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FOSTERING THE DEVELOPMENT OF MENTAL HEALTH – RISK AND PROMOTIVE FACTORS

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Abstract

The Developmental Origins of Health and Disease (DOHaD) framework posits that foundations of mental health can be traced to the earliest stages of life, namely to the prenatal and early childhood periods. Evidence exists that early life stress (ELS) in childhood, including e.g., physical and emotional maltreatment, and in the prenatal period, including e.g., maternal psychological distress during pregnancy, is associated with adverse mental health and psychological development in the offspring. According to extensive evidence, the adverse effects of ELS extend to mental health in early adulthood, but less is known about whether ELS is associated with the risk of psychopathology still in late adulthood. Moreover, much less is known about whether there may be promotive and protective factors for offspring mental health during pregnancy, such as positive maternal mental health.

This thesis investigates the associations of positive maternal mental health during pregnancy, including maternal positive emotions and social support, with mental health and cognitive development in the offspring, utilizing two prospective longitudinal pregnancy cohorts. Furthermore, the thesis investigates the associations of childhood ELS with late adulthood anxiety, utilizing a third birth cohort. The thesis consists of four studies. Studies I−II investigated the associations of positive maternal mental health during pregnancy with child mental and behavioral disorders among 3378 mother-child-dyads (Study I) and with psychiatric problems in children in early and late childhood among 2636 mother-child-dyads (Study II) of the Finnish Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) study. Study III investigated the associations and timing effects of maternal social support during and after pregnancy on child cognitive development, more specifically general cognitive ability in late childhood, among 5784 mother-child-dyads of the UK-based Avon Longitudinal Study of Parents and Children (ALSPAC) and among 420 mother-child-dyads of the PREDO studies. Finally, Study IV examined the association of ELS, defined here as physical and emotional maltreatment, parental divorce, death of a family member, low socioeconomic status (SES) and separation from parents in childhood, with anxiety symptoms at age 65−77 years among 1872 participants of the Finnish Helsinki Birth Cohort Study (HBCS).

The results of this thesis indicated that positive maternal mental health during pregnancy was associated with a lower risk of mental and behavioral disorders from birth to 8.4−12.8 years of age and with lower dimensionally assessed psychiatric problems at 1.9−5.9 and at 7.1−12.1 years of age among children. Furthermore, higher perceived maternal social support during and after pregnancy was associated with higher general cognitive ability among children at 8 years of age; pregnancy emerged as a potential sensitive period for the beneficial effects of maternal social support on

cognitive ability in children. The associations in all three studies were independent of maternal depressive and/or anxiety symptoms during pregnancy and of lifetime mental and behavioral disorders. The associations were also independent of later positive maternal mental health. Finally, experiencing physical and emotional maltreatment and lower SES in childhood were associated with higher anxiety symptoms in late adulthood, and these early life adversities and parental divorce in childhood were further associated with a risk of clinically relevant anxiety symptoms. The accumulation of ELS experiences was associated with higher risks of both dimensionally assessed and clinically relevant anxiety symptoms.

The findings of this thesis support the DOHaD framework by suggesting that both the prenatal and postnatal environment contribute to the programming of child development, and that this programming extends from early adversities to promotive features such as positive maternal mental health during pregnancy. Positive maternal mental health provided protection also to children exposed to co-occurring maternal psychological distress during pregnancy. The effects of positive maternal mental health during pregnancy may persist throughout childhood. Similarly supporting the DOHaD framework, the findings on the association between ELS and anxiety in late adulthood suggest that the adverse effects of ELS experienced in childhood may extend throughout the life course until late adulthood. Together these findings suggest that preventive efforts to diminish the risk of ELS and to promote positive environments should be directed to early life, already to the prenatal period.

Keywords

Early life stress; Prenatal distress; Psychological distress during pregnancy; Positive maternal mental health; Pregnancy; Mental health; Social support; Psychiatric problems; Mental and behavioral disorders; Cognitive development; Developmental Origins of Health and Disease; Longitudinal studies; Cohort studies

Tiivistelmä

Mielenterveys alkaa kehittyä jo elämän varhaisimmissa vaiheissa, alkaen sikiöajasta. Aiemmat tutkimukset osoittavat, että koettu varhainen stressi, esimerkiksi fyysinen ja emotionaalinen kaltoinkohtelu lapsuudessa sekä altistuminen äidin raskaudenaikaiselle psykologiselle stressille sikiöaikana, vaikuttavat negatiivisesti lapsen mielenterveyteen ja psykologiseen kehitykseen ja lisäävät esimerkiksi psykiatristen oireiden ja häiriöiden riskiä. Laajan tutkimusnäytön perusteella tiedetään, että lapsuudenaikaiset stressikokemukset vaikuttavat negatiivisesti mielenterveyteen vielä aikuisiällä. Vähemmän tutkimusnäyttöä on siitä, yltävätkö varhaisen stressin negatiiviset vaikutukset myöhäisaikuisuuden mielenterveyteen. Varhaisen stressin vaikutuksiin verrattuna vähemmän tutkittuja ovat myös mahdolliset lapsen mielenterveyttä ja kehitystä suojaavat tekijät. Yksi mahdollinen suojaava tekijä on äidin positiivinen mielenterveys raskausaikana.

Tämä väitöskirja tutkii äidin raskaudenaikaisen positiivisen mielenterveyden, tarkemmin määriteltynä positiivisten tunteiden sekä koetun vahvemman sosiaalisen tuen, yhteyttä lapsen mielenterveyteen ja kognitiiviseen kehitykseen. Väitöskirjassa näitä yhteyksiä tutkitaan kahdessa pitkittäistutkimuskohortissa. Lisäksi väitöskirja tutkii kolmannessa syntymäkohortissa, ovatko lapsuusiän varhaiset stressikokemukset yhteydessä ahdistusoireisiin myöhäisaikuisuudessa.

Väitöskirja koostuu neljästä osatutkimuksesta. Osatutkimukset I−II tarkastelivat suomalaisessa Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) -raskauskohortissa äidin raskaudenaikaisen positiivisen mielenterveyden yhteyttä lapsen mielenterveyden häiriöiden esiintyvyyteen (Osatutkimus I; n=3378) sekä lapsen psykiatrisiin oireisiin (Osatutkimus II; n=2636). Osatutkimus III tarkasteli äidin kokeman raskaudenaikaisen sekä lapsen syntymän jälkeisen sosiaalisen tuen yhteyttä lapsen kognitiiviseen kehitykseen kahdessa raskauskohortissa: englantilaisessa Avon Longitudinal Study of Parents and Children (ALSPAC) -kohortissa (n=5784) sekä suomalaisessa PREDO-kohortissa (n=420). Osatutkimus IV tarkasteli suomalaisessa Helsinki Birth Cohort Study (HBCS) 1934−44 -kohortissa (n=1872) varhaisten stressikokemusten, tarkemmin määriteltynä lapsuus- ja nuoruusiän fyysisen ja emotionaalisen kaltoinkohtelun, vanhempien avioeron, perheenjäsenen kuoleman, perheen matalan sosioekonomisen aseman sekä erokokemusten vanhemmista yhteyttä ahdistusoireisiin 65−77 vuoden iässä.

Väitöskirjan löydökset osoittivat, että äidin korkeampi positiivinen mielenterveys raskausaikana oli yhteydessä lapsen matalampaan mielenterveyden häiriöiden riskiin 8.4−12.8 ikävuoteen mennessä sekä vähempiin psykiatrisiin oireisiin 1.9−5.9 vuoden ja 7.1−12.1 vuoden iässä. Lisäksi äidin korkeampi koettu sosiaalinen tuki raskausaikana ja lapsen syntymän jälkeen ennustivat lapsen

parempaa kognitiivista suoriutumista 8 vuoden iässä. Äidin raskausaikana kokeman sosiaalisen tuen myönteiset vaikutukset lapsen kognitiiviseen kehitykseen näyttäytyivät voimakkaampina kuin äidin lapsen syntymän jälkeen kokeman sosiaalisen tuen myönteiset vaikutukset. Kaikki edellä kuvatut yhteydet olivat riippumattomia äidin samanaikaisista masennus- ja ahdistusoireista ja/tai mielenterveyden häiriöistä ennen raskautta tai raskausaikana. Yhteydet olivat riippumattomia myös äidin raskauden jälkeisestä positiivisesta mielenterveydestä. Lisäksi lapsuusiässä koettu fyysinen ja emotionaalinen kaltoinkohtelu sekä matala sosioekonominen asema olivat yhteydessä korkeampiin ahdistusoireisiin myöhäisaikuisuudessa. Nämä stressikokemukset sekä lapsuusiässä koettu vanhempien avioero lisäsivät myös myöhäisaikuisuudessa kliinisesti merkittävien ahdistusoireiden riskiä. Varhaisten stressikokemusten kumuloituminen oli yhteydessä sekä korkeampiin ahdistusoireisiin että kliinisesti merkittävien ahdistusoireiden riskiin.

Väitöskirjan tulokset ovat linjassa aiempien tutkimuslöydösten kanssa antaen tukea hypoteesille, että sekä sikiöaikainen että lapsuusiässä koettu ympäristö ovat yhteydessä lapsen mielenterveyteen ja kognitiiviseen kehitykseen. Väitöskirja antaa tärkeää uutta tietoa siitä, että mielenterveyden kehittymiseen vaikuttavat varhaisten stressikokemusten lisäksi varhaisen, etenkin raskaudenaikaisen ympäristön myönteiset ja suojaavat piirteet, kuten äidin positiivinen mielenterveys, ja että nämä myönteiset vaikutukset säilyvät läpi lapsuuden. Äidin raskaudenaikainen koettu positiivinen mielenterveys suojasi myös niiden lasten mielenterveyden kehitystä, jotka altistuivat samanaikaisesti äidin psykologiselle stressille. Varhaisen ympäristön merkitystä tukivat myös löydökset lapsuudenaikaisten stressikokemusten ja myöhäisaikuisuuden ahdistusoireiden välisestä yhteydestä, osoittaen että varhaiset kokemukset voivat heijastua mielenterveyteen läpi elämänkaaren. Kaiken kaikkiaan väitöskirjan tulokset korostavat aikaisiin elämänvaiheisiin ajoitettujen ennaltaehkäisevien tukitoimien merkitystä pyrkimyksissä sekä vähentää varhaisten stressikokemusten riskiä, että myös tukea positiivisia kehitysympäristöjä, lähtien jo raskausajasta.

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Abbreviations

ACE	Adverse Childhood Experience
ALSPAC	Avon Longitudinal Study of Parents and Children
BAI	Beck Anxiety Inventory
BRLM	Bayesian Relevant Life course Modelling
CBCL	Child Behavior Checklist
CCEI	Crown-Crisp Experiential Index
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence interval
DNAm	Deoxyribonucleic acid methylation
DSM	Diagnostic and Statistical Manual of mental and behavioral disorders
ELS	Early life stress
EPDS	Edinburgh Postnatal Depression Scale
GWAS	Genomic-wide association study
HBCS	Helsinki Birth Cohort Study
HILMO	Care Register for Health Care (Hoitoilmoitusrekisteri)
HPA	Hypothalamus-pituitary-adrenal
HR	Hazard ratio
ICD	International Classification of Diseases
IQ	Intelligence Quotient
IQR	Interquartile range
MBR	Medical Birth Register
PANAS	Positive and Negative Affect Schedule
PCA	Principal Component Analysis
PREDO	Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study
PTSD	Posttraumatic stress disorder
OR	Odds Ratio
SD	Standard deviation
SES	Socioeconomic status
SSQ	Social Support Questionnaire
STAI	Spielberger State-Trait Anxiety Inventory
TEC	Traumatic Experiences Checklist
VAS	Visual Analogue Scale
WHO	World Health Organization
WISC	Wechsler Intelligence Scale for Children

List of original publications

I **Lähdepuro, A.,** Lahti-Pulkkinen, M., Pyhälä, R., Tuovinen, S., Lahti, J., Heinonen, K., Laivuori, H., Villa, P.M., Reynolds, R.M., Kajantie, E., Girchenko, P. & Räikkönen, K. (2023). Positive maternal mental health during pregnancy and mental and behavioral disorders in children: A prospective pregnancy cohort study. *Journal of Child Psychology and Psychiatry,* 64(5), 807−816. doi:10.1111/jcpp.13625.

II **Lähdepuro, A**., Lahti-Pulkkinen, M, Girchenko, P., Villa, P. M., Heinonen, K., Lahti, J., Pyhälä, R., Laivuori, H., Kajantie, E. & Räikkönen, K. (2023). Positive maternal mental health during pregnancy and psychiatric problems in children from early childhood to late childhood. *Development and Psychopathology,* 1−13. doi:10.1017/S0954579423001244.

III **Lähdepuro, A.,** Räikkönen, K., Pham, H., Thompson-Felix, T., Eid, R. S., O'Connor, T., Glover, V., Lahti, J., Heinonen, K., Wolford, E., Lahti-Pulkkinen, M. & O'Donnell, K. J. (2023). Maternal social support during and after pregnancy and child cognitive ability: examining timing effects in two cohorts. *Psychological Medicine.* 1−10. doi: 10.1017/S0033291723003550.

IV **Lähdepuro, A.,** Savolainen, K., Lahti-Pulkkinen, M., Eriksson, J. G., Lahti, J., Tuovinen, S., Kajantie, E., Pesonen, A-K., Heinonen, K. & Räikkönen, K. (2019). The impact of early life stress on anxiety symptoms in late adulthood. *Scientific Reports,* 9(1). doi: 10.1038/s41598-019-40698-0.

1 Introduction

Mental and behavioral disorders carry an enormous societal and economic burden. They rank among the top five causes of years lived with disability (Mokdad et al., 2016; Vos et al., 2017), causing 7% of disability-adjusted life years globally (Rehm & Shield, 2019) and predicting an average of 10.5 years less contributing to work force (Plana-Ripoll et al., 2023) and a 15−20 years shorter life expectancy (Nordentoft et al., 2013). Positive psychological development such as higher cognitive ability in childhood and adolescence is, in turn, positively associated with long-term educational, occupational and health outcomes such as educational attainment (Blair, 2016) and better physical and mental health (Wraw, Deary, Der, & Gale, 2016; Wraw, Deary, Gale, & Der, 2015) later in life. Identifying risk and resilience factors for mental and behavioral disorders and their symptoms as well as developmental precursors of healthy cognitive development is thus needed (Arango et al., 2018).

A growing consensus exists that adversities emerging as early in life as in the prenatal period contribute to the individual's vulnerability to later psychopathology (e.g., MacKinnon, Kingsbury, Mahedy, Evans, & Colman, 2018; Madigan et al., 2018; Manzari, Matvienko-Sikar, Baldoni, O'Keeffe, & Khashan, 2019; Monk, Lugo-Candelas, & Trumpff, 2019; Robinson, Lahti-Pulkkinen, Heinonen, Reynolds, & Räikkönen, 2019; Van den Bergh et al., 2020). Maternal psychopathology is among the known early life stress (ELS) experiences in the prenatal period. Maternal prenatal mental health, along with mental health after the child's birth, is a public health issue that has great implications for both maternal and child health and well-being (Meaney, 2018; O'Donnell & Meaney, 2017). If untreated, maternal prenatal psychopathology has vast economic, humane and societal consequences (Bauer, Parsonage, Knapp, Iemmi, & Adelaja, 2014; Howard & Khalifeh, 2020; Stein et al., 2014), including adverse health consequences both for the mother and the offspring (Bauer et al., 2014). Investing in maternal prenatal mental health is thus an investment not only in the mothers, but in the offspring. While much of the research to date has focused on maternal psychopathology during pregnancy and in childhood (Madigan et al., 2018; Manzari et al., 2019; Tarabulsy et al., 2014), much less is known about potentially protective and promotive factors early in life that contribute to building resilience, better mental health, and healthy cognitive development in the offspring.

Beyond pregnancy, ELS in childhood contributes to the development of mental health. Experiencing ELS, such as childhood physical or emotional maltreatment, interpersonal loss (e.g., separation from parents, parental divorce, or parental death) and low socioeconomic status (SES) (Gilbert et al., 2009; Sahle et al., 2022), is consistently associated with a range of later psychopathology (e.g., Gardner,

Thomas, & Erskine, 2019; Hughes et al., 2017; Humphreys et al., 2020; Li, D'Arcy, & Meng, 2016; Macpherson et al., 2021; Norman et al., 2012; Sahle et al., 2022; Wang, Chen, Zhou, & Zhang, 2022). Less is known of whether the association between ELS and psychopathology persists into late adulthood.

The aim of this thesis is to expand earlier research on the effects of maternal mental health during pregnancy on offspring mental health and psychological development, shifting the focus from stressful environments such as maternal psychopathology to positive environments, namely positive maternal mental health. I investigate whether positive maternal mental health is associated with offspring mental health and psychological development and whether it may mitigate the effects of concurrent maternal psychological distress on these outcomes. Another aim is to add to the existing evidence on the far-reaching adverse effects of childhood ELS experiences on mental health, investigating whether the associations between different types of ELS and anxiety symptoms found in previous research are still evident in late adulthood.

2 Review of the literature

2.1 Mental health and psychological development across the life course

The following chapter defines the indicators of offspring mental health and psychological development that I use in this thesis. I use the term offspring to cover individuals of all ages. Of note, while there is no uniform definition for "mental health", consensus exists that mental health consists of several aspects of cognitive-emotional functioning, sense of autonomy and agency, subjective well-being, and social health, and does not merely reflect the presence or absence of mental disorders (Manwell et al., 2015; Westerhof & Keyes, 2010; World Health Organization, 2004). Indicators of offspring mental health and psychological development covered in this thesis are mental and behavioral disorders, psychiatric problems, anxiety symptoms and general cognitive ability; these indicators are described in detail in the following chapter.

Mental and behavioral disorders are defined as syndromes that cause clinically significant disturbance in an individual's cognition, emotional regulation, or behavior, and reflect a dysfunction in the psychological, biological or developmental processes underlying mental functioning, causing distress in e.g., social, educational, and occupational activities (American Psychiatric Association, 2013; World Health Organization, 2019). Diagnoses of mental and behavioral disorders are most commonly based on two international classification systems: the International Classification of Diseases, with 11th Revision (ICD-11) as the most recent revision (World Health Organization, 2019) and the Diagnostic and Statistical Manual of Mental Disorders, with the 5th Revised Revision (DSM-5-TR) as the most recent revision (American Psychiatric Association, 2022). Of note, the ICD-11 has replaced the previous definition "mental and behavioral disorders" with "mental, behavioral or neurodevelopmental disorders" (World Health Organization, 2019); however, since this thesis is based on the earlier revisions of the ICD, and the ICD-10 is still in use in Finland at the time of submission of this thesis, for the purpose of clarity and conciseness I use the term "mental and behavioral disorders", in which neurodevelopmental disorders are included.

Globally, the point prevalence for mental and behavioral disorders is estimated to be 13% (World Health Organization, 2022). Moreover, according to meta-analytic evidence, the projected cumulative risk for a lifetime mental or behavioral disorder by age 75 years is 46.4−53.1%, meaning that approximately half of the population will develop some mental or behavioral disorder during their lifetime (McGrath et al., 2023). Among mental and behavioral disorders, anxiety (31%) and depressive (28%) disorders are the most common (World Health Organization, 2022).

Often, mental and behavioral disorders have their origins early in life: overall, 48.4% of those diagnosed with a mental and behavioral disorder receive their diagnosis by the age of 18 years (Solmi et al., 2022). Other estimates suggest that the peak age of onset for mental and behavioral disorders is around the age of 14−15 years (Kessler et al., 2005; McGrath et al., 2023). Particularly neurodevelopmental disorders, with a median age of onset at 12 years (interquartile range (IQR) 7−16 years), and anxiety disorders, with a median age of onset at 17 years (IQR 9−25 years), typically occur in childhood or adolescence and are diagnosed by the age of 18 (Solmi et al., 2022). Diagnoses of both of the aforementioned categories peak at the age of 5.5 years (Solmi et al., 2022). By this age, many children are enrolled in school or daycare; in a novel learning environment with increasing demands, difficulties with neurodevelopment or emotion regulation may become more evident and are more likely to be detected.

While mental and behavioral disorders represent the more severe end on the continuum of psychopathology, psychiatric problems refer to dimensionally assessed symptoms that may or may not reach a diagnosis level. Psychiatric problems in childhood are often further categorized to internalizing and externalizing problems. Internalizing problems are characterized by emotional reactivity, anxiety, depression, withdrawal, and somatic complaints, while externalizing problems are characterized by problems related to impulsivity, aggression and rule-breaking behavior (Achenbach, Ivanova, Rescorla, Turner, & Althoff, 2016; Achenbach & Rescorla, 2000). Internalizing problems have been described to cause distress within the individual, while externalizing problems may be more likely to cause distress also in the individual's environment (Oldehinkel & Ormel, 2023).

The prevalence of psychiatric problems among children has remained relatively stable for the past decades, apart from increasing internalizing problems among adolescent girls (Bor, Dean, Najman, & Hayatbakhsh, 2014; Sourander, Lempinen, & Brunstein Klomek, 2016). In Finland, the prevalence of parent-reported total psychiatric problems among 8-year-old children remained similar from 1989 to 2013, with 11.8−19.7% of boys and 7.9−10.1% of girls scoring above the clinically relevant threshold of psychiatric problems over a 24-year period (Sourander et al., 2016). One Austrian study among a population-based sample of 10 to 18-year-old adolescents estimated the prevalence of clinically relevant internalizing problems to be 17.8% and externalizing problems to be 7.4% (Philipp et al., 2018).

Psychiatric problems and mental and behavioral disorders show relatively high continuity over time, and psychiatric problems in early childhood predict later psychopathology (Mesman & Koot, 2001; Oldehinkel & Ormel, 2023; Pihlakoski et al., 2006; Sallis et al., 2019). The continuity is mainly homotypic, e.g., with internalizing symptoms most likely predicting future internalizing, rather than

externalizing symptoms (Oldehinkel & Ormel, 2023); however, heterotypic continuity, e.g., one type of psychopathology predicting another type of psychopathology later in life, also occurs (Shevlin, McElroy, & Murphy, 2017). The onset of childhood psychopathology has been associated with a range of other adverse outcomes such as reduced well-being and lower academic achievement, more years lived with disability, and other negative social, health-related, legal, and economic consequences in late adolescence and early adulthood (Copeland, Angold, Shanahan, & Costello, 2014; Kim-Cohen et al., 2003; Sallis et al., 2019). Psychopathology is among the most common causes of years lived with disability and shorter life expectancy (Mokdad et al., 2016; Nordentoft et al., 2013; Plana-Ripoll et al., 2023; Rehm & Shield, 2019; Vos et al., 2017). This emphasizes the importance of early detection and prevention of psychiatric problems and mental and behavioral disorders.

The prevalence of mental and behavioral disorders in general is estimated to decrease towards late adulthood (Kessler et al., 2005). However, mental and behavioral disorders and their symptoms are still evident in late adulthood and can have detrimental effects on health, as reviewed below. Anxiety disorders are among the most prevalent mental and behavioral disorders in late adulthood, with an estimated prevalence of 15.3% among older adults at or above the age of 60 years (Kessler et al., 2005). Another systematic review has estimated the prevalence of anxiety disorders to vary between 1.2−14% in community samples of adults over 60 years of age (Bryant, Jackson, & Ames, 2008). Anxiety disorders, more specifically, are characterized by excessive anxiety and fear and related behavioral disturbances that cause significant distress and impairment in personal, social, occupational, or other functioning (World Health Organization, 2019). According to ICD-11, the key feature that differentiates anxiety disorders is the disorder-specific trigger of anxiety or fear; for example, in social anxiety disorder, anxiety and related thoughts and behaviors are related to social situations, whereas in agoraphobia, anxiety and related thoughts and behaviors are related to public spaces (World Health Organization, 2019).

Whereas anxiety disorders, by definition, cause significant distress and impairment in the individual's functioning, anxiety symptoms can be seen as a continuum, including anxiety symptoms that do not necessarily reach the diagnostic criteria (American Psychiatric Association, 2013; World Health Organization, 2022). Anxiety symptoms that are elevated but below the level fulfilling diagnostic criteria are more common than diagnosed anxiety disorders in late adulthood (Bryant et al., 2008; Grenier et al., 2011). While anxiety disorders generally have a young age at onset (Solmi et al., 2022), the developmental risk factors for late-life anxiety are poorly understood.

Anxiety has deteriorating effects on the functioning of elderly adults: it has been associated with lower cognitive performance, memory problems, sleep disturbances, and higher risk of dementia and somatic illnesses (Butters et al., 2011; Gimson, Schlosser, Huntley, & Marchant, 2018; Palmer, Jeste, & Sheikh, 1997; Spira, Stone, Beaudreau, Ancoli-Israel, & Yaffe, 2009; Yochim, Mueller, & Segal, 2013). These impairments have been estimated to be equally severe with anxiety disorders and subclinical anxiety symptoms (Grenier et al., 2011; Yochim et al., 2013). The adverse effects of anxiety on the well-being of elderly adults call for early identification of anxiety and its risk factors in the life course.

Another aspect of mental health and psychological functioning is cognitive development. Cognitive development is often operationalized as general cognitive ability, which encompasses cognitive skills such as verbal comprehension, perceptual reasoning, working memory, and processing speed (Wechsler, 2010). In addition, general cognitive ability encompasses executive functioning, which covers a wide range of cognitive functions related to working memory, inhibitory control, and attention shifting (Blair, 2016), and thus plays an important role in psychological functioning. Of note, cognitive ability and psychiatric problems may have a bidirectional association: lower cognitive ability has been shown to longitudinally predict higher psychiatric problems later in childhood, and vice versa psychiatric problems among children increase their risk for poorer cognitive ability (Halse, Steinsbekk, Hammar, & Wichstrøm, 2022; Weeks et al., 2014).

Cognitive ability has an extensive impact on well-being at both individual and societal/economic level (Blair, 2016; Calvin et al., 2011; OECD, 2010; Wraw et al., 2016, 2015). The development of executive functioning in early childhood has been associated with later educational attainment (Blair, 2016). Furthermore, general cognitive ability in adolescence has been associated with better physical and mental health later in life: for example, in a longitudinal cohort of ca. 4000 participants, higher general cognitive ability at 14−21 years of age, operationalized as intelligence quotient (IQ), was associated with better physical health at 50 years of age (Wraw et al., 2015) and with a lower risk of self-reported psychopathology at 50 years of age (Wraw et al., 2016). According to a meta-analysis, a one standard deviation (SD) increase in standardized cognitive test scores in childhood/adolescence is associated with a 24% lower risk of death at follow-up from 17 to 69 years of age (Calvin et al., 2011). On a more societal level, investing in early preventive efforts to support children's cognitive development has significant economic benefits for the whole society (Heckman & Masterov, 2007).

2.2 Early life origins of mental health and psychological development – underlying theoretical frameworks

Mental health and psychological development has its origins in early life. Several theoretical frameworks have been postulated to address these early life origins of mental health and psychological development, describing how risk and promotive factors early in life contribute to later well-being. This chapter aims to give an overview of these underlying theoretical frameworks. While the emphasis is on the Developmental Origins of Health and Disease framework (DOHaD), several related theories are reviewed that address questions of risk and promotive factors of offspring mental health and psychological development.

2.2.1 The Developmental Origins of Health and Disease (DOHaD)

The DOHaD framework posits that characteristics of the early life environment, occurring already in the prenatal period or early in childhood, may "program" the structure and functioning of the developing organs and biological systems, thereby enhancing individual differences in later reactivity and adaptation to environmental influences (Barker, 2007, 2004; O'Donnell & Meaney, 2017; Van den Bergh et al., 2020). According to Barker who initially introduced the DOHaD framework, many developing organs of the offspring are particularly plastic and sensitive to environmental influences already *in utero* (Barker, 2004). This early life programming may then lead to a higher sensitivity to health adversities such as chronic physical health conditions and mental and behavioral disorders in subsequent life (Barker, 2007, 2004; O'Donnell & Meaney, 2017; Van den Bergh et al., 2020).

The DOHaD framework was first introduced based on research on the associations between low birthweight and later risk of coronary heart disease; this finding led to the hypothesis that offspring exposure to stressful environments such as undernutrition already *in utero* had permanent effects on the body composition and metabolism of the individual (Barker, 2007). Since the postulation of the DOHaD framework, it has been widened to cover other stressful environments during pregnancy such as maternal psychological distress during pregnancy, as well as psychological health in the offspring such as mental and behavioral disorders and their symptoms and cognitive development (Van Den Bergh, 2011; Van den Bergh et al., 2020). A multitude of interrelated biological systems are involved in prenatal programming, including the central and autonomic nervous system, cardiovascular and immune systems, and the neuro-endocrine system, namely the hypothalamus-pituitary-adrenal (HPA) axis, which is a central part of stress regulation (Monk et al., 2019; Van den Bergh et al., 2020). Hartman and colleagues have recently extended the DOHaD framework by suggesting that via these

mechanisms, prenatal stress may influence the prenatal programming of postnatal sensitivity to environmental effects (Hartman, Belsky, & Pluess, 2023); that is, the conditions in the prenatal environment may contribute to the offspring's response to positive and negative features in their environment after birth.

2.2.2 The Life Cycle Model of Stress

In line with the DOHaD framework, *the life cycle model of stress* (Lupien, McEwen, Gunnar, & Heim, 2009) posits that early life exposure to stress or adversities may contribute to persistent changes in the individuals' biological stress regulation systems such as the HPA axis. This propensity to changes may be more pronounced during pregnancy and in childhood due to the particularly rapid development of these biological systems in early life (Lupien et al., 2009). Indeed, the first 1000 days of life, encompassing approximately the pregnancy period and the first two years of life, are particularly important for the development of the brain, which is especially sensitive to environmental changes during the pre- and postnatal period (Cusick & Georgieff, 2016). For example the hippocampus, a brain structure involved in the downregulation of the HPA axis, develops most rapidly until the age of two years (Lupien et al., 2009).

According to the life cycle model of stress, changes in biological systems following stress may also differ at different developmental stages (Lupien et al., 2009; Raymond et al., 2021). For example, exposure to ELS during pregnancy (e.g., maternal psychological distress) and in childhood (e.g., childhood maltreatment) has been associated with both hyper- and hypoactivity of the HPA axis (Lupien et al., 2009; Raymond et al., 2021; Van den Bergh et al., 2020). Changes in the HPA axis functioning and in the related brain regions, in turn, are associated with higher vulnerability to mental and behavioral disorders, including mood, anxiety, and trauma-related disorders (Lupien et al., 2009; Sprooten et al., 2017; Zorn et al., 2017).

2.2.3 The Diathesis-Stress, Differential Susceptibility, and Vantage Sensitivity models

In the past decades, several theoretical frameworks have highlighted the individual differences in environmental sensitivity, suggesting that individuals respond in different ways to stressful (diathesis-stress models), supportive (vantage sensitivity), or both of these environmental characteristics (differential susceptibility) (review: Slagt, Dubas, Deković, & van Aken, 2016). Below I introduce these theoretical frameworks more in detail.

The diathesis-stress model (e.g., Bleuler, 1963), posits that individuals exposed to stressors vary in their diathesis, i.e., vulnerability to mental health adversities following this stressor. According to the diathesis-stress model, those with an underlying diathesis who experience stressors are more likely to develop psychopathology; in other words, a stressor may activate an underlying diathesis, thus leading to the development of psychopathology (Monroe & Simons, 1991). Examples of underlying diatheses include genetic liability, biological markers, temperament, cognitive ability, and other social and psychological vulnerability factors (Monroe & Simons, 1991; Slagt et al., 2016).

While the focus of the diathesis-stress model is on risk factors for mental health and psychological development (Monroe & Simons, 1991), not all children exposed to ELS end up developing psychopathology or other adversities. This highlights the importance of identifying environmental factors early in life which may promote the mental health and psychological development of the offspring, despite underlying diatheses or encountered stressors. Extending from the diathesis-stress model, *the differential susceptibility model* posits that individuals differ not only in their vulnerability to stressors, but also in their susceptibility to the beneficial effects of positive environments (Belsky & Pluess, 2009, 2013). According to the differential susceptibility model, individuals who are more vulnerable to the adverse effects of stress may also be more sensitive to the beneficial effects of positive environments (Belsky & Pluess, 2009). The markers of differential susceptibility may also include genetic, physiological stress regulatory, temperamental, and behavioral factors (Pluess & Belsky, 2013; van IJzendoorn, Bakermans-Kranenburg, Coughlan, & Reijman, 2020). Environmental factors early in life, including in pregnancy, may influence these markers, thus altering the individual's susceptibility to risk and promotive factors later in life (Pluess & Belsky, 2011; Slagt et al., 2016; van IJzendoorn et al., 2020); this has been referred to as "prenatal programming of postnatal plasticity" (Pluess & Belsky, 2011) and "prenatal programming or environmental sensitivity" (Hartman et al., 2023).

Based on the differential susceptibility model, another model was developed that focuses particularly on the individual differences in how the individual benefits from positive environmental features; this was named *the vantage sensitivity model* (Pluess & Belsky, 2013). According to this model, some individuals benefit greatly from positive environments (showing vantage sensitivity), while others fail to benefiting from these environments (showing vantage resistance) (Pluess & Belsky, 2013); however, this does not imply that the individuals varying in vantage sensitivity would differ in their susceptibility to adverse environments. In other words, Pluess and Belsky argue that while some may be more sensitive to the benefits of positive environments, the same individuals may not be more

susceptible to the negative effects of adverse environments; therefore, a differentiation should be made between differential susceptibility and vantage sensitivity.

To summarize, despite the similarities of the diathesis-stress, vantage sensitivity, and differential susceptibility models, they differ from one another in how they perceive environmental risk and promotive factors. The diathesis-stress model emphasizes individual differences in vulnerability, the vantage sensitivity model emphasizes differences in benefiting from promotive factors, and the differential susceptibility model emphasizes differences in both. Pluess and Belsky (2013) also highlight that not all vulnerability factors will by default function as promotive factors and vice versa; therefore, different theoretical frameworks may fit different vulnerability and different environmental factors. For example, one large meta-analysis showed evidence supporting both the diathesis-stress, differential susceptibility, and vantage sensitivity models on the modifying effects of temperament traits on children's sensitivity to parenting when predicting their socioemotional developmental (Slagt et al., 2016).

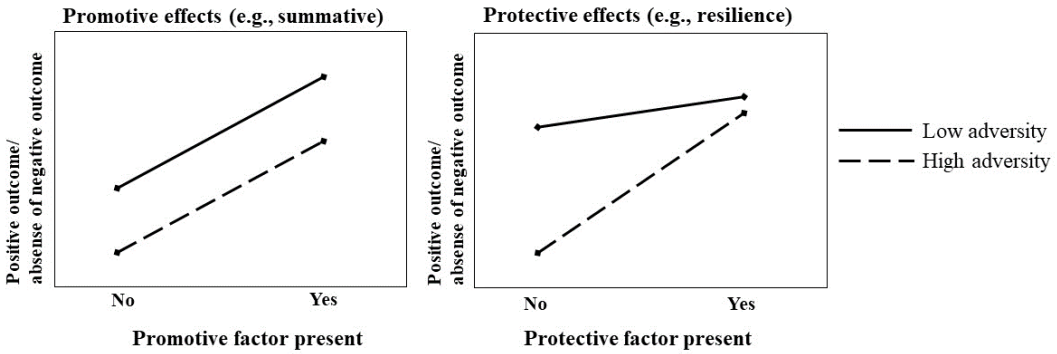
2.2.4 The concepts of resilience and promotive effects

Another concept close to differential susceptibility (Belsky & Pluess, 2009), particularly in light of early adversities, is the concept of *resilience*. Broadly defined, resilience refers to reduced vulnerability to environmental risk factors, more likely overcoming adversity, the ability to maintain good mental or physical health *despite* adversities, and the absence of expected maladaptive outcomes after encountering a risk factor (Liu, Reed, & Girard, 2017; Rutter, 1987, 2006, 2012; Zimmerman et al., 2013). Therefore, resilience does not refer to the absence of adversities, but to the positive adaptation in the face of adversities (Herrman et al., 2011; Rutter, 2012). Furthermore, resilience does not imply superior well-being, but rather, relatively good well-being in relation to the well-being of those exposed to similar adversities (Rutter, 2012).

