to daughter anxiety/depression was still significant, whereas the direct
385 path from maternal anxiety/depression was not. This path was, however, not significantly
386 different for daughters and sons (Wald test of parameter constraints (1) = 1.181, $p = .28$), and
387 when constraining the parameters to be equal for both daughters and sons, both maternal and
388 paternal anxiety/depression were significantly associated with anxiety/depression in both
389 daughters and sons. Thus, parental anxiety/depression was still significantly directly
390 associated with offspring anxiety/depression in adolescence. The direct and indirect effects
391 were not significantly different either for daughters (b (SE) = .021 (.026), $p = .412$) or sons (b
392 (SE) = -.028 (.031), $p = .368$). Thus, parental and adolescent anxiety/depression were partly
393 directly associated and partly mediated by a low adolescent self-esteem.

394 **Does adolescent physical activity protect against familial aggregation of**
395 **anxiety/depression?**

396 Finally, we examined whether adolescent physical activity moderated the direct or indirect
397 paths associating parental anxiety/depression with offspring anxiety/depression. We
398 conducted multi-group analyses with two groups consisting of adolescents who responded
399 “low” vs. “regular” on self-initiated physical activity. In this model, we did not distinguish

400 between daughters and sons because there were no significant sex differences in the previous
401 model (reported above) and because the proportion of daughters and sons were the same in
402 both the low (50.9% daughters) and the regular (50.2% daughters) physical activity group
403 ($Z=-0.353$; $p=.726$). The fit indices for the model were good ($\chi^2(553, N=5732) = 3973, p <$
404 $.001$; CFI = .955; TLI = .955; RMSEA = .046).

405 This model (see Figure 6) showed that the difference between the direct associations between
406 maternal and offspring anxiety/depression was significant in the low vs. regular activity
407 groups ($b(SE) = -.124(.051), p = .015$). This indicates that maternal and offspring
408 anxiety/depression were not directly associated among adolescents exercising at least once a
409 week outside of school hours. The drop in estimates between maternal anxiety/depression and
410 offspring self-esteem was, however, not significant ($b(SE) = -.057(.054), p = .291$). The
411 direct and indirect paths were significantly different ($b(SE) = .628(.039), p < .001$),
412 indicating that regular physical activity moderated the direct path between maternal and
413 offspring anxiety/depression but not the indirect paths between maternal and offspring
414 anxiety/depression via offspring self-esteem. Physical activity did not moderate the
415 associations between paternal and adolescent anxiety/depression either directly ($b(SE) = -$
416 $.007(.058), p = .911$) or indirectly via offspring self-esteem ($b(SE) = -.014(.039), p = .710$).
417 Thus, only the direct path between maternal and adolescent anxiety/depression was
418 moderated by physical activity. Although the indirect paths between parental and offspring
419 anxiety/depression via self-esteem were not moderated, the regular activity group did have a
420 significantly higher self-esteem than the low activity group ($b(SE) = .346(.043), p < .001$).

421 **Discussion**

422 Our results showed that parental anxiety/depression when offspring were of a preschool age
423 is associated with such problems in adolescent offspring, but these associations are entirely

424 mediated by current parental symptoms. The familial associations are evident for both
425 daughters and sons regardless of whether anxiety/depression is present in mothers or fathers,
426 thus extending previous research findings to also include paternal symptoms. Our findings
427 also indicated that adolescent self-esteem partly mediates the associations between
428 anxiety/depression in parents and their offspring. Finally, physical activity seems to moderate
429 the direct associations between anxiety/depression in mothers and offspring, whereas no such
430 moderating effect is evident with regard to paternal anxiety/depression. To our knowledge,
431 the present study was the first to suggest that physical activity may protect against familial
432 aggregation of anxiety/depression.

433 **Familial aggregation of anxiety/depression**

434 Parental anxiety/depression when offspring were of a preschool age was weakly associated
435 with such problems in offspring in adolescence, and this relationship was entirely mediated
436 by current anxiety/depression in parents. This may imply that the stability of parental mental
437 health problems leads to problems in offspring, although our findings may also support
438 previous research suggesting a reciprocal relationship between at least maternal and offspring
439 depressive symptoms in children ages 5-7 [19]. Whereas we lacked information about
440 offspring mental health at a preschool age to test this more directly, this directionality is
441 partly supported by studies showing that improvement in parental depression leads to
442 improvement in offspring psychopathology [78,79], whereas continued maternal symptoms
443 are related to fewer declines or elevations of symptoms in offspring [20]. That this effect was
444 fully mediated by parental anxiety/depression in adolescence in our study suggests a 10-year
445 stability of these problems among adults. Furthermore, our findings may reflect the chronic
446 nature of anxiety and depression, which has also been reported in previous studies [80,81].
447 Studies show that recurrent maternal depression is related to a higher risk of such problems in
448 offspring [22], and nearly 60% of adolescents with anxiety and depression have further

449 episodes in adulthood [82]. These findings point to the risk associated with stability, and
450 likely chronicity, in parental anxiety/depression, and indicates that it is vital to prevent
451 familial aggregation of these problems as early as possible. Our results may suggest that
452 parental psychopathology in the early years of life may have long-term implications for
453 offspring and trigger negative developmental cascades. Thus, health professionals working
454 with adults with anxiety/depression should be aware of the possible negative consequences
455 for offspring and seek to prevent the development of such symptoms in the offspring.
456 Furthermore, these findings emphasize the importance of addressing mental health problems
457 in a familial context. Our study expands on previous research by examining associations
458 between recurrent paternal anxiety/depression and such problems in offspring. We found that
459 both maternal and paternal problems were associated with offspring anxiety/depression, and
460 there were no significant sex differences. This underscores the importance of including both
461 mothers and fathers when studying familial aggregation of mental health problems and
462 highlights the fact that paternal anxiety and depression is just as important for the mental
463 well-being of adolescents as maternal problems. Thus, our findings point to the importance of
464 assessing the mental status of the entire immediate family both in clinical practice and in
465 research, as we also reported in a previous study [2].

466 **Self-esteem as a mediator in familial aggregation of anxiety/depression**

467 The fact that low self-esteem partially mediated the associations between parental and
468 offspring anxiety/depression is in accordance with the developmental model detailing that
469 children of depressed mothers are exposed to risks that may eventually create a vulnerability
470 for low self-esteem, which over time increases the risk for depression, especially in
471 adolescence [34,35]. Our findings also support previous studies showing that children of
472 parents with depression have lower self-esteem than children of healthy parents [2,29-32].
473 Likewise, our results support previous findings that offspring self-worth partly mediates the

474 associations between maternal and offspring depression [22]. Again, our study demonstrates
475 the role of fathers by indicating that self-esteem also partly mediates associations between
476 paternal and offspring symptoms of anxiety/depression in addition to associations between
477 maternal and offspring symptoms. These results also emphasise the importance of including
478 both mothers and fathers in studies of familial aggregation of mental health problems.
479 Additionally, our findings indicated that self-esteem partly mediates the associations between
480 symptoms of both anxiety and depression, as suggested in the tripartite model [58], and not
481 only symptoms of depression. Future research should examine whether self-esteem also
482 mediates parental and offspring anxiety. Because different anxiety disorders are differently
483 related to the factors of the tripartite model [83,84], it will also be important to distinguish
484 among anxiety disorders when further examining the etiological role of self-esteem.

485 **Physical activity as a moderator in familial aggregation of anxiety/depression**

486 Our findings suggested that physical activity moderates the direct associations between
487 maternal and offspring anxiety/depression but not between paternal and offspring
488 anxiety/depression. Additionally, physical activity did not moderate the indirect paths
489 associating parental and offspring anxiety/depression via self-esteem. As we have not been
490 able to find studies examining the role of physical activity in familial aggregation of anxiety
491 and depression, these findings should serve as the basis for further research on this subject.
492 Nonetheless, our findings support studies showing an inverse association between physical
493 activity and anxiety/depression [42,43,45] because maternal and adolescent
494 anxiety/depression were not associated in adolescents reporting self-initiated physical activity
495 beyond that prescribed in school. This indicates that physical activity can act as an important
496 protective factor against anxiety/depression in adolescents with mothers with such problems.
497 Hence, beyond treating adults with symptoms of anxiety/depression, it is important that

498 professionals working in the primary care services also inform about the positive effects of
499 and encourage physical activity in the family.

500 Physical activity did not moderate the associations between paternal and offspring
501 anxiety/depression. This may be explained by the fact that a father's physical activity is
502 shown to be one of the strongest predictors for physical activity in adolescents, whereas a
503 mother's physical activity appears less important [85-87]. This is corroborated by the finding
504 that fathers with anxiety/depression were significantly less physically active than healthy
505 fathers. Thus, the offspring of fathers with anxiety/depression may also be less physically
506 active, whereas in families with a healthy and physically active father, adolescents most
507 likely exercise more. Further research is necessary to examine these hypotheses.