Related to the differential susceptibility and vantage sensitivity models, a distinction can be made between resilience, more closely related to differential susceptibility, and *promotive factors*, more closely related to vantage sensitivity. According to Rutter (2012), resilience indicates an interaction between risk and promotive factors, rather than their summative effects. Similarly, Zimmerman and colleagues (2013) conceptualize a distinction between *protective* factors, promoting well-being particularly in individuals facing distress (similarly to resilience), and *universal* promotive factors, promoting well-being in all individuals regardless of their risk status (similarly to summative effects). In other words, protective factors operate via moderating the effects of simultaneously experienced

risk factors and thus increasing resilience (Luthar, Sawyer, & Brown, 2006; Rutter, 2012; Zimmerman et al., 2013), whereas promotive factors have a direct, independent effect on well-being that is opposite in direction than potential risk factors (Rutter, 2012; Zimmerman et al., 2013). Figure 1 illustrates this distinction between promotive and protective effects (e.g., summative effects vs. resilience effects).

Figure 1. Promotive effects (e.g., summative) vs. protective effects (e.g., resilience) of risk and promotive/protective factors.



Pluess and Belsky (2013) also point out that the same promotive factors may serve both as universal and resilience-promoting; that is, the same factor may increase vantage sensitivity in a supportive environment and provide protection in an adverse environment. For example, the beneficial effects of positive environments such as social support may be driven by their ability to buffer the negative effects of concurrent distress on the outcome, serving as a protective factor (Cohen, 2004), or they may compensate the effects of concurrent distress via independent pathways, serving as a universal promotive factor. Of note, in this thesis, I use the terms resilience and protective factors interchangeably.

Resilience theories, along with the vulnerability and differential susceptibility theories, emphasize the importance of enhancing promotive and protective factors, instead of merely aiming to reduce risk factors, in the efforts to support offspring mental health and psychological development (Zimmerman et al., 2013). Sources of resilience can be biological, psychological, dispositional and related to the environment, such as the social network (Herrman et al., 2011). According to the multi-systems model of resilience (Liu et al., 2017), resilience can be viewed as a three-layered construct

of core resilience, internal resilience, and external resilience. Core resilience refers to relatively stable, trait-like intra-individual characteristics such as the biological stress reactivity that regulate the individual's ability to adapt to stressors. Internal resilience refers to the individual's interpersonal and psychological resources such as coping skills, self-efficacy, emotion regulation, and social support. Finally, external resilience refers to the wider socio-ecological environment of the individual, such as SES and access to services (Liu et al., 2017).

2.2.5 Summary of theoretical frameworks

To conclude, several theories – the DOHaD, the life cycle model of stress, the diathesis-stress/differential susceptibility/vantage sensitivity models, and resilience theories – posit that experiences in early life, already during pregnancy and in childhood, may shape the individual's development in ways that make them more vulnerable − or more resilient − towards adverse mental health and poorer cognitive ability, and may also promote better mental health and cognitive ability. While much of the focus of previous research and theoretical frameworks has been on vulnerability factors, differential susceptibility and vantage sensitivity models highlight that individuals may also differ in their ability to benefit from positive environmental factors. Integrating the different theoretical frameworks, prenatal and childhood exposures to both negative and positive experiences may shape this susceptibility to later environments, thus contributing to later developmental pathways. Furthermore, life cycle models highlight the potential timing effects in these experiences, informing research and practice on whether there are developmental periods at which the exposures carry most relevance to later development.

2.3 Early risk and promotive factors of mental health and psychological development

The following chapter focuses on defining the risk and promotive factors for offspring mental health and psychological development that are included in this thesis. I use the term "risk factor" to describe ELS experiences during pregnancy and in childhood or adolescence that may increase the offspring's vulnerability to adverse mental health and psychological development. I use the term "promotive factor" to describe environmental factors during pregnancy and in childhood that enhance the offspring's positive development and decrease their risk of adverse mental health. These promotive factors may show universal beneficial effects for all individuals, or they may show protective effects particularly in the face of adversity, increasing resilience (Rutter, 2012), as described in Chapter 2.2.4.

2.3.1 Early life stress as a risk factor

ELS refers to stressful life experiences occurring early in development; in this thesis I include ELS experienced during pregnancy and in childhood. This chapter aims to give an overview of common ELS experiences both during pregnancy and in childhood. Previous research on the associations of these ELS experiences with offspring mental health and psychological development are reviewed in Chapter 2.4.1.

2.3.1.1 Early life stress during pregnancy

During pregnancy, the fetus may encounter stressful environments *in utero*. Among the known indicators of stressful environments is exposure to maternal psychological and physiological distress during pregnancy. Maternal psychological distress (i.e., negative maternal mental health) includes e.g., maternal depressive and anxiety symptoms and disorders, exposure to major disasters and stressful life events, perceived stress and pregnancy specific stress (i.e., stress originating from pregnancy-specific issues) (Lobel et al., 2008; Van den Bergh et al., 2020). Maternal physiological distress includes e.g., maternal substance use and cardiometabolic conditions during pregnancy (e.g., obesity, diabetes, and hypertensive disorders) which have been associated with an increased risk of psychopathology and adverse neurodevelopment among the offspring (Flak et al., 2014; Girchenko et al., 2018; Pyman, Collins, Muggli, Testa, & Anderson, 2021; Robinson et al., 2021). Of note, in this thesis I define prenatal ELS as maternal psychological distress, covering maternal depressive and anxiety symptoms during pregnancy and lifetime mental and behavioral disorders; other psychological and physiological ELS types during pregnancy are beyond the scope of the current thesis.

Maternal psychological distress during pregnancy is highly prevalent: for example, according to meta-analytic evidence, the prevalence of maternal depressive disorder during pregnancy, according to diagnostic interviews, varies between 9−17% (Dennis, Falah-Hassani, & Shiri, 2017; Roddy Mitchell et al., 2023; Wallwiener et al., 2019). The prevalence estimates of clinically relevant depressive and anxiety symptoms not necessarily reaching the diagnostic criteria for a disorder are generally higher than the prevalence estimates of diagnosed disorders, varying between 20−33% (Dennis et al., 2017; Lahti et al., 2017; Meaney, 2018; Molyneaux, Poston, Ashurst-Williams, & Howard, 2014; Tuovinen et al., 2018). Depressive symptoms show high continuity from pregnancy to the postpartum period (Evans, Heron, Francomb, Oke, & Golding, 2001; Lahti et al., 2017; Putnam et al., 2015).

2.3.1.2 Early life stress in childhood

In childhood, ELS most commonly encompasses experiences of childhood maltreatment, namely physical, emotional and sexual abuse and physical and emotional neglect before the age of 18 years (see e.g., the reviews and meta-analyses Gilbert et al., 2009; Norman et al., 2012; Wang et al., 2023 for more specific definitions). More specifically, physical abuse refers to the intentional use of force that results in, or has the potential to result in, physical injury, such as hitting, kicking, pushing, etc.; emotional abuse refers to intentional behavior that is insensitive to the child's emotional needs and conveys to a child that he/she is worthless or flawed, such as blaming, belittling, intimidating, etc.; sexual abuse refers to any completed or attempted sexual act with a child; and neglect refers to the failure to meet a child's basic physical, emotional, medical, or educational needs (Gilbert et al., 2009). In addition, ELS in childhood includes other potentially stressful early life experiences, such as interpersonal loss (e.g., death of a family member, separation from parents, parental divorce) and low family SES, e.g., access to economic, educational, and social resources (Peverill et al., 2021; Sahle et al., 2022). Of note, research in the field of ELS often uses a synonymous term of adverse childhood experiences (ACEs); for clarity and coherence purposes, I refer to stressful/adverse childhood experiences as ELS throughout this thesis.

In this thesis, I define ELS in childhood as physical maltreatment, emotional maltreatment (including both emotional abuse and neglect), separation from parents, parental divorce, death of a family member, and low SES occurring before the age of 18. Of note, this definition covers stressful experiences in both childhood and adolescence; to be consistent with previous study literature, I use the term "childhood" to cover both of these developmental periods. While sexual abuse is another ELS type associated with a higher risk of psychopathology (Gardner et al., 2019; Humphreys et al., 2020), it was not included in the current thesis. Furthermore, other types of ELS in childhood are also identified, including for example exposure to intimate partner violence, family dysfunction such as parental mental disorders and substance use problems, bullying, and stressful life events, that have been associated with a higher risk of psychopathology (meta-analyses: Gilbert et al., 2009; McKay, Cannon, Chambers, et al., 2021; Sahle et al., 2022), but these forms of ELS are beyond the scope of the current thesis. Moreover, while maternal psychological distress such as depressive symptoms show continuity from pregnancy to the postnatal period (Evans et al., 2001; Lahti et al., 2017; Putnam et al., 2015), exposure to maternal psychological distress in childhood was not investigated in this thesis and is thus beyond the scope of this review.

Different types of ELS vary in their estimated prevalence. The prevalence estimates for childhood maltreatment range between 4−22.6% for physical abuse and 10−36.3% for emotional abuse (Gilbert et al., 2009; Stoltenborgh, Bakermans-Kranenburg, Alink, & van IJzendoorn, 2015). In Finland, a recent study reported that ca. 14% of 4-year-old children had been exposed to physical abuse and ca. 44% to psychological abuse within the past year, according to parental reports (Leppäkoski, Vuorenmaa, & Paavilainen, 2021). Prevalence of childhood maltreatment is difficult to estimate due to the likely underreporting of incidences (Gilbert et al., 2009). Differences in estimates are also likely to stem from differences in assessment methods and sources of information: for example, the prevalence estimates are much higher in studies using self-report than informant studies (Stoltenborgh et al., 2015). The number of children living in families with low SES is likely to vary according to the country of origin and other cultural determinants. For example, in 2017, ca. 17.5% of children in the US lived in families below the federal poverty line (Peverill et al., 2021). Likewise, the number of children experiencing parental divorce, separation from parents, and death of a family member is likely to vary greatly. ELS experiences in childhood often co-occur, and children with previous ELS are at a higher risk for recurring ELS (Gilbert et al., 2009).

2.3.2 Positive maternal mental health as a promotive factor

This chapter reviews the concept of positive maternal mental health, including positive emotions and perceived social support, during and after pregnancy. Previous research on the associations between positive maternal mental health and offspring mental health and psychological development is reviewed in Chapter 2.4.2.

Positive mental health comprises different aspects of psychological well-being and can be conceptualized as domains of hedonic well-being, encompassing positive affect (e.g., excitement, enthusiasm, curiosity, activeness, determination) and life satisfaction, and eudaimonic well-being, encompassing e.g., self-acceptance, feelings of meaningfulness, autonomy, and pursuing life goals (Joshanloo, 2016; Phua, Kee, & Meaney, 2020; Ryan & Deci, 2001; Watson, Clark, & Tellegen, 1988; Westerhof & Keyes, 2010). Several studies have found these domains of positive mental health to be correlated but distinct (Joshanloo, 2016; Keyes, Shmotkin, & Ryff, 2002; Ryan & Deci, 2001). However, the grouping of positive mental health into hedonic and eudaimonic well-being has also been criticized, and some studies suggest that they capture the same phenomenon of positive mental health (Disabato, Goodman, Kashdan, Short, & Jarden, 2016). In addition, positive mental health comprises a domain of social well-being, including social integration, contribution, coherence,

actualization, and acceptance (Keyes, 1998; Westerhof & Keyes, 2010). Experiencing social well-being builds on experiencing social support from others. Social support can be further conceptualized as social network size, i.e., social embeddedness, referring to the number of connections that an individual has with significant others, and as perceived social support, referring to the cognitive appraisal of the quality of social relationships and being reliably connected to others (Barrera, 1986; Sarason, Sarason, Shearin, & Pierce, 1987).

A large body of research shows that while positive mental health and negative mental health (i.e., psychological distress, including mental disorders) are negatively correlated (Moeller, Ivcevic, Brackett, & White, 2018), positive mental health can be regarded as a distinct construct with separate origins, biological and sociodemographic correlates, and health effects (Chida & Steptoe, 2008; Folkman & Moskowitz, 2000; Fredrickson, Mancuso, Branigan, & Tugade, 2000; Moeller et al., 2018; Monteiro, Fonseca, Pereira, & Canavarro, 2021; Phua et al., 2017; Ryff et al., 2006; Verner et al., 2021; Watson et al., 1988). Also among postpartum women, positive mental health and the absence of negative mental health have been associated with distinct sociodemographic and infant-related factors (Monteiro et al., 2021). Positive and negative mental health may co-occur within an individual and even in the same situation (Moeller et al., 2018). Positive mental health does therefore not merely indicate the absence of negative mental health (Westerhof & Keyes, 2010).

Overall, positive mental health may also mitigate the effects of psychological and physiological stress on well-being (Fredrickson et al., 2000; Southwick, Vythilingam, & Charney, 2005; Trompetter, de Kleine, & Bohlmeijer, 2017; Tugade & Fredrickson, 2004), independently of depressive symptoms (Steptoe, O'Donnell, Badrick, Kumari, & Marmot, 2007), and shows protective effects against psychopathology (Keyes, Dhingra, & Simoes, 2010). Among pregnant women, positive mental health may reduce concurrent psychological distress during pregnancy: for example, higher social support has been associated with lower maternal depressive and anxiety symptoms and lower psychological and physiological stress during pregnancy (Friedman, Gelaye, Sanchez, & Williams, 2020; Racine, Plamondon, Hentges, Tough, & Madigan, 2019; Walsh et al., 2019), and may buffer the effects of stressful life events on clinically relevant depressive symptoms during pregnancy (Kishore et al., 2018). Low perceived social support, on the other hand, increases the risk of depression, anxiety and self-harm during pregnancy (Bedaso, Adams, Peng, & Sibbritt, 2021) as well as depression in the postpartum period (Bales et al., 2023). Positive maternal mental health, including positive emotions and social support, may thus be a modifiable target in reducing or buffering the adverse effects of maternal distress during pregnancy.

2.3.3 Life course models on the continuity and timing effects of risk and promotive factors

The DOHaD framework includes a presumption that during gestation, there are sensitive periods during which environmental influences may have differential influences on offspring health and well-being (Barker, 2004). Based on this presumption, studies investigating the associations of early life exposures to risk and promotive factors with later mental health and psychological development have aimed at disentangling whether exposures to risk or promotive factors at different developmental stages during or after pregnancy, coinciding with different developmental windows (e.g. *in utero*, neonatal period, or beyond), carry differential relevance to offspring development.

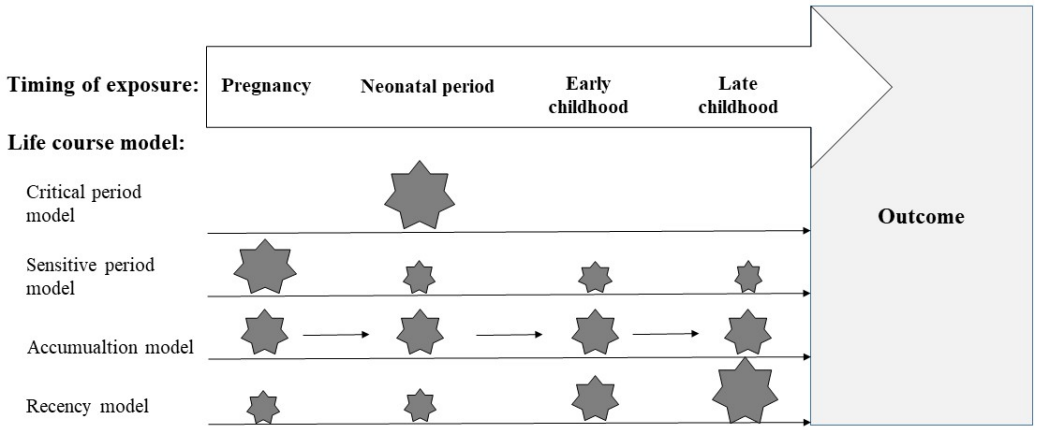
Investigating these potential sensitive periods requires repeated, prospective assessments of exposures at different developmental periods (Gabard-Durnam & McLaughlin, 2019). Previous studies addressing the independent effects and potential sensitive periods for exposures have often investigated this by simultaneously adjusting for exposures assessed at the different developmental periods (e.g., Pearson et al., 2013). However, this approach has methodological shortcomings. First, including repeated, often highly correlated exposures into the same statistical model may induce multicollinearity into the models, increasing the risk of affecting the coefficients. Second, while investigating the exposures in the same model may show which exposure periods have independent effects on the outcome, they do not provide information on whether the exposures show differential relevance, e.g., different effect size in relation to the outcome.

Life course models provide a way of investigating timing effects and comparing different life course models (Chumbley, Xu, Potente, Harris, & Shanahan, 2021; Madathil, Joseph, Hardy, Rousseau, & Nicolau, 2018; Smith et al., 2016; Zuber et al., 2023). The benefits of these life course models include their ability to include repeated, correlated measures, and their ability to compare the model fit of different life course models: more specifically, these models aim at identifying critical or sensitive periods during development and/or whether the effects of the exposure accumulate across time. According to the critical period model, only a certain developmental stage is relevant for the outcome; exposures outside this critical period do not have a relevant effect on the outcome. The sensitive period model, in turn, implies that while exposures at several developmental stages may have an effect on the outcome, different developmental stages have a differential relevance in relation to the outcome. For example, during the critical or sensitive periods of human development, neuroplasticity may be particularly elevated, leading to experiences having a particularly profound effect on the outcome (Schaefer, Cheng, & Dunn, 2022). The accumulation model, in turn, assumes that the effects of exposures accumulate across time and carry an equal relevance to the outcome. Finally, the recency

model implies that exposure at the most recent developmental stage carries most relevance in relation to the outcome (Smith et al., 2016; Zuber et al., 2023). Figure 2 illustrates different life course models.

Understanding timing effects and identifying potential sensitive or critical periods of the exposures, both to risk factors and to promotive factors, in relation to later mental health and psychological development, may help in planning and implementing preventive measures and interventions. When investigating and interpreting timing effects, it should be noted that several different developmental processes contribute to the outcome, for example psychiatric problems or cognitive ability, and that these developmental processes may have different sensitive periods (Woodard & Pollak, 2020).

Figure 2. An illustration of different life course models on the effect of repeated exposures at different time periods (in this example, pregnancy, neonatal period, early childhood, and late childhood) on the outcome. A star indicates that an effect of the exposure exists, and the size of the star indicates the relative effect size of each exposure. In this example, the critical period model shows that exposure only during the neonatal period has an effect on the outcome. The sensitive period model shows that exposure at each time period has on effect on the outcome, and in this example, pregnancy shows the largest effect. The accumulation model shows that the effects of exposures on the outcome are similar and accumulate across time periods. In the recency model, exposure at each time period has an effect on the outcome, with the most recent exposure in late childhood having the largest effect.



2.4 Previous evidence on the associations between risk and promotive factors and offspring mental health and psychological development

The following sections aim to synthesize previous research literature on the associations between exposure to risk and promotive factors during pregnancy and in childhood and later mental health and psychological development in the context of DOHaD and related theoretical frameworks. While emphasis to date has been on ELS during the pregnancy and in childhood (chapter 2.4.1), the role of promotive factors already in the prenatal period is increasingly recognized (chapter 2.4.2). The previous findings on the timing effects of prenatal and childhood experiences are discussed in Chapter 2.4.3.

2.4.1 Early life stress and offspring mental health and psychological development

2.4.1.1 Early life stress during pregnancy

In line with the DOHaD framework, meta-analytic evidence and evidence from multiple longitudinal studies shows that ELS during pregnancy, particularly maternal psychological distress, is associated with the offspring's adverse mental health and psychological development (Madigan et al., 2018; Manzari et al., 2019; Rogers et al., 2020; Tarabulsy et al., 2014; Van den Bergh et al., 2020). Among these adverse offspring outcomes are socioemotional and behavioral problems ranging from problems in self-regulation to mental and behavioral disorders. For example, two large meta-analyses including 73 and 191 studies, respectively, found that maternal depression and/or anxiety during pregnancy was associated with a higher risk of socioemotional problems in the offspring, including e.g., internalizing and externalizing problems, lower social and emotional competence, negative affectivity and difficult temperament, peer problems, and crying/colic (Madigan et al., 2018; Rogers et al., 2020). Systematic reviews and a meta-analysis also suggest an association between maternal psychological distress during pregnancy and offspring mental and behavioral disorders, including neuropsychiatric disorders (Manzari et al., 2019; Robinson et al., 2019; Van den Bergh et al., 2020) and "difficult" temperament traits such as higher negative affectivity and lower effortful control (Korja, Nolvi, Grant, & McMahon, 2017; Rogers et al., 2020; Spry et al., 2020; Van den Bergh et al., 2020).

Moreover, maternal psychological distress during pregnancy has been associated with poorer neurodevelopment in the offspring (Manzari et al., 2019; Pearson et al., 2016; Tuovinen et al., 2018; Van den Bergh et al., 2020), including lower cognitive development (Evans et al., 2012; O'Connor et al., 2022; Power, van IJzendoorn, Lewis, Chen, & Galbally, 2021; Rogers et al., 2020; Tarabulsy et al., 2014; van der Waerden et al., 2017). For example, two meta-analyses, both including 11 studies,

found a consistent, albeit small association between higher maternal psychological distress during pregnancy and poorer child cognitive and language development (Rogers et al., 2020; Tarabulsy et al., 2014).

The adverse effects of maternal psychological distress during pregnancy seem to persist throughout childhood and adolescence up until emerging adulthood (O'Donnell, Glover, Barker, & O'Connor, 2014; Pearson et al., 2013). Moreover, the adverse effects of maternal psychological distress on maternal parenting behavior and on child psychiatric problems are not limited to exposures to the most severe end of maternal distress, such as diagnoses of depression, but associations are found across the continuum of maternal psychological distress (Goodman et al., 2011; Lovejoy, Graczyk, O'Hare, & Neuman, 2000). However, some studies suggest that the associations may be genetically confounded (Havdahl et al., 2022), and not related to *in utero* exposure to psychological distress *per se*.

2.4.1.2 Early life stress in childhood

In this chapter, I will first review previous evidence on the associations between ELS in childhood and psychopathology up until adulthood. I will then move on to reviewing the existing evidence on the associations of childhood ELS with anxiety in late adulthood, an age group that has been more scarcely studied and is the focus of this thesis.

ELS exposure in childhood is associated with an increased risk of a range of psychopathology by adulthood, as shown by a large body of meta-analytic evidence (Gardner et al., 2019; Hughes et al., 2017; Humphreys et al., 2020; M. Li et al., 2016; Muzi Li et al., 2023; Jiaqi Liu, Deng, Zhang, & Tang, 2023; McKay, Cannon, Chambers, et al., 2021; Norman et al., 2012; Sahle et al., 2022). For example, an umbrella review of 68 systematic reviews an meta-analyses found that exposure to at least one ELS experience in childhood, most frequently physical, emotional or sexual abuse, parental mental disorders, and inter-parental conflict, was associated with a two-fold increase in the risk of depression and anxiety disorders (Sahle et al., 2022). In other meta-analyses, ELS, most frequently physical, emotional or sexual maltreatment and exposure to intimate partner violence, has been associated with a 2.03−2.48 -fold risk of depression and a 1.67−2.70 -fold risk of anxiety disorders (Gardner et al., 2019; M. Li et al., 2016; Jiaqi Liu et al., 2023). The strength of these associations are estimated to be similar in studies using prospective and retrospective reports of ELS (Gardner et al., 2019; Scott, McLaughlin, Smith, & Ellis, 2012).

The effects of childhood maltreatment on adult psychopathology are estimated to be more consistent than the effects of interpersonal loss such as death of a family member, separation from parents, or parental divorce. For example, meta-analytic evidence on the association between parental divorce in childhood and offspring's later depressive and anxiety disorders is inconsistent (Auersperg, Vlasak, Ponocny, & Barth, 2019; Sands, Thompson, & Gaysina, 2017). Other meta-analyses have shown an association between any parental loss (e.g., death of a parent, parental separation, or divorce) (McKay, Cannon, Chambers, et al., 2021) and more specifically death of a parent in childhood (McKay, Cannon, Healy, et al., 2021) and higher risks of mental and behavioral disorders; however, these meta-analyses did not look at the associations with specific mental and behavioral disorders. Other individual studies have not found an association between parental death in childhood and depressive and anxiety disorders or their symptoms in adulthood (van Heijningen et al., 2023).

Regarding low childhood SES, meta-analytic evidence shows an association between lower SES and a higher risk of psychopathology across childhood and adolescence (Peverill et al., 2021). In line with this meta-analysis, a previous study in the Helsinki Birth Cohort Study (HBCS) cohort found that lower childhood SES was associated with a higher risk of lifetime mental and behavioral disorders (Räikkönen et al., 2011). However, studies not detecting an association between low childhood SES and anxiety symptoms or disorders in adulthood also exist (Power et al., 2007; Räikkönen et al., 2011). Different operationalizations of low SES may show differential associations with later psychopathology: for example, one study found that financial hardship in childhood (e.g., receiving food stamps or other types of government assistance) was associated with a lifetime risk of mental and behavioral disorders, whereas parental education level was associated with the persistence and severity of these disorders in adulthood (McLaughlin et al., 2011).

Different types of ELS are estimated to increase the risk of different types of psychopathology in a similar, consistent manner (Gardner et al., 2019; Li et al., 2016; Norman et al., 2012; Schaefer et al., 2022). Other adverse outcomes associated with ELS in childhood include substance use disorders (Norman et al., 2012; Räikkönen et al., 2011), personality disorders (Johnson, Cohen, Brown, Smailes, & Bernstein, 1999; Lahti et al., 2012), posttraumatic stress disorder (Gardner et al., 2019), psychosis (Varese et al., 2012), and suicidality (Angelakis, Gillespie, & Panagioti, 2019; Dube et al., 2001; Norman et al., 2012; Sahle et al., 2022). ELS in childhood has also been associated with impairments in cognitive functioning (Johnson et al., 2021; Su, D'Arcy, Yuan, & Meng, 2019), although one systematic review showed that the evidence is much less consistent for cognitive functioning in late adulthood (Patel & Oremus, 2023).

The accumulation of several ELS experiences further increases the risk of psychopathology in adults: for example, a meta-analysis including ca. 104000 and 38000 participants found that exposure to four or more ELS experiences was associated with a 4.40-fold risk of depression and a 3.70-fold risk of anxiety, respectively (Hughes et al., 2017). These risk estimates are much higher than the estimates of the association between separately occurring ELS experiences and psychopathology, as reviewed above. To summarize, previous studies consistently link ELS and its accumulation to psychopathology still in adulthood, even though one meta-analysis reported that the association between emotional abuse and depression was somewhat stronger in childhood than in adulthood (Humphreys et al., 2020).

Extending these findings to later life, accumulating evidence suggests that the association between ELS and psychopathology, particularly depression, persists until late adulthood. These studies are summarized in Table 1 and described more in detail below. One recent meta-analysis of 10 studies, including ca. 30300 participants, found that physical and emotional abuse and neglect in childhood were associated with the risk of depression in adults aged 60 years and older (Wang et al., 2023). Studies on the association between ELS and psychopathology in late adulthood have more often focused on depression, but some have also examined the association between ELS and late-adulthood anxiety, which is the focus of this thesis. In a study of ca. 7000 participants above the age 65 years, Raposo and colleagues (2014) found that childhood physical and emotional abuse and neglect and their accumulation were associated with a higher risk of anxiety disorders in late adulthood. In another study, participants approaching late adulthood (aged 50 years and older) reporting childhood abuse had more anxiety disorders compared to those without childhood abuse (Sachs-Ericsson et al., 2010). A similar association was found between childhood physical abuse and clinically relevant anxiety symptoms not necessarily implying anxiety disorder diagnoses: In a study of ca. 22000 older adults above the age 60 years, retrospectively self-reported childhood physical abuse was associated with higher anxiety symptoms in late adulthood (Draper et al., 2008). Also in late adulthood, the accumulation of childhood maltreatment experiences has been associated with higher levels of anxiety symptoms and disorders (Bakouni, Ouimet, Desjardins, Forget, & Vasiliadis, 2023; Raposo, Mackenzie, Henriksen, & Afifi, 2014).

Some studies have investigated ELS experiences other than physical, emotional and sexual maltreatment in relation to late-life psychopathology, such as low childhood SES and interpersonal loss (i.e., separation from parents, death of a family member, and parental divorce); these studies to date have mainly focused on psychopathology other than anxiety. Regarding interpersonal loss, two studies in the Finnish HBCS cohort found associations between separation from parents in childhood

due to World War II evacuations and higher depressive symptoms among older adults (Pesonen et al., 2007) and a higher risk of severe lifetime mental and behavioral disorders across adult ages, albeit not depressive or anxiety disorders (Räikkönen et al., 2011). Similarly, a UK-based study on World War II evacuations found that separation from parents in early childhood (i.e., age 4−6 years), but not later in childhood, was associated with elevated depressive and anxiety symptoms in late adulthood (Rusby & Tasker, 2009). On the other hand, no association was found between death of a parent in childhood and depressive symptoms in late adulthood (Yang, Hu, Silventoinen, & Martikainen, 2020). Lower childhood SES, in turn, has been associated with higher depressive symptoms in late adulthood (Angelini, Howdon, & Mierau, 2019; Tani et al., 2016; Yang et al., 2020); two of these studies (Angelini et al., 2019; Tani et al., 2016) showed that the associations were independent of adulthood SES. Moreover, one previous study in the HBCS cohort found an association of lower childhood SES, operationalized as father's lower occupational status, with higher trait anxiety in older adults (Lahti et al., 2010).

Table 1. A summary of the previous literature on the associations between ELS and psychopathology in late adulthood.

Study	Cohort / Country	N	Indicator of ELS	Participant age at psychopathology assessment	Indicator of psychopathology
Angelini et al., 2019	SHARE, Europe	21989	low SES	mean age 66.1 years	depressive symptoms
Draper et al., 2008	DEPS-GP, Australia	21822	physical and sexual abuse	mean age 71.9 years	depressive and anxiety symptoms
Lahti et al., 2010	HBCS, Finland	1698	low SES	mean age 63.4 years	trait anxiety
Pesonen et al., 2007	HBCS, Finland	1658	separation from parents	mean age 61.6 years and 63.4 years	depressive symptoms
Raposo et al., 2014	NESARC, USA	7080	physical, emotional and sexual abuse, physical and emotional neglect, household dysfunction	>65 years	past-year diagnoses of depressive/anxiety disorders; lifetime personality disorders
Rusby & Tasker,	UK	870	separation from parents	62-72 years	depression and anxiety
Räikkönen et al., 2011	HBCS, Finland	12747	separation from parents	lifetime	severe mental and behavioral disorders
Sachs-Ericsson et al., 2010	Physical Health and Disability Study, USA	1982	physical, emotional and sexual abuse	>50 years (mean age 67 years)	internalizing disorders (including depressive and anxiety disorders)
Tani et al., 2016	JAGES, Japan	10458	low SES	>65 years	depressive symptoms
Wang et al., 2022	meta-analysis	30308	physical, emotional and sexual abuse, physical and emotional neglect	>60 years on average	depressive symptoms and disorders
Yang et al., 2020	CHARLS, China	13710	physical abuse, emotional neglect, death of a parent, low SES	45-98 years	depressive symptoms

ELS=Early life stress; SES=Socioeconomic status.

The comorbidity of stressful experiences in childhood is high, with especially emotional maltreatment often co-occurring with other types of ELS (Kaplan, Pelcovitz, & Labruna, 1999). It is therefore difficult to assess which types of ELS have the strongest association with later anxiety. However, accumulating evidence suggests that emotional maltreatment such as emotional abuse and neglect predicts depression (Humphreys et al., 2020; Infurna et al., 2016; Norman et al., 2012), anxiety (Jiaqi Liu et al., 2023), mental and behavioral disorders (Macpherson et al., 2021), and other

psychopathology (Norman et al., 2012) more strongly than other types of ELS do; in contrast, one small-scale study of 260 participants found that physical abuse, but not emotional abuse in childhood was associated with a higher risk of generalized anxiety disorder in late adulthood (Santos et al., 2023). To my knowledge, no other studies have investigated this particularly among the elderly. Some studies also suggest that the association of certain types of ELS with later anxiety, for example physical maltreatment and low SES, may be explained by other types of ELS due to their co-occurrence (Cougle, Timpano, Sachs-Ericsson, Keough, & Riccardi, 2010; Fergusson, Boden, & Horwood, 2008; Stansfeld, Clark, Rodgers, Caldwell, & Power, 2011).

To summarize, meta-analytic evidence and findings in longitudinal cohort studies give support to the DOHaD framework suggesting that ELS experiences both during pregnancy and in childhood increase the risk of mental health adversities such as psychiatric symptoms and disorders and adverse cognitive development later in life. Regarding childhood ELS experiences, consistent meta-analytic evidence shows associations with psychopathology up until adulthood; while associations in late adulthood have been studied less extensively, evidence is beginning to accumulate that the adverse effects of ELS extend until this life stage. However, less of the previous research has investigated the associations of ELS particularly with anxiety in late adulthood, or addressed other types of ELS in addition to childhood emotional and physical maltreatment.

2.4.2 Positive maternal mental health and offspring mental health and psychological development

While much of the previous research has focused on the adverse effects of maternal psychological distress during pregnancy for the offspring, studies on the potential beneficial effects of positive maternal mental health on offspring mental health and psychological development are beginning to emerge. These studies are summarized in Table 2 and described in detail in this chapter. The few existing studies suggest that positive maternal mental health shows promotive effects on child psychological development and mental health (Braeken, Jones, Otte, Nyklíček, & Van den Bergh, 2017; Clayborne et al., 2023; DiPietro, Novak, Costigan, Atella, & Reusing, 2006; Estinfort et al., 2022; Phua et al., 2017; van den Heuvel, Johannes, Henrichs, & Van den Bergh, 2015; Wei et al., 2023).

Table 2. A summary of the previous literature on the associations between positive maternal mental health and offspring mental health and psychological development.

Study	Cohort / Country	N	Indicator of positive maternal mental health	Timing of positive maternal mental health measure	Offspring age at assessment	Indicator of offspring mental health and psychological development
Braeken et al., 2017	The Netherlands	109	mindfulness skills	gw 15-22	4 months	social-emotional development
Clayborne et al., 2023	MoBa, Norway	36584	self-efficacy, self-esteem, enjoyment	gw 30 + 6, 18 and 36 months postpartum	5 years	internalizing & externalizing problems
DiPietro et al., 2006	USA	90	pregnancy-related feelings of uplifts	gw 32	24 months	child development
Estinfort et al., 2022	LEAPP-HIT, Taiwan	454	subjective well-being	repeatedly across 3 trimesters + 1 and 6 months + 1 and 2 years postpartum	6-24 months	developmental delay
Lewinn et al., 2020	CANDLE, USA	1055	social network size	3rd trimester + 2 years postpartum	4-6 years	general cognitive ability
Parkes & Sweeting, 2018	Growing Up in Scotland, Scotland	2649	perceived social support	22 months postpartum	90 months	socioemotional adjustment
Phua et al., 2017	GUSTO, Singapore	1066	positive mood; positive self-perception	gw 26	12-24 months	socioemotional behavior, autism symptoms, cognitive development
Shin et al., 2019	CANDLE, USA	1082	cohabitation, social network size, neigborhood	4 weeks postpartum	2 years	cognitive development
van den Heuvel et al., 2015	The Netherlands	90	mindfulness skills	gw 15-22	10 months	socioemotional development, temperament traits
Wei et al., 2023	Shanghai MCPC, China	4412	positive life events	+/-3 months around conception	2, 6, 12 and 24 months postpartum	neurodevelopment

gw=gestation week.