508 Biochemical, physiological and psychological mechanisms explaining the relationships
509 between physical activity and anxiety/depression have been proposed [14,88,89]. One of the
510 most important psychological mechanisms is the distraction hypothesis, which posits that the
511 "time out" from difficult thoughts during exercise results in reduced anxiety and depression
512 [90]. Another possible mechanism stems from the self-determination theory [41], which
513 claims that physical activity may increase feelings of autonomy, competence and provide
514 more possibilities for social interaction, which are properties shown to increase self-esteem
515 and reduce anxiety and depression [91]. Finally, physical activity may reduce anxiety and
516 depression by increasing self-esteem [49], but in this study, physical activity did not affect
517 the paths associating parental and offspring anxiety/depression via self-esteem. However, the
518 regular activity group did have a significantly higher self-esteem than the low activity group.
519 Physical activity may potentially increase self-esteem or vice versa, but further research is
520 necessary to explore the precise nature of these relationships.

521 As mentioned previously, there is ambiguity with regard to the effect of physical activity on
522 anxiety and depression in existing research [46]. This study expands on previous research by
523 suggesting that adolescents exercising with moderate to vigorous intensity at least once a
524 week outside of school may be protected against symptoms of anxiety and depression when
525 having a mother with such symptoms. The differential susceptibility hypothesis [92] claiming
526 that children at risk (e.g. due to having parents with anxiety/depression) may be more
527 strongly influenced by positive environmental experiences might be relevant for our findings.
528 Physical activity may be a positive experience affecting children of parents with
529 anxiety/depression more strongly than children of healthy parents, and thus partly account for
530 the previous ambiguous findings in this research area. Future research should examine the
531 possible thresholds for positive consequences of physical activity and the cause-effect
532 relationships between physical activity and symptoms of anxiety/depression further, for
533 example by employing latent class analysis, cross-lagged autoregressive analysis, or possibly
534 conducting a randomized controlled trial.

535 **Strengths and limitations**

536 The inclusion of a large number of fathers (> 3000) is an important addition to previous
537 research examining familial aggregation of anxiety/depression and the mediational role of
538 self-esteem. Additionally, our study is the first that we have been able to find that examines
539 whether physical activity moderates the associations between parental and offspring
540 anxiety/depression. Such investigations examining the factors important for positive mental
541 health have been suggested by the ROAMER project [9]. In addition, we assessed moderated
542 mediation by examining whether physical activity affected the mediational paths from
543 parental to offspring anxiety/depression via offspring self-esteem using advanced statistical
544 methods. Using data from a large community sample with a high response rate also made it
545 possible to examine sex differences without jeopardising the statistical power. There was a

546 low degree of missing values in the present study (< 4.0%), which removed the need to use
547 multiple imputation to handle the missing values. Finally, we were able to examine some of
548 the hypotheses using a long-term longitudinal design.

549 There are several limitations in the current study. First, because this is a correlational study,
550 causal processes cannot be determined. Thus, even though we emphasised the interpretation
551 that parental mental health problems likely lead to problems in offspring, the reverse or
552 reciprocity cannot be ruled out. Additionally, our assumption that self-esteem leads to
553 depression was based on previous research findings and was not examined in the present
554 study. Further longitudinal studies can advance inferences about the direction of associations
555 between the variables measured in our study. Using data from a large community sample
556 with a high response rate would usually indicate representative results, but the adolescents
557 without participating parents in the HUNT3 study had slightly more symptoms of
558 anxiety/depression, had lower self-esteem, and were less physically active than the
559 adolescents with participating parents. This might result in an underestimation of the
560 observed associations in the present study, but the small effect size should partially abate that
561 concern. Additionally, the participation rate of adolescents not in school was too low to be
562 representative, possibly leading to an underestimation of associations because this group may
563 have a worse mental health and life style. Also, the generalizability of our findings to other
564 cultures may be limited. Norway is a wealthy country with significant resources available to
565 the whole population, including prominently universal public health insurance coverage and
566 equal status of the sexes. The socioeconomic health inequalities in the county of Nord-
567 Trøndelag are, however, comparable to other countries in Northern Europe [93], suggesting
568 that the findings at least may be representative for other North European countries. Future
569 research should examine whether our findings also can be generalized to other cultures.
570 Although self-reports may be biased, studies generally find self-reports of mental health and

571 physical activity to be valid [94]. With the measures used here, we were not able to
572 differentiate between anxiety and depression. However, because the comorbidity between
573 these problems is high [57], this limitation may be mitigated. Other relevant mediators and
574 moderators were not examined; thus, future research should include more variables to
575 broaden the understanding of familial aggregation of anxiety and depression.

576 **Conclusions**

577 Our findings suggest that the children of parents with anxiety/depression problems are at a
578 sustained risk for mental health problems due to the chronic nature of these symptoms, as
579 shown by the apparent 10-year stability of both maternal and paternal anxiety/depression.
580 Thus, preventing familial aggregation of these problems as early as possible seems vital.
581 Because our study indicates that the associations between parental and offspring
582 anxiety/depression are partially mediated by offspring self-esteem, efforts could be aimed at
583 increasing self-esteem in vulnerable children as early as possible in life. Engaging in
584 activities that fulfil an individual's basic needs of autonomy, competence, and relatedness has
585 been shown to increase self-esteem [91]; thus, encouraging such activities may also serve to
586 mitigate familial aggregation of anxiety/depression. Furthermore, because this study is one of
587 the first to suggest that physical activity can reduce familial aggregation of
588 anxiety/depression, this could be an important focus for future prevention and treatment
589 efforts. Thus, clinicians should view symptoms of anxiety and depression as a familial
590 problem, and inform about the possible positive consequences of physical activity and work
591 to increase motivation and possibly prescribe exercise programs for adolescents exercising
592 less than once a week outside of school. From a public health perspective, it seems important
593 to encourage physical activity in the offspring of parents with anxiety/depression, possibly
594 from early in life.

595 **Endnotes**

596 ^aIt should be noted that these recommendations are based on simulation studies using
597 maximum likelihood estimations of continuous data. No standards for such evaluations of
598 alternative fit indices exist for WLSMV estimations [95], although there are some indications
599 that the WLSMV Δ RMSEA performs particularly well [96]. ^bThe adjustment for cluster
600 effects is not available with bootstrapping. Thus, we examined the differences between
601 bootstrapped estimates without clustering and non-bootstrapped estimates with clustering.
602 Not adjusting for clustering resulted in lower chi-square values but no evident differences in
603 the standard errors.

604 **Abbreviations**

605 HUNT, the Nord-Trøndelag Health Study; SCL, symptom check list; WHO HBSC, World
606 Health Organization Health Behaviour in School-aged Children; VO₂ peak, maximal oxygen
607 uptake; CONOR-MHI, Cohort Norway Mental Health Index; HADS, Hospital Anxiety and
608 Depression Scale; WLSMV, weighted least squares mean and variance adjusted estimator;
609 CFI, comparative fit index; TLI, Tucker-Lewis Index; RMSEA, root mean square error of
610 approximation; CR, composite reliability; FIML, full information maximum likelihood.

611 **Competing interests**

612 The authors declare that they have no competing interests.

613 **Authors' contributions**

614 IR was mainly responsible for the design, analyses and drafting of the manuscript. FS
615 contributed to the design, analyses, and interpretation of the results. CAK supervised in
616 conducting the statistical analyses and interpreting the findings. JW and TJ contributed to the

617 design and supervised the whole process. All authors critically reviewed and revised versions
618 of the manuscript. All authors read and approved the final manuscript.

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905 **Figure legends**

906 **Figure 1 – Conceptual model examined in the present study**

907 We tested for invariance across sexes and different levels of offspring physical activity.

908 **Figure 2 – Flowchart of the participants in the present study**

909 **Figure 3 – Associations between parental anxiety/depression when offspring were at**
910 **preschool age and offspring anxiety/depression in adolescence**

911 Standardised coefficients and p values are presented. Associations for daughters are presented
912 in the upper part of the figure; associations for sons are presented in the lower part of the
913 figure.

914 **Figure 4 – Parental anxiety/depression in adolescence as a mediator**

915 The associations between parental anxiety/depression when offspring were preschool aged
916 and offspring anxiety/depression in adolescence mediated by parental anxiety/depression in
917 adolescence for daughters (the upper part of the figure) and sons (the lower part of the
918 figure), presented with standardised coefficients and p values (statistically significant paths
919 are in black ($p < .05$), non-significant paths are in grey).

920 **Figure 5 – Adolescent self-esteem as a mediator**

921 The associations between parental anxiety/depression and adolescent offspring
922 anxiety/depression mediated by adolescent self-esteem presented with standardised
923 coefficients and p values. Associations for daughters are presented in the upper part of the
924 figure; associations for sons are presented in the lower part of the figure.

925 **Figure 6 – Adolescent physical activity level as a moderator**

926 The associations between parental anxiety/depression and offspring anxiety/depression in
927 adolescence mediated by adolescent self-esteem for the two physical activity groups (low and
928 regular) is presented with standardised coefficients and p values (statistically significant paths

929 are in black ($p < .05$), non-significant paths are in grey). Associations for the low physical
930 activity group are presented in the upper part of the figure; associations for the regular
931 physical activity group are presented in the lower part of the figure.