Previous studies investigating the effects of positive maternal emotions during pregnancy as an indicator of positive mental health have mostly focused on socioemotional development and developmental milestones of infants and toddlers as offspring outcomes. In a Singapore-based study of 1066 mother-child dyads, positive maternal mood and self-perception at 26 weeks of gestation were associated with improved objectively assessed socioemotional and cognitive skills, but not with communication or motor skills, in children at ages 12−24 months (Phua et al., 2017). In another study among 90 mothers and their children in the US, maternal pregnancy-related feelings of uplifts at 32 gestational weeks were associated with enhanced infant orientation, engagement and emotion regulation skills but not with motor development skills at age 24 months (DiPietro et al., 2006). In a Taiwanese study of ca. 450 mother-infant dyads, higher maternal eudaimonic well-being during pregnancy was associated with a decreased risk of infant developmental delay at 6−24 months among multiparous mothers (Estinfort et al., 2022). Another Shanghai-based study including over 4400 mother-child dyads found that a higher number of maternal positive life events around the time of conception (from ca. 3 months before conception until the first 3 months of pregnancy) was associated with better communication skills and problem solving skills among infants at 12−24 months of age (Wei et al., 2023). Furthermore, the infants of mothers reporting positive life events were at a lower risk for suspected developmental delay in gross motor and personal-social skills during their first 24 months of life. On the other hand, no associations were found between positive maternal life events and suspected offspring developmental delay in overall development or communication, fine motor, and problem solving skills (Wei et al., 2023).

Some studies have also assessed maternal mindfulness skills during pregnancy as a proxy for positive maternal mental health. Two studies among 109 and 90 participants in the Netherlands showed that higher maternal mindfulness between 15 and 22 weeks of gestation, reflecting a disposition to positive mental health and adaptive coping strategies, was associated with more adaptive socioemotional functioning in 4-month-old infants (Braeken et al., 2017) and with better self-regulatory capacity and lower scores on negative affectivity at 10 months (van den Heuvel et al., 2015). In contrast, mindfulness was not associated with levels of infant communication, interaction or affective problems at either 4 or 10 months or with adaptive functioning or extraversion at 10 months of age (Braeken et al., 2017; van den Heuvel et al., 2015).

To my knowledge, only two studies have investigated the association between positive maternal mental health during pregnancy and offspring mental health (Clayborne et al., 2023; Phua et al., 2017). In Phua and colleagues' study (2017) reviewed above, positive maternal mood during pregnancy was associated with lower autism symptoms and, surprisingly, higher peer aggression in

infants, whereas no association was found with other externalizing problems, dysregulation, or internalizing problems (Phua et al., 2017). Another study among ca. 36000 Norwegian mother-child-dyads investigated the associations of positive maternal mental health, namely maternal self-efficacy, self-esteem and enjoyment averaged from assessments during pregnancy at 30 gestation weeks and after pregnancy at 6, 18 and 36 months postpartum, with internalizing and externalizing problems in 5-year-old children (Clayborne et al., 2023). This study found that positive maternal mental health was associated with lower internalizing problems in girls and externalizing problems in girls and boys, and that higher positive mental health also buffered the effects of maternal prenatal stress on child internalizing problems. However, the study did not disentangle the effects of maternal positive mental health during pregnancy from the effects of positive mental health after pregnancy.

To my knowledge, the effects of another indicator of positive maternal mental health during pregnancy, perceived social support, on offspring mental health and psychological development remain largely uninvestigated. Regarding mental health, one Finnish study among 122 mother-child-dyads found that lack of maternal social support during pregnancy was associated with higher internalizing, although not externalizing problems in children at adolescence, but not at middle childhood (Luoma, Korhonen, Puura, & Salmelin, 2019). After pregnancy, one UK-based study of ca. 2600 mother-child-dyads found that higher maternal perceived social support in the child's infancy (at 22 months of age) was associated with lower internalizing and externalizing problems in infants at age 90 months (Parkes & Sweeting, 2018). This association was partly mediated by lower maternal distress. The association between maternal social support during and after pregnancy and cognitive development in the offspring has been investigated in two studies of a US-based cohort, including ca. 1000 mother-child-dyads (Lewinn, Bush, Batra, Tylavsky, & Rehkopf, 2020; Shin et al., 2019). These studies found that maternal social support network size at 4 weeks postpartum was associated with higher child cognitive ability at 2 years of age (Shin et al., 2019), whereas maternal social support at 2 years of age, but not during pregnancy, was associated with child cognitive ability at 4−6 years of age (Lewinn et al., 2020).

Taken together, emerging evidence suggests that positive maternal mental health during pregnancy, including positive emotions and perceived social support, shows beneficial effects for child mental health and cognitive development. However, previous research in still scarce and, to my knowledge, no earlier studies have extended the follow-up of the offspring beyond infancy or early childhood or investigated the effects of positive maternal mental health on the change in offspring mental health across childhood; the longest follow-ups to date have investigated the children at 6 years of age. Furthermore, no previous studies have investigated the associations of positive maternal mental health

during pregnancy and the more severe end of the continuum of child psychopathology, namely mental and behavioral disorders. Finally, the evidence on whether the associations are independent of concurrent maternal psychological distress or whether positive maternal mental health may moderate and thus buffer the adverse effects of maternal psychological distress, is still scarce.

2.4.3 Timing and continuity of risk and promotive factors

While ELS, for example maternal psychological distress both during (Madigan et al., 2018; Manzari et al., 2019; Rogers et al., 2020; Tarabulsy et al., 2014; Van den Bergh et al., 2020) and after (Goodman et al., 2011; Rogers et al., 2020; Spry et al., 2020) pregnancy is associated with adverse offspring development and mental health, two large systematic reviews indicate that sensitive developmental periods may vary greatly according to the exposures and outcomes studied, and no clear, consistent sensitive periods have been identified for exposures during pregnancy (Van den Bergh et al., 2020) or in childhood (Schaefer et al., 2022). Evidence on potential timing effects of childhood ELS such as maltreatment on later psychopathology is mixed. One recent large meta-analysis of 58 studies, including ca. 33000 participants, found that while exposure to childhood physical, emotional or sexual abuse at all ages was associated with later depression, the association was strongest in middle childhood, at age 6−13 years (Li et al., 2023); however, the timing effects differed regarding different types of childhood maltreatment. Another meta-analysis, on the other hand, found that the association between childhood ELS and later psychopathology did not differ according to child age (Sahle et al., 2022). Research on the timing effects of *promotive* factors is still in its initial stages (Zimmerman et al., 2013).

Studies utilizing life course modelling (described more in detail in Chapter 2.3.3) in investigating potential timing effects of ELS are emerging. A recent study of ca. 3300 mother-child-dyads of a UK-based cohort utilized a life course modelling approach, more specifically a structured life course model, in investigating the relative relevance of maternal depression at 13 different prenatal and postnatal periods in relation to depression among children in early adulthood (Lacey et al., 2023). This study found that the accumulation maternal depression across time was the most appropriate life course model to account for depressive symptoms among male offspring, whereas middle childhood was a sensitive period of exposure to account for depressive symptoms among female offspring (Lacey et al., 2023). Another study investigated potential sensitive periods for childhood maltreatment in different developmental stages of childhood: this study of 2892 African American adults primarily from low SES background found that individuals who reported childhood

maltreatment in early childhood at age 0−5 years experienced higher depressive and posttraumatic stress disorder (PTSD) symptoms compared to individuals with maltreatment experiences later in childhood (Dunn, Nishimi, Powers, & Bradley, 2017). Furthermore, exposure to other types of interpersonal violence, such as witnessing violence, was associated with higher depressive and PTSD symptoms particularly when the exposure happened in middle childhood (6−10 years). Taken together, studies on the timing effects of ELS show mixed results.

I am not aware of studies utilizing life course models to investigate the relative relevance of promotive factors such as social support during or after pregnancy in relation to child mental health and development. The Bayesian relevant life course modelling (BRLM) (Madathil et al., 2018) is a statistical approach that has been suggested as one mean of estimating the relative relevance of exposures and comparing different life course models; this approach was used in this thesis and is described more in detail in Chapter 4.5.1.3.

2.5 Summary of the literature

Taken together, there is a well-established association between ELS during pregnancy, namely maternal psychological distress, and a risk of psychopathology (Madigan et al., 2018; Manzari et al., 2019; Rogers et al., 2020; Tarabulsy et al., 2014; Van den Bergh et al., 2020) and adverse cognitive development (Evans et al., 2012; O'Connor et al., 2022; Power et al., 2021; Rogers et al., 2020; Tarabulsy et al., 2014) among the offspring. ELS during childhood, of which physical and emotional abuse and neglect and sexual abuse are the most studied types, also shows consistent associations with psychopathology (Gardner et al., 2019; Hughes et al., 2017; Humphreys et al., 2020; M. Li et al., 2016; Norman et al., 2012; Sahle et al., 2022), and the associations seem to persist into late adulthood (Wang et al., 2023). Less is known about whether the effects of childhood ELS particularly on anxiety are still evident late adulthood, and whether different types of ELS carry differential or additive effects on anxiety symptoms in late adulthood.

The potentially beneficial role of positive maternal mental health during and after pregnancy remains much less investigated; only few studies have addressed its associations with offspring mental health and psychological development. The available evidence shows that positive maternal mental health including positive emotions and social support both during and after pregnancy is associated with beneficial mental health and psychological development among the offspring (Clayborne et al., 2023; Lewinn et al., 2020; Parkes & Sweeting, 2018; Phua et al., 2017; Wei et al., 2023). However, previous research has not extended the follow-up of the offspring beyond early childhood or investigated

whether positive maternal mental health during pregnancy is associated with trajectories in mental health across childhood, e.g. change in psychiatric problems from early childhood to later childhood. Nor have these studies addressed potential timing effects of positive maternal mental health during and after pregnancy on offspring mental health or psychological development, or addressed the associations between positive maternal mental health during pregnancy and the more severe end of the continuum of child psychopathology. Finally, to my knowledge, previous studies have scarcely addressed whether the associations are independent of, or may potentially mitigate the effects of concurrent maternal psychopathology.

3 Aims of the current study

Building on the DOHaD framework and the related life-cycle model of stress, diathesis-stress, differential susceptibility and vantage sensitivity models, my aim in this thesis was to investigate whether promotive factors during and after pregnancy, operationalized here as positive maternal mental health encompassing positive emotions and perceived social support, are associated with better mental health and cognitive development in the offspring. I hypothesized that positive maternal mental health during and after pregnancy may provide long-lasting benefits to the offspring's mental health and cognitive development. Building on resilience theories, I also investigated whether positive maternal mental health shows universal promotive effects for the offspring or protective effects particularly for those exposed to concurrent maternal psychological distress. My second aim was to investigate the long-term effects of ELS experiences on anxiety symptoms in late adulthood. I hypothesized that ELS in childhood increases the risk of anxiety symptoms still in late adulthood. The main study questions are presented in Table 3, and the specific aims of the four included studies were as follows:

3.1 Study I

To investigate the association between positive maternal mental health during pregnancy, defined here as positive emotions and social support, and the incidence of mental and behavioral disorders among children from birth until the age of 8.4−12.8 years. Additionally, to investigate whether the potential association between positive maternal mental health during pregnancy and lower incidence of mental and behavioral disorders in the offspring extends to children of mothers with clinically relevant depressive symptoms during pregnancy and/or with mental and behavioral disorders diagnosed before or during pregnancy.

3.2 Study II

To investigate the association between positive maternal mental health during pregnancy, as described above, and psychiatric problems in the offspring in early childhood at 1.9−5.9 years of age and in late childhood at 7.1−12.1 years of age. Additionally, to examine whether positive maternal mental health during pregnancy predicts change in psychiatric problems from early childhood to late childhood, and to examine whether positive maternal mental health mitigates the effects of maternal psychological distress, e.g. maternal depressive symptoms during pregnancy and/or mental and

behavioral disorders before or during pregnancy, on child psychiatric problems or on the change in psychiatric problems. Finally, to investigate whether positive maternal mental health in child's late childhood mediates the effects of positive maternal mental health during pregnancy on child psychiatric problems.

3.3 Study III

In two longitudinal pregnancy cohorts, to investigate the association between maternal perceived social support during pregnancy and after pregnancy and the objectively assessed general cognitive ability among the offspring at 8 years of age, and whether these associations are independent of or moderate the effects of concurrent maternal depressive and anxiety symptoms on child cognitive ability. Additionally, to investigate the potential timing effects of maternal social support during and after pregnancy in relation to child general cognitive ability in order to determine whether social support at different developmental periods carries differential relevance to child cognitive ability.

3.4 Study IV

To investigate the association of ELS experiences in childhood, operationalized here as physical and emotional maltreatment, separation from parents, parental divorce, death of a family member, and low childhood SES, with self-reported anxiety symptoms in late adulthood at age 65−77 years. Additionally, to investigate whether the accumulation of different ELS experiences is associated with higher anxiety symptoms, and whether these associations extend to anxiety symptoms exceeding the clinically relevant threshold.

Table 3. Main study questions, cohorts, participants and assessment methods included in the four studies of the thesis.

	Study I	Study II	Study III	Study IV
Main study question	Is there an association between positive maternal mental health during pregnancy and mental and behavioral disorders in children?	Is there an association between positive maternal mental health during pregnancy and psychiatric problems in children from early childhood to late childhood?	Is there an association between maternal social support during and after pregnancy and cognitive ability in children?	Is there an association between ELS in childhood and anxiety symptoms in late adulthood?
Participants				
Name(s) of the cohort	PREDO	PREDO	ALSPAC; PREDO	HBCS
Country of origin of the cohort	Finland	Finland	United Kingdom; Finland	Finland
Sample size	3378	2636	5784 (ALSPAC); 420 (PREDO)	1872
Birth years of the participants	2006-2010	2006-2010	1991-1992 (ALSPAC); 2006-2010 (PREDO)	1934-1944
Assessment methods				
Exposure	Positive maternal mental health		Maternal perceived social support	ELS experiences
Timing of exposure	Pregnancy	Pregnancy	During pregnancy and at child age 8 months (ALSPAC) or 8 years (PREDO)	Childhood (before age 18 years)
Source of exposure data	Self-reported	Self-reported	Self-reported	Self-reported and register-based
Assessment method	PANAS; STAI Curiosity scale; VAS social support scale	PANAS; STAI Curiosity scale; VAS social support scale	Social support questionnaire (ALSPAC); SSQ-6 (PREDO)	*Register-based:* Low SES, parental separation; *Self-reported:* TEC (emotional & physical maltreatment, parental divorce, death of a family member)
Outcome	Mental and behavioral disorders in childhood	Psychiatric problems in childhood	General cognitive ability in childhood	Anxiety symptoms in late adulthood
Timing of assessment	8.4-12.8 years	1.9-5.9 years & 7.1-12.1 years	7.4-10.5 years (ALSPAC); 7.0-11.9 years (PREDO)	65-77 years
Source of data	National HILMO register	Mother-reported	Neuropsychological assessment	Self-reported
Assessment method	ICD-10, F00-F99	CBCL	WISC-III (ALSPAC); WISC-IV (PREDO)	BAI

ELS=Early life stress. PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction study. ALSPAC=The Avon Longitudinal Study of Parents and Children. HBCS=The Helsinki Birth Cohort Study. PANAS=Positive and Negative Affect Schedule. STAI=Spielberger State Anxiety Inventory. VAS=Visual Analogue Scale. SSQ=Social Support Questionnaire. TEC=Traumatic Events Checklist. SES=Socioeconomic status. ICD-10=International Statistical Classification of Diseases and Related Health Problems, 10th (ICD-10) Revision. HILMO=Hoitoilmoitusrekisteri, national care register for healthcare. CBCL=Child Behavior Checklist. WISC=Wechsler Intelligence Scale for Children. BAI=Beck Anxiety Inventory.

4 Methods

4.1 Participants

Studies I−III utilized the Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) cohort (Girchenko et al., 2017), Study III additionally utilized the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort (Boyd et al., 2013; Fraser et al., 2013), and Study IV utilized the Helsinki Birth Cohort Study (HBCS) cohort (Eriksson, Forsén, Tuomilehto, Osmond, & Barker, 2001). Characteristics of the cohorts in each study are presented in Table 3 and described more in detail below.

4.1.1 The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) study – studies I−III

The PREDO study, described in detail elsewhere (Girchenko et al., 2017) included 4777 pregnancies that resulted in a birth of a singleton live child in 2006−2010. The women were recruited during their first ultrasound screening visit between 12+0 and 13+6 gestation weeks and days at one of the ten participating study hospitals in Southern and Eastern Finland. Three women have since withdrawn from the study. Of the participating 4774 women, 3402 (71.3%) filled in a battery of questionnaires biweekly up to 14 times throughout their pregnancy, including e.g., reports of their positive and negative mental health.

For Study I, data on diagnoses of mental and behavioral disorders were available for 3378 children (99.3%) of the 3402 mothers with available questionnaire data from pregnancy, and this data was utilized. At the end of the register follow-up the children were 8.4−12.8 years of age (median=10.2, interquartile range (IQR) 9.7−10.8).

For Study II, data from two follow-ups were utilized for the assessment of psychiatric problems among the offspring. In 2011−2012, 4586 of the original 4774 mother-child-dyads were invited to a follow-up (three children had died, 33 did not have available medical birth register data, 55 women had declined participation in a follow up, and addresses for 100 women could not be traced). Of these, 2296 dyads (67.5%) of the 3402 with available positive and negative mental health data during pregnancy participated the follow-up at the child's median age of 3.5 years (IQR 3.0−4.1 years). In 2016, 4505 mother-child-dyads with available contact information were again invited to a follow-up. At this follow-up, 2001 (58.8%) of those with positive mental health data during pregnancy filled out

the questionnaire on psychiatric problems in children at their median age of 9.4 years (IQR 8.9−10.1 years). Overall, 2636 mother-child-dyads (77.5% of those with available pregnancy data) provided data for psychiatric problems in children in at least one of the follow-ups, and 1661 mother-child-dyads (48.8% of those with available pregnancy data) provided data at both follow-ups.

Study III utilized data primarily from the 1079 pregnant women recruited to the clinical arm of the PREDO study (Girchenko et al., 2017), 969 (89.8%) of whom had one or more known risk factors for preeclampsia and intrauterine growth restriction. This sample was further appended by 89 pregnant women from the control arm of the study who were recruited independently of their risk factor status and donated placenta samples after delivery; together, the sample consisted of 1168 pregnant women. Of these women, 828 (70.9%) reported their perceived social support during pregnancy with a self-report questionnaire. These 828 women did not differ from the original PREDO sample in their self-reported perceived social support (mean difference 0.06 units; t=0.34, p=.73). Of the 828 women, 497 (60.0 %) reported their perceived social support again after pregnancy at child age 8 years. Neurocognitive assessment data were available for 420 (50.7%) children of mothers with social support data from pregnancy, and for 370 (74.4%) children of mothers with social support data from pregnancy and after pregnancy, at median child age of 8.5 years (range 7.0−11.9).

4.1.2 Avon Longitudinal Study of Parents and Children (ALSPAC) – study III

The ALSPAC study is an ongoing population-based cohort study (Boyd et al., 2013; Fraser et al., 2013) that recruited pregnant women living in the Avon area, United Kingdom, who had their expected dates of delivery between 1st April 1991 and 31st December 1992. Initially, the study comprised 14541 pregnancies in which mothers completed questionnaires during pregnancy; these pregnancies resulted in 14,062 live births and 13,988 children who were alive at 1 year of age. The ALSPAC study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool that can be found at http://www.bristol.ac.uk/alspac/researchers/our-data/.

Of the participating women with singleton pregnancies (n=14,468), 10,528 (72.8%) reported their perceived social support during pregnancy with a questionnaire. Of them, 9,175 (87.1%) reported their perceived social support again after pregnancy at child age 8 months. Neurocognitive assessment data were available for 5,784 (54.9%) children of mothers with social support data from pregnancy, and for 5,498 (59.9%) children of mothers with social support data from pregnancy and after pregnancy, at median child age of 8.5 years (range 7.4−10.5).

4.1.3 The Helsinki Birth Cohort Study (HBCS) – study IV

The sample of this study is a part of the HBCS cohort that originally comprises 13,345 singleton participants (52.3% male) born in one of the two main maternity hospitals in Helsinki, Finland, between 1934 and 1944. The HBCS has been described in detail elsewhere (Eriksson et al., 2001). In 2001−2004, at the age of 57−70 years, a subsample of the cohort was invited to a clinical examination (Kajantie, Barker, Osmond, Forsen, & Eriksson, 2008), during which they completed a questionnaire on ELS experiences. In 2009−2010, when members of the cohort were aged 65−77 years, a battery of psychological questionnaires including a questionnaire on anxiety symptoms was administered to 4147 randomly selected participants of the original HBCS study (Tuovinen et al., 2014), 1893 (45.6%) of whom returned the questionnaire. The final sample comprised 1872 participants (57.8% male) who completed the anxiety questionnaire. Of these 1872 participants, 1277 (68.2%) had also completed the questionnaire on ELS experiences in 2001−2004. The mean time difference between completing the questionnaires on ELS and on anxiety was 5.68 years (SD 0.45, range 4.66–6.37 years).

4.2 Ethical considerations

All of the cohort studies used in this thesis were conducted in accordance with the Helsinki Declaration and have been reviewed and approved by relevant national and institutional boards, as described more in detail below.

The PREDO study protocol was approved by the Ethics committee of the Helsinki and Uusimaa Hospital District. All participants gave their written informed consent, also enabling linkage of the questionnaire data with nationwide health register data for the women, their spouses, and children. Register data were obtained by permission of the relevant register authorities.

Ethical approval for the ALSPAC study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. All mothers gave their written informed consent to participate; children provided their consent after receiving a full explanation of the study. Approval for secondary data analyses was obtained from Yale University Institutional Review Board (Protocol ID: 2000036041).

The HBCS study has been approved by the Ethics Committee of the National Public Health Institute (now called The Finnish Institute for Health and Welfare) and was carried out in accordance with the relevant guidelines and regulations. All participants gave their written informed consent to participate.

4.3 Data attrition

Table 4 shows the comparisons of the participants included in Studies I−III with the non-participants of the PREDO and ALSPAC cohorts regarding the relevant covariates in each study. Briefly, in comparison to the sample that had no data on the exposures/outcomes and were therefore not included in the analyses in Studies I−III, the samples with all data available comprised women who were older, more often primiparous, more likely to be married/cohabiting and to have a higher education level, and more likely to report substance use in early pregnancy; the only exception was the subsample of the PREDO cohort included in Study III, in which the participating mothers had a higher education level but did not differ from the non-participating mothers regarding other covariates. In Studies I−II, participants were additionally less likely than non-participants to have a cardio-metabolic pregnancy condition or any lifetime mental or behavioral disorder. In Study I, the children of the subsample with available pregnancy and diagnostic data were less likely to have a mental or behavioral disorder diagnosis by follow-up (10.6% vs. 12.7%, p=.04). The participants of the PREDO subsamples in Studies I−III did not differ from the non-participants in child sex, birth weight, gestational age, or the prevalence of mental and behavioral disorders of the father. In ALSPAC, the participating children of Study III were more often female, White and with a higher birthweight and gestational age, in comparison with the non-participating children of the cohort.

In Study IV, compared to the non-participants of the initial HBCS cohort of 13345 participants, the participants included in the current study sample (n=1872) were more often male (51.4% vs. 57.8%, respectively, p<.001) and had been less often separated from their parents due to war time evacuations in childhood based on register-data (13.7% vs. 11.2%, p=.004). The non-participant and participant groups did not differ in low childhood SES (44.7% vs. 42.5%, p=.09). In comparison with the participants who provided data on anxiety symptoms at 65−77 years of age but did not complete the questionnaire on ELS experiences at 57−70 years of age and were thus excluded from the analyses regarding self-reported ELS (e.g., physical and emotional maltreatment, parental divorce, and death of a family member), the participants who did provide data on these ELS experiences were older (mean difference 0.89 years, p<.001) and reported higher anxiety symptoms in late adulthood (mean difference 0.18 SD units, p<.001).

Table 4. Differences between the participants of the analytic subsample in Studies I-III and the non-participants of the initial cohort that were not included in the analyses of each study.

	Study I			Study II			Study III					
							ALSPAC			PREDO		
	Participants (N=3378)	Non-participants (N=1396)	P-value	Participants (n=2636)	Non-participants (n=2138)	P-value	Participants (N=5784)	Non-participants (N=8684)	P-value	Participants (N=420)	Non-participants (N=748)	P-value
MATERNAL CHARACTERISTICS												
Age at delivery (years), mean (SD)	31.8 (4.7)	30.8 (5.3)	**<.001**	31.90 (4.62)	31.00 (5.16)	**<.001**	29.23 (4.49)	27.09 (5.11)	**<.001**	33.39 (5.41)	32.82 (5.96)	.11
Unknown, no. (%)	-	10 (0.7)			10 (0.5)		-	572 (6.6)		-	-	
Parity, N (%)			**<.001**			**<.001**			**.001**			.48
Primiparous	1379 (40.8)	476 (34.1)		1102 (41.8)	753 (35.2)		2605 (45.0)	3137 (36.1)		145 (34.5)	243 (32.5)	
Multiparous	1999 (59.2)	920 (65.9)		1534 (58.2)	1385 (64.8)		3051 (52.7)	4125 (47.5)		275 (65.5)	505 (67.5)	
Missing							128 (2.2)	1422 (16.4)		-	-	
Education level, N (%)												
ALSPAC									**<.001**			
Degree							959 (16.6)	625 (7.2)				
A-levels							1539 (26.6)	1231 (14.2)				
O-levels							2001 (34.6)	2266 (26.1)				
None/CSE/vocational							1179 (20.4)	2524 (29.1)				
Missing							106 (1.8)	2038 (23.5)				
PREDO			**.008**			**<.001**						**<.001**
Upper tertiary	1153 (34.1)	299 (21.4)		1060 (40.2)	531 (24.8)					167 (39.8)	205 (27.4)	
Lower tertiary	872 (25.8)	265 (19.0)		831 (31.5)	449 (21.0)					132 (31.4)	187 (25.0)	
Primary/secondary	1348 (39.9)	454 (32.5)		745 (28.3)	820 (38.4)					121 (28.8)	326 (43.6)	
Missing	5 (0.1)	378 (27.1)		-	338 (15.8)					-	30 (4.0)	
Household crowding index (number of people by room)									**<.001**	N/A		
0-0.50							2812 (48.6)	2607 (30.0)				
0.50-0.75							1761 (30.4)	2329 (26.8)				
0.75-1							864 (14.9)	1770 (20.4)				
>1							197 (3.4)	702 (8.1)				
Missing							150 (2.6)	1276 (14.7)				
Marital/cohabiting status, N (%)			**<.001**			**<.001**			**<.001**	N/A		
Married/cohabiting	3293 (97.5)	1277 (91.5)		2582 (98.0)	1988 (93.0)		5326 (92.1)	6463 (74.4)				
Not cohabiting	76 (2.2)	56 (4.0)		50 (1.9)	82 (3.8)		413 (7.1)	1210 (13.9)				
Missing	9 (4.5)	63 (4.5)		4 (0.2)	68 (3.2)		45 (0.8)	1011 (11.6)				
Substance use during pregnancy[a)]			**.007**			**.01**			**<.001**			.73
No	2690 (76.6)	1140 (81.7)		2092 (79.4)	1738 (81.3)		2133 (36.9)	2480 (28.6)		329 (78.3)	478 (63.9)	
Yes	687 (20.3)	232 (16.6)		544 (20.6)	375 (17.5)		3595 (62.2)	4806 (55.3)		86 (20.5)	132 (17.6)	
Missing	1 (0.03)	24 (1.7)		-	25 (1.2)		56 (1.0)	1398 (16.1)		5 (1.2)	138 (18.4)	
Cardio-metabolic pregnancy conditions[b)], N(%)			**.04**			**.004**	N/A					.88
Yes	1432 (42.4)	632 (45.3)		1092 (41.4)	972 (45.5)					138 (32.9)	249 (33.3)	
No	1706 (50.5)	640 (45.8)		1358 (51.5)	988 (46.2)					282 (67.1)	499 (66.7)	
Only before current pregnancy	234 (6.9)	103 (7.4)		183 (6.9)	154 (7.2)					-	-	
Unknown	6 (0.2)	21 (1.5)		3 (0.1)	24 (1.1)					-	-	

Mental and behavioral disorders before/during pregnancy[c], N(%)			**<.001**			**<.001**			N/A			
No	3084 (91.3)	1173 (84.0)		2425 (92.0)	1832 (85.7)							
Yes	294 (8.7)	203 (14.5)		211 (8.0)	286 (13.4)							
Missing	-	20 (1.4)		-	20 (0.9)							
Mental and behavioral disorders by the child's first mental or behavioral disorder[c], N(%)			**<.001**			**<.001**			N/A			
No	2849 (84.3)	1068 (76.5)		2250 (85.4)	1643 (77.6)							
Yes	529 (15.7)	308 (22.1)		386 (14.6)	475 (22.4)							
Missing	-	20 (1.4)		-	20 (0.9)							
CHILD CHARACTERISTICS												
Sex, N (%)			.18			.07			**.001**			.05
Male	1743 (51.6)	741 (53.1)		1345 (51.0)	1139 (53.3)		2895 (50.1)	4319 (49.7)		208 (49.5)	415 (55.5)	
Female	1635 (48.4)	638 (45.7)		1291 (49.0)	982 (45.9)		2889 (49.9)	3853 (44.4)		212 (50.5)	333 (44.5)	
Missing	-	17 (0.4)		-	17 (0.8)		-	512 (5.9)		-	-	
Birth weight (grams), mean (SD)	3526.5 (517.2)	3546.3 (538.4)	.24	3522.95 (514.00)	3543.80 (534.88)	.17	3435.65 (534.18)	3362.79 (593.76)	**<.001**	3492.68 (554.66)	3526.60 (596.80)	.34
Missing, N (%)	11 (0.3)	33 (2.3)		7 (0.3)	26 (0.5)		67 (1.2)	680 (7.8)		-	-	
Gestational age (weeks), mean (SD)	39.9 (1.6)	39.9 (1.7)	.48	39.91 (1.55)	39.86 (1.67)	.31	39.49 (1.80)	37.69 (6.84)	**<.001**	39.74 (1.55)	39.62 (1.95)	.24
Missing, N (%)	-	4 (0.3)		-	4 (0.2)		-	44 (0.5)		-	-	
Ethnic background	N/A			N/A					**<.001**	N/A		
White							5399 (93.3)	5983 (68.9)				
Non-white							198 (3.4)	404 (4.7)				
Missing							187 (3.2)	2297 (26.5)				
PATERNAL CHARACTERISTICS												
Mental and behavioral disorders by the child's first mental or behavioral disorder[c]			.68	N/A					N/A			
Yes	126 (3.7)	38 (2.7)										
No	1680 (49.7)	548 (39.3)										
Missing	1572 (46.5)	810 (58.0)										

PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study. ALSPAC=Avon Longitudinal Study of Parents and Children.

a) Smoking and/or alcohol use during pregnancy.

b) Studies I-II: Early pregnancy body mass index [BMI]≥25kg/m2, hypertensive disorders of pregnancy, and/or type 1, type 2 or gestational diabetes. Study III: Hypertensive disorders of pregnancy.

c) All mental disorder diagnoses based on the International Classification of Diseases 8th (ICD-8; codes 290−315) and 9th (ICD-9; codes 290−319) Revisions and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10; codes F00−F99).

4.4 Assessment methods

Specific assessment methods used to investigate each exposure and outcome of interest are presented in Table 3 and described more in detail below.

4.4.1 Positive maternal mental health during and after pregnancy

Positive maternal mental health during and after pregnancy was operationalized as positive emotions and/or perceived social support in Studies I−III. In Studies I−II in the PREDO cohort, maternal positive emotions were assessed with two scales. The positive scale of The Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) comprises 10 positive mood items such as "excited" or "interested". Each item is assessed on a 5-point scale from 1 (not at all) to 5 (very much). The score thus ranges from 10 to 50, higher score reflecting more positive emotions. The second scale, the Curiosity subscale of Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, 1983), is a 40-item questionnaire assessing state-like anxiety symptoms and trait-like anxiety. The STAI Curiosity subscale comprises 10 items measuring positive emotionality at the moment of assessment, assessed on a 4-point scale ranging from 1 (not at all) to 4 (very much), score thus ranging from 10 to 40 (Spielberger & Reheiser, 2009). Previous studies indicate that positively worded subscales of frequently used psychological distress screening tools such as the STAI can be used as measures of positive mental health (Hernandez-Martinez et al., 2011; Kvaal et al., 2001; Phua et al., 2017; Shafer, 2006). To report social well-being in Studies I−II, mothers assessed their level of perceived social support with a Visual Analogue Scale (VAS), placing a mark on a 65 millimeters long line indicating how much support they felt they had received from others during the past two weeks ("Not at all" to "Very much").

Psychometric properties are good for PANAS (Crawford & Henry, 2004; Terracciano et al., 2003; Watson et al., 1988) and for STAI (Spielberger, 1983), also in pregnant populations (Grant et al., 2008; Meades & Ayers, 2011; Sinesi et al., 2019). In the samples of Studies I and II, the internal consistencies of the scales were good, α=.91−.94 for PANAS and α=.94−.95 for STAI Curiosity across the biweekly measurement points.

The participants completed the PANAS, STAI and VAS questionnaires biweekly up to 14 times throughout pregnancy, starting at 12+0/13+6 gestation weeks and days, and continuing up to 38+0/39+6 gestation weeks and days or delivery. A trimester-weighted mean of all measurement points was used for each questionnaire, e.g. the mean was first calculated for each pregnancy trimester

(only gestation week 12 in the first trimester, mean of gestation weeks 14−28 in the second trimester, and mean of gestation weeks 29−delivery in the third trimester) and the mean score was then calculated from these three trimester means. The participants also completed the same three questionnaires at the late childhood follow-up of Study II, at the child's median age of 9.4 years (IQR 8.9−10.1 years).

In Study III in the PREDO cohort, mothers assessed their perceived satisfaction with social support by completing a six-item Sarason's Social Support Questionnaire (SSQ-6) (Sarason et al., 1987). First, mothers reported on each item the number of people that would provide them social support (e.g. "Whom can you count on to console you when you are very upset?"), followed by satisfaction with this support on a six-point scale (ranging from "not at all satisfied" (1) to "very satisfied" (6) for each item). The SSQ-6 satisfaction sum score therefore ranged from 6−36, higher score indicating higher satisfaction with social support. Mothers completed the SSQ-6 once in pregnancy, at median gestational week 12, and again approximately at the child's age 8 years. The questionnaire shows good psychometric properties (Friedman et al., 2018; Rascle & Bruchon-Schweitzer, 2005). In the current sample, reliability was excellent during (α=.92) and after pregnancy (α=.93).

In Study III in the ALSPAC cohort, mothers assessed their perceived satisfaction with social support both during and after pregnancy with a ten-item questionnaire (e.g., "There are other pregnant women with whom I can share my experiences", "My partner provides the emotional support I need"). Each item was rated on a four-point scale (ranging from "often feel" (0) to "never feel" (3)). If the woman reported not having a partner during their pregnancy, partner-related items were coded as "never feel". Positively worded items were reverse-coded, resulting in a sum score ranging from 0−30; higher score indicated higher satisfaction with social support. Mothers completed the questionnaire once during pregnancy, at median gestational week 24, and again approximately at the child's age 8 months. The questionnaire, developed by the ALSPAC study team, shows good predictive validity (Thomson et al., 2014; Tracy, Salo, & Appleton, 2018); in the current sample, reliability was acceptable during (α=.73) and after pregnancy (α=.74).

4.4.2 Maternal psychological distress during and after pregnancy and parental mental and behavioral disorders

To assess whether the associations of positive maternal mental health with offspring psychopathology and cognitive ability were independent of maternal psychological distress in Studies I−III, maternal psychological distress was operationalized as depressive symptoms and/or anxiety symptoms and/or

as lifetime mental and behavioral disorders. Additionally, paternal mental and behavioral disorders were considered in Study I. Indicators of maternal and paternal psychological distress are described in detail below.

In Studies I−II, indicators of psychological distress included maternal depressive symptoms during pregnancy and mental and behavioral disorders before or during pregnancy. Maternal depressive symptoms were assessed with the Centre for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). CES-D is a 20-item scale assessing depressive symptoms during the past week. CES-D has excellent psychometric properties (Radloff, 1977; Shafer, 2006) also in pregnant populations (Maloni et al., 2005; Nast et al., 2013). A cut-off score of 16 was used to identify women with clinically relevant depressive symptoms, as suggested by previous studies (Radloff, 1977; Vilagut, Forero, Barbaglia, & Alonso, 2016). Similarly to positive maternal mental health measures described above, a trimester-weighted mean of biweekly CES-D reports throughout pregnancy was used in Studies I−II.

Physician-diagnosed lifetime maternal mental and behavioral disorders were identified from the Finnish nationwide Care Register for Health Care (HILMO) which is a validated register for studying mental and behavioral disorders (Sund, 2012). This register provides data of mental and behavioral disorder diagnoses classified using the International Classification of Diseases 8th (ICD-8; codes 290−315) and 9th (ICD-9; codes 290−319) Revisions and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10; codes F00−F99). I identified all primary and subsidiary diagnoses of maternal hospital treatments in Finland since 1969 and of all outpatient treatments in public specialized medical care in Finland since 1998 until each relevant follow-up of Studies I−II. For each study question, I then included diagnoses from the time period that was relevant for the study question, as described in the Statistical analyses section. In Study I, I also included data on paternal mental and behavioral disorders derived from HILMO similarly to data on maternal mental and behavioral disorders.

In Study III, indicators of psychological distress included maternal depressive and anxiety symptoms during and after pregnancy, reported concurrently with the reports of perceived social support. The PREDO cohort assessed maternal depressive symptoms with the CES-D scale and anxiety symptoms with the 20-item State-version of the STAI scale; both scales are described above. For this study, reports from gestational week 12 were used from pregnancy as they coincided with maternal reports of social support with the SSQ-6 questionnaire. Depressive symptoms and anxiety symptoms were reported again when the children were approximately 8 years of age. In Study III, the reliabilities were α=.91 and α=.88 for CES-D scales and α=.95 and α=.94 for STAI scales during and after

pregnancy, respectively. The ALSPAC cohort assessed maternal depressive symptoms using the self-reported ten-item Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, & Sagovsky, 1987), and anxiety symptoms using the self-reported eight-item anxiety subscale of the Crown-Crisp Experiential Index (CCEI) (Birtchnell, Evans, & Kennard, 1988). Mothers completed both questionnaires at gestational week 18 during pregnancy, and again at child age 8 months, concurrently with reporting their perceived social support. Both questionnaires show good psychometric properties (Birtchnell et al., 1988; Cox et al., 1987; Hewitt et al., 2009); in this study, the reliabilities were α=.85 and α=.86 for EPDS scales and α=.79 and α=.84 for CCEI anxiety scales during and after pregnancy, respectively.

4.4.3 ELS in childhood

In Study IV, six indices of ELS were included: physical and emotional maltreatment, separation from parents, death of a family member, parental divorce, and low childhood SES. These variables are described more in detail below.

Participants retrospectively self-reported their childhood physical and emotional maltreatment experiences with the Traumatic Experiences Checklist (TEC) (Nijenhuis, Van der Hart, & Kruger, 2002). The original TEC comprises 29 items describing potentially traumatic life events. Six specific items are used to report physical maltreatment (e.g., "physical abuse (e.g., being hit, tortured, or wounded) by your parents, brothers, or sisters", "unexpected/bizarre punishment") and six specific items are used to measure emotional maltreatment, including emotional abuse (e.g., "emotional abuse (e.g. being belittled, teased, called names, threatened verbally, or unjustly punished) by your parents, brothers, or sisters") and neglect (e.g., "emotional neglect (e.g., being left alone, insufficient affection)". These six items for each type of maltreatment (physical and emotional) were included in this study. Participants were also asked to report the age in which the maltreatment had occurred. Binary variables of the occurrence of physical and emotional maltreatment were formed, "yes" indicating that the participant had experienced at least one of the six physical or emotional maltreatment experiences in childhood. Participants not reporting physical or emotional maltreatment and those reporting maltreatment only in adulthood (>18 years of age) were used as a control group. Participants with missing values either in the question on the maltreatment experience or on the age of maltreatment were excluded from the analyses regarding physical or emotional maltreatment in childhood. The TEC has good psychometric properties (Nijenhuis et al., 2002; Schumacher, 2012).

Data on parental divorce and on the death of a family member during childhood were also collected from the TEC questionnaire, by using dichotomic items "your parent's divorce" and "loss of a family member when you were a child (brother, sister, parent)" and the reported age at which parental divorce/death of a family member occurred. Participants reporting no parental divorce/death of a family member or parental divorce/death of a family member at the age of 18 or older were used as a control group.

Data on separation from parents were derived from a register in the Finnish National Archives, which comprises data on World War II -related child evacuations, age at first evacuation, and duration of separation from parents. During the war, approximately 80000 Finnish children were evacuated from their homes due to wartime insecurity. Many of the children were sent to Sweden and Denmark unaccompanied by their parents, and siblings were often placed in different families to promote learning the new language faster (Kavén, 1985). For the participants that had been evacuated according to the register data, the evacuation happened at the mean age of 4.42 years (SD 2.33, range 0−10 years) and for a mean duration of 1.76 years (SD 1.05, range 0−7 years). Additionally, some participants reported having been evacuated during World War II although no data on the evacuation were found in the register. These participants may have been separated from their parents through other means, for example through being accommodated by relatives. Participants with self-reported separation were thus included in the analyses as a separate group, while participants with register-based separation or both self-reported and register-based separation were coded to the same category of register-based separation.

Data on childhood SES was based on the highest recorded occupational status (manual worker, clerical worker (including both upper and lower clerical worker status)) of either parent. Register data of the occupational status of the parents were extracted from birth-, child welfare clinic-, and school healthcare records. Low childhood SES was defined as "manual worker" being the highest occupational status of either parent; "clerical worker" status served as the reference group.

4.4.4 Mental health and cognitive ability in the offspring

Offspring outcomes in Studies I−III, namely mental and behavioral disorders, psychiatric problems, and cognitive ability in children, were assessed by using data from national registers, maternal reports, and standardized objective measures, respectively. Assessment methods used in each study are described more in detail below.

In Study I, data on child mental and behavioral disorder diagnoses (F-codes 00−99 in ICD-10; World Health Organization, 2004) was obtained from the HILMO register, described in detail in Chapter 4.4.2. The follow-up data includes all diagnoses from the child's birth until 31 December 2018, by which the children were aged 8.4−12.8 years. The study used any mental and behavioral disorder diagnosis as the diagnostic outcome as this outcome had sufficient statistical power to reliably address the study questions in this age group. The HILMO register has been validated for certain childhood mental and behavioral disorders such as autism and ADHD (Joelsson et al., 2016; Lampi et al., 2010).

In Study II, child psychiatric problems were mother-assessed at the two follow-ups with age-appropriate versions of the Child Behavior Checklist (CBCL): CBCL for ages 1½−5 years (CBCL/1½−5) (Achenbach & Rescorla, 2000) at the early childhood follow-up and CBCL for ages 6−18 years (CBCL/6−18) (Achenbach & Rescorla, 2001) at the late childhood follow-up. CBCL scales comprise 99 and 119 problems, respectively, that the caregiver rates on a three-point scale from "not true" (0) to "very true/often true" (2). Both scale versions show excellent validity and reliability (Achenbach & Rescorla, 2001, 2000; Kristensen, Henriksen, & Bilenberg, 2010; Rescorla, 2005). CBCL scales yield three main scales, namely total, internalizing and externalizing problems (Achenbach & Rescorla, 2001, 2000). I used the Total problem scale as the main outcome, and Internalizing and Externalizing problem scales as secondary outcomes. CBCL scores were converted to age- and sex-standardized t-scores according to the manuals (Achenbach & Rescorla, 2001, 2000), enabling the investigation of change in psychiatric problems across the two follow-ups and across the two questionnaire versions.

In Study III, general cognitive ability (IQ) in children was assessed with the most current version of the Wechsler Intelligence Scale for Children (WISC) at the time of the assessment in both cohorts. In ALSPAC, the WISC 3rd UK edition (WISC-III) (Wechsler, Golombok, & Rust, 1992) was used to during an in-person visit. The WISC-III was administered by a member of the psychology team of the ALSPAC research group. In the short version of the WISC-III that was used in this study, items in each subtest were alternated, beginning with item 1 in each subtest; as an exception, the coding subtest was administered in its full form. Each short-form subtest scores were then multiplied in order to generate scores that were comparable to the original WISC-III scales. Finally, scores were age-scaled to form a Total IQ score that has a mean of 100 and a SD of 15. Total IQ score was obtained based on the UK normative data provided by the WISC-III manual (Wechsler et al., 1992). In PREDO, a short form of the WISC 4th Finnish edition (WISC-IV) (Wechsler, 2010), described in detail elsewhere (Crawford, Anderson, Rankin, & MacDonald, 2010), was used to objectively assess children's IQ during an in-person visit. The WISC-IV was administered by a neuropsychologist or a

psychology student supervised by a neuropsychologist, usually in a home setting. In the short-form WISC-IV, seven subtests of the WISC-IV were administered, and a full-scale IQ score was formed and converted to a scale that has a mean of 100 and SD of 15, based on Finnish normative data (Wechsler, 2010). The reliability of the short-version Full-scale IQ is excellent, and it correlates strongly with the full-length WISC-IV Full-scale IQ score (Crawford et al., 2010).

4.4.5 Anxiety symptoms in late adulthood

In Study IV, anxiety symptoms were assessed using the Finnish version of the Beck Anxiety Inventory (BAI) (Beck, Epstein, Brown, & Steer, 1988). The BAI comprises 21 items describing symptoms typical to anxiety, including both somatic anxiety symptoms (e.g., "numbness or tingling") and subjective feelings of anxiety and panic (e.g., "fear of worst happening"). The participants report how much they have experienced the symptom in question in the past week. The total BAI score varies on a scale from 0 to 63, a higher score reflecting more severe anxiety symptoms. According to the BAI manual and a meta-analysis, a cutoff score of 16 refers to clinically relevant anxiety symptoms, described as "moderate" or "severe" symptoms (Bardhoshi, Duncan, & Erford, 2016; Beck & Steer, 1993). This cutoff score was used to additionally investigate if the association between different types of ELS and anxiety symptoms exceeding the clinically relevant threshold. The participants reported their anxiety symptoms in late adulthood at the mean age of 68.73 years (SD = 2.84, range 65–77).

The BAI has good psychometric properties (Bardhoshi et al., 2016; Beck et al., 1988; Steer, Ranieri, Beck, & Clark, 1993), also among elderly participants (Kabacoff, Segal, Hersen, & Van Hasselt, 1997). In this study, the internal consistency of the BAI scale was α=.86.

4.4.6 Relevant covariates included in each study

This chapter outlines the covariates previously associated with maternal mental health during pregnancy and/or offspring mental health (Girchenko et al., 2018; Lahti et al., 2017; Lewinn et al., 2020; O'Connor et al., 2022; Tuovinen et al., 2018) and with ELS in childhood and/or anxiety in late adulthood (Lahti et al., 2010; Räikkönen et al., 2011; Stansfeld et al., 2011) that were therefore included as covariates in the studies of this thesis.

Covariates in Studies I−II included maternal age at delivery (years), parity (primiparous, multiparous), marital status (cohabiting or married, single parent), cardio-metabolic pregnancy

conditions (no pregnancy condition, hypertension or gestational diabetes only before current pregnancy, early pregnancy body mass index [BMI]≥25kg/m^2/chronic hypertension/preeclampsia/ gestational hypertension/unspecified hypertension in current pregnancy [ICD-10: I10, 010−011, O13−O16]/and/or type 1 or type 2 diabetes or gestational diabetes in current pregnancy [ICD-10: E08−E14, O24]), and child's sex, birth year, gestational age (weeks) and birth weight (grams); data on these covariates were derived from the Finnish nationwide Medical Birth Register (MBR) (Gissler, Louhiala, & Hemminki, 1997) and/or the HILMO register. Mothers self-reported their education level (primary or secondary, lower tertiary, upper tertiary) in early pregnancy. Data on maternal substance use during pregnancy was based on MBR data on smoking (no smoking, quit during 1st trimester or smoked throughout pregnancy) and self-reported data on alcohol consumption during early pregnancy (no, yes). Additional analyses were adjusted for maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder or the end of the follow-up.

In Study III, covariates in both cohorts included maternal age at delivery (years), parity (primiparous, multiparous), education level, substance use during early pregnancy (no substance use, any smoking and/or alcohol use), and, and child age at cognitive assessment (years). Maternal age and parity were self-reported in ALSPAC and derived from MBR in PREDO. Education level was self-reported in both cohorts; in ALSPAC, education level was defined as the highest educational attainment within the UK educational system, ranging from none/Certificate of Secondary Education (CSE) or vocational training, O-levels, A-levels, to university degree or higher, whereas in PREDO, education level was defined as primary or secondary, lower tertiary, or upper tertiary degree. Substance use during early pregnancy was self-reported and/or derived from MBR. Data on child sex, birthweight and gestational age were derived from medical records in both cohorts, and child age at cognitive assessment (years+months) was recorded during the in-person assessment visit. Additionally in the ALSPAC cohort, covariates included self-reported household crowding index (number of people in the household divided by the number of rooms: <0.5, ≥0.50–0.75, >0.75–1.00, >1.00, higher number indicating higher crowding), marital/cohabiting status during pregnancy (married or cohabiting, not cohabiting), and ethnic background of the child (White, non-White). In the PREDO subsample, only 2.4% of the 420 mothers in Study III were not married/cohabiting during pregnancy, and marital/cohabiting status was therefore not included as a covariate. Data on household crowding and child ethnic background were unavailable in PREDO. Additionally in the PREDO cohort, analyses were adjusted for the presence or absence of maternal hypertensive disorders during pregnancy (preeclampsia, eclampsia, gestational or chronic hypertension, and unspecified hypertension;

International Classification of Diseases, 10th revision codes: I10, O10, O12−O16), since the clinical study sample was enriched for women at elevated risk of preeclampsia (Girchenko et al., 2017). Data on hypertensive disorders were derived from the MBR, medical records, and Care Register for Health Care (Sund, 2012) and operationalized as a binary variable (none, one or more).

In Study IV, the participant's sex based on register data and self-reported age at completing the BAI questionnaire were included as covariates in all models. In the analyses regarding ELS based on the TEC (physical and emotional maltreatment, parental divorce, and death of a family member), the time interval between completing the TEC and the BAI was also included as a covariate in order to account for the potential effect of variation in the time interval. Additional analyses examined whether adulthood SES modified the associations between ELS and anxiety symptoms; in these analyses, adulthood SES was included as an additional covariate. Data on adulthood SES of the participants was based on the participant's own highest lifetime level of education achieved (upper secondary school education or lower, tertiary education (including lower and upper tertiary education)). Low adulthood SES was defined as an education level of upper secondary school or lower; tertiary education served as a reference category. Information on adulthood SES was derived from Statistics Finland and was available for all 1872 participants.

4.5 Statistical analyses

The main statistical analyses of this thesis were conducted with linear and logistic regression analyses, mixed models, Cox proportional hazards models, and Bayesian relevant life course modelling. These statistical methods and their application for each study question are described in more detail below. Complete-case analyses were conducted in all of the studies; the sample size for each statistical model is presented in Table 5, and the number and percentage of missing data for each variable are presented in Tables 6 and 11. There was one exception: data on paternal mental and behavioral disorders was missing from 46.5% of the participants, and missing data on this variable was coded as a separate analytic category. To facilitate effect size interpretation, all continuous independent variables were standardized. When necessary, square-root or rank-order transformations were used to correct for skewness in the continuous scales. Statistical analyses were conducted using IBM SPSS Statistics 26−29, R4.0.3−4.1.0, and Stata 17. Table 5 presents the covariates included in each statistical model in Studies I−IV.

Table 5. Covariates included in each statistical model in Studies I-IV.

	Study I	Study II	Study III	Study IV
Model 1	*child-related:* sex assigned at birth, birth year	*child-related:* sex assigned at birth, age at assessment	*child-related:* sex assigned at birth, age at assessment	age at assessment, sex, time interval between reporting ELS and anxiety symptoms
N for Model 1	*3378*	*2296 (early childhood); 2001 (late childhood)*	*ALSPAC: 5784/5498 (during/after pregnancy) PREDO: 420/370 (during/after pregnancy)*	*1023-1872 for each ELS type*
Model 2 ***(in addition to covariates of Model 1)***	*mother-related:* age at childbirth, parity, marital status, education level, substance use during pregnancy, cardio-metabolic pregnancy conditions; *child-related:* birthweight, gestational age	*mother-related:* age at childbirth, parity, marital status, education level, substance use during pregnancy, cardio-metabolic conditions, negative mental health; *child-related:* birthweight, gestational age	*mother-related:* age at childbirth, parity, education level, substance use during pregnancy (both cohorts), household crowding & marital status (ALSPAC), hypertensive disorders in pregnancy (PREDO); *child-related:* birthweight, gestational age (both cohorts), ethnic background (ALSPAC)	other ELS types included in the study (e.g., physical and emotional maltreatment, separation from parents, death of a family member, parental divorce, low SES)
N for Model 2	*3354*	*2289 (early childhood); 1993 (late childhood)*	*ALSPAC: 5300/5090 (during/after pregnancy) PREDO: 415/366 (during/after pregnancy)*	*1023-1872 for each ELS type*
Model 3 ***(in addition to covariates of Model 2)***	maternal clinically relevant depressive symptoms during pregnancy, maternal mental disorders by childbirth		*mother-related:* depressive and anxiety symptoms concurrently with social support assessment	adulthood SES
N for Model 3	*3353*		*ALSPAC: 5209/5088 (during/after pregnancy) PREDO: 415/362 (during/after pregnancy)*	*1023-1872 for each ELS type*

ELS=Early life stress. SES=Socioeconomic status. ALSPAC=Avon Longitudinal Study of Parents and Children. PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study.

Moreover, since the indices of positive maternal mental health included in Studies I−II (e.g., positive affect, curiosity and social support) were highly interrelated, I first conducted a principal component analysis (PCA) to reduce the dimensionality of the data while retaining maximum statistical power. Eigenvalue criterion 1 was used to extract the principal components. In the subsample of Study I, the PCA yielded one principal component (eigenvalue = 2.00; loadings 0.87, 0.87 and 0.70 for PANAS, STAI Curiosity and VAS, respectively), explaining 66.6% of the total variance. In the subsample of Study II, the PCA yielded one principal component both during pregnancy and in late childhood; this principal component explained 66.7% (eigenvalue 2.0, loadings 0.87, 0.87 and 0.70) and 60.7% (eigenvalue 1.8, loadings 0.85, 0.85 and 0.61) of the total variance during pregnancy and in late childhood, respectively. In the subsequent analyses of Studies I−II, the PCA-based composite score was used as the primary index of positive maternal mental health during pregnancy.

4.5.1 Positive maternal mental health and offspring mental health and psychological development (Studies I−III)

In Study I, the associations of the PCA-based positive maternal mental health composite score with mental and behavioral disorders in children were investigated with Cox proportional hazards models. The children were followed from birth until their first mental and behavioral disorder diagnosis, and were censored from the analyses at death, moving abroad, or at the end of the follow-up in 31/12/2018. Utilizing the Cox models enabled me to accommodate the fact that the length of the follow-up varies by individual based on their birth date. Cox models provide hazard ratios (HR) and 95% Confidence Intervals (CI) for the cumulative incidence of mental and behavioral disorders. Before applying the Cox models, time-dependent Cox regression was applied to test whether the HRs changed across time; maternal substance use showed time-dependent associations with child mental and behavioral disorders (p=.007), and subsequent Cox models were stratified for substance use. The Cox models were initially adjusted for child's sex and birth year (Model 1), following other relevant covariates (Model 2; Table 5). Additional adjustments were made for maternal mental and behavioral disorders and clinically relevant depressive symptoms during pregnancy, along with the covariates of Model 2. Additionally, both maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder were included as covariates in a separate analysis.

In Studies II and III, linear regression analyses were applied to investigate the associations of positive maternal mental health (e.g., positive emotions and/or social support) with total, internalizing and externalizing psychiatric problems in children in early childhood and in late childhood (Study II) and with child cognitive ability (Study III). In both studies, analyses were adjusted for child sex and age at assessment (Model 1), followed by other relevant covariates (Model 2; Table 5). In Study III, additional adjustments were made for concurrent maternal depressive and anxiety symptoms (Model 3), while adjusting also for the covariates of Model 2. Additionally, I conducted sensitivity analyses in Study III that excluded children with an IQ score below 70 in the WISC assessment, as this may be an indicator of a potential intellectual disability (Wechsler, 2010; Wechsler et al., 1992).

4.5.1.1 Associations of positive maternal mental health with change in psychiatric problems

In Study II, linear mixed models for longitudinal data were applied to study whether positive maternal mental health during pregnancy was associated with *change* in the children's total psychiatric problems from early childhood to late childhood. Only children with both CBCL assessments available (n=1661) were included in the change analyses. Total psychiatric problems in early

childhood and in late childhood represented the within-person outcome, positive maternal mental health composite score the between-person predictor, and child age at the two follow-ups the within-person predictor. The interaction term between positive maternal mental health and child age addressed the question of change in child psychiatric problems. In the presence of significant interactions, two separate sub-analyses were conducted investigating change in psychiatric problems from early childhood to late childhood among children of mothers reporting low (below median) or high (at/above median) levels of positive mental health during pregnancy.

4.5.1.2 Mitigation of maternal psychological distress effects by positive maternal mental health

In Studies I−III, Cox proportional hazards models, linear regression models and linear mixed models investigated whether positive maternal mental health (positive emotions and/or social support) during pregnancy (Studies I−II) or during and after pregnancy (Study III) protected the children of mothers experiencing concurrent psychological distress before or during pregnancy from developing mental health adversities. Interaction terms of positive maternal mental health and maternal psychological distress variables relevant for each study were included, followed by the main effects of these variables (e.g., 'Positive maternal mental health composite score x clinically relevant depressive symptoms and/or mental and behavioral disorders' in Studies I−II; 'Perceived maternal social support during/after pregnancy x co-occurring anxiety/depressive symptoms' in Study III). Interaction terms were built separately for each indicator of maternal psychological distress. In Studies I−II, the associations of positive maternal mental health with mental and behavioral disorders and psychiatric symptoms in children were then tested among subgroups of mothers with/without clinically relevant depressive symptoms during pregnancy, and among subgroups of mothers with/without mental and behavioral disorders before or during pregnancy. According to Luthar et al. (2006), this subgroup approach may prove useful in investigating potential protective factors at different risk levels, thus identifying intervention priorities.

To further investigate whether positive maternal mental health mitigated the effects of maternal psychological distress on the *change* in psychiatric problems among children in Study II, linear mixed models were applied, including three-way interaction terms between child age, positive maternal mental health, and maternal psychological distress. Three separate interaction models were run in which CES-D scores were treated as continuous, mental and behavioural disorders as dichotomous, and combined maternal psychological distress as dichotomous variables. Change in psychiatric problems from early childhood to late childhood was then investigated among children of mothers

reporting lower (below median) and higher (at/above median) levels of positive mental health in the subgroups of mothers with and without psychological distress before or during pregnancy.

4.5.1.3 Timing effects of positive maternal mental health

In Study I, I further investigated whether the associations between each index of positive maternal mental health (PANAS, STAI Curiosity, and VAS) and mental and behavioral disorders in children varied by gestational stage by applying reverse temporal mixed effects models. In these analyses, maternal biweekly reports of positive affect/curiosity/social support were defined as outcomes; mental and behavioral disorders in children were defined as a between-person predictor, gestational week at the time of assessment of positive maternal mental health was defined as a within-person predictor, and their interaction tested if the associations varied by gestational week. Child sex was included as a fixed effect and length of diagnostic follow-up for the child as both a fixed and random effect covariate.

In Study III, the BRLM (Madathil et al., 2018) was applied to investigate timing effects of maternal social support on child cognitive ability, adjusting for child's sex assigned at birth and age at cognitive assessment. First, the BRLM estimates the presence or absence of a lifetime effect of repeatedly assessed exposures on an outcome of interest, defined as delta (δ) with a corresponding 95% Credible Interval (CrI). In this study, the delta refers to the lifetime effect of maternal social support on child cognitive ability. Next, the model estimates weights (w) for each exposure period that indicate the proportion of the lifetime effect explained by each exposure period. These weights are presented as percentages, the sum of all weights being fixed at 100% (i.e., $w_1+w_2=100$). I tested if maternal social support at two different time points (during and after pregnancy) has comparable or differing effects on child cognitive ability, and evaluated evidence for the life course models described in Chapter 2.3.3, namely: 1) a critical period model (e.g., $w_1=100$, $w_2=0$), 2) a sensitive period model (e.g., $w_1=66$, $w_2=33$), or 3) an accumulation model (e.g., $w_1=50$, $w_2=50$). Posterior probabilities and Euclidean distances were used to evaluate which life-course model is best supported by the data; the model with the shortest Euclidean distance is considered the best-fitting model (Madathil et al., 2018).

To similarly investigate the relative relevance of positive maternal mental health during pregnancy and positive maternal mental health in late childhood follow-up in relation to child total psychiatric problems in late childhood, additional BRLM analyses were conducted in Study II as described above. In these analyses, participants with all data available were included (n=1962).

4.5.2 ELS and anxiety symptoms in late adulthood (Study IV)

In Study IV, linear regression analyses investigated the associations of physical and emotional maltreatment, low childhood SES, separation from parents, parental divorce, death of a family member, and the accumulation of these six stressors, with anxiety symptoms in late adulthood. Logistic regression analyses investigated whether each ELS type and their accumulation was associated with clinically relevant anxiety symptoms in late adulthood (BAI≥16). Associations with clinically relevant anxiety symptoms are presented as odds ratios (OR). The individual associations of each ELS type with anxiety were first studied by adjusting for participant sex, age, and the time interval between the TEC and the BAI where applicable (Model 1). The independence of these associations from other ELS types was then studied in Model 2, where all ELS types were entered to the analyses simultaneously while adjusting for covariates of Model 1 (Table 5). This multiple individual risks modelling approach (Lanoue, George, Helitzer, & Keith, 2020) enabled the comparison of whether some ELS types had a stronger effect on late adulthood anxiety symptoms in the presence of other ELS types. Finally, to investigate the independence of the associations from adulthood SES, additional linear and logistic regression analyses were applied including adulthood SES as a covariate, while also adjusting for the covariates of Model 2 (Model 3; Table 5). To investigate the accumulation of different types of ELS, an ordinal variable of 0, 1, 2, or 3 or more separate ELS types was used as an independent variable. Participants with missing values regarding one ELS variable were included in the analyses regarding all other ELS variables by encoding missing values as a separate category in each ELS variable.

4.5.3 Mediation effects by later exposures (Studies II and IV)

Studies II and IV further investigated whether the effects of early exposures, namely exposure to positive maternal mental health during pregnancy in Study II and to low childhood SES in Study IV, were mediated by later exposures. Mediation analyses were conducted using the Process Macro 3.5.3 for SPSS (Hayes, 2022). The Process Macro is a regression-based method for observed variables that uses bootstrapping with 5000 resamples with replacement and bias corrected confidence intervals in order to assess the presence of an indirect effect via a mediator (Abu-Bader & Jones, 2021; Hayes, 2009, 2013, 2022; Igartua & Hayes, 2021). This mediation analysis method has shown robustness regarding statistical assumptions, higher study power and a lower risk of falsely rejecting the null hypothesis (Abu-Bader & Jones, 2021; Hayes, 2009, 2013; Igartua & Hayes, 2021).

In Study II, I investigated whether positive maternal mental health in the late childhood follow-up mediated the association between positive maternal mental health during pregnancy and total psychiatric problems among children in late childhood. The conditions for mediation analysis were met, as the associations between positive maternal mental health composite score assessed during pregnancy and in the late childhood follow-up (unstandardized b=0.49, 95%CI 0.45, 0.53; p<.001), and in the late childhood follow-up between the positive maternal mental health composite score and child total psychiatric problems (unstandardized b=−3.08, 95%CI −3.51, −2.65; p<.001) were significant. In Study IV, I examined whether adulthood SES mediated the association of low childhood SES with late-life anxiety symptoms. The conditions for mediation analysis were met also in this study: childhood SES was significantly associated with adulthood SES (unstandardized b=0.22, 95%CI 0.17, 0.26; p<.001), and lower adulthood SES predicted higher late-life anxiety symptoms (unstandardized b=0.39, 95%CI 0.30, 0.48; p<.001).

4.5.4 Sex-specific effects

In Studies I−IV, I additionally investigated with interaction analyses whether the associations between the early life exposures and the study-specific outcomes were different among male and female participants.

5 Results

Table 6 presents the characteristics of the participating mother-child-dyads of the PREDO and ALSPAC cohorts in Studies I-III. The characteristics of the participants in the HBCS cohort in Study IV are presented later in this thesis in Table 11.

The associations of the covariates and indices of parental psychological distress with each study-specific outcome of Studies I−III are shown in Table 7. In Study I, maternal lower education, non-cohabiting during pregnancy, substance use during early pregnancy, cardio-metabolic pregnancy conditions, and mental and behavioral disorders, and child's male sex were associated with higher hazards of mental and behavioral disorders in children. In Study II, children of younger, primiparous and single mothers, of mothers with lower education, who reported substance use and psychological distress during pregnancy or by early childhood/late childhood follow-up, and younger children, boys, and those with lower birth weight scored higher on total psychiatric problems in early childhood and/or late childhood. In Study III, lower maternal education level was associated with lower child cognitive ability in both cohorts; additionally in ALSPAC, maternal multiparity, younger age, non-cohabiting during pregnancy, higher depressive and anxiety symptoms during or after pregnancy, and lower birthweight and gestational age of the child were associated with lower child cognitive ability, when adjusting for child sex and age. In Study IV, women [mean difference 2.02 (95% CI 1.48–2.56), $p < 0.001$] and older participants [$r = 0.14$, $p < 0.001$] reported higher anxiety symptoms.

Table 6. Characteristics of the analytic samples of the PREDO cohort (Studies I-III) and the ALSPAC cohort (Study III).

	Study I PREDO	Study II PREDO	Study III ALSPAC	Study III PREDO
	N (%) / Mean (SD)	N (%) / Mean (SD)	N (%) / Mean (SD)	N (%) / Mean (SD)
Sample size (N)	3378	2636	5784	420
MATERNAL CHARACTERISTICS				
Age at delivery (years), mean (SD)	31.80 (4.7)	31.90 (4.62)	29.23 (4.49)	33.39 (5.41)
Parity, N (%)				
Primiparous	1379 (40.8)	1102 (41.8)	2605 (45.0)	145 (34.5)
Multiparous	1999 (59.2)	1534 (58.2)	3051 (52.7)	275 (65.5)
Missing	-	-	128 (2.2)	-
Education level, N (%)				
ALSPAC				
Degree			959 (16.6)	
A-levels			1539 (26.6)	
O-levels			2001 (34.6)	
None/CSE/vocational			1179 (20.4)	
Missing			106 (1.8)	
PREDO				
Upper tertiary	1153 (34.1)	1060 (40.2)		155 (36.9)
Lower tertiary	872 (25.8)	831 (31.5)		102 (24.3)
Primary/secondary	1348 (39.9)	745 (28.3)		163 (38.8)
Missing	5 (0.1)	-		-
Household crowding index (number of people by room)				
0-0.50			2812 (48.6)	
0.50-0.75			1761 (30.4)	
0.75-1			864 (14.9)	
>1			197 (3.4)	
Missing			150 (2.6)	
Marital/cohabiting status, N (%)				N/A
Married/cohabiting	3293 (97.5)	2582 (98.0)	5326 (92.1)	
Not cohabiting	76 (2.2)	50 (1.9)	413 (7.1)	
Missing	9 (0.3)	4 (0.2)	45 (0.8)	
Substance use during pregnancy[a)]				
No	2690 (79.7)	2092 (79.4)	1564 (27.0)	329 (78.3)
Yes	687 (20.3)	544 (20.6)	4136 (71.5)	86 (20.5)
Missing	1 (0.03)	-	84 (1.5)	5 (1.2)
Cardio-metabolic pregnancy conditions[b)], N(%)				
Yes	1432 (42.4)	1092 (41.4)		138 (32.9)
No	1706 (50.5)	1358 (51.5)		282 (67.1)
Only before current pregnancy	234 (6.9)	183 (6.9)		
Unknown	6 (0.2)	3 (0.1)		
Psychological distress during pregnancy				
Depressive symptoms[c)], mean (SD)	11.47 (6.39)	11.39 (6.36)	6.61 (4.84)	11.60 (6.90)
Missing, N (%)	1 (0.03)	-	102 (1.8)	-
Anxiety symptoms[d)], mean (SD)	N/A	N/A	4.83 (3.46)	33.52 (8.01)
Missing, N (%)			154 (2.7)	-
Mental and behavioral disorders before/during pregnancy[e)], N(%)			N/A	N/A
No	3084 (91.3)	2425 (92.0)		
Yes	294 (8.7)	211 (8.0)		
Missing	-	-		
Psychological distress after pregnancy				
Depressive symptoms at child follow-up[c)], mean (SD)	N/A	N/A	5.94 (5.07)	8.58 (8.80)
Missing, N (%)			908 (15.7)	51 (12.1)
Anxiety symptoms at child follow-up[d)], mean (SD)	N/A	N/A		
Missing, N (%)				
Mental and behavioral disorders by the child's first mental or behavioral disorder[e)], N(%)			N/A	N/A
No	2849 (84.3)	2250 (85.4)		
Yes	529 (15.7)	386 (14.6)		
Missing	-	-		
Positive mental health during pregnancy, mean (SD)				
Positive affect (PANAS)	30.28 (6.76)	30.15 (6.74)		
Curiosity (STAI)	31.40 (4.87)	31.46 (4.84)		
Social support (VAS/ALSPAC questionnaire/SSQ-6)	44.22 (11.19)	44.37 (11.03)	20.09 (4.75)	31.02 (4.78)

Positive mental health after pregnancy, mean (SD)	N/A			
Positive affect (PANAS)		31.04 (8.31)		
Curiosity (STAI)		32.46 (5.77)		
Social support (VAS/ALSPAC questionnaire/ SSQ-6)		38.01 (17.66)	20.08 (4.97)	29.86 (5.98)
CHILD CHARACTERISTICS				
Sex, N (%)				
Male	1743 (51.6)	1345 (51.0)	2895 (50.1)	208 (49.5)
Female	1635 (48.4)	1291 (49.0)	2889 (49.9)	212 (50.5)
Birth weight (grams), mean (SD)	3526.5 (517.2)	3522.95 (514.00)	3435.65 (534.18)	3492.68 (554.66)
Missing, N (%)	11 (0.3)	7 (0.3)	67 (1.2)	-
Gestational age (weeks), mean (SD)	39.9 (1.6)	39.91 (1.55)	39.49 (1.80)	39.74 (1.55)
Ethnic background	N/A	N/A		N/A
White			5399 (93.3)	
Non-white			198 (3.4)	
Missing			187 (3.2)	
PATERNAL CHARACTERISTICS				
Mental and behavioral disorders by the child's first mental or behavioral disorder[e)]		N/A	N/A	N/A
Yes	126 (3.7)			
No	1680 (49.7)			
Missing	1572 (46.5)			
INDEX OF CHILD MENTAL HEALTH OR DEVELOPMENT:				
Age at assessment (years), mean (SD)	10.23 (0.74)	3.52 (0.71) (early childhood); 9.40 (0.79) (late childhood)	8.62 (0.28)	8.68 (0.92)
Study I: Any mental and behavioral disorder[e)], n(%)				
Yes	359 (10.6)			
No	3019 (89.4)			
Study II: Total psychiatric problems[f)], mean (SD)				
Early childhood follow-up		46.37 (9.16)		
Late childhood follow-up		46.80 (10.22)		
Study III: General cognitive ability[g)], mean (SD)			104.48 (16.42)	100.35 (13.60)

PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study. ALSPAC=Avon Longitudinal Study of Parents and Children. SD=Standard Deviation. PANAS=Positive and Negative Affect Schedule. STAI=Spielberger State Anxiety Inventory. VAS=Visual Analogue Scale. SSQ-6=Social Support Questionnaire.

a) Smoking and/or alcohol use during pregnancy.

b) Studies I-II: Early pregnancy body mass index [BMI]≥25kg/m2, hypertensive disorders of pregnancy, and/or type 1, type 2 or gestational diabetes. Study III: Hypertensive disorders of pregnancy.

c) In PREDO, reported with Center for Epidemiologic Studies Depression Scale (CES-D). In ALSPAC, reported with Edinburgh Postnatal Depression Scale (EPDS).

d) In PREDO, reported with State-Trait-Anxiety Inventory (STAI). In ALSPAC, reported with Crown-Crisp Experimental Index (CCEI).

e) All mental disorder diagnoses based on the International Classification of Diseases 8th (ICD-8; codes 290−315) and 9th (ICD-9; codes 290−319) Revisions and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10; codes F00−F99).

f) Total psychiatric problem t-scores reported with Child Behavior Checklist (CBCL).

g) In ALSPAC, Total IQ of the Wechsler Intelligence Scale for Children, 3rd edition (WISC-III). In PREDO, Full-scale IQ of the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV).