932

933 **Table**934 **Table 1 – Correlations of the variables (standard errors in parentheses)**

935 Daughters are below the diagonal and sons are above the diagonal. All correlations were
 936 statistically significant ($p < .05$), except if otherwise indicated by a superscript.

Daughters \ Sons	1	2	3	4	5	6	7
1. Offspring anxiety/depression		.571 (.020)	.119 (.024)	-.118 (.028)	-.138 (.031)	-.103 (.031)	-.093 (.035)
2. Offspring self-esteem	.640 (.015)		.225 (.022)	-.075 (.028)	-.107 (.030)	-.066 (.031)	-.092 (.033)
3. Offspring physical activity	.134 (.022)	.195 (.021)		-.071 (.024)	-.076 (.026)	-.069 (.027)	-.080 (.030)
4. Maternal anxiety/depression	-.129 (.026)	-.106 (.025)	-.027 (.023) ^{n.s.}		.231 (.035)	.506 (.025)	.149 (.038)
5. Paternal anxiety/depression	-.202 (.027)	-.102 (.029)	-.131 (.026)	.263 (.032)		.209 (.038)	.551 (.030)
6. Maternal preschool anxiety/depression	-.090 (.027)	-.109 (.029)	-.055 (.026)	.495 (.025)	.146 (.036)		.323 (.040)
7. Paternal preschool anxiety/depression	-.096 (.033)	-.138 (.034)	-.107 (.031)	.060 (.037) ^{n.s.}	.546 (.027)	.208 (.039)	