Table 7. Associations of the covariates and the indices of parental psychological distress with mental and behavioral disorders (Study I), total psychiatric problems (Study II) and general cognitive ability (Study III) among children in the ALSPAC and PREDO cohorts.

Cohort	Study I PREDO		Study II PREDO				Study III ALSPAC		Study III PREDO	
Index of child mental health or development	Mental and behavioral disorders in children (F00-F99)[a]		CBCL Total problems				WISC-III Total IQ		WISC-IV Full-scale IQ	
			Early childhood		Late childhood					
	HR (95%CI)	P-value	B (95%CI)	p	B (95%CI)	p	B (95%CI)	p	B (95%CI)	p
MATERNAL CHARACTERISTICS										
Age at delivery (years), mean (SD)	0.99 (0.97, 1.02)	.62	**-0.23 (-0.31, -0.15)**	**<.001**	-0.17 (-0.27, -0.08)	**<.001**	**0.63 (0.54, 0.73)**	**<.001**	-0.08 (-0.31, 0.17)	.54
Parity, N (%)										
Primiparous	[ref]		[ref]		[ref]		[ref]		[ref]	
Multiparous	0.87 (0.71, 1.07)	.19	**-3.18 (-3.93, -2.44)**	**<.001**	**-2.68 (-3.58, -1.77)**	**<.001**	**-2.55 (-3.40, -1.71)**	**<.001**	-1.35 (-4.08, 1.38)	.33
Education level, N (%)										
Degree							[ref]			
A-levels							**-7.41 (-8,63, -6.19)**	**<.001**		
O-levels							**-12.51 (-13.67, -11.35)**	**<.001**		
None/CSE/vocational							**-18.06 (-19.35, -16.76)**	**<.001**		
Upper tertiary	[ref]		[ref]		[ref]				[ref]	
Lower tertiary	**1.63 (1.20, 2.22)**	**.002**	**1.23 (0.34, 2.12)**	**.01**	**2.54 (1.51, 3.57)**	**<.001**			**-6.93 (-9.84, -4.03)**	**<.001**
Primary/secondary	**2.21 (1.69, 2.88)**	**<.001**	**1.50 (0.59, 2.42)**	**.001**	**3.53 (2.43, 4.64)**	**<.001**			**-10.42 (-13.41, -7.43)**	**<.001**
Household crowding index (number of people by room)										
0-0.50							[ref]			
0.50-0.75							**-3.79 (-4.74, -2.85)**	**<.001**		
0.75-1							**-8.47 (-9.68, -7.26)**	**<.001**		
>1							**-9.86 (-12.15, -7.57)**	**<.001**		
Marital/cohabiting status, N (%)										
Married/cohabiting	[ref]		[ref]		[ref]		[ref]			
Not cohabiting	**2.39 (1.49, 3.83)**	**<.001**	0.28 (-2.51, 3.07)	.84	**4.76 (1.41, 8.10)**	**.01**	**-5.23 (-6.85, -3.62)**	**<.001**		
Cardio-metabolic pregnancy conditions[b]										
No	[ref]		[ref]		[ref]				[ref]	
Yes	**1.74 (1.40, 2.16)**	**<.001**	0.40 (-0.38, 1.19)	.32	0.84 (-0.09, 1.77)	.08			-0.89 (-3.66, 1.88)	.53
Other	0.92 (0.56, 1.50)	.74	-0.35 (-1.82, 1.12)	.64	-0.40 (-2.23, 1.43)	.67			-	
Substance use during pregnancy[c]										
No	[ref]		[ref]		[ref]		[ref]		[ref]	
Yes	**1.28 (1.00, 1.62)**	**.046**	0.92 (-0.01, 1.85)	.05	**1.11 (0.002, 2.23)**	**.05**	0.21 (-0.65, 1.08)	.63	-0.97 (-4.17, 2.23)	.55
Psychological distress during pregnancy										
Depressive symptoms[d]			**2.87 (2.51, 3.22)**	**<.001**	**3.35 (2.93, 3.78)**	**<.001**	**-1.64 (-2.07, -1.22)**	**<.001**	-0.54 (-1.83, 0.75)	.41
Below clinically relevant symptoms	[ref]		[ref]		[ref]					
Clinically relevant symptoms	**1.80 (1.44, 2.24)**	**<.001**	**5.22 (4.33, 6.11)**	**<.001**	**5.78 (4.70, 6.86)**	**<.001**				
Anxiety symptoms[e]							**-0.77 (-1.20, -0.35)**	**<.001**	-0.50 (-1.79, 0.79)	.45
Mental and behavioral disorders before/during pregnancy[f]										
No	[ref]		[ref]		[ref]					
Yes	**2.60 (1.99, 3.39)**	**<.001**	1.18 (-0.18, 2.55)	.09	**3.25 (1.58, 4.92)**	**<.001**				

Psychological distress after pregnancy										
Depressive symptoms[d]							**-0.78 (-1.20, -0.35)**	**<.001**	0.05 (-1.31, 1.40)	.95
Anxiety symptoms[e]							-0.27 (-0.69, 0.16)	.22	-0.94 (-2.27, 0.40)	.17
Mental and behavioral disorders by the child's first mental or behavioral disorder[f]										
No	[ref]		[ref]		[ref]					
Yes	**1.89 (1.49, 2.39)**	**<.001**	**1.79 (0.57, 3.01)**	**.004**	**4.34 (3.07, 5.62)**	**<.001**				
CHILD CHARACTERISTICS										
Sex										
Male	[ref]		[ref]		[ref]		[ref]		[ref]	
Female	-2.16 (-2.71, -1.73)	**<.001**	**-1.39 (-2.14, 0.64)**	**<.001**	**-2.40 (-3.29, -1.51)**	**<.001**	-0.38 (-1.22, 0.46)	.37	2.55 (-0.03, 5.13)	.05
Birth weight (grams), mean (SD)	1.00 (-1.00, 1.00)	.81	**-0.001 (-0.002, 0.00)**	**.001**	-0.001 (-0.001, 0.00)	.20	**1.30 (0.88, 1.72)**	**<.001**	-0.05 (-1.28, 1.18)	.93
Gestational age (weeks), mean (SD)	0.98 (0.92, 1.04)	.43	-0.20 (-0.44, 0.04)	.11	0.05 (-0.25, 0.34)	.76	**0.23 (0.002, 0.47)**	**.048**	-0.11 (-0.96, 0.74)	.80
Ethnic background										
White							[ref]			
Non-white							0.03 (-2.27, 2.32)	.98		
PATERNAL CHARACTERISTICS										
Mental and behavioral disorders by the child's first mental or behavioral disorder[f]										
No	[ref]									
Yes	1.46 (0.86, 2.49)	.16								

PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study. ALSPAC=Avon Longitudinal Study of Parents and Children. SD=Standard Deviation. CBCL=Child Behavior Checklist. WISC=Wechsler Intelligence Scale for Children. BAI=Beck Anxiety Inventory. HR=Hazard Ratio. OR=Odds Ratio. CI=Confidence Interval.

a) All mental and behavioral disorder diagnoses classified using the International Statistical Classification of Diseases and Related Health Problems, 10th (ICD-10) Revision (codes F00-F99).

b) Studies I-II: Early pregnancy body mass index [BMI]≥25kg/m2, hypertensive disorders of pregnancy, and/or type 1, type 2 or gestational diabetes. Study III: Hypertensive disorders of pregnancy.

c) Smoking and/or alcohol use during pregnancy.

d) In PREDO, reported with Center for Epidemiologic Studies Depression Scale (CES-D). In ALSPAC, reported with Edinburgh Postnatal Depression Scale (EPDS).

e) In PREDO, reported with State-Trait-Anxiety Inventory (STAI). In ALSPAC, reported with Crown-Crisp Experimental Index (CCEI).

f) All mental disorder diagnoses based on the International Classification of Diseases 8th (ICD-8; codes 290−315) and 9th (ICD-9; codes 290−319) Revisions and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10; codes F00−F99).

Additionally, in Studies I−III, mothers who reported higher depressive and anxiety symptoms, clinically relevant depressive symptoms and/or had a mental or behavioral disorder before or during pregnancy reported lower levels of positive emotions and social support than mothers without these indices of psychological distress (Table 8).

Positive maternal mental health showed high continuity from pregnancy to the childhood assessment: in Study II, positive maternal mental health composite scores during pregnancy and in child's late childhood had a correlation of r=.48, and in Study III, maternal perceived social support during pregnancy and after pregnancy had correlations of r=.61 in ALSPAC and r=.41 in PREDO. Moreover, psychiatric problems among children showed continuity across childhood (correlations for CBCL t-scores r=.55 for total problems, r=.44 for internalizing problems, and r=.51 for externalizing problems; p<.001 for all correlations).

Table 8. Associations between the indices of positive maternal mental health (the composite score in Studies I-II and social support in Study III) and the indices of maternal psychological distress in Studies I-III.

	Maternal clinically relevant depressive symptoms during pregnancy			Maternal mental and behavioral disorders diagnosed before or during pregnancy			ALSPAC				PREDO			
	CES-D<16 Mean (SD)	CES-D≥16 Mean (SD)	Difference between groups P-value	No diagnoses Mean (SD)	Has diagnoses Mean (SD)	Difference between groups P-value	Concurrent depressive symptoms r	P-value	Concurrent anxiety symptoms r	P-value	Concurrent depressive symptoms r	P-value	Concurrent anxiety symptoms r	P-value
Positive mental health composite score, SD units														
Study I	0.29 (0.85)	-1.04 (0.80)	<.001	0.04 (0.98)	-0.46 (1.07)	<.001								
Study II	0.28 (0.85)	-1.05 (0.78)	<.001	0.04 (0.99)	-0.44 (1.05)	<.001								
Social support (Study III), SD units														
During pregnancy							-0.31	<.001	-0.23	<.001	-.38	<.001	-.29	<.001
After pregnancy							-0.40	<.001	-0.34	<.001	-.46	<.001	-.39	<.001

SD=Standard deviation. r=correlation coefficient. P-value refers to the significance of the difference between group means. ALSPAC=Avon Longitudinal Study of Parents and Children. PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study.

5.1 Positive maternal mental health and offspring mental health

5.1.1 Association of positive maternal mental health with child mental health and psychological development

In Study I, higher positive maternal mental health principal component score during pregnancy was associated with a lower hazard of any mental and behavioral disorder in children; the association was significant across the adjustment models (Table 9). Figure 3 shows the cumulative incidence of mental and behavioral disorders in children whose mothers reported low (below median) and high (at/above median) positive mental health during pregnancy. Moreover, the association of positive maternal mental health with the lower hazard of offspring mental and behavioral disorders was independent of maternal clinically relevant depressive symptoms during pregnancy and/or maternal mental and behavioral disorders before or during pregnancy (HR=0.86, 95% CI=0.76-0.98, p=.02), and of both maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder diagnosis or the end of the follow-up (HR=0.87, 95% CI=0.77−0.99, p=.03).

Extending these findings to dimensionally assessed psychiatric problems among children, Study II showed that higher positive maternal mental health composite score during pregnancy was associated with lower total problem t-scores and lower internalizing and externalizing problem t-scores in children both in early childhood and in late childhood (Table 9). These associations were also independent of mother- and child-related sociodemographic characteristics and of maternal depressive symptoms during pregnancy and mental and behavioral disorders diagnosed by the early childhood/late childhood follow-up (Model 2, Table 9).

In Study III, Higher maternal social support *during* pregnancy was associated with higher child cognitive ability in both cohorts across Models 1−2 (Table 9). Higher maternal social support *after* pregnancy, in turn, was associated with higher child cognitive ability in ALSPAC across Models 1−2, whereas no such association was found in PREDO (Table 9). The associations of maternal social support during pregnancy with child cognitive ability were independent of maternal concurrent depressive and anxiety symptoms during pregnancy in both ALSPAC and PREDO (Model 3; Table 9). In ALSPAC, the positive association between maternal social support after pregnancy with child cognitive ability was also independent of maternal concurrent depressive and anxiety symptoms (Model 3; Table 9). Supplementary sensitivity analyses showed that the associations of maternal social support during and after pregnancy with child cognitive ability remained similar in both cohorts when excluding children with an IQ score below 70 (data not shown).

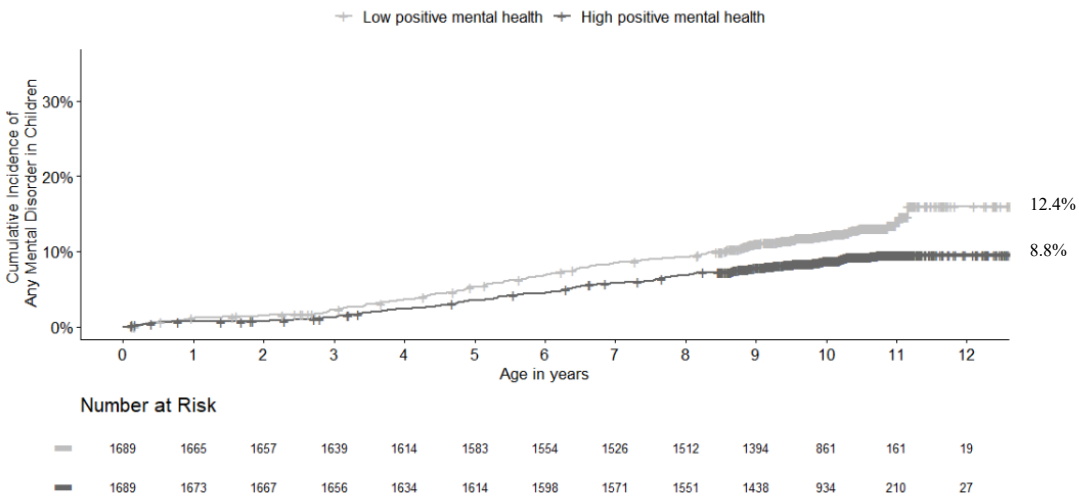
Table 9. The association of positive maternal mental health with any mental and behavioral disorder (Study I), total psychiatric problems (Study II) and child general cognitive ability (Study III) in the ALSPAC and PREDO cohorts. The covariates of different statistical models in each study are described in Table 5.

	INDEX OF CHILD MENTAL HEALTH OR PSYCHOLOGICAL DEVELOPMENT									
	Mental and behavioral disorders (F00-F99)[a]		Psychiatric problems (CBCL)				Cognitive ability (WISC)			
			Early childhood		Late childhood		ALSPAC		PREDO	
	HR (95%CI)	P-value	B (95%CI)	p	B (95%CI)	p	B (95%CI)	p	B (95%CI)	p
INDEX OF POSITIVE MATERNAL MENTAL HEALTH										
Studies I-II: Positive mental health composite score during pregnancy (SD units)			**Total problems**							
Model 1	**0.79 (0.71, 0.87)**	**<.001**	**-1.61 (-1.98, -1.24)**	**<.001**	**-2.03 (-2.46, -1.59)**					
Model 2	**0.79 (0.71, 0.88)**	**<.001**	**-1.37 (-1.79, -0.95)**	**<.001**	**-1.75 (-2.24, -1.26)**					
			Internalizing problems							
Model 1			**-1.39 (-1.77, -1.01)**	**<.001**	**-1.78 (-2.21, -1.36)**					
Model 2			**-1.27 (-1.70, -0.83)**	**<.001**	**-1.55 (-2.03, -1.08)**					
			Externalizing problems							
Model 1			**-1.37 (-1.73, -1.01)**	**<.001**	**-1.57 (-2.00, -1.15)**					
Model 2			**-1.08 (-1.50, -0.66)**	**<.001**	**-1.49 (-1.97, -1.00)**					
Study III: Maternal social support (SD units)										
During pregnancy										
Model 1							**1.58 (1.16, 2.00)**	**<.001**	**1.75 (0.47, 3.03)**	**.007**
Model 2							**0.79 (0.37, 1.20)**	**<.001**	**1.50 (0.27, 2.74)**	**.02**
Model 3							**0.67 (0.23, 1.11)**	**.003**	**1.62 (0.29, 2.95)**	**.02**
After pregnancy										
Model 1							**1.25 (0.82, 1.67)**	**<.001**	0.08 (-1.28, 1.45)	.90
Model 2							**0.65 (0.23, 1.07)**	**.002**	0.01 (-1.30, 1.31)	.99
Model 3							**0.62 (0.16, 1.07)**	**.01**	0.06 (-1.44, 1.55)	.94

PREDO=The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction Study. ALSPAC=Avon Longitudinal Study of Parents and Children. SD=Standard Deviation. CBCL=Child Behavior Checklist. WISC=Wechsler Intelligence Scale for Children. HR=Hazard Ratio. CI=Confidence Interval.

a) All mental and behavioral disorder diagnoses classified using the International Statistical Classification of Diseases and Related Health Problems, 10th (ICD-10) Revision (codes F00-F99).

Figure 3. The cumulative incidence of mental and behavioral disorders in children whose mothers reported low (below median) and high (at/above median) positive mental health during pregnancy.



5.1.2 Associations of positive maternal mental health with change in child psychiatric problems

In Study II, Positive maternal mental health composite score interacted significantly with child age in predicting total psychiatric problems in children in the linear mixed models (B=-0.10, 95% CI -0.17, -0.02 for interaction; p=.01). In the analyses among subgroups of women with below median/at or above median levels of positive mental health during pregnancy, the total problems t-scores were at a lower level and remained stable from early childhood to late childhood among children of mothers with high positive mental health (composite score at or above median; B=0.18, 95% CI -0.44, 0.80; p=.57). The total problems t-scores were consistently higher and increased among children of mothers with low levels of positive mental health during pregnancy (composite score below median; B=0.68, 95% CI 0.05, 1.30; p=.03).

5.1.3 Mitigation of maternal psychological distress effects on child mental health by positive maternal mental health

Consistently across Studies I−III, no interactions were detected between the indices of positive maternal mental health during or after pregnancy (i.e., the PCA-based composite score or

perceived social support) and the indices of maternal psychological distress (i.e., depressive and anxiety symptoms and/or mental and behavioral disorders) (Table 10).

Subgroup analyses in Study I showed that higher positive maternal mental health composite score during pregnancy was associated with a lower hazard of any mental and behavioral disorder among children of mothers with (HR=0.80, 95%CI 0.64, 1.00; p=.047) but not among children of mothers without (HR=0.91, 95%CI 0.78, 1.05; p=.19) clinically relevant depressive symptoms during pregnancy, and both among children of mothers with (HR=0.69, 95% CI 0.55-0.86; p=.001) and without (HR=0.87, 95% CI 0.78, 0.98; p=.02) any mental and behavioral disorder before or during pregnancy.

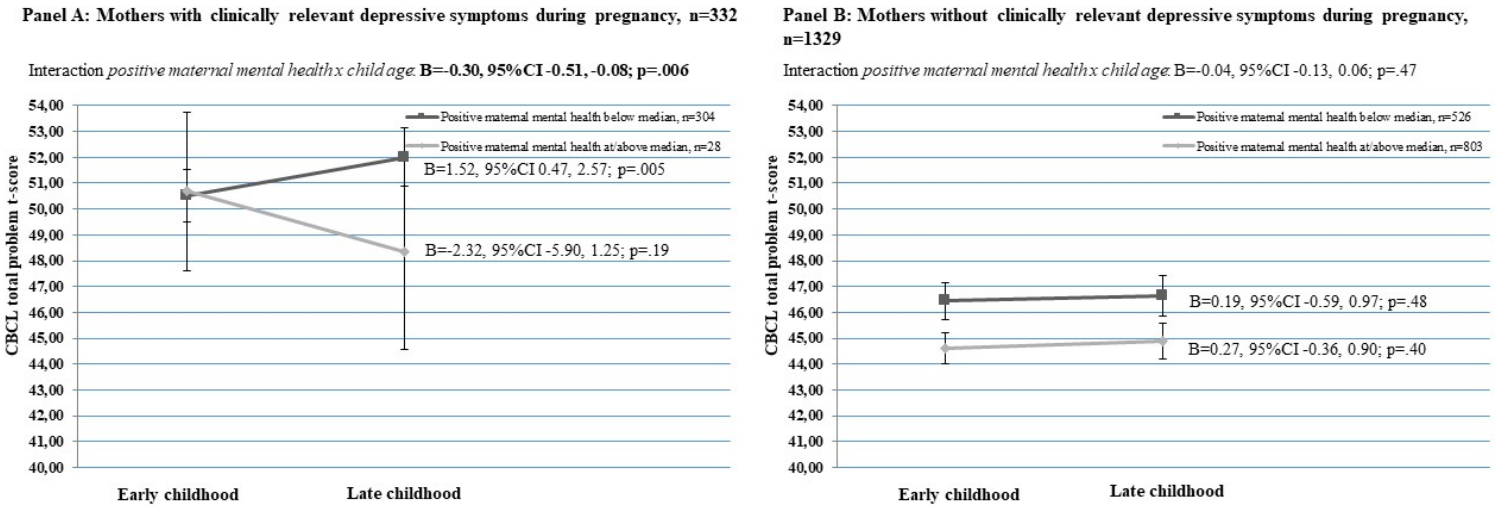
In Study II, positive maternal mental health was associated with lower total psychiatric problems in the subgroups of children with or without psychological distress before or during pregnancy (coefficients between B=-0.84, B=-2.88 among the subgroups; 95%CI's between -4.51, -0.15; p-values between .02 and <.001); the only exception was the subgroup of children whose mothers had clinically relevant depressive symptoms during pregnancy, in which subgroup the association was not significant (B=0.53, 95%CI -0.50, 1.55; p=.31 in early childhood; B=-0.52, 95%CI -1.83, 0.79; p=.43 in late childhood).

Further three-way interaction analyses in Study II investigated whether positive maternal mental health during pregnancy mitigated the effects of maternal psychological distress on the *change* in psychiatric problems: these analyses showed a significant interaction between positive maternal mental health × continuous CES-D score during pregnancy × child age (B=-0.08, 95%CI -0.14, -0.02; p=.008). In the subgroup of mothers reporting clinically relevant depressive symptoms during pregnancy, total psychiatric problems did not increase among children of mothers concurrently reporting higher levels of positive mental health during pregnancy, but did increase among children of mothers reporting lower levels of positive mental health during pregnancy (Figure 4, Panel A). Total problems did not increase from early childhood to late childhood among children of mothers with lower than clinically relevant depressive symptoms, regardless of whether the mother reported higher or lower positive mental health during pregnancy (Figure 4, Panel B). There were no significant three-way interactions regarding maternal mental and behavioral disorders before or during pregnancy or the combination of mental and behavioral disorders and/or clinically relevant depressive symptoms before or during pregnancy (p-values for interactions ≥.46).

Table 10. Interactions between the indices of positive maternal mental health and the indices of maternal psychological distress in Studies I-III.

	INDEX OF CHILD MENTAL HEALTH OR PSYCHOLOGICAL DEVELOPMENT				
	Mental and behavioral disorders (F00-F99)[a)]	**Total problems (CBCL)**		**Cognitive ability (WISC)**	
	HR (95%CI)	**Early childhood B (95%CI)**	**Late childhood B (95%CI)**	**ALSPAC B (95%CI)**	**PREDO B (95%CI)**
STUDY I					
During pregnancy					
Positive mental health x depressive symptoms	0.89 (0.68, 1.16)				
Positive mental health x mental disorders	0.80 (0.62, 1.02)				
STUDY II					
During pregnancy					
Positive mental health x Continuous depressive symptoms		0.18 (-0.10, 0.46)	-0.18 (-0.52, 0.17)		
Positive mental health x mental disorders		-0.84 (-2.15, 0.47)	-1.01 (-2.55, 0.54)		
Positive mental health x clinically relevant depressive symptoms and/or mental disorders		-0.20 (-1.14, 0.75)	-0.48 (-1.62, 0.65)		
STUDY III					
During pregnancy					
Social support x depressive symptoms				0.33 (-0.05, 0.72)	0.16 (-1.09, 1.40)
Social support x anxiety symptoms				-0.08 (-0.49, 0.33)	-0.03 (-1.28, 1.22)
After pregnancy					
Social support x depressive symptoms				0.17 (-0.24, 0.57)	0.50 (-0.79, 1.78)
Social support x anxiety symptoms				0.02 (-0.38, 0.42)	-0.03 (-1.36, 1.31)

Figure 4. Change in total psychiatric problems t-scores from early childhood to late childhood among children of mothers with low (below median) and high (at or above median) levels of positive mental health composite score during pregnancy, in the subgroups of mothers with (Panel A)/without (Panel B) clinically relevant depressive symptoms during pregnancy. Analyses are adjusted for child's sex, and conducted among mother-child-dyads with psychiatric problems data available at both follow-ups (n=1661).



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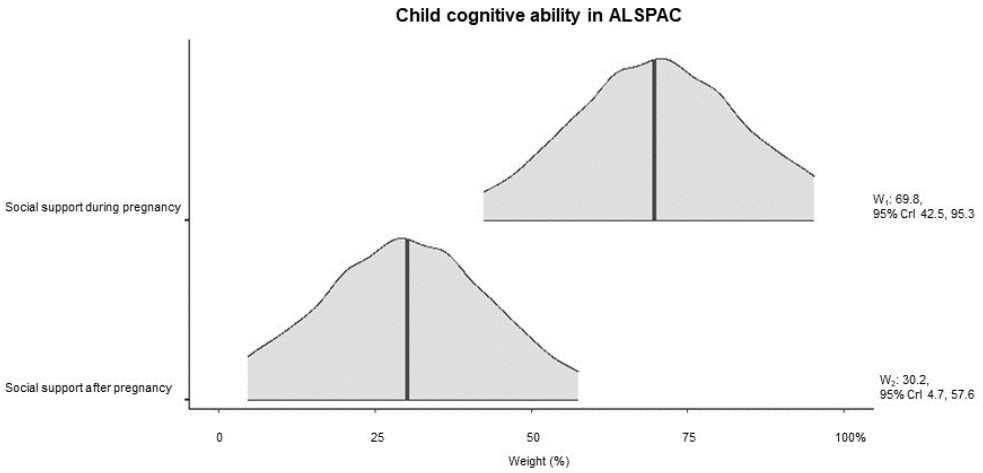
5.1.4 Timing effects of positive maternal mental health

Regarding the timing effects of positive maternal mental health within pregnancy (Study I), no gestation stage specificity was detected in the associations of positive affect, curiosity, and social support with any mental and behavioral disorder in children (estimates<0.01, 95%CIs -0.04−0.05, p-values ≥.24 for interactions between gestational week x any mental and behavioral disorder in children). In other words, the associations between positive maternal mental health during pregnancy and child mental and behavioral disorders were similar regardless of gestational week.

In Study III, BRLM analyses in the ALSPAC cohort showed that higher maternal social support during and after pregnancy had a combined lifetime effect (δ) of 1.87 IQ points on child cognitive ability (95% CrI 1.39, 2.37). The contributions of maternal social support during pregnancy (w_1) and after pregnancy (w_2) were 69.8% and 30.2% of the lifetime effect on child cognitive ability, respectively (Figure 5). Pregnancy was a sensitive period for the effects of maternal social support with a 92.0% posterior probability; this life course model also provided the shortest Euclidean distance (data not shown). In PREDO, the BRLM analyses showed no lifetime effect of maternal social support during and after pregnancy on child cognitive ability (δ=0.50 IQ points, 95% CrI -0.88, 1.88); therefore, I did not estimate weights for maternal social support during or after pregnancy in PREDO.

Figure 5. Posterior densities of weights of maternal social support during pregnancy (w^1) and at child age 8 months (^{w2}) on the lifetime effect of social support on child general cognitive ability (IQ) at child age 8 years in the ALSPAC cohort (n=5498). Posterior densities are presented as percentages (range 0−100%); the area in gray presents 95% credible interval (CrI) for the mean posterior density.



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Additional BRLM analyses in Study II showed that the lifetime effect of positive maternal mental health on child total problem t-scores was δ= -3.17 (95%CrI -3.66, -2.68). Positive maternal mental health in the late childhood follow-up (w_2) carried a higher relevance to child total problems, contributing to 82.0% of the lifetime effect (95%CrI 67.9, 95.8), while positive maternal mental health during pregnancy (w_1) contributed to 18.0% of the lifetime effect (95%CrI 4.2, 32.2) (Lähdepuro et al., unpublished results). Data gave most support for the late childhood follow-up being a sensitive period for the effects of positive maternal mental health on child total problems, with a 99.9% posterior probability and the shortest Euclidean distance (data not shown).

5.2 ELS and anxiety symptoms in late adulthood

Table 11 shows the characteristics of the study sample in the HBCS cohort (Study IV). The mean BAI score among the participants was 6.31 (SD 5.84, range 0–42), and 151 (8.1%) of the participants reported anxiety symptoms above the clinically relevant threshold.

Table 11. Characteristics of the analytic sample of the HBCS cohort.

	N (%) / Mean (SD)
Age at anxiety assessment, mean (SD)	68.73 (2.84)
Sex, n (%)	
Male	1082 (57.8)
Female	790 (42.2)
Anxiety symptoms[a)], mean (SD)	6.31 (5.84)
Below clinically relevant, n (%)	1721 (91.9)
Above clinically relevant, n (%)	151 (8.1)
ELS experiences:	
Physical maltreatment experienced in childhood[b)], n (%)	
Yes	278 (26.70)
No	762 (73.3)
Missing	832
Number of physical maltreatment experiences in childhood, mean (SD)	0.63 (1.07)
Emotional maltreatment experienced in childhood[b)], n (%)	
Yes	299 (29.20)
No	724 (70.8)
Missing	849
Number of emotional maltreatment experiences in childhood, mean (SD)	0.66 (1.19)
Childhood SES based on parental occupational status[c)], n (%)	
Manual worker	796 (42.50)
Clerical worker	1075 (57.50)
Missing	1
Separation from parents in childhood, n (%)	
Evacuated	210 (11.20)
Self-reported evacuation	140 (7.50)
Not evacuated	1522 (81.30)
Age at evacuation (registered evacuees)	4.42 (2.33)
Parental divorce in childhood, n (%)	
Yes	97 (8.00)
No	1116 (92.00)
Missing	659
Age at parental divorce in childhood (years), mean (SD)	8.64 (4.94)
Death of a family member in childhood, n (%)	
Yes	186 (15.60)
No	1009 (84.4)
Missing	677
Age at death of a family member in childhood (years), mean (SD)	8.73 (4.85)
Accumulation of ELS experiences, n (%)	
0 ELS types	309 (24.40)
1 ELS type	472 (37.30)
2 ELS types	292 (23.10)
3 or more ELS types	193 (15.20)
Missing	606

HBCS=Helsinki Birth Cohort Study. ELS=Early life stress.
a) Reported with the Beck Anxiety Inventory (BAI).
b) Reported with the Traumatic Events Checklist (TEC). The participants reporting no maltreatment or maltreatment only in adulthood were used as a control group.
c) Highest recorded occupational status of either the father or the mother of the participant in their childhood.

Emotional and physical maltreatment and low childhood SES were associated with higher dimensionally assessed anxiety symptoms in late adulthood both when assessed in separate models and when adjusting for co-occurring other types of ELS (Models 1 and 2; Table 12). Furthermore,

emotional and physical maltreatment and parental divorce were individually associated with an increased risk of anxiety symptoms exceeding the clinically relevant threshold (Model 1). The risk of clinically relevant anxiety symptoms remained significant for emotional maltreatment and parental divorce but not for physical maltreatment when adjusting for other ELS types (Model 2; Table 12). Separation from parents and death of a family member were not associated with either dimensionally assessed or clinically relevant anxiety symptoms in late adulthood.

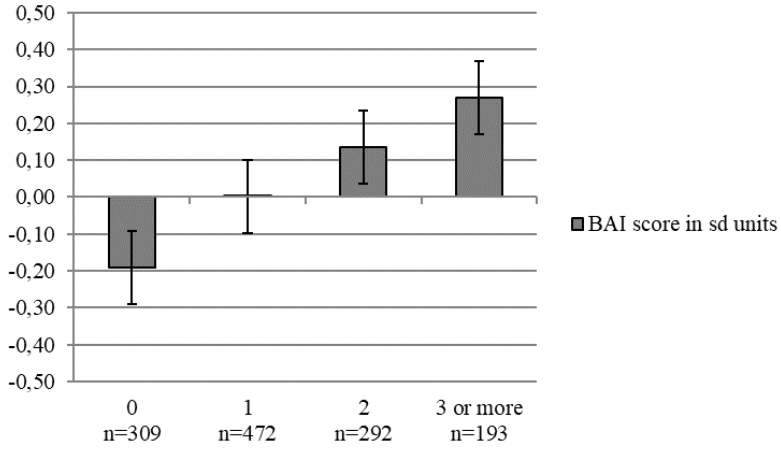
The accumulation of different types of ELS (0, 1, 2, or 3 or more) was associated with higher anxiety symptoms in late adulthood (Table 12; Figure 6). Furthermore, reporting two or more ELS types significantly increased the risk of anxiety symptoms exceeding the clinical threshold (Table 12).

Table 12. The association of ELS experiences and their accumulation with dimensionally assessed and clinically relevant anxiety symptoms in Study IV. The covariates of different statistical models in each study are described in Table 5.

	Anxiety symptoms (BAI)			
	Dimensionally assessed continuous score		Above clinically relevant threshold	
	B (95%CI)	p	OR (95%CI)	p
ELS experiences (yes vs. no)				
Physical maltreatment				
Model 1	**0.33 (0.20, 0.46)**	**<.001**	**1.73 (1.10, 2.74)**	**.02**
Model 2	**0.17 (0.01, 0.32)**	**.03**	1.04 (0.61, 1.78)	.88
Model 3	**0.18 (0.03, 0.32)**	**.02**	1.05 (0.61, 1.82)	.87
Emotional maltreatment				
Model 1	**0.44 (0.31, 0.58)**	**<.001**	**2.78 (1.78, 4.33)**	**<.001**
Model 2	**0.37 (0.22, 0.53)**	**<.001**	**2.59 (1.53, 4.39)**	**<.001**
Model 3	**0.38 (0.22, 0.53)**	**<.001**	**2.77 (1.60, 4.78)**	**<.001**
Low SES				
Model 1	**0.10 (0.01, 0.19)**	**.02**	1.36 (0.98, 1.91)	.07
Model 2	**0.12 (0.03, 0.21)**	**.01**	**1.42 (1.01, 2.00)**	**.05**
Model 3	0.05 (-0.04, 0.14)	.27	1.19 (0.84, 1.69)	.34
Separation from parents				
Register-based - Model 1	0.08 (-0.07, 0.23)	.31	1.44 (0.88, 2.35)	.14
Register-based - Model 2	0.02 (-0.13, 0.17)	.81	1.24 (0.75, 2.05)	.40
Register-based - Model 3	-0.01 (-0.15, 0.14	.90	1.16 (0.70, 1.93)	.56
Self-reported - Model 1	0.14 (-0.03, 0.32)	.11	1.26 (0.71, 2.25)	.44
Self-reported - Model 2	0.08 (-0.10, 0.26)	.38	1.01 (0.55, 1.83)	.99
Self-reported - Model 3	0.05 (-0.12, 0.23	.55	0.92 (0.51, 1.69)	.80
Parental divorce				
Model 1	0.16 (-0.05, 0.36)	.13	**2.37 (1.33, 4.19)**	**.003**
Model 2	0.09 (-0.11, 0.30)	.36	**2.14 (1.18, 3.88)**	**.01**
Model 3	0.05 (-0.15, 0.25)	.60	**1.93 (1.05, 3.54)**	**.03**
Death of a family member				
Model 1	0.06 (0.10, 0.21)	.46	1.09 (0.64, 1.84)	.75
Model 2	0.04 (-0.12, 0.19)	.63	1.03 (0.60, 1.77)	.92
Model 3	0.03 (-0.12, 0.18)	.71	0.98 (0.56, 1.70)	.93
Accumulation of ELS experiences				
0	[ref]		[ref]	
1	**0.19 (0.05, 0.33)**	**.01**	1.43 (0.79, 2.59)	.24
2	**0.33 (0.17, 0.48)**	**<.001**	**1.94 (1.04, 3.60)**	**.04**
3 or more	**0.46 (0.28, 0.63)**	**<.001**	**2.91 (1.55, 5.46)**	**.001**

BAI=Beck Anxiety Inventory. OR=Odds Ratio. CI=Confidence Interval. ELS=Early life stress. SES=Socioeconomic status.

Figure 6. The accumulation of different ELS types predicting anxiety symptoms in late adulthood, while adjusting for participant age and sex. Error bars represent the 95% confidence intervals.



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The associations between ELS types and anxiety symptoms in late adulthood were independent of adulthood SES, with one exception: the association of low childhood SES and anxiety symptoms was no longer significant when adjusting for adulthood SES (Model 3; Table 12).

5.3 Mediation effects by later exposures

The mediation analyses in Study II showed that positive maternal mental health composite score in the late childhood follow-up mediated a significant proportion of the association between the positive maternal mental health composite score during pregnancy and total psychiatric problems among children in late childhood (Figure 7); the effect size proportion mediated was 66.7%.

Similarly in Study IV, the mediation analyses showed that adulthood SES mediated the association between childhood SES and anxiety symptoms in late adulthood (Figure 8); the direct association between childhood SES and late-life anxiety symptoms was no longer significant when taking into account adulthood SES. The effect size proportion mediated was 66.7%.

Figure 7. The mediation effect of positive maternal mental health composite score in the late childhood follow-up on the association between positive maternal mental health composite score during pregnancy and child's total psychiatric problems in late childhood (n=1962). Mediation analyses are adjusted for child sex and age in late childhood.

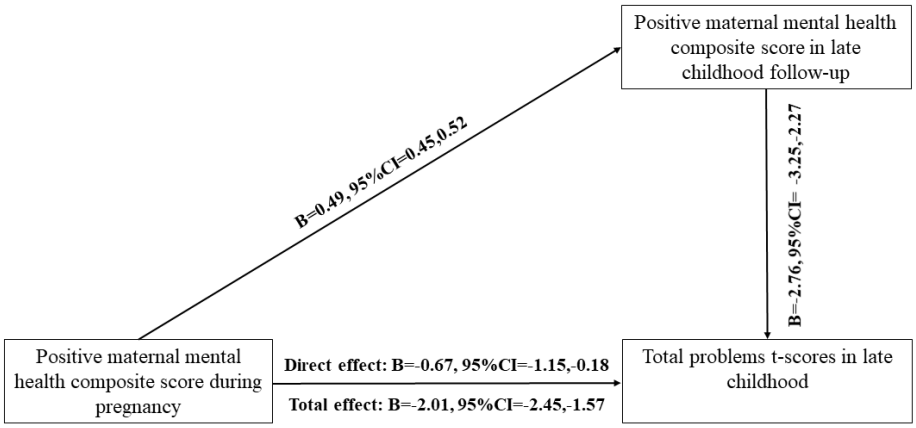

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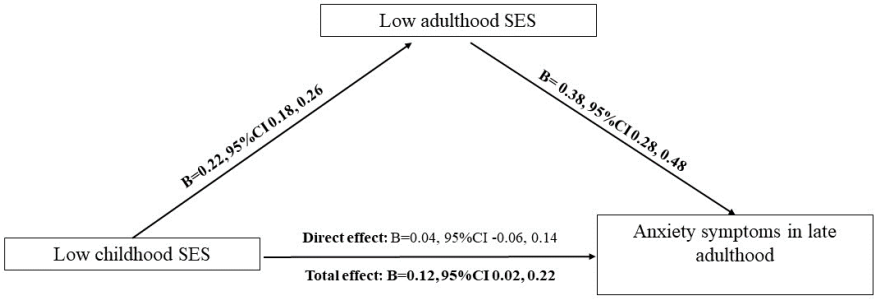
Figure 8. The mediation effect of low adulthood SES on the association between low childhood SES and anxiety symptoms in late adulthood.



5.4 Sex-specific effects

Studies I−IV additionally investigated any potential interactions between participant sex and the exposure (positive maternal mental health in Studies I−III; ELS in Study IV) in relation to mental health or psychological development. In Study I, a significant interaction was detected between positive maternal mental health composite score and child sex when predicting mental and behavioral disorders in children (OR=0.79, 95%CI 0.64, 0.99; p=.04). Sex-stratified analyses showed that positive maternal mental health during pregnancy was more strongly associated with a lower hazard of mental and behavioral disorders in girls (OR=0.67, 95%CI 0.56, 0.81; p<.001) than in boys (OR=0.85, 95%CI 0.75, 0.96, p=.007); the association was significant among both girls and boys. In Study II, on the other hand, positive maternal mental health during pregnancy did not show sex-specific effects on total psychiatric problems in early childhood (B=0.09, 95%CI -0.65, 0.82; p=.81) or in late childhood (B=0.32, 95%CI -0.56, 1.20; p=.48). Same was found for child internalizing and externalizing problems among (all p-values for interactions ≥.15). Similarly, Study III found no interactions between child sex and maternal social support in ALSPAC during pregnancy (B=-0.45, 95%CI -1.08, 0.58; p=.56) or after pregnancy (B=0.09, 95%CI -0.76, 0.94; p=.83) or in PREDO during pregnancy (B=0.51, 95%CI -2.06, 3.08; p=.70) or after pregnancy (B=1.93, 95%CI -0.79, 4.65; p=.16), when predicting child general cognitive ability.

Finally in Study IV, no interactions were detected between participant sex and ELS types, namely emotional maltreatment (B=.08, 95%CI -0.20, 0.36; p=.56), physical maltreatment (B=-0.07, 95%CI -0.35, 0.20; p=.60), low childhood SES (B=-0.05, 95%CI -0.23, 0.13; p=.57), separation from parents (B=.03, 95%CI -0.26, 0.31; p=.86), parental divorce (B=-0.10, 95%CI -0.54, 0.34; p=.65), or death of a family member (B=.05, 95%CI -0.27, 0.37; p=.77 for interactions).

6 Discussion

This thesis investigated the developmental origins of mental health throughout the life course, building on the DOHaD framework and utilizing three longitudinal cohort studies that included a combination of register-based, self-reported, and objectively assessed data spanning from the pregnancy period until late adulthood. This approach enabled me to form a comprehensive picture of the early risk and promotive factors for the offspring's mental health and psychological development. Extending from previous studies that have focused mainly on early life risk factors during pregnancy and in childhood, this thesis sought to identify potential promotive factors for offspring mental health and psychological development that occur already during pregnancy, such as positive maternal mental health. The thesis highlights the importance of positive maternal mental health during pregnancy, including positive emotions and social support, for the development of offspring mental health. Additionally, the thesis adds to earlier research literature investigating the lifelong associations of ELS with anxiety symptoms in late adulthood. Converging with earlier evidence, this thesis shows that the association of ELS in childhood, particularly emotional and physical maltreatment and low childhood SES, with higher anxiety symptoms is evident still in late adulthood.

In the following chapters I discuss the study findings more in detail.

6.1 Positive maternal mental health and mental health and cognitive development among children

Overall, the findings of this thesis indicate an association of higher levels of positive maternal mental health during pregnancy with lower hazards of mental and behavioral disorders, lower levels of total, internalizing and externalizing psychiatric problems, and with higher general cognitive ability among the offspring. Studies I and II among 3378 and 2636 mother-child-dyads of the PREDO cohort, respectively, found that maternal positive emotions, curiosity, social support, and their composite score during pregnancy were associated with a lower hazard of any mental and behavioral disorder in children by child age 8.4−12.8 years and with lower total, internalizing and externalizing problems among children both in early childhood at age 1.9−5.9 years and in late childhood at age 7.1−12.1 years. Study III among 5784 and 420 mother-child dyads in the ALSPAC and PREDO cohorts, respectively, showed that higher maternal perceived social support during pregnancy was associated with higher general cognitive ability among children at 8 years of age. In ALSPAC, higher maternal perceived social support after pregnancy was also associated with higher cognitive ability in the offspring; however, life course modelling analyses suggested that pregnancy may be a sensitive

period for the effects of maternal social support on child cognitive development. In all of the three studies, associations were independent of the included sociodemographic and perinatal covariates such as child birth weight and gestational age and, importantly, of maternal psychological distress preceding or co-occurring with positive maternal mental health. The associations were detected among both boys and girls.

The findings of this thesis are in line with earlier evidence suggesting associations between higher positive maternal mental health during pregnancy and beneficial psychological development and lower psychiatric problems among children (Braeken et al., 2017; Clayborne et al., 2023; DiPietro et al., 2006; Lewinn et al., 2020; Phua et al., 2017; Shin et al., 2019; van den Heuvel et al., 2015; Wei et al., 2023). Earlier studies have focused on infants and preschool aged children, while the three studies of this thesis followed up the children until late childhood, thus suggesting that the beneficial effects of positive maternal mental health during pregnancy may persist beyond infancy and early childhood.

Moreover, Study I extends the evidence from earlier studies that have focused on psychological development and psychiatric problems to the more severe end of the continuum of child psychopathology, namely to diagnosed mental and behavioral disorders. This finding suggests that the protective effects of positive maternal mental health during pregnancy may extend to alleviating the risk of the more severe psychopathology among children, in addition to continuously assessed symptoms of psychopathology, which I also examined in Study II. Study II was to my knowledge the first to show that higher positive maternal mental health during pregnancy was associated with a lack of increase in total psychiatric problems from early childhood to late childhood, while such increase was found among children of women with lower positive mental health during pregnancy. This is in line with previous meta-analytic evidence on maternal psychological distress during pregnancy, showing no weakening in the association between maternal perinatal depression and anxiety and psychiatric problems in children from infancy through adolescence (Rogers et al., 2020).

In general, the positive associations of positive maternal mental health on child mental health and cognitive development showed relatively small effect sizes across Studies I−III. It should be noted that in the PREDO and ALSPAC cohorts, mothers generally scored high in positive emotions and social support during pregnancy (Table 6); it may be that relatively low variance in positive maternal mental health resulted in smaller effect sizes than could be expected in populations with more varying levels of positive mental health. However, small effects at the population level may nonetheless translate into clinically meaningful findings when targeting positive mental health interventions to mothers experiencing marked isolation and low positive emotions.

6.1.1 Mitigation of maternal psychological distress effects by positive maternal mental health

Higher positive maternal mental health, including positive emotions and higher social support both during and after pregnancy, was associated with lower concurrent psychological distress such as depressive and anxiety symptoms and a history of mental and behavioral disorders, consistently with earlier evidence (Bedaso et al., 2021; Friedman et al., 2020; Hetherington, McDonald, Williamson, Patten, & Tough, 2018; Racine et al., 2019). Importantly, however, positive maternal mental health during pregnancy was associated with mental health and cognitive development in children independently of these concurrent indicators of maternal psychological distress, indicating that the beneficial effects of positive maternal mental health were not merely explained by the absence of concurrent psychological distress.

Studies I−II showed that positive maternal mental health during pregnancy was associated with lower hazards of mental and behavioral disorders and lower psychiatric problems also among children of mothers who reported clinically relevant depressive symptoms during pregnancy and/or who had a mental or behavioral disorder before or during pregnancy. This is in line with another study reporting that positive maternal mental health in the perinatal period was associated with lower internalizing and externalizing problems among girls independently of maternal stress, and that positive maternal mental health buffered the effects of maternal stress on child mental health (Clayborne et al., 2023). The lack of interactions between indicators of positive maternal mental health and maternal psychological distress in Studies I−III suggests that positive maternal mental health provides universal beneficial effects for the children, regardless of whether their mothers experienced concurrent or lifetime psychological distress. On the other hand, Study II suggested that particularly among children of mothers with clinically relevant depressive symptoms, positive maternal mental health may mitigate the effects of maternal depressive symptoms during pregnancy on the *increase* of psychiatric problems from early childhood to late childhood, suggesting resilience effects. It should be noted, however, that the sample size of clinically depressed pregnant women was relatively small; these findings should be interpreted with caution.

The potential mitigation effects of positive maternal mental health can be interpreted in light of the resilience effects of protective factors vs. summative effects of promotive factors, described more in detail in Chapter 2.2.4. According to this conceptualization, resilience effect would imply that exposure to positive maternal mental health *in utero* would be particularly beneficial for those children who are exposed to concurrent maternal psychological distress during pregnancy, such as

maternal prenatal depression, anxiety and stress, whereas it would have less effects for those not exposed to concurrent adversities. Summative effects, in turn, would imply that the promotive effects of positive maternal mental health during pregnancy would be present universally for all children, regardless of their risk factors. The findings of Studies I−III suggest that the beneficial effects of positive maternal mental health extend both to children of mothers with and without concurrent psychological distress; the effects were not limited to those experiencing co-occurring risk factors. According to Luthar et al. (2006, 2012) and Zimmerman et al. (2013), the findings of Studies I-III give most support to positive maternal mental health as a universally promotive factor, rather than a specific protective factor that would work by counteracting the negative effects of adversities. According to the vantage sensitivity model, it could also be formulated that positive maternal mental health during pregnancy may increase the offspring's vantage sensitivity to benefit from later environments (Pluess & Belsky, 2013).

On the other hand, resilience may be defined differently among mothers and the offspring. The multi-systems model of resilience (Liu et al., 2017), introduced in Chapter 2.2.4, describes resilience at different levels, and differentiates core resilience including for example biological stress regulation and internal resilience including for example interpersonal and psychological resources such as coping skills, self-efficacy, emotion regulation, and social support. In this context, positive maternal mental health during pregnancy could be seen as internal resilience factor among *mothers*. Furthermore, positive maternal mental health may strengthen the development of core resilience among *children* via influencing the development of HPA axis and other biological systems related to stress regulation and adaptive functioning. Therefore, in light of the multi-systems model of resilience, positive maternal mental health during pregnancy may then contribute in the developmental origins of resilience.

6.1.2 Timing effects of positive maternal mental health

Positive maternal mental health showed high continuity from pregnancy to the late childhood follow-up; this calls for interventions supporting positive mental health at the early stages, already during pregnancy. The finding in Study III that maternal social support *during* pregnancy was consistently associated with child cognitive ability and may be a sensitive period for the promotive effects further emphasizes the importance of social support during this period. While there was also an association between maternal perceived social support after pregnancy and child cognitive ability in ALSPAC, no such association was detected in the smaller PREDO cohort. It should be noted that maternal social

support after pregnancy was reported at child age 8 months in the ALSPAC and at child age 8 years in the PREDO, reflecting very different developmental periods and potentially contributing to the discrepant findings. Neurodevelopmental processes such as synaptogenesis, synaptic pruning, and white matter development are especially dynamic during pregnancy and the first 2−3 years of life (Cusick & Georgieff, 2016), and therefore maternal social support during this period may have a larger effect on child cognitive development than maternal social support later in childhood.

The findings regarding pregnancy as a sensitive period for maternal social support are somewhat in contrast with an earlier study of ca. 1000 mother-child-dyads which reported an association between maternal social network size after pregnancy, but not during pregnancy, and child cognitive ability (Lewinn et al., 2020). Of note, this earlier study focused on maternal social network size instead of perceived satisfaction with social support. It has been suggested that the perceived quality of social support is more predictive of positive health outcomes than the quantity and frequency of social interactions (Barrera, 1986; Sarason et al., 1987); for example, the quality of a romantic relationship, rather than the presence of a romantic partner *per se*, may provide protective effects against distress among pregnant women (Ungar et al., 2019).

Somewhat in contrast with the findings of Study III regarding child cognitive ability, Study II suggested that late childhood may be a potential sensitive period for positive maternal mental health in relation to offspring psychiatric problems, with higher relevance than the positive maternal mental health during the pregnancy period. Positive maternal mental health in the late childhood follow-up also mediated a large proportion of the association between positive maternal mental health during pregnancy and total psychiatric problems in late childhood. In addition to the mediation effects, however, a direct association between positive maternal mental health during pregnancy and lower total problems in children existed independently of positive maternal mental health at child's late childhood. The findings are in line with earlier studies regarding maternal psychological distress during pregnancy, showing that the effects of maternal distress during pregnancy on child mental health are partly, but not fully mediated by maternal distress after pregnancy (Hentges, Graham, Plamondon, Tough, & Madigan, 2019; Lahti et al., 2017). It should also be noted that in Study II, child psychiatric problems were mother-assessed, whereas in Study III child cognitive ability was objectively assessed. The source of assessment may contribute to the recency effects of positive maternal mental health in relation to child psychiatric problems (Madathil et al., 2018; Zuber et al., 2023).

Taken together, the findings on the beneficial effects of positive maternal mental health, including positive emotions and social support, on the mental health and psychological development of the

offspring suggest that positive maternal mental health during and after pregnancy may promote mental health of not only the mother, but also of the offspring. The findings support the DOHaD framework, which suggests that already during pregnancy and early in childhood, the fetal environment contributes in programming the developing brain and other organs of the child (Barker, 2007; Van den Bergh et al., 2020).

6.2 Early life stress and late adulthood anxiety

Study IV found that low childhood SES and emotional and physical maltreatment in childhood were associated with higher anxiety symptoms in late adulthood. Furthermore, the study found that these types of ELS and additionally parental divorce were associated with a higher risk of clinically relevant anxiety symptoms. These findings are in line with a wide body of research showing that ELS, particularly low SES and emotional and physical maltreatment, may increase the risk for anxiety, depression and other psychiatric problems throughout the life course (Gardner et al., 2019; Hughes et al., 2017; Humphreys et al., 2020; M. Li et al., 2016; Norman et al., 2012; Sahle et al., 2022), and that the associations extend to late adulthood (Angelini et al., 2019; Draper et al., 2008; Pesonen et al., 2007; Räikkönen et al., 2011; Raposo et al., 2014; Rusby & Tasker, 2009; Sachs-Ericsson et al., 2010; Tani et al., 2016; Wang et al., 2023).

Additionally, the accumulation of different types of ELS was associated with higher dimensionally assessed anxiety symptoms and a higher risk of clinically relevant anxiety in late adulthood. This is in line with earlier studies linking the accumulation of ELS with adverse outcomes in adulthood: for example, a meta-analysis found the accumulation of four or more ELS experiences to be associated with a 3.70-fold risk of anxiety (Hughes et al., 2017).

Of the studied types of ELS, emotional maltreatment was most strongly and consistently associated with dimensionally assessed and clinically relevant anxiety symptoms in late adulthood. This is in line with the converging evidence that the association between emotional maltreatment and later psychopathology is stronger than the association of other maltreatment types, such as physical abuse (Humphreys et al., 2020; Infurna et al., 2016; Macpherson et al., 2021; Norman et al., 2012); also among elderly adults, emotional neglect has been found to be most strongly associated with depression (Wang et al., 2023). Emotional maltreatment is a form of ELS that often remains undetected, and emotional and physical maltreatment also often co-occur; for example in the current sample of the HBCS cohort, 66.4% of those reporting physical maltreatment also reported emotional

maltreatment. This high co-occurrence may contribute to the blunted association between physical maltreatment and clinically relevant anxiety symptoms when adjusting for emotional maltreatment.

This thesis also adds to the evidence that low childhood SES is a type of ELS that has a negative impact on mental health throughout the life course (Peverill et al., 2021), an effect that was mediated by adulthood SES. Low childhood SES often co-occurs with other stressors and is associated with a higher risk of childhood abuse (Yang et al., 2021). In this study, however, the association of childhood SES with anxiety symptoms was independent of other types of ELS, contrasting some previous studies that have suggested that other types of ELS may mediate the effects of low childhood SES on psychopathology (McLaughlin et al., 2011; Yang et al., 2021).

In this study, associations between other types of ELS (physical and emotional maltreatment, parental divorce, and accumulation of ELS) and late-life anxiety were independent of adulthood SES, also in line with an earlier study among older adults (Yazawa et al., 2022). It should be noted, however, that adulthood SES fully mediated the association between childhood SES and late-life anxiety, suggesting that the continuity of low SES throughout the life course, rather than low SES in childhood specifically, increases the risk of anxiety symptoms in late adulthood. A similar mediation effect has been found in other studies (Stansfeld et al., 2011), whereas associations between low childhood SES and late-life depressive symptoms have also been found independently of adulthood SES (Tani et al., 2016). Additionally, Yazawa and colleagues showed that adulthood SES moderated the effects of ELS on late-adulthood depressive symptoms; this suggests that higher SES in adulthood may buffer some of the adverse effects of ELS on later mental health. Preliminary analyses in the HBCS data (Lähdepuro et al., unpublished results) suggest that also in this cohort, adulthood SES may moderate the effects of childhood emotional maltreatment on anxiety symptoms in late adulthood; among participants with a higher adulthood SES, the association between childhood emotional maltreatment and clinically relevant anxiety symptoms was no longer significant. Higher adulthood SES may thus mitigate some of the effects of ELS in childhood; this is an interesting finding that should be investigated further.

This study found no association between childhood separation from parents due to wartime evacuations and anxiety symptoms in late adulthood. The finding is somewhat in line with previous research finding an association between childhood separation from parents and the risk of psychopathology, but not with anxiety symptoms (Pesonen et al., 2007; Räikkönen et al., 2011; Rusby & Tasker, 2009). Of note, the findings regarding parental separation due to war-time evacuation cannot be generalized to all separation from parents due to special characteristics related specifically to war-time conditions. Also, the participants of Study IV who were not separated were exposed to

war-time conditions, which may have been a remarkable stressor as such; this may partly explain why no associations were detected between parental separation in childhood and anxiety symptoms in late adulthood.

No associations were found between death of a family member in childhood and anxiety symptoms in late adulthood. This is in line with an earlier study which found no association between death of a parent in childhood and depressive symptoms in middle age or late adulthood (Yang et al., 2020). The finding that parental divorce was not associated with dimensionally assessed anxiety symptoms is corresponding to previous studies not finding an association between parental divorce and anxiety symptoms in adulthood (Sands et al., 2017; Spinhoven et al., 2010), but parental divorce was associated with an increased risk of clinically relevant anxiety symptoms in late adulthood. This finding is, to my knowledge, novel. One possible explanation for this may be that since the participants in the HBCS cohort had experienced parental divorce between the 1940s and the early 1970s, the consequences of the parental divorce on e.g. the social and economic situation of the family may have differed from more recent study cohorts. The finding also suggests that participants experiencing parental divorce in childhood were either highly affected by the experience or not.

6.3 Potential mechanisms underlying the DOHaD framework

This thesis found that positive maternal mental health both during and after pregnancy, contributing to positive fetal and childhood environments, may have versatile promotive effects on child mental health and psychological development, and that pregnancy may even be a sensitive period for some of these promotive effects. Furthermore, this thesis provided further evidence that the adverse effects of ELS on anxiety symptoms extend throughout the life course until late adulthood. Together, the findings provide further support to the DOHaD framework. Importantly, the current findings extend this framework from risk factors to potentially promotive factors that contribute to the prenatal programming of mental health and psychological development of the offspring. The importance of investigating the positive prenatal environments in the context of DOHaD in increasingly acknowledged (Meaney, 2018; Monk et al., 2019); the current research contributes to this emerging field of research.

According to the DOHaD framework, prenatal and early life programming in response to the fetal and childhood environment may contribute to changes that prepare the individual to adapt to the expected environment (Barker, 2007). This has also been called “meta-plasticity” and “prenatal programming of postnatal plasticity/environmental sensitivity” (Hartman et al., 2023; O’Donnell &

Meaney, 2017; Pluess & Belsky, 2011). From an evolutionary perspective, the goal of adapting to environmental features during and after pregnancy is to enhance future survival by helping the fetus or child to prepare for the environment predicted by these features (Glover, 2011). In other words, the early environment may predict the later environment of the offspring, and biological alterations related to exposures to stressful or beneficial environments may aim at enhancing adaptive reactions to future environments (Belsky & Pluess, 2013; Glover, O'Donnell, O'Connor, & Fisher, 2018; Monk et al., 2019). Extending from the evolutionary perspective on prenatal distress, it could be speculated that a positive prenatal environment such as prenatal positive maternal mental health may provide evolutionary benefits for the offspring. For example, a less vigilant individual may have more curiosity and capacity to explore their environment, and may experience lower reactivity to stressors.

Several biological mechanisms underlying the DOHaD framework, related to the mother and the placental functioning, have been recognized (Monk et al., 2019; Van den Bergh et al., 2020). While this thesis does not directly address the mechanisms underlying its findings, potential biological and other mechanisms underlying the effects of prenatal and childhood environments on offspring mental health and psychological development are reviewed below. To the best of my knowledge, no studies have directly investigated the potential mechanisms linking positive maternal mental health during pregnancy to offspring mental health and psychological development. Regarding prenatal mechanisms, I therefore review the literature focusing on the effects of maternal psychological distress during pregnancy on offspring mental health and psychological development, reflecting on how similar mechanisms may underlie the effects of positive maternal mental health during pregnancy.

6.3.1 Changes in physiology and the HPA axis

Pregnancy is associated with a host of physiological changes in the mother that involve several organs and tissues, including hormonal activity and alterations in the brain structure; many of these changes and their relevance to the mother-child-dyad are still poorly known (Galea, Qiu, & Duarte-Guterman, 2018). Accumulating evidence also shows that maternal psychological distress during pregnancy is associated with changes in maternal and fetal physiology (reviews: Monk et al., 2019; Van den Bergh et al., 2020) and in offspring brain volumes and structures such as the hippocampus, amygdala and the prefrontal cortex (reviews: Hartman et al., 2023; O'Donnell & Meaney, 2017).

Among the most studied potential mechanisms of ELS during pregnancy and in childhood is the HPA axis. The lifecycle model of stress suggest that chronic or repeated exposure to stress may have a

long-term effect on the development of the HPA axis and the related brain structures involved in stress regulation, such as the amygdala, hippocampus and frontal cortex, and that these brain structures are particularly sensitive to stress during early development (Lupien et al., 2009). Exposure to prolonged ELS may cause long-term alterations in the developing brain by modifying the functioning of the HPA axis and the aforementioned associated brain areas involved in the stress system (Jawahar, Murgatroyd, Harrison, & Baune, 2015; Lai & Huang, 2011; Lupien et al., 2009; Silberman, Acosta, & Zorrilla Zubilete, 2016).

During pregnancy, maternal psychological distress has been associated with altered HPA functioning both among the mothers and the offspring (Lupien et al., 2009; Monk et al., 2019; Van den Bergh et al., 2020); however, one systematic review found that the majority of the included studies did not detect an association between maternal psychological distress during pregnancy, more specifically depression, and maternal cortisol (Orta, Gelaye, Bain, & Williams, 2018). Among the studies that have detected an association, the direction of the association is not consistent across studies, as psychological distress during pregnancy has been associated with both increased and decreased cortisol responses (Lupien et al., 2009; Van den Bergh et al., 2020). Exposure to excess glucocorticoids during pregnancy has been associated with adverse mental health and cognitive development in the offspring (Bergman, Sarkar, Glover, & O'Connor, 2010), although evidence of this association is inconclusive (Van den Bergh et al., 2020).

On the other hand, previous findings have linked positive emotions and social support, also among pregnant women, with *beneficial* effects in the stress regulation system and maternal cortisol levels (Fredrickson et al., 2000; Giesbrecht, Poole, Letourneau, Campbell, & Kaplan, 2013; Nierop, Wirtz, Bratsikas, Zimmermann, & Ehlert, 2008; Pluess et al., 2012; Southwick et al., 2005). Furthermore, in an earlier study, higher social support during pregnancy was shown to moderate the effects of psychosocial stress on maternal cortisol level increase, thus potentially buffering the effects of maternal psychological distress during pregnancy on the fetus (Giesbrecht et al., 2013). These potential alterations in maternal physiology following higher levels of positive mental health during pregnancy allude that the associations between positive maternal mental health during pregnancy and offspring mental health may associate with similar physiological mechanisms. Among other potential hormonal mechanisms underlying the association between positive maternal mental health during pregnancy and offspring development is oxytocin, a hormone that is involved in social behaviors and in pregnancy and childbirth (Phua et al., 2020). Positive emotions and social support have been associated with increased oxytocin levels (Ozbay et al., 2007), which in turn have been linked to the activation of parenting practices (Phua et al., 2020).

In childhood, chronic stress has been associated with dysregulation of the HPA axis and particularly its negative feedback system that aims at returning the homeostatic balance of the stress hormone level when the perceived stress is over (Jawahar et al., 2015). Furthermore, exposure to stressful life events early in life may modify brain structures in a way that enhances stronger reactivity to new potentially stressful life events (Anisman, Merali & Stead, 2008); this may contribute to the association between the accumulation of ELS and later anxiety. Higher sensitivity to stress may then increase the individual's risk for psychopathology (Lupien et al., 2009). Indeed, altered HPA axis functioning and changes in the structure and functioning of hippocampus and amygdala have been consistently found in mental and behavioral disorders, including anxiety disorders (Sprooten et al., 2017; Zorn et al., 2017).

Exposure to ELS at different developmental stages may have differential effects on cortisol reactivity: for example, Raymond and colleagues (2021) found that participants exposed to ELS in early childhood at age 3−7 years, approximately co-occurring with early development of the amygdala in the brain, showed a higher cortisol awakening response and a blunted cortisol reactivity to a stressor, compared with participants exposed to ELS in infancy (0−2 years) and in later childhood (over 7 years) (Raymond et al., 2021). Of note, ELS has been associated with both hyper- and hypoactivity of the HPA axis (Brindle, Pearson, & Ginty, 2022; Bunea, Szentágotai-Tătar, & Miu, 2017; Lupien et al., 2009); particularly childhood neglect has been associated with lower glucocorticoid levels among children (Lupien et al., 2009). Of note, however, one meta-analysis found an association between objectively confirmed maltreatment experiences and low wake-up cortisol, whereas no associations were found for self-reported maltreatment (Bernard, Frost, Bennett, & Lindhiem, 2017). In late adulthood, increased glucocorticoid levels have been linked with decreases in hippocampal volume and memory performance (Lupien et al., 2009). These changes may potentially elicit anxiety in older adults.

6.3.2 Genetic and epigenetic mechanisms

The promotive effects of positive maternal mental health during pregnancy on offspring mental health and psychological development may be at least in part explained by shared genetic variance of the mother-child-dyad, as has been suggested for the effects of maternal psychological distress during pregnancy (Hannigan et al., 2018; Havdahl et al., 2022). Regarding positive mental health, it is estimated that approximately 30-40% of the variation in subjective well-being is genetically determined (Diener, Oishi, & Tay, 2018). Polygenic scores for extraversion and neuroticism have

been associated with higher and lower positive mental health, respectively (Weiss et al., 2016). On the other hand, a recent study conducted in the ALSPAC and PREDO cohorts showed that the genetic risk only partially explains the association between maternal psychological distress during pregnancy and offspring psychiatric problems, accounting for ca. 45% of the association, while maternal psychological distress also carried independent effects (Chen et al., 2023). In this thesis, the associations between positive maternal mental health and offspring mental health found in Studies I−II were independent of maternal and/or paternal mental and behavioral disorders which are a strong indicator of familial confounding. These findings allude that other underlying mechanisms in addition to genetic heritability exist.

Underlying genetic confounding may also link ELS experiences with anxiety throughout the life course. For example, parents experiencing anxiety and other psychiatric problems may be at a higher risk of perpetrating maltreatment on their children, while at the same time shared genetic propensity increases the risk for anxiety and other psychiatric problems among these children. Indeed, a meta-analysis of genomic-wide association studies (GWAS) found a heritability component in childhood maltreatment (Warrier et al., 2021). Mendelian randomization analyses of the same study found evidence for a causal association between child maltreatment and depression, ADHD and schizophrenia; for depression, this association was unidirectional (Warrier et al., 2021).

While the genes remain largely static throughout development, inter-individual differences in how the genes are expressed, and therefore how they affect the brain and behavior, may occur (O'Donnell & Meaney, 2020). This process, known as epigenetics, refers to changes in the chromatin structure that regulate genomic transcription and therefore gene expression (Cao-Lei et al., 2020). Among the most commonly studied epigenetic changes is DNA methylation (DNAm), meaning an addition or removal of a methyl group into a cytosine that induce changes in gene expression (Cao-Lei et al., 2020; Smeeth, Beck, Karam, & Pluess, 2021). Epigenetic changes are dynamic and can occur throughout development, and they can also be inherited by the offspring (Cao-Lei et al., 2020).

Converging evidence suggests that epigenetic mechanisms may underlie the association between maternal psychological distress during pregnancy and child mental health (Cao-Lei et al., 2020; Monk et al., 2019; Provençal et al., 2020; Suarez et al., 2018; Van den Bergh et al., 2020). Epigenetic changes may also occur in the placenta during pregnancy, thereby increasing fetal exposure to glucocorticoids (Hartman et al., 2023). To my knowledge, no studies have investigated whether positive maternal mental health during pregnancy is associated with epigenetic changes. However, Smeeth and colleagues (2021) have presented a framework involving different pathways through which epigenetics may be involved in psychological resilience. First, epigenetic modifications

fostering resilience may be inherited or affected by genetic variation. Second, early environment may modify the individual's epigenome in ways that foster resilience when facing adversities later in life. Third, promotive factors co-occurring with adversities may modify the effect of adversity on the individual's epigenome (Smeeth et al., 2021). In the context of positive maternal mental health and the findings of this thesis, the potential resilience effect may occur via the third pathway, e.g. mitigating the negative effects of concurrent adversity. Indeed, there is evidence in human offspring that after pregnancy, positive environmental factors such as positive maternal care practices have an impact on infant DNAm and may moderate the effects of adverse environments such as maternal depressive symptoms during pregnancy, as reviewed by Provenzi and colleagues (2019); similar patterns may be present for prenatal positive environments.

Also in childhood, the associations between ELS and later psychopathology risk may be mediated via epigenetic mechanisms. More specifically, research on epigenetic factors suggests that ELS exposure is linked with hypermethylation of the glucocorticoid receptor gene NR3C1 (Palma-Gudiel, Córdova-Palomera, Leza, & Fañanás, 2015; Turecki & Meaney, 2016; Tyrka, Ridout, & Parade, 2016) which is involved in the regulation the HPA axis, potentially altering its negative feedback system (Tyrka et al., 2016; Wadji et al., 2021). Hypermethylation of the NR3C1 has also been associated with an increased risk of psychopathology (Wadji et al., 2021; Zhu, Bo, Liu, & Jia, 2023).

While DNAm is dynamic and occurs throughout the life course, it has been suggested that there may be sensitive periods for epigenetic changes related to ELS, and that experiences early in development may contribute to more stable DNAm changes (Dunn et al., 2019). In their study comparing DNAm among participants who were exposed to ELS before 3 years of age, 3−5 years of age, or 6−7 years of age in the ALSPAC cohort, Dunn and colleagues found that ELS exposure before 3 years of age was most strongly associated with DNAm changes (Dunn et al., 2019). In the same cohort, another study found that downward mobility in the family SES across developmental stages and financial hardship particularly in middle childhood were associated with alterations in the offspring DNAm (Liu et al., 2023). In light of these findings, it is possible that DNAm plays a role particularly in the effects of early exposures to positive maternal mental health, such as maternal social support during pregnancy and in offspring infancy, while this mechanism may be less relevant in late childhood.

6.3.3 Other biological mechanisms

Inflammation may be among other potential biological mechanisms underlying the association between positive maternal mental health during pregnancy and offspring mental health and

psychological development. Maternal psychological distress during pregnancy has been associated with increased inflammation levels in pregnancy (Lahti-Pulkkinen et al., 2020; Van den Bergh et al., 2020), and in turn, maternal infections and inflammation during pregnancy have been associated with adverse neurodevelopment in the offspring (Girchenko et al., 2020; Nazzari et al., 2020; O'Connor et al., 2022); furthermore, higher maternal inflammation levels during pregnancy may partially mediate the effects of prenatal stressful environments, namely maternal psychological distress and cardiometabolic pregnancy disorders, on the higher risk of developmental delay among the offspring (Girchenko et al., 2020). On the contrary, higher social support during pregnancy has been associated with lower inflammation levels among pregnant women (Coussons-Read, Okun, & Nettles, 2007; Ross et al., 2017). There is also some evidence that higher levels of positive emotions are associated with lower inflammation levels particularly when facing simultaneous stress, thus potentially buffering the negative effects of stress on inflammation (Blevins et al., 2017). The abovementioned oxytocin hormone, associated with positive maternal mental health, has also been associated with beneficial effects in the immune system functioning (Feldman, 2020).