937

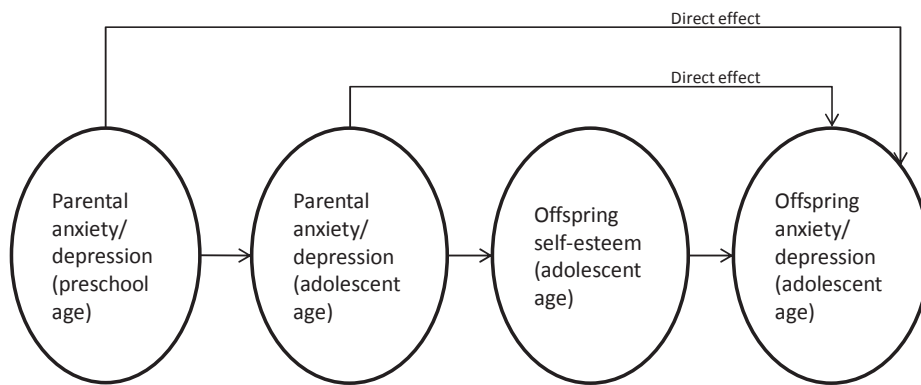


Figure 1

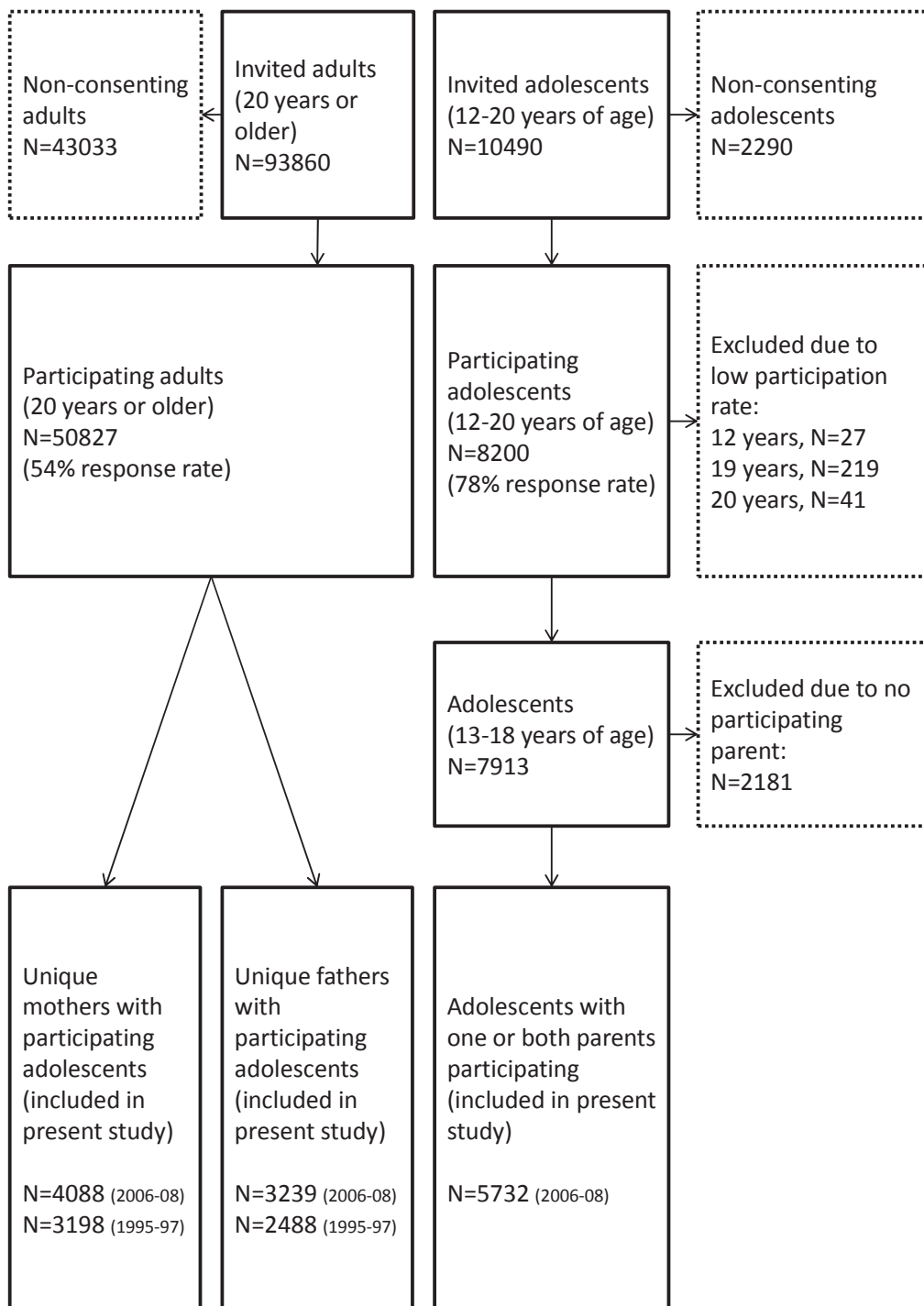


Figure 2