Another potential biological mechanism of interest may be alterations in offspring telomere length. Exposure to ELS both during pregnancy, such as maternal psychological distress, and in childhood, such as childhood maltreatment, have been associated with shorter telomere length (Chen, Lo, Chan, Leung, & Ip, 2022; Savolainen et al., 2014; Van den Bergh et al., 2020). Shorter telomere length, in turn, has been associated with stress biology and with a higher risk of mental and behavioral disorders (Van den Bergh et al., 2020). On the other hand, a history of mental and behavioral disorders severe enough to warrant hospital treatment has been associated with longer, rather than shorter telomere length among older adults (Savolainen et al., 2012). Regarding promotive effects of positive environments, an earlier study in the PREDO cohort found an association between positive maternal mental health during pregnancy a longer newborn telomere length in fetal cord blood, independently of concurrent maternal psychological distress (Verner et al., 2021). These longer telomeres may have protective effects on offspring mental health and psychological development.

Emerging evidence also shows that stress-related changes in maternal intestinal microbiota may contribute to linking prenatal maternal distress with offspring outcomes (reviews: Hartman et al., 2023; Monk et al., 2019). Microbiome-related mechanisms potentially associated with positive maternal mental health are yet to be investigated. Finally, one small-scale study among 37 neonates found that maternal cohabiting status during pregnancy, potentially reflecting higher social support, moderated the association of low SES with neonatal brain volumes in areas associated with e.g. emotion regulation, attention, sensory processing, and language, thus showing protective effects on

brain development (Spann, Bansal, Hao, Rosen, & Peterson, 2020). Therefore, structural changes in the offspring's brain may be potentially interesting pathways between risk and promotive factors and offspring mental health and development that should be explored further.

6.3.4 Bonding and the attachment relationship

Attachment refers to the emotional relationship or "bond" between the caregiver and the infant that shapes the infant's perception of other people and the surrounding world (Ainsworth, 1979; Bowlby, 1969, 1988). Secure attachment to the caregiver enables the child to explore the surroundings and use the caregiver as a "secure base" and a source of safety and comfort. An insecure attachment, on the other hand, disturbs these processes and has been consistently associated with a higher risk of psychopathology in both children and adults (meta-analyses: Herstell et al., 2021; Madigan, Brumariu, Villani, Atkinson, & Lyons-Ruth, 2016; Spruit et al., 2020). Meta-analytic evidence shows that childhood maltreatment increases the risk of insecure attachment (Cyr, Euser, Bakermans-Kranenburg, & Van Ijzendoorn, 2010). Of note, the same meta-analysis found no association between low family SES and insecure attachment.

Maternal attachment and bonding to the offspring starts developing already during pregnancy (Condon, 1993; Trombetta et al., 2021). Maternal psychological distress both during and after pregnancy is associated with poorer maternal bonding and a higher risk of insecure attachment (Le Bas et al., 2021; Stein et al., 2014), whereas maternal satisfaction with their social support has been associated with higher maternal bonding with the fetus (Hopkins et al., 2018). Higher positive maternal mental health during and after pregnancy may thus enhance bonding and sensitive parenting, which in turn have been associated with beneficial development in children (Le Bas et al., 2021, 2020) and with smaller and less prolonged stress-related activations of the offspring HPA axis (Lupien et al., 2009). Mother-infant attachment and the quality of early social interactions are also associated with infant cognitive and brain development (de Mendonça Filho et al., 2022; Ilyka, Johnson, & Lloyd-Fox, 2021; Ronfani et al., 2015). In light of these findings, maternal positive emotions and satisfaction with their perceived social support may benefit child development by supporting maternal attachment and interactions with their infant. This hypothesis is supported by a systematic review of 55 studies that found evidence of associations between mother-infant interactions, attachment quality and a range of functional brain outcomes of the offspring (Ilyka et al., 2021). Moreover, postnatal mother-infant attachment has been shown to moderate the effects of prenatal glucocorticoid exposure on child cognitive development, thus potentially buffering the

adverse effects of negative prenatal exposures (Bergman et al., 2010). Promoting mother-infant attachment via supporting positive maternal mental health already during pregnancy may thus contribute to mitigating the effects of maternal psychological distress during pregnancy on child mental health and development, in addition to the beneficial effects of attachment *per se*.

6.3.5 Cognitive and behavioral mechanisms

During pregnancy, positive maternal mental health may protect the mother-child-dyad from the effects of stressors by influencing the mother's cognitive appraisals of stressful life events (Ungar, Hadfield, Bush, Quesnel-Vallée, & Pekelny, 2019), potentially mitigating the effect of stressful events on the subjective experiences of stress. Experiencing positive mood and social support in the perinatal period may also enhance positive parenting and engaging in positive care practices such as breastfeeding postpartum (Chae, Chae, Kandula, & Winter, 2017; McManus, Khalessi, Lin, Ashraf, & Reich, 2017; Mercan & Tari Selcuk, 2021; Phua et al., 2020). Breastfeeding, in turn, consistently shows beneficial effects on child cognitive development (Horta, Loret de Mola, & Victora, 2015; Kramer et al., 2008; Lewinn et al., 2020). Furthermore, higher levels of perceived maternal social support during pregnancy may reflect on the early caregiving environment of the child, particularly via shared caregiving: Higher social support during pregnancy may indicate that there are other people to share caregiving responsibilities with, and who interact with the growing child. This, in turn, may contribute in providing a more stimulating growing environment that benefits cognitive and emotional development among children (National Scientific Council on the Developing Child, 2004; Shin et al., 2019; Tooley, Bassett, & Mackey, 2021).

Several cognitive and behavioral processes may also mediate the association between childhood ELS and late-life anxiety. ELS occurring during early development may profoundly impact the individual's perceptions of themselves and their environment. Based on early experiences in attachment relationships with the caregivers, the child begins to form internal working models of themselves, others, and future attachment relationships (Bowlby, 1988; Trombetta et al., 2021); stressful experiences in these early attachment relations may negatively impact the internal working models, increasing the risk of insecure attachment style later in life and potentially eliciting anxiety. ELS may also elicit negative cognitive appraisals of both the stressful event and of oneself and their surroundings, provoking a sense of continuing threat (Ehlers & Clark, 2000) and a lower perception of one's own ability to face challenges and to endure stress (Nishimi et al., 2020), eliciting anxiety symptoms. Furthermore, the accumulation of ELS, particularly repeated exposure to physical and

sexual abuse in childhood, shows associations with lower social cognition skills among girls in early adolescence (Crawford et al., 2022). Social cognition skills play a role in understanding, interpreting and participating in social relationships, and may thus contribute in the development of psychopathology following ELS. Finally, ELS experiences have been associated with unhealthy and risky lifestyle behaviors such as risky sexual behavior (Norman et al., 2012) and smoking, alcohol use, overweight and diet (Yang et al., 2022). These behaviors may contribute to the association between ELS in childhood and later psychopathology.

6.4 Strengths and limitations of the studies

6.4.1 Strengths

This thesis investigates the DOHaD framework from a wide perspective, focusing on exposures at different developmental periods both during pregnancy and in childhood. Moreover, the studies extend the DOHaD perspective from exposure to prenatal and early life stressors to positive environments, thus adding novelty to previous findings. The thesis also included both dimensional and categorical indicators of mental health across the life course, focusing on mental health and psychological development in early childhood and late childhood but also extending the assessment to mental health in late adulthood, an age group that remains somewhat underrepresented in ELS studies.

One of the key strengths of this thesis is utilization of three large, longitudinal cohorts with multiple repeated assessment points. The utilization of longitudinal birth cohorts is in line with the recommendation of the World Health Organization (WHO) which recognizes the importance of investing in birth cohort studies and other longitudinal follow-ups in promoting life-course approach to health (Kuruvilla et al., 2018). This thesis utilizes several different analytic approaches and assessment methods: outcomes included in this thesis are based on nationwide healthcare registers (Study I) and objective neuropsychological assessments (Study III), as well as parent-reported (Study II) and self-reported (Study IV) questionnaire data collected with validated instruments. Together, the assessment tools used build a comprehensive picture of offspring mental health and psychological development, covering childhood and late adulthood and both dimensionally assessed mental health and the more severe end of the continuum of psychopathology.

Particularly the use of objective assessment methods such as register-based diagnostic data and standardized neuropsychological assessment data is a strength of this thesis and has been

recommended in the efforts to study the DOHaD hypothesis in humans (Glover, O'Connor, & O'Donnell, 2023). This approach precludes the issue of shared method variance bias related to many studies that rely on maternal reports of both their own and their child's mental health. On the other hand, even though Study II relied on maternal reports of both their own and their children's mental health, this is unlikely to significantly bias the found associations: a previous study found maternal psychiatric symptoms to have only a small effect on their reports of their offspring's psychiatric problems (Olino, Michelini, Mennies, Kotov, & Klein, 2021). In addition, Study III utilized a coordinated data analysis approach (Zuber et al., 2023) which enables the comparison and replication of associations across two different cohorts. Coordinated data analysis in several cohorts is a recommended method particularly for life course modelling, since it enables the investigation of generalizability of potential sensitive periods across different populations (Zuber et al., 2023).

Studies I−III were also able to take into account several relevant mother- and child-related covariates. For example, the associations between positive maternal mental health and child mental health were independent of obstetric factors across studies; while positive maternal mental health has been associated with better obstetric outcomes such as a lower risk of preterm delivery in previous studies (Feldman, Dunkel-Schetter, Sandman, & Wadhwa, 2000; Hernandez-Martinez, Val, Murphy, Busquets, & Sans, 2011; Hetherington et al., 2015; Pesonen et al., 2016; Voellmin, Entringer, Moog, Wadhwa, & Buss, 2013), the current findings suggest that the associations found in this thesis are not explained by the effects of positive maternal mental health on obstetric outcomes.

6.4.2 Limitations

A general limitation of the thesis is that in all of the three included cohorts, selective attrition occurred; this is inherent to most longitudinal studies and may bias the findings and limit their generalizability. The participants included in the current studies were in general with higher education, stronger social support network, and less likely to have health problems. More specifically in Studies I−III, women who reported on their mental health during pregnancy experienced fewer sociodemographic and health-related risk factors for adverse child mental health and psychological development, and their children had a lower incidences of psychopathology compared to women who did not report on their mental health during pregnancy. Previous studies have also shown that particularly individuals experiencing higher psychological distress are less likely to continue participating in longitudinal studies (Wolke et al., 2009). As the participating individuals are more likely to experience better mental health than those not participating in the follow-up, it could be hypothesized that the selective

attrition would more likely result in underestimating, rather than overestimating the association of ELS and positive maternal mental health with offspring mental health and psychological development. For example, the participants of Study III showed fewer risk factors for low social support, and generally scored high on the social support scale in both the ALSPAC and PREDO cohorts; in the case that there was a threshold effect to "sufficient" prenatal social support, the findings would not capture the effects of extremely low levels of social support on child cognitive development.

A key limitation specific to Study III was the inability to adjust the analyses for maternal IQ, a strong predictor of child cognitive ability that may confound the association between maternal prenatal mental health and child cognitive development (Faleschini, Rifas-Shiman, Tiemeier, Oken, & Hivert, 2019). Instead, I used maternal educational attainment as a proxy for the familial and socioenvironmental factors influencing child cognitive development. The lack of adjustment of maternal IQ sets limitations to the interpretation of findings. On the other hand, an earlier study found associations between maternal social support after pregnancy and child cognitive ability to be independent of maternal IQ (Lewinn et al., 2020).

While Study II utilized repeated assessments of psychiatric problems among children to investigate change in these problems, the main limitation of Study IV was that anxiety symptoms were reported only at one time point in late adulthood; it was therefore not possible to specify whether anxiety symptoms had been persistent throughout the life course or were only manifested later in life. However, a previous study using repeated assessment of anxiety in late adulthood found that higher number of ELS experiences was associated with both persistence of anxiety across a four-year assessment period and with incidence of anxiety symptoms at the later follow-up (Bakouni et al., 2023) and another study found an association between ELS and the onset of mental and behavioral disorders in middle age and late adulthood even in the absence of a prior history of mental and behavioral disorders (Macpherson et al., 2021). These findings suggest that ELS may increase the risk of chronic anxiety, but also of new episodes of anxiety in late adulthood.

Another limitation of Study IV was that some of the ELS experiences were retrospectively self-reported. The agreement between prospective and retrospective reports of ELS is generally poor, implying that prospective and retrospective studies of ELS may capture somewhat different phenomena (Baldwin, Reuben, Newbury, & Danese, 2019; Danese & Widom, 2020). On the other hand, an earlier meta-analysis found no difference in the associations of prospective and retrospective assessments of ELS with later psychopathology (Gardner et al., 2019). Moreover, retrospective self-report is more likely associated with under-reporting, rather than over-reporting, past

stressful/traumatic events (Hardt & Rutter, 2004), and people are fairly consistent in their recall of ELS across time (Hardt, Sidor, Bracko, & Egle, 2006; Yancura & Aldwin, 2009). Moreover, concurrent psychopathology is estimated to have a low impact on the association between retrospective reports of ELS and lifetime psychopathology (Danese & Widom, 2020). While a large proportion of the studies investigating the association between ELS and psychopathology rely on self-reports of ELS, a meta-analysis found evidence of the association also when only taking into account objective reports of ELS (Li et al., 2016). While prospective, objective reports of ELS experiences may provide higher specificity, retrospective reports of ELS have higher sensitivity and therefore capture cases that may be undetected by objective assessment methods. Prospectively and retrospectively reported ELS experiences may also vary in their duration and severity, which may contribute to differential associations with psychopathology (Danese & Widom, 2020).

6.5 Implications and future research

6.5.1 Public health implications

The importance of considering the full spectrum of mental health, including positive mental health, is increasingly acknowledged from the public health perspective. In fact, the WHO has acknowledged already in 2004 that positive mental health is an important aspect of well-being (World Health Organization, 2004). From a public health perspective, positive mental health is viewed as something all individuals can enhance, regardless of their mental illness status (Orpana, Vachon, Dykxhoorn, McRae, & Jayaraman, 2016). Some countries such as the United Kingdom and Canada are already regularly surveying indicators of positive mental health among their residents (Office of National Statistics, 2023; Orpana et al., 2016). These indicators focus on mapping indicators such as self-rated mental health and happiness, life satisfaction, and psychological and social well-being (Public Health Agency of Canada Centre for Surveillance and Applied Research, 2022). The findings of this thesis further highlight the importance of screening for positive mental health, also among pregnant women.

Social disconnectedness is a growing concern that has been called a global behavioral epidemic (Na, Jeste, & Pietrzak, 2023), further emphasized by the Covid-19 pandemic. Importantly, while satisfaction with social support shows continuity over the perinatal period in this and other studies (Junttila et al., 2015), a previous study in a Finnish cohort showed that 5.0% of mothers experienced increasing social loneliness, and 8.7% of mothers experienced increasing emotional loneliness from pregnancy to the child's toddlerhood (Junttila et al., 2015). This highlights the importance of

identifying and supporting the women's social support networks already during pregnancy, as transitioning to parenthood may change the availability of and need for social support.

Furthermore, the concerningly high prevalence of ELS, particularly physical and emotional maltreatment in childhood (see Chapter 2.3.1), and its adverse consequences spanning from poor mental health to for example low educational achievement, poor health behaviors, and criminality (Gilbert et al., 2009), makes ELS in childhood a public health issue. The findings regarding the long-term adverse effects of low childhood SES are concerning in light of the notion that rates of child poverty have increased for example in the United Kingdom in the past decade (Marmot, Allen, Boyce, & Goldblatt, 2020). In Finland, the number of children living in poverty also increased by ca. 3% during 2022 (Kela, 2022). Together, these findings emphasize the importance of preventive efforts to diminish the effects of physical and emotional maltreatment, low family SES, and other types of ELS among children.

6.5.2 Policy implications

If untreated, maternal psychological distress during and after pregnancy has vast economic, humane and societal consequences (Bauer et al., 2014; Howard & Khalifeh, 2020; Stein et al., 2014); therefore, perinatal mental health needs to be taken into account in health policy planning. One of the benefits of the DOHaD framework has been the shift of the scientific, clinical and health policy focus from the postnatal period to begin already during pregnancy (Glover et al., 2023). The findings of this thesis further underscore the need for early interventions in promoting mental health and well-being in the offspring. Furthermore, shifting the focus from maternal prenatal psychological distress to positive maternal mental health may reduce the potential stigma related to the "prenatal programming" hypothesis that pregnant women with high levels of psychological distress may experience (Glover et al., 2023).

The high burden and long-lasting consequences of childhood ELS such as childhood maltreatment also call for preventive policies aiming to reduce ELS in early childhood (Gilbert et al., 2009). A meta-analysis on the association between ELS and later depression and anxiety disorders estimated that globally, based on the self-reported incidence of childhood maltreatment, a 10 percent reduction in the incidence of childhood maltreatment could prevent 31.36 million cases of depression and anxiety (Li et al., 2016). Policies targeting the effects of ELS should implement multisectoral preventive strategies that include for example national-level actions, healthcare systems, and policies that target behavioral health (Jacob & Hanson, 2020).

Preventive policies can ultimately be divided into three groups: 1) universal prevention which targets the whole population regardless of their known risk factors for adverse outcomes, 2) selective prevention which targets subgroups showing some risk factors, and 3) indicated prevention which targets individuals who already show subthreshold problems (Arango et al., 2018). In the context of policies promoting positive maternal mental health, universal prevention strategies could encompass policies that promote well-being during the perinatal period such as paid parental leave; according to a systematic review, paid parental leave of at least 2−3 months shows protective effects on maternal mental health (Heshmati, Honkaniemi, & Juárez, 2023). Selective prevention strategies could include measures such as screening for social support networks among mothers with a history of mental and behavioral disorders. Finally, indicated prevention strategies could encompass psychological interventions focusing on the promotion of positive mental health among mothers who report elevated depressive and anxiety symptoms during pregnancy. In this thesis, Study I suggested that positive maternal mental health during pregnancy was particularly protective for children of mothers who had a history of mental and behavioral disorders before or during pregnancy. This finding supports the previous suggestion that preventive efforts could be directed already to the preconception period particularly among women with prior psychopathology (Catalao, Mann, Wilson, & Howard, 2020); this could entail, for example, mapping social support networks among women with a history of mental and behavioral disorders who are planning pregnancy. Currently, women of reproductive age with previous mental and behavioral disorders are not systematically provided with pregnancy-counselling, although women experiencing psychological distress are at a higher risk of unintended pregnancy (Hall, Kusunoki, Gatny, & Barber, 2014; Schonewille et al., 2022).

In the context of preventing ELS in childhood, universal prevention strategies could include for example policies that aim at reducing child poverty: the WHO suggests that reducing child poverty and economically strengthening families is in itself a strategy that reduces child maltreatment (World Health Organization, 2018). Selective prevention strategies could be aimed for example at parents showing more permissive attitudes toward corporal punishment of the child: in a Finnish study, parents who reported approving corporal punishment were ca. 13 times more likely to report child physical abuse in their families (Leppäkoski et al., 2021). Finally, indicated prevention strategies could entail family intervention programs designed to reduce child maltreatment in families showing high risk, as described in Chapter 6.4.3.

6.5.3 Implications for interventions

The findings of this thesis suggest, in line with the DOHaD framework, that directing attention to preventive strategies and interventions early in life, already during pregnancy, may not only benefit the mother, but also the offspring. Several interventions have been developed that aim at supporting maternal mental health during pregnancy and preventing ELS in childhood. Utilizing life course modelling in research may have significant benefits in identifying time periods in which intervention measures may be most beneficial (Zuber et al., 2023). Furthermore, in addition to the efforts of diminishing maternal psychological distress during pregnancy, interventions should be aimed at supporting positive mental health among pregnant women. It is possible that promotive factors such as positive maternal mental health are more easily modifiable than risk factors such as maternal psychological distress, for example via increasing maternal perceived social support with peer support; however, to my knowledge, no studies have addressed this.

In the perinatal period, current psychological interventions show limited benefits for the mental health of women (Martín-Gómez et al., 2022; Matvienko-Sikar et al., 2021). According to a systematic review and meta-analysis, psychological interventions aiming at preventing postpartum depression among non-depressed women showed significant but clinically very small effects (Martín-Gómez et al., 2022). This meta-analysis did not differentiate psychological interventions targeted to the prenatal vs. postnatal period; this precludes conclusions about the optimal timing of the interventions. Another meta-analysis has also showed inconsistent results regarding the effectiveness of current psychosocial interventions in reducing maternal distress in in the perinatal period (Matvienko-Sikar et al., 2021). On the other hand, in another meta-analysis, psychotherapeutic interventions showed moderate beneficial effects in reducing depressive symptoms among women with diagnosed depressive disorder (Ravesteyn, Berg, Hoogendijk, & Kamperman, 2017). These findings suggest that women with more severe psychological distress during pregnancy may benefit more from the interventions. Regarding child mental health and development, current prenatal non-pharmacological interventions targeted at reducing maternal psychological distress during pregnancy show fairly little effects on the offspring (Brouwer et al., 2018).

A recent review suggests that combining current treatments with interventions targeting to increase positive maternal mental health may prove beneficial (Phua et al., 2020). Positive maternal mental health interventions may target maternal perceived social support, feelings of competence, better physical health, active lifestyle, self-compassion, mindfulness, and resilience (Monteiro et al., 2021; Rodriguez-Ayllon et al., 2021; Taylor, Cavanagh, & Strauss, 2016; Ungar et al., 2019; Varin et al., 2020). Group-based interventions may also improve maternal perceived social support from peers

(Chae et al., 2017); according to Chae and colleagues, attending a group-based intervention during pregnancy was associated with increases in perceived psychological and physical quality of life. Recent findings also suggest that music and singing interventions (Wulff et al., 2021) and lower levels of sedentary time, reflecting an active lifestyle (Rodriguez-Ayllon et al., 2021), may enhance positive affect, lower cortisol levels, and/or higher oxytocin levels among pregnant women. Interventions supporting positive maternal mental health already during pregnancy may also promote higher parenting self-efficacy and thus enhance positive parenting practices after the child's birth (Phua et al., 2020).

Findings on the effectiveness of perinatal positive mental health in interventions in aiming to reduce maternal psychological distress are beginning to emerge. One systematic review found evidence that resilience-enhancing interventions targeting e.g. mindfulness, coping, acceptance, and self-esteem show efficiency in reducing maternal depressive symptoms during pregnancy (Walker et al., 2022). However, Walker and colleagues found the methodological quality of the studies investigating this association to be generally low. In another meta-analysis, mindfulness-based interventions in the perinatal period were associated with a reduction in depressive and anxiety symptoms among pregnant women, but this reduction did not differ from women in the control group (Taylor et al., 2016). One small-scale quasi-experimental study of pregnant Iranian women found that an intervention targeting positive maternal mental health during pregnancy was as effective as cognitive-behavioral therapy intervention in diminishing anxiety symptoms and improving self-reported quality of life and resilience during pregnancy (Jafari, Basharpour, Bazazorde, & Hajlo, 2022). Another small-scale randomized controlled trial in Iran also showed that a positive psychology based intervention increased positive mental health among women with unintended pregnancies (Rastad, Golmohammadian, Jalali, Kaboudi, & Kaboudi, 2021).

Studies investigating the effects of prenatal positive mental health interventions on offspring outcomes are, to my knowledge, scarce. One review of randomized trials found that providing additional emotional, instrumental or informational social support for women at risk for preterm or low birth weight birth slightly reduced the risk of offspring being born preterm of with a low birthweight, and may reduce the risk of cesarean section and hospitalizations (East, Biro, Fredericks, & Lau, 2019). I am not aware of studies that have investigated whether the effects of positive mental health interventions among mothers extend to the offspring's mental health. However, one previous study among 1135 mother-child dyads of the French EDEN cohort found that while maternal clinically relevant depressive and anxiety symptoms during pregnancy were associated with higher psychiatric problem trajectories among their 3 to 11-year-old children, this association was attenuated

among dyads in which mother had sought psychiatrist or psychologist consultation during pregnancy (Kallas et al., 2023).

Regarding childhood ELS, several universal, selective and indicative interventions have also been developed that target ELS in childhood, particularly childhood maltreatment. Meta-analytic evidence gives support for the effectiveness of these interventions in both preventing and reducing child maltreatment (van der Put, Assink, Gubbels, & Boekhout van Solinge, 2018).

The WHO highlights that interventions targeted at supporting parents in developing positive parenting, such as affection, quality time, praise, and dealing with difficult child behavior in healthy ways, are among the most cost-effective ways of preventing childhood maltreatment (World Health Organization, 2018). Parenting programs may include aspects of learning about child development, strengthening non-violent and positive parenting practices, managing behavioral problems, and improving parent-child-relationships (Altafim & Linhares, 2016; Branco, Altafim, & Linhares, 2022). Systematic reviews have consistently shown that parenting programs may improve positive parenting skills and reduce the risk of child maltreatment such as harsh parenting, physical punishment, and emotional abuse (Altafim & Linhares, 2016; Branco et al., 2022); for example, in a systematic review by Branco and colleagues (2022), 91% of the included studies that evaluated these outcomes showed improvement, suggesting that interventions improving parenting practices are effective in reducing child maltreatment risk. According to a meta-analysis, parenting interventions that focus on increasing the parents' self-confidence may be particularly beneficial for preventive interventions, whereas in indicative interventions targeted at maltreating parents, parenting interventions aimed at improving parenting and personal skills, addressing parental mental health problems, providing social and emotional support, and improving child well-being may be particularly beneficial (van der Put et al., 2018). Parenting programs also show other benefits for family health such as decreasing the risk of behavioral problems in children and improving mental health, self-efficacy and perceived social support among parents (Altafim & Linhares, 2016; Branco et al., 2022).

Regarding indicated intervention strategies for individuals reporting ELS, it should be noted that while ELS is associated with a higher risk of later anxiety at a group level, it shows low accuracy in predicting individual-level health outcomes (Baldwin et al., 2021). Nevertheless, identifying ELS experiences, also among older adults, may be important in planning the length and intensity of treatment interventions, and ELS experiences should be addressed in psychotherapeutic treatment. For example, a meta-analysis of 26 studies indicated that depressed individuals with experiences of ELS showed poorer treatment outcomes than depressed individuals with no experiences of ELS

(Nanni, Uher, & Danese, 2012); this suggests that more intense treatment may be needed among those exposed to ELS. Higher social support has also been suggested to be a potential resilience factor for children experiencing ELS (Herrman et al., 2011), and there is evidence that higher perceived social support may buffer the effects of ELS on mental health (Kaufman et al., 2006). These findings suggest that interventions promoting social support among individuals with ELS experiences may prove beneficial.

6.5.4 Future directions for research

This thesis has extended the consideration of maternal mental health during and after pregnancy from maternal psychological distress to positive mental health. Future research should acknowledge the dimension of positive mental health also when defining offspring outcomes of interest: it would be important to investigate if positive maternal mental health or maternal psychological distress are associated with the positive mental health, such as positive emotions and perceived satisfaction with social relationships, of the offspring. Furthermore, while this research was conducted in two high-income countries with relatively good access to healthcare and support services, it would be important to extend the research on the long-term effects of childhood ELS, as well as the potential promotive and protective effects of positive maternal mental health, also to low- and middle-income countries.

Future studies should also aim at including fathers and their preconception and perinatal mental health, including positive mental health, in studying the intergenerational effects of mental health (Jacob & Hanson, 2020). This is important since paternal mental disorders are also consistently associated with higher psychiatric problems among children (Scarlett, Moirangthem, & van der Waerden, 2023). Emerging evidence suggests trait resilience and higher satisfaction with social support may attenuate the association between prior stressful experiences and psychological distress during pregnancy among fathers (Kumar, Franz, DiLillo, & Brock, 2022; Mondolin et al., 2024), but not among mothers (Kumar et al., 2022; Mondolin et al., 2024; Racine, Zumwalt, McDonald, Tough, & Madigan, 2020). Of note, in Kumar and colleagues' study, the association between a history of stressful life events and depressive symptoms during pregnancy was stronger among mothers than fathers, and on the other hand satisfaction with the intimate partner relationship was lower among mothers than among fathers; this may contribute to the found moderation effects.

Integrating the findings of this thesis, an interesting research question in the future would be to investigate the potentially protective effects of positive maternal mental health during pregnancy on child mental health and psychological development among mothers with a history of ELS experiences

in childhood. Earlier studies have associated ELS with a higher risk of psychological distress during pregnancy (Racine et al., 2021), and the transition to parenthood may be particularly challenging for individuals with a history of childhood maltreatment. Maternal history of childhood maltreatment is also associated with a higher risk of psychiatric problems and mental and behavioral disorders among their children (Airikka et al., 2022). It would therefore be important to identify potential protective factors among this group with higher vulnerability to adversities.

Furthermore, while this study was able to adjust for several potential confounding factors in investigating early life risk and promotive factors for mental health and psychological development, future studies would benefit from including more comprehensive assessments of important sociodemographic factors such as family socioeconomic status and also from integrating objective and self-reported psychological assessment data with biological measures such as cortisol reactivity of the mother and the child. Finally, observational measures of parenting behaviors and parent-child attachment would enable research on whether these factors contribute to the associations of positive maternal mental health and exposure to ELS with offspring mental health.

6.6 Conclusion

To conclude, this thesis gives support to the DOHaD framework, suggesting that both positive and negative experiences already in the prenatal period and later in childhood contribute to the development of mental health and cognitive ability. The effects of the early life environment seem to span throughout the life course, from the pregnancy period until childhood and from childhood until late adulthood. This thesis identified positive maternal mental health during pregnancy, including maternal positive emotions and higher perceived social support, as a promotive factor for the development of mental health and cognitive ability among children. Moreover, the thesis found further support to previous findings that ELS in childhood, particularly emotional and physical maltreatment and low childhood SES, continue to increase the risk of anxiety still in late adulthood.

The findings of this thesis are based on three large, longitudinal birth cohorts combining data from objective assessment methods, nationwide healthcare registers, and self-reports from parents and the offspring. The comprehensive use of assessment methods and different analytical methods strengthen the reliability of the findings. The current research findings call for directing preventive and supportive efforts to early life, already to the prenatal period, and extending the focus of research and interventions from adverse early life experiences to positive experiences in promoting mental health and psychological development.

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The weight of the average placenta is roughly one and a half pounds. A disposable organ where nutrients, hormones, and waste are passed between mother and fetus. In this way, the placenta is a kind of language – perhaps our first one, our true mother tongue.

- Ocean Wuong, in *On Earth We're Briefly Gorgeous*

Doing a large part of my PhD during the years of a global pandemic made the experience very different than it may have been otherwise. The road was certainly much lonelier than I anticipated. Still, I am immensely thankful for all the people whom I have gotten to know and who have guided and supported me along the way.

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8 References

Abu-Bader, S., & Jones, T. V. (2021). Statistical Mediation Analysis Using the Sobel Test and Hayes SPSS Process Macro. *International Journal of Quantitative and Qualitative Research Methods*, *9*, 42–61.

Achenbach, T. M., Ivanova, M. Y., Rescorla, L. A., Turner, L. V., & Althoff, R. R. (2016). Internalizing/Externalizing Problems: Review and Recommendations for Clinical and Research Applications. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(8), 647–656. https://doi.org/10.1016/j.jaac.2016.05.012

Achenbach, T. M., & Rescorla, L. (2001). *Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment.* Burlington, VT: Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Achenbach, T. M., & Rescorla, L. A. (2000). *Manual for the ASEBA preschool forms & profiles: An integrated system of multi-informant assessment.* Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Ainsworth, M. S. (1979). Infant-mother attachment. *American Psychologist*, *34*(10), 932–937. https://doi.org/10.1037/0003-066X.34.10.932

Airikka, A., Lahti-Pulkkinen, M., Tuovinen, S., Heinonen, K., Lahti, J., Girchenko, P., … Räikkönen, K. (2022). Maternal exposure to childhood maltreatment and mental and behavioral disorders in children. *European Child and Adolescent Psychiatry*, *1*, 3. https://doi.org/10.1007/s00787-022-02090-8

Altafim, E. R. P., & Linhares, M. B. M. (2016). Universal violence and child maltreatment prevention programs for parents: A systematic review. *Psychosocial Intervention*, *25*(1), 27–38. https://doi.org/10.1016/j.psi.2015.10.003

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*. Washington, DC.

American Psychiatric Association. (2022). *Diagnostic and Statistical Manual of Mental Disorders, 5th ed., text rev.* Washington, DC.

Angelakis, I., Gillespie, E. L., & Panagioti, M. (2019). Childhood maltreatment and adult suicidality: A comprehensive systematic review with meta-analysis. *Psychological Medicine*, *49*(7), 1057–1078. https://doi.org/10.1017/S0033291718003823

Angelini, V., Howdon, D. D. H., & Mierau, J. O. (2019). Childhood Socioeconomic Status and Late-Adulthood Mental Health: Results from the Survey on Health, Ageing and Retirement in Europe. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *74*(1), 95–104. https://doi.org/10.1093/geronb/gby028

Arango, C., Díaz-Caneja, C. M., McGorry, P. D., Rapoport, J., Sommer, I. E., Vorstman, J. A., … Carpenter, W. (2018). Preventive strategies for mental health. *The Lancet Psychiatry*, *5*(7), 591–604. https://doi.org/10.1016/S2215-0366(18)30057-9

Auersperg, F., Vlasak, T., Ponocny, I., & Barth, A. (2019). Long-term effects of parental divorce on mental health – A meta-analysis. *Journal of Psychiatric Research*, *119*, 107–115. https://doi.org/10.1016/j.jpsychires.2019.09.011

Bakouni, H., Ouimet, M. C., Desjardins, S., Forget, H., & Vasiliadis, H. M. (2023). Childhood abuse/neglect and temporal patterns in late-life anxiety. *Aging and Mental Health*, *27*(5), 973–

982. https://doi.org/10.1080/13607863.2022.2076204

Baldwin, J. R., Caspi, A., Meehan, A. J., Ambler, A., Arseneault, L., Fisher, H. L., … Danese, A. (2021). Population vs Individual Prediction of Poor Health from Results of Adverse Childhood Experiences Screening. *JAMA Pediatrics*, *175*(4), 385–393. https://doi.org/10.1001/jamapediatrics.2020.5602

Baldwin, J. R., Reuben, A., Newbury, J. B., & Danese, A. (2019). Agreement between prospective and retrospective measures of childhood maltreatment: A systematic review and meta-analysis. *JAMA Psychiatry*, *76*(6), 584–593. https://doi.org/10.1001/jamapsychiatry.2019.0097

Bales, M., Pambrun, E., Maguet, C., van der Waerden, J., Glangeaud-Freudenthal, N., Charles, M.-A., … Sutter-Dallay, A.-L. (2023). Pathways between Risk/Protective Factors and Maternal Postnatal Depressive Symptoms: The ELFE Cohort. *Journal of Clinical Medicine*, *12*(9), 3204. https://doi.org/10.3390/jcm12093204

Bardhoshi, G., Duncan, K., & Erford, B. T. (2016). Psychometric Meta-Analysis of the English Version of the Beck Anxiety Inventory. *Journal of Counseling and Development*, *94*(3), 356–373. https://doi.org/10.1002/jcad.12090

Barker. (2007). The origins of the developmental origins theory. *Journal of Internal Medicine*, *261*(5), 412–417. https://doi.org/10.1111/j.1365-2796.2007.01809.x

Barker, D. J. P. (2004). The developmental origins of well-being. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *359*(1449), 1359–1366. Royal Society. https://doi.org/10.1098/rstb.2004.1518

Barrera, M. (1986). Distinctions Between Social Support Concepts, Measures, and Models I. *American Journal of Community Psychology*, *14*(4).

Bauer, A., Parsonage, M., Knapp, M., Iemmi, V., & Adelaja, B. (2014). *The costs of perinatal mental health problems*. London.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An Inventory for Measuring Clinical Anxiety: Psychometric Properties. *Journal of Consulting and Clinical Psychology*, *56*(6), 893–897. https://doi.org/10.1037/0022-006X.56.6.893

Beck, A. T., & Steer, R. A. (1993). *Beck Anxiety Inventory Manual*. Psychological Corporation.

Bedaso, A., Adams, J., Peng, W., & Sibbritt, D. (2021). The relationship between social support and mental health problems during pregnancy: a systematic review and meta-analysis. *Reproductive Health*, *18*(1), 162. https://doi.org/10.1186/s12978-021-01209-5

Belsky, J., & Pluess, M. (2009). Beyond Diathesis Stress: Differential Susceptibility to Environmental Influences. *Psychological Bulletin*, *135*(6), 885–908. https://doi.org/10.1037/a0017376

Belsky, J., & Pluess, M. (2013). Beyond risk, resilience, and dysregulation: Phenotypic plasticity and human development. *Development and Psychopathology*, *25*, 1243–1261. https://doi.org/10.1017/S095457941300059X

Bergman, K., Sarkar, P., Glover, V., & O'Connor, T. G. (2010). Maternal Prenatal Cortisol and Infant Cognitive Development: Moderation by Infant-Mother Attachment. *Biological Psychiatry*, *67*(11), 1026–1032. https://doi.org/10.1016/j.biopsych.2010.01.002

Bernard, K., Frost, A., Bennett, C. B., & Lindhiem, O. (2017). Maltreatment and diurnal cortisol regulation: A meta-analysis. *Psychoneuroendocrinology*, *78*, 57–67.

https://doi.org/10.1016/j.psyneuen.2017.01.005

Birtchnell, J., Evans, C., & Kennard, J. (1988). The total score of the Crown-Crisp Experiential Index: A useful and valid measure of psychoneurotic pathology. *British Journal of Medical Psychology*, *61*(3), 255–266. https://doi.org/10.1111/j.2044-8341.1988.tb02787.x

Blair, C. (2016). Executive function and early childhood education. *Current Opinion in Behavioral Sciences*, *10*, 102–107. https://doi.org/10.1016/j.cobeha.2016.05.009

Bleuler, M. (1963). Conception of Schizophrenia Within-the Last Fifty Years and Today. *Proceedings of the Royal Society of Medicine*, *56*, 25–32.

Bor, W., Dean, A. J., Najman, J., & Hayatbakhsh, R. (2014). Are child and adolescent mental health problems increasing in the 21st century? A systematic review. *Australian and New Zealand Journal of Psychiatry*, *48*(7), 606–616. https://doi.org/10.1177/0004867414533834

Bowlby, J. (1969). *Attachment and Loss. Volume I. Attachment*. London: Hogarth Press.

Bowlby, J. (1988). *A Secure Base: Clinical Applications of Attachment Theory*. New York: Routledge.

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., … Smith, G. D. (2013). Cohort profile: The 'Children of the 90s'-The index offspring of the avon longitudinal study of parents and children. *International Journal of Epidemiology*, *42*(1), 111–127. https://doi.org/10.1093/ije/dys064

Braeken, M. A. K. A., Jones, A., Otte, R. A., Nyklíček, I., & Van den Bergh, B. R. H. (2017). Potential benefits of mindfulness during pregnancy on maternal autonomic nervous system function and infant development. *Psychophysiology*, *54*(2), 279–288. https://doi.org/10.1111/psyp.12782

Branco, M. S. S., Altafim, E. R. P., & Linhares, M. B. M. (2022). Universal Intervention to Strengthen Parenting and Prevent Child Maltreatment: Updated Systematic Review. *Trauma, Violence, and Abuse*, *23*(5), 1658–1676. https://doi.org/10.1177/15248380211013131

Brindle, R. C., Pearson, A., & Ginty, A. T. (2022, March 1). Adverse childhood experiences (ACEs) relate to blunted cardiovascular and cortisol reactivity to acute laboratory stress: A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews*, Vol. 134, p. 104530. Elsevier Ltd. https://doi.org/10.1016/j.neubiorev.2022.104530

Brouwer, M. E., Williams, A. D., Van Grinsven, S. E., Cuijpers, P., Lambregtse-Van Den Berg, M. P., Burger, H., & Bockting, C. L. H. (2018). Offspring outcomes after prenatal interventions for common mental disorders: A meta-analysis. *BMC Medicine*, *16*(1). https://doi.org/10.1186/s12916-018-1192-6

Bryant, C., Jackson, H., & Ames, D. (2008). The prevalence of anxiety in older adults: Methodological issues and a review of the literature. *Journal of Affective Disorders*, *109*(3), 233–250. https://doi.org/10.1016/j.jad.2007.11.008

Bunea, I. M., Szentágotai-Tătar, A., & Miu, A. C. (2017). Early-life adversity and cortisol response to social stress: A meta-analysis. *Translational Psychiatry*, *7*(12), 1274. https://doi.org/10.1038/s41398-017-0032-3

Butters, M. A., Bhalla, R. K., Andreescu, C., Wetherell, J. L., Mantella, R., Begley, A. E., & Lenze, E. J. (2011). Changes in neuropsychological functioning following treatment for late-life generalised anxiety disorder. *British Journal of Psychiatry*, *199*(3), 211–218. https://doi.org/10.1192/bjp.bp.110.090217

Calvin, C. M., Deary, I. J., Fenton, C., Roberts, B. A., Der, G., Leckenby, N., & Batty, G. D. (2011). Intelligence in youth and all-cause-mortality: systematic review with meta-analysis. *International Journal of Epidemiology*, *40*(3), 626–644. https://doi.org/10.1093/ije/dyq190

Cao-Lei, L., de Rooij, S. R., King, S., Matthews, S. G., Metz, G. A. S., Roseboom, T. J., & Szyf, M. (2020). Prenatal stress and epigenetics. *Neuroscience and Biobehavioral Reviews*, *117*, 198–210. https://doi.org/10.1016/j.neubiorev.2017.05.016

Catalao, R., Mann, S., Wilson, C., & Howard, L. M. (2020). Preconception care in mental health services: Planning for a better future. *British Journal of Psychiatry*, *216*(4), 180–181. https://doi.org/10.1192/bjp.2019.209

Chae, S. Y., Chae, M. H., Kandula, S., & Winter, R. O. (2017). Promoting improved social support and quality of life with the CenteringPregnancy® group model of prenatal care. *Archives of Women's Mental Health*, *20*(1), 209–220. https://doi.org/10.1007/s00737-016-0698-1

Chen, L. M., Pokhvisneva, I., Lahti-Pulkkinen, M., Kvist, T., Baldwin, J. R., Parent, C., … O'Donnell, K. J. (2023). Independent Prediction of Child Psychiatric Symptoms by Maternal Mental Health and Child Polygenic Risk Scores. *Journal of the American Academy of Child & Adolescent Psychiatry*. https://doi.org/10.1016/j.jaac.2023.08.018

Chen, X. Y., Lo, C. K. M., Chan, K. L., Leung, W. C., & Ip, P. (2022). Association between Childhood Exposure to Family Violence and Telomere Length: A Meta-Analysis. *International Journal of Environmental Research and Public Health*, *19*(19). https://doi.org/10.3390/ijerph191912151

Chida, Y., & Steptoe, A. (2008). Positive psychological well-being and mortality: A quantitative review of prospective observational studies. *Psychosomatic Medicine*, *70*(7), 741–756. https://doi.org/10.1097/PSY.0b013e31818105ba

Chumbley, J., Xu, W., Potente, C., Harris, K. M., & Shanahan, M. (2021). A Bayesian approach to comparing common models of life-course epidemiology. *International Journal of Epidemiology*. https://doi.org/10.1093/ije/dyab073

Clayborne, Z. M., Nilsen, W., Torvik, F. A., Gustavson, K., Bekkhus, M., Gilman, S. E., … Colman, I. (2023). Positive maternal mental health attenuates the associations between prenatal stress and children's internalizing and externalizing symptoms. *European Child and Adolescent Psychiatry*, *32*, 1781–1794. https://doi.org/10.1007/s00787-022-01999-4

Cohen, S. (2004). Social relationships and health. *American Psychologist*, *59*(8), 676–684. https://doi.org/10.1037/0003-066X.59.8.676

Condon, J. T. (1993). The assessment of antenatal emotional attachment: Development of a questionnaire instrument. *British Journal of Medical Psychology*, *66*(2), 167–183. https://doi.org/10.1111/j.2044-8341.1993.tb01739.x

Copeland, W. E., Angold, A., Shanahan, L., & Costello, E. J. (2014). Longitudinal patterns of anxiety from childhood to adulthood: The great smoky mountains study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(1), 21–33. https://doi.org/10.1016/j.jaac.2013.09.017

Cougle, J. R., Timpano, K. R., Sachs-Ericsson, N., Keough, M. E., & Riccardi, C. J. (2010). Examining the unique relationships between anxiety disorders and childhood physical and sexual abuse in the National Comorbidity Survey-Replication. *Psychiatry Research*, *177*(1–2), 150–155. https://doi.org/10.1016/j.psychres.2009.03.008

Coussons-Read, M. E., Okun, M. L., & Nettles, C. D. (2007). Psychosocial stress increases inflammatory markers and alters cytokine production across pregnancy. *Brain, Behavior, and Immunity*, *21*(3), 343–350. https://doi.org/10.1016/j.bbi.2006.08.006

Cox, J., Holden, J., & Sagovsky, R. (1987). Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*, *150*, 782–786.

Crawford, J. R., Anderson, V., Rankin, P. M., & MacDonald, J. (2010). An index-based short-form of the WISC-IV with accompanying analysis of the reliability and abnormality of differences. *British Journal of Clinical Psychology*, *49*(2), 235–258. https://doi.org/10.1348/014466509X455470

Crawford, K. M., Choi, K., Davis, K. A., Zhu, Y., Soare, T. W., Smith, A. D. A. C., … Dunn, E. C. (2022). Exposure to early childhood maltreatment and its effect over time on social cognition. *Development and Psychopathology*, *34*(1), 409–419. https://doi.org/10.1017/S095457942000139X

Cusick, S. E., & Georgieff, M. K. (2016). The Role of Nutrition in Brain Development: The Golden Opportunity of the "First 1000 Days." *Journal of Pediatrics*, *175*, 16–21. https://doi.org/10.1016/j.jpeds.2016.05.013

Cyr, C., Euser, E. M., Bakermans-Kranenburg, M. J., & Van Ijzendoorn, M. H. (2010). Attachment security and disorganization in maltreating and high-risk families: A series of meta-analyses. *Development and Psychopathology*, *22*(1), 87–108. https://doi.org/10.1017/S0954579409990289

Danese, A., & Widom, C. S. (2020). Objective and subjective experiences of child maltreatment and their relationships with psychopathology. *Nature Human Behaviour*, *4*(8), 811–818. https://doi.org/10.1038/s41562-020-0880-3

de Mendonça Filho, E. J., Frechette, A., Pokhvisneva, I., Arcego, D. M., Barth, B., Tejada, C. A. V., … Silveira, P. P. (2022). Examining attachment, cortisol secretion, and cognitive neurodevelopment in preschoolers and its predictive value for telomere length at age seven. *Frontiers in Behavioral Neuroscience*, *16*. https://doi.org/10.3389/fnbeh.2022.954977

Dennis, C. L., Falah-Hassani, K., & Shiri, R. (2017). Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *British Journal of Psychiatry*, *210*(5), 315–323. https://doi.org/10.1192/bjp.bp.116.187179

Diener, E., Oishi, S., & Tay, L. (2018). Advances in subjective well-being research. *Nature Human Behaviour*, *2*(4), 253–260. https://doi.org/10.1038/s41562-018-0307-6

DiPietro, J. A., Novak, M. F. S. X., Costigan, K. A., Atella, L. D., & Reusing, S. P. (2006). Maternal Psychological Distress During Pregnancy in Relation to Child Development at Age Two. *Child Development*, *77*(3), 573–587. https://doi.org/10.1111/j.1467-8624.2006.00891.x

Disabato, D. J., Goodman, F. R., Kashdan, T. B., Short, J. L., & Jarden, A. (2016). Different types of well-being? A cross-cultural examination of hedonic and eudaimonic well-being. *Psychological Assessment*, *28*(5), 471–482. https://doi.org/10.1037/pas0000209

Draper, B., Pfaff, J. J., Pirkis, J., Snowdon, J., Lautenschlager, N. T., Wilson, I., & Almeida, O. P. (2008). Long-term effects of childhood abuse on the quality of life and health of older people: Results from the depression and early prevention of suicide in general practice project. *Journal of the American Geriatrics Society*, *56*(2), 262–271. https://doi.org/10.1111/j.1532-5415.2007.01537.x

Dube, S. R., Anda, R. F., Felitti, V. J., Chapman, D. P., Williamson, D. F., & Giles, W. H. (2001). Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span: Findings from the adverse childhood experiences study. *JAMA*, *286*(24), 3089–3096. https://doi.org/10.1001/jama.286.24.3089

Dunn, E. C., Nishimi, K., Powers, A., & Bradley, B. (2017). Is developmental timing of trauma exposure associated with depressive and post-traumatic stress disorder symptoms in adulthood? *Journal of Psychiatric Research*, *84*, 119–127. https://doi.org/10.1016/j.jpsychires.2016.09.004

Dunn, E. C., Soare, T. W., Zhu, Y., Simpkin, A. J., Suderman, M. J., Klengel, T., … Relton, C. L. (2019). Sensitive Periods for the Effect of Childhood Adversity on DNA Methylation: Results From a Prospective, Longitudinal Study. *Biological Psychiatry*, *85*(10), 838–849. https://doi.org/10.1016/j.biopsych.2018.12.023

East, C. E., Biro, M. A., Fredericks, S., & Lau, R. (2019). Support during pregnancy for women at increased risk of low birthweight babies. *Cochrane Database of Systematic Reviews*, *2019*(4). https://doi.org/10.1002/14651858.CD000198.pub3

Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, *38*(4), 319–345. https://doi.org/10.1016/S0005-7967(99)00123-0

Eriksson, J. G., Forsén, T., Tuomilehto, J., Osmond, C., & Barker, D. J. P. (2001). Early growth and coronary heart disease in later life: Longitudinal study. *British Medical Journal*, *322*, 949–953. https://doi.org/10.1136/bmj.322.7292.949

Estinfort, W., Huang, J.-P., Au, H.-K., Lin, C.-L., Chen, Y.-Y., Chao, H. J., … Chen, Y.-H. (2022). Effects of prenatal subjective well-being on birth outcomes and child development: A longitudinal study. *European Psychiatry*, *65*(1), e77. https://doi.org/10.1192/j.eurpsy.2022.2338

Evans, J., Heron, J., Francomb, H., Oke, S., & Golding, J. (2001). Cohort study of depressed mood during pregnancy and after childbirth. *British Medical Journal*, *323*, 257–260. https://doi.org/10.1136/bmj.323.7307.257

Evans, Melotti, R., Heron, J., Ramchandani, P., Wiles, N., Murray, L., & Stein, A. (2012). The timing of maternal depressive symptoms and child cognitive development: a longitudinal study. *Journal of Child Psychology and Psychiatry*, *53*(6), 632–640. https://doi.org/10.1111/j.1469-7610.2011.02513.x

Faleschini, S., Rifas-Shiman, S. L., Tiemeier, H., Oken, E., & Hivert, M. F. (2019). Associations of prenatal and postnatal maternal depressive symptoms with offspring cognition and behavior in mid-childhood: A prospective cohort study. *International Journal of Environmental Research and Public Health*, *16*(6). https://doi.org/10.3390/ijerph16061007

Feldman, P. J., Dunkel-Schetter, C., Sandman, C. A., & Wadhwa, P. D. (2000). Maternal Social Support Predicts Birth Weight and Fetal Growth in Human Pregnancy. *Psychosomatic Medicine*, *62*(5), 715–725.

Feldman, R. (2020). What is resilience: an affiliative neuroscience approach. *World Psychiatry*, *19*(2), 132–150. https://doi.org/10.1002/wps.20729

Fergusson, D. M., Boden, J. M., & Horwood, L. J. (2008). Exposure to childhood sexual and physical abuse and adjustment in early adulthood. *Child Abuse and Neglect*, *32*(6), 607–619. https://doi.org/10.1016/j.chiabu.2006.12.018

Flak, A. L., Su, S., Bertrand, J., Denny, C. H., Kesmodel, U. S., & Cogswell, M. E. (2014). The Association of Mild, Moderate, and Binge Prenatal Alcohol Exposure and Child

Neuropsychological Outcomes: A Meta-Analysis. *Alcoholism: Clinical and Experimental Research*, *38*(1), 214–226. https://doi.org/10.1111/acer.12214

Folkman, S., & Moskowitz, J. T. (2000). Positive affect and the other side of coping. *American Psychologist*, *55*(6), 647–654. https://doi.org/10.1037/0003-066X.55.6.647

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Davey Smith, G., … Lawlor, D. A. (2013). Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *International Journal of Epidemiology*, *42*(1), 97–110. https://doi.org/10.1093/ije/dys066

Fredrickson, B. L., Mancuso, R. A., Branigan, C., & Tugade, M. M. (2000). The undoing effect of positive emotions. *Motivation and Emotion*, *24*(4), 237–258. https://doi.org/10.1023/A:1010796329158

Friedman, L. E., Gelaye, B., Sanchez, S. E., & Williams, M. A. (2020). Association of social support and antepartum depression among pregnant women. *Journal of Affective Disorders*, *264*, 201–205. https://doi.org/https://doi.org/10.1016/j.jad.2019.12.017

Friedman, L. E., Manriquez Prado, A. K., Santos Malavé, G. F., Vélez, J. C., Gillibrand Esquinazi, R. W., Sanchez, S., … Williams, M. A. (2018). Construct validity and factor structure of a Spanish-language Social Support Questionnaire during early pregnancy. *International Journal of Women's Health*, *Volume 10*, 379–385. https://doi.org/10.2147/IJWH.S160619

Gabard-Durnam, L. J., & McLaughlin, K. A. (2019). Do Sensitive Periods Exist for Exposure to Adversity? *Biological Psychiatry*, *85*(10), 789–791. https://doi.org/10.1016/j.biopsych.2019.03.975

Galea, L. A., Qiu, W., & Duarte-Guterman, P. (2018). Beyond sex differences: short and long-term implications of motherhood on women's health. *Current Opinion in Physiology*, *6*, 82–88. https://doi.org/10.1016/j.cophys.2018.06.003

Gardner, M. J., Thomas, H. J., & Erskine, H. E. (2019). The association between five forms of child maltreatment and depressive and anxiety disorders: A systematic review and meta-analysis. *Child Abuse and Neglect*, *96*, 104082. https://doi.org/10.1016/j.chiabu.2019.104082

Giesbrecht, G. F., Poole, J. C., Letourneau, N., Campbell, T., & Kaplan, B. J. (2013). The Buffering Effect of Social Support on Hypothalamic-Pituitary-Adrenal Axis Function During Pregnancy. *Psychosomatic Medicine*, *75*(9), 856–862. https://doi.org/10.1097/PSY.0000000000000004

Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., & Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. *The Lancet*, *373*(9657), 68–81. https://doi.org/10.1016/S0140-6736(08)61706-7

Gimson, A., Schlosser, M., Huntley, J. D., & Marchant, N. L. (2018). Support for midlife anxiety diagnosis as an independent risk factor for dementia: A systematic review. *BMJ Open*, *8*(4). https://doi.org/10.1136/bmjopen-2017-019399

Girchenko, P., Lahti-Pulkkinen, M., Heinonen, K., Reynolds, R. M., Laivuori, H., Lipsanen, J., … Räikkönen, K. (2020). Persistently High Levels of Maternal Antenatal Inflammation Are Associated With and Mediate the Effect of Prenatal Environmental Adversities on Neurodevelopmental Delay in the Offspring. *Biological Psychiatry*, *87*(10), 898–907. https://doi.org/10.1016/j.biopsych.2019.12.004

Girchenko, P., Lahti, M., Tuovinen, S., Savolainen, K., Lahti, J., Binder, E. B., … Räikkönen, K. (2017). Cohort Profile: Prediction and prevention of preeclampsia and intrauterine growth

restriction (PREDO) study. *International Journal of Epidemiology*, *46*(5), 1380–1381. https://doi.org/10.1093/ije/dyw154

Girchenko, P., Tuovinen, S., Lahti-Pulkkinen, M., Lahti, J., Savolainen, K., Heinonen, K., … Räikkönen, K. (2018). Maternal early pregnancy obesity and related pregnancy and pre-pregnancy disorders: Associations with child developmental milestones in the prospective PREDO Study. *International Journal of Obesity*, *42*(5), 995–1007. https://doi.org/10.1038/s41366-018-0061-x

Gissler, M., Louhiala, P., & Hemminki, E. (1997). Nordic Medical Birth Registers in epidemiological research. *European Journal of Epidemiology*, *13*(2), 169–175. https://doi.org/10.1023/A:1007379029182

Glover, V. (2011). Annual Research Review: Prenatal stress and the origins of psychopathology: an evolutionary perspective. *Journal of Child Psychology and Psychiatry*, *52*(4), 356–367. https://doi.org/10.1111/j.1469-7610.2011.02371.x

Glover, V., O'Connor, T. G., & O'Donnell, K. J. (2023). Fetal Programming and Public Policy. *Journal of the American Academy of Child and Adolescent Psychiatry*, *62*(6), 618–620. https://doi.org/10.1016/j.jaac.2022.11.010

Glover, V., O'Donnell, K. J., O'Connor, T. G., & Fisher, J. (2018). Prenatal maternal stress, fetal programming, and mechanisms underlying later psychopathology - A global perspective. *Development and Psychopathology*, *30*(3), 843–854. https://doi.org/10.1017/S095457941800038X

Goodman, S. H., Rouse, M. H., Connell, A. M., Broth, M. R., Hall, C. M., & Heyward, D. (2011, March 4). Maternal Depression and Child Psychopathology: A Meta-Analytic Review. *Clinical Child and Family Psychology Review*, Vol. 14, pp. 1–27. Springer. https://doi.org/10.1007/s10567-010-0080-1

Grenier, S., Préville, M., Boyer, R., O'Connor, K., Béland, S. G., Potvin, O., … Brassard, J. (2011). The impact of DSM-IV symptom and clinical significance criteria on the prevalence estimates of subthreshold and threshold anxiety in the older adult population. *American Journal of Geriatric Psychiatry*, *19*(4), 316–326. https://doi.org/10.1097/JGP.0b013e3181ff416c

Hall, K. S., Kusunoki, Y., Gatny, H., & Barber, J. (2014). The risk of unintended pregnancy among young women with mental health symptoms. *Social Science and Medicine*, *100*, 62–71. https://doi.org/10.1016/j.socscimed.2013.10.037

Halse, M., Steinsbekk, S., Hammar, Å., & Wichstrøm, L. (2022). Longitudinal relations between impaired executive function and symptoms of psychiatric disorders in childhood. *Journal of Child Psychology and Psychiatry*, *63*(12), 1574–1582. https://doi.org/10.1111/jcpp.13622

Hannigan, L. J., Eilertsen, E. M., Gjerde, L. C., Reichborn-Kjennerud, T., Eley, T. C., Rijsdijk, F. V., … McAdams, T. A. (2018). Maternal prenatal depressive symptoms and risk for early-life psychopathology in offspring: genetic analyses in the Norwegian Mother and Child Birth Cohort Study. *The Lancet Psychiatry*, *5*(10), 808–815. https://doi.org/10.1016/S2215-0366(18)30225-6

Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *Journal of Child Psychology and Psychiatry*, *45*(2), 260–273. https://doi.org/10.1111/j.1469-7610.2004.00218.x

Hardt, J., Sidor, A., Bracko, M., & Egle, U. T. (2006). Reliability of Retrospective Assessments of

Childhood Experiences in Germany. *Journal of Nervous & Mental Disease*, *194*(9), 676–683. https://doi.org/10.1097/01.nmd.0000235789.79491.1b

Hartman, S., Belsky, J., & Pluess, M. (2023). Prenatal programming of environmental sensitivity. *Translational Psychiatry*, *13*(1), 1–10. https://doi.org/10.1038/s41398-023-02461-y

Havdahl, A., Wootton, R. E., Leppert, B., Riglin, L., Ask, H., Tesli, M., … Stergiakouli, E. (2022). Associations Between Pregnancy-Related Predisposing Factors for Offspring Neurodevelopmental Conditions and Parental Genetic Liability to Attention-Deficit/Hyperactivity Disorder, Autism, and Schizophrenia: The Norwegian Mother, Father and Child Cohort Study (MoBa). *JAMA Psychiatry*, *79*(8), 799–810. https://doi.org/10.1001/jamapsychiatry.2022.1728

Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical Mediation Analysis in the New Millennium. *Communication Monographs*, *76*(4), 408–420. https://doi.org/10.1080/03637750903310360

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis: a regression-based approach.* New York: Guilford Publications.

Hayes, A. F. (2022). *Introduction to Mediation, Moderation, and Conditional Process Analysis* (3rd editio). New York: Guilford Press.

Heckman, J. J., & Masterov, D. V. (2007). The productivity argument for investing in young children. *Review of Agricultural Economics*, *29*, 446–493. https://doi.org/10.1111/j.1467-9353.2007.00359.x

Hentges, R. F., Graham, S. A., Plamondon, A., Tough, S., & Madigan, S. (2019). A Developmental Cascade from Prenatal Stress to Child Internalizing and Externalizing Problems. *Journal of Pediatric Psychology*, *44*(9), 1057–1067. https://doi.org/10.1093/jpepsy/jsz044

Hernandez-Martinez, C., Val, V. A., Murphy, M., Busquets, P. C., & Sans, J. C. (2011). Relation Between Positive and Negative Maternal Emotional States and Obstetrical Outcomes. *Women & Health*, *51*(2), 124–135. https://doi.org/10.1080/03630242.2010.550991

Herrman, H., Stewart, D. E., Diaz-Granados, N., Berger, E. L., Jackson, B., & Yuen, T. (2011). What is resilience? *Canadian Journal of Psychiatry*, *56*(5), 258–265. https://doi.org/10.1177/070674371105600504

Herstell, S., Betz, L. T., Penzel, N., Chechelnizki, R., Filihagh, L., Antonucci, L., & Kambeitz, J. (2021). Insecure attachment as a transdiagnostic risk factor for major psychiatric conditions: A meta-analysis in bipolar disorder, depression and schizophrenia spectrum disorder. *Journal of Psychiatric Research*, *144*, 190–201. https://doi.org/10.1016/j.jpsychires.2021.10.002

Heshmati, A., Honkaniemi, H., & Juárez, S. P. (2023). The effect of parental leave on parents' mental health: a systematic review. *The Lancet. Public Health*, *8*(1), e57–e75. https://doi.org/10.1016/S2468-2667(22)00311-5

Hetherington, E., Doktorchik, C., Premji, S. S., McDonald, S. W., Tough, S. C., & Sauve, R. S. (2015). Preterm Birth and Social Support during Pregnancy: a Systematic Review and Meta-Analysis. *Paediatric and Perinatal Epidemiology*, *29*(6), 523–535. https://doi.org/10.1111/ppe.12225

Hetherington, E., McDonald, S., Williamson, T., Patten, S. B., & Tough, S. C. (2018). Social support and maternal mental health at 4 months and 1 year postpartum: Analysis from the All Our Families cohort. *Journal of Epidemiology and Community Health*, *72*(10), 933–939.

https://doi.org/10.1136/jech-2017-210274

Hewitt, C. E., Gilbody, S. M., Brealey, S., Paulden, M., Palmer, S., Mann, R., … Richards, D. (2009). *Methods to identify postnatal depression in primary care: an integrated evidence synthesis and value of information analysis*. *13*, 36. https://doi.org/10.3310/hta13360

Hopkins, J., Miller, J. L., Butler, K., Gibson, L., Hedrick, L., & Boyle, D. A. (2018). The relation between social support, anxiety and distress symptoms and maternal fetal attachment. *Journal of Reproductive and Infant Psychology*, *36*(4), 381–392. https://doi.org/10.1080/02646838.2018.1466385

Horta, B. L., Loret de Mola, C., & Victora, C. G. (2015). Breastfeeding and intelligence: a systematic review and meta-analysis. *Acta Paediatrica*, *104*, 14–19. https://doi.org/10.1111/apa.13139

Howard, L. M., & Khalifeh, H. (2020). Perinatal mental health: a review of progress and challenges. *World Psychiatry*, *19*(3), 313–327. https://doi.org/10.1002/wps.20769

Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., … Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *The Lancet Public Health*, *2*(8), e356–e366. https://doi.org/10.1016/S2468-2667(17)30118-4

Humphreys, K. L., LeMoult, J., Wear, J. G., Piersiak, H. A., Lee, A., & Gotlib, I. H. (2020). Child maltreatment and depression: A meta-analysis of studies using the Childhood Trauma Questionnaire. *Child Abuse and Neglect*, *102*, 104361. https://doi.org/10.1016/j.chiabu.2020.104361

Igartua, J. J., & Hayes, A. F. (2021). Mediation, Moderation, and Conditional Process Analysis: Concepts, Computations, and Some Common Confusions. *Spanish Journal of Psychology*, *24*(6), e49. https://doi.org/10.1017/SJP.2021.46

Ilyka, D., Johnson, M. H., & Lloyd-Fox, S. (2021). Infant social interactions and brain development: A systematic review. *Neuroscience and Biobehavioral Reviews*, *130*, 448–469. https://doi.org/10.1016/j.neubiorev.2021.09.001

Infurna, M. R., Reichl, C., Parzer, P., Schimmenti, A., Bifulco, A., & Kaess, M. (2016). Associations between depression and specific childhood experiences of abuse and neglect: A meta-analysis. *Journal of Affective Disorders*, *190*, 47–55. https://doi.org/10.1016/j.jad.2015.09.006

Jacob, C. M., & Hanson, M. (2020). Implications of the Developmental Origins of Health and Disease concept for policy-making. *Current Opinion in Endocrine and Metabolic Research*, *13*, 20–27. https://doi.org/10.1016/j.coemr.2020.08.001

Jafari, M., Basharpour, S., Bazazorde, M., & Hajlo, N. (2022). Cognitive Behavioral Training and Positive Psychology Training for Pregnant Women's Psychological Health. *Psychological Studies*, *67*(4), 419–431. https://doi.org/10.1007/s12646-022-00673-8

Jawahar, M. C., Murgatroyd, C., Harrison, E. L., & Baune, B. T. (2015). Epigenetic alterations following early postnatal stress: A review on novel aetiological mechanisms of common psychiatric disorders. *Clinical Epigenetics*, *7*(1), 1–13. https://doi.org/10.1186/s13148-015-0156-3

Joelsson, P., Chudal, R., Gyllenberg, D., Kesti, A. K., Hinkka-Yli-Salomäki, S., Virtanen, J. P., … Sourander, A. (2016). Demographic Characteristics and Psychiatric Comorbidity of Children and Adolescents Diagnosed with ADHD in Specialized Healthcare. *Child Psychiatry and Human Development*, *47*(4), 574–582. https://doi.org/10.1007/s10578-015-0591-6

Johnson, D., Policelli, J., Li, M., Dharamsi, A., Hu, Q., Sheridan, M. A., … Wade, M. (2021, November 1). Associations of Early-Life Threat and Deprivation with Executive Functioning in Childhood and Adolescence: A Systematic Review and Meta-analysis. *JAMA Pediatrics*, Vol. 175. American Medical Association. https://doi.org/10.1001/jamapediatrics.2021.2511

Johnson, J. G., Cohen, P., Brown, J., Smailes, E. M., & Bernstein, D. P. (1999). Childhood maltreatment increases risk for personality disorders during early adulthood. *Archives of General Psychiatry*, *56*(7), 600–608. https://doi.org/10.1001/archpsyc.56.7.600

Joshanloo, M. (2016). Revisiting the Empirical Distinction Between Hedonic and Eudaimonic Aspects of Well-Being Using Exploratory Structural Equation Modeling. *Journal of Happiness Studies*, *17*(5), 2023–2036. https://doi.org/10.1007/s10902-015-9683-z

Junttila, N., Ahlqvist-Björkroth, S., Aromaa, M., Rautava, P., Piha, J., & Räihä, H. (2015). Intercorrelations and developmental pathways of mothers' and fathers' loneliness during pregnancy, infancy and toddlerhood - STEPS study. *Scandinavian Journal of Psychology*, *56*(5), 482–488. https://doi.org/10.1111/sjop.12241

Kabacoff, R. I., Segal, D. L., Hersen, M., & Van Hasselt, V. B. (1997). Psychometric properties and diagnostic utility of the Beck Anxiety Inventory and the State-Trait Anxiety Inventory with older adult psychiatric outpatients. *Journal of Anxiety Disorders*, *11*(1), 33–47. https://doi.org/10.1016/S0887-6185(96)00033-3

Kajantie, E., Barker, D. J. P., Osmond, C., Forsen, T., & Eriksson, J. G. (2008). Growth before 2 years of age and serum lipids 60 years later: The Helsinki Birth Cohort Study. *International Journal of Epidemiology*, *37*(2), 280–289. https://doi.org/10.1093/ije/dyn012

Kallas, K. A., Marr, K., Moirangthem, S., Heude, B., Koehl, M., van der Waerden, J., & Downes, N. (2023). Maternal Mental Health Care Matters: The Impact of Prenatal Depressive and Anxious Symptoms on Child Emotional and Behavioural Trajectories in the French EDEN Cohort. *Journal of Clinical Medicine*, *12*(3), 1120. https://doi.org/10.3390/jcm12031120

Kaplan, S. J., Pelcovitz, D., & Labruna, V. (1999). Child and adolescent abuse and neglect research: A review of the past 10 years. Part I: Physical and emotional abuse and neglect. *Journal of the American Academy of Child and Adolescent Psychiatry*, *38*(10), 1214–1222. https://doi.org/10.1097/00004583-199910000-00009

Kaufman, J., Yang, B.-Z., Douglas-Palumberi, H., Grasso, D., Lipschitz, D., Houshyar, S., … Gelernter, J. (2006). Brain-Derived Neurotrophic Factor-5-HTTLPR Gene Interactions and Environmental Modifiers of Depression in Children. *Biological Psychiatry*, *59*(8), 673–680. https://doi.org/10.1016/j.biopsych.2005.10.026

Kavén, P. (1985). *70000 pientä kohtaloa. Suomen sotalapset.* Helsinki: Otava.

Kela. (2022). Hintojen nousun vaikutuksia lapsiperheköyhyyteen voidaan lieventää vain vähän lapsilisäjärjestelmän muutoksilla. Retrieved from https://tutkimusblogi.kela.fi/arkisto/6774

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, *62*(6), 593–602. https://doi.org/10.1001/archpsyc.62.6.593

Keyes. (1998). Social well-being. *Social Psychology Quarterly*, *61*(2), 121–137. https://doi.org/10.2307/2787065

Keyes, C. L. M., Dhingra, S. S., & Simoes, E. J. (2010). Change in level of positive mental health as

a predictor of future risk of mental Illness. *American Journal of Public Health*, *100*(12), 2366–2371. https://doi.org/10.2105/AJPH.2010.192245

Keyes, Shmotkin, D., & Ryff, C. D. (2002). Optimizing well-being: The empirical encounter of two traditions. *Journal of Personality and Social Psychology*, *82*(6), 1007–1022. https://doi.org/10.1037/0022-3514.82.6.1007

Kim-Cohen, J., Caspi, A., Moffitt, T. E., Harrington, H. L., Milne, B. J., & Poulton, R. (2003). Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. *Archives of General Psychiatry*, *60*(7), 709–717. https://doi.org/10.1001/archpsyc.60.7.709

Kishore, M. T., Satyanarayana, V., Ananthanpillai, S. T., Desai, G., Bhaskarapillai, B., Thippeswamy, H., & Chandra, P. S. (2018). Life events and depressive symptoms among pregnant women in India: Moderating role of resilience and social support. *International Journal of Social Psychiatry*, *64*(6), 570–577. https://doi.org/10.1177/0020764018789193

Korja, R., Nolvi, S., Grant, K. A., & McMahon, C. (2017). The Relations Between Maternal Prenatal Anxiety or Stress and Child's Early Negative Reactivity or Self-Regulation: A Systematic Review. *Child Psychiatry and Human Development*, *48*(6), 851–869. https://doi.org/10.1007/s10578-017-0709-0

Kramer, M. S., Aboud, F., Mironova, E., Vanilovich, I., Platt