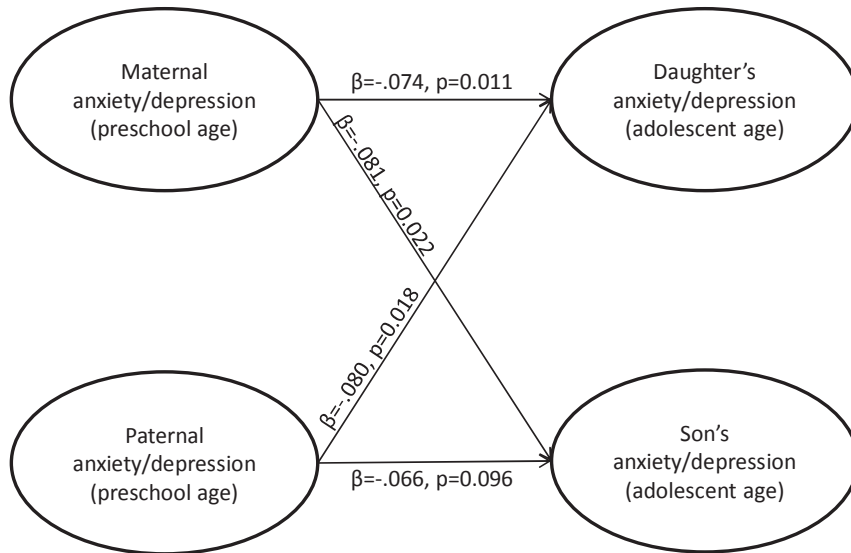


Figure 3

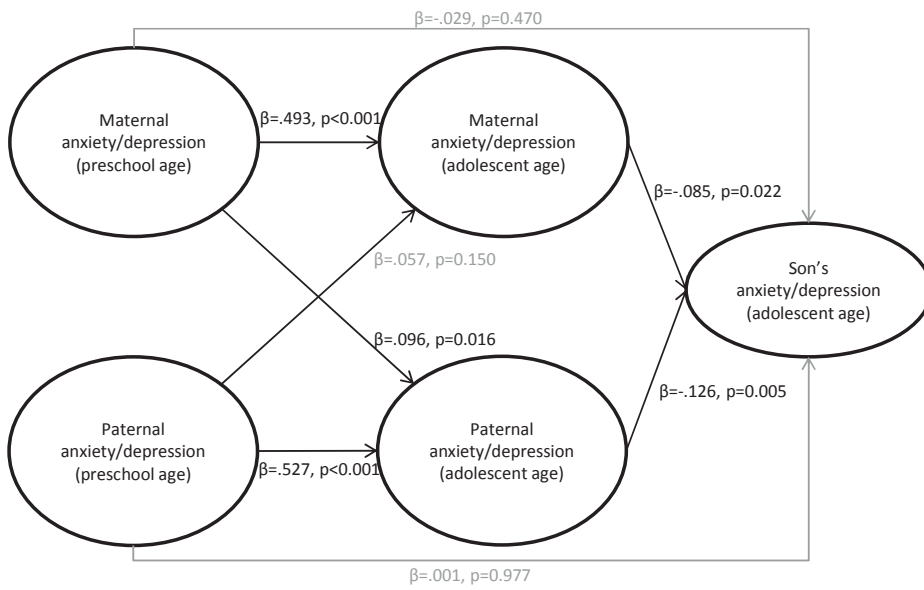
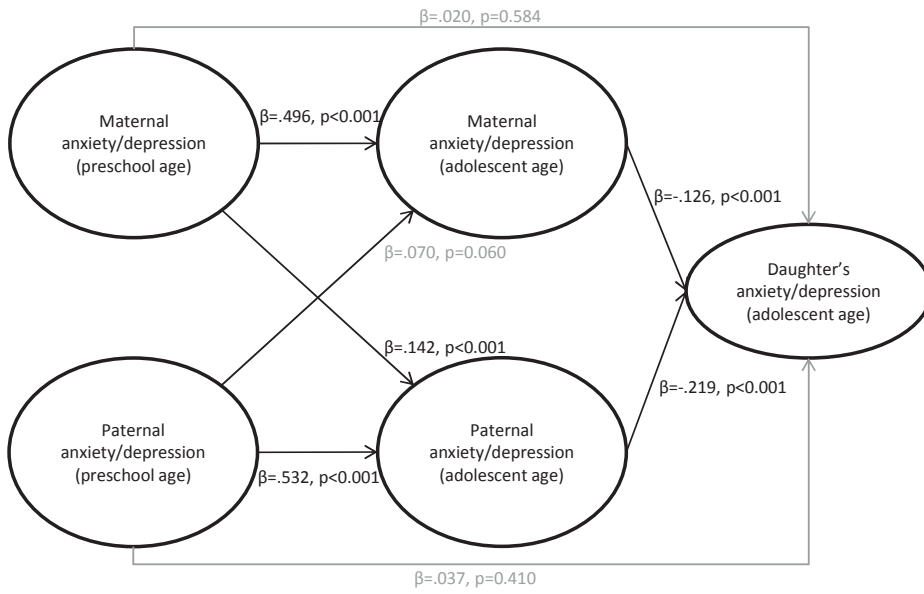


Figure 4

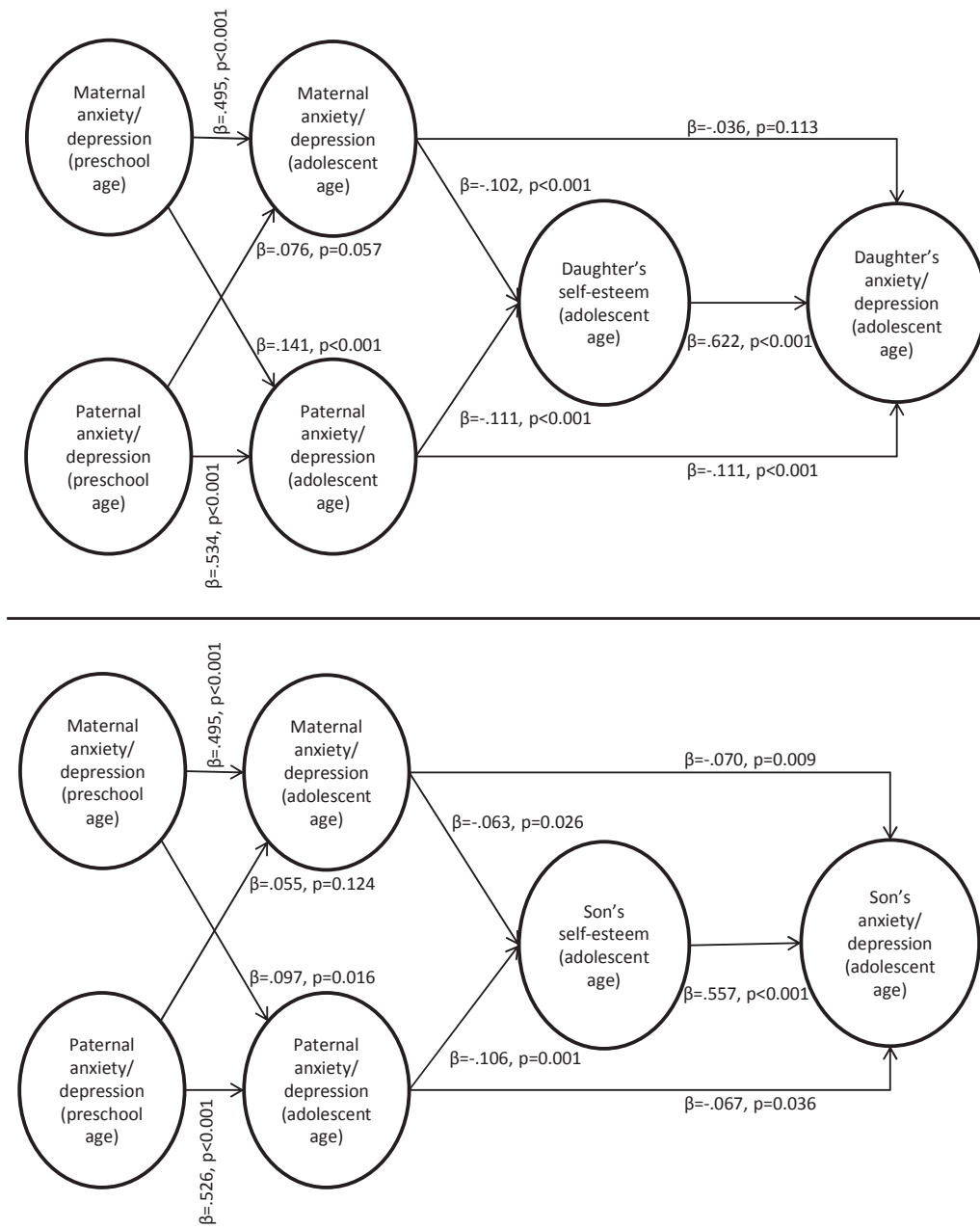
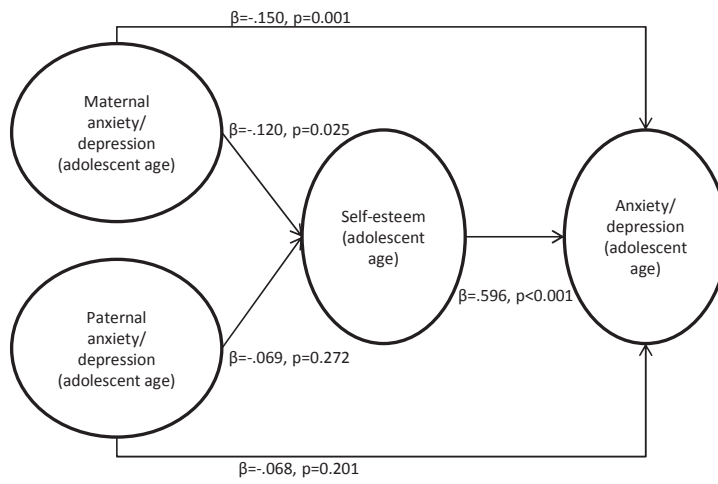


Figure 5

Adolescent low physical activity:



Adolescent regular physical activity:

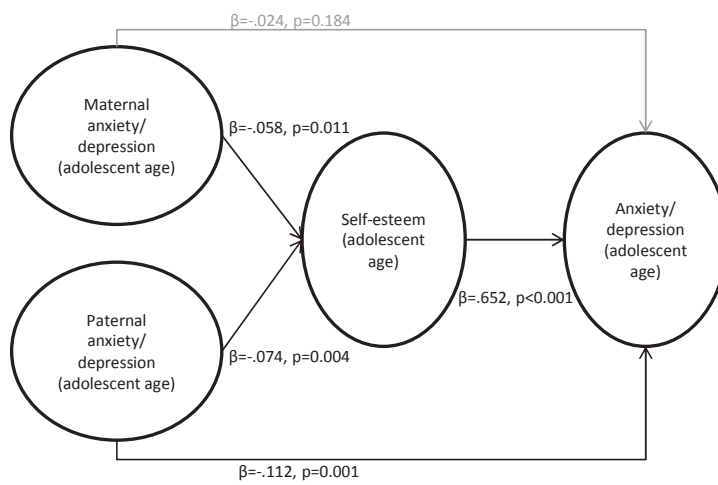


Figure 6

Paper III

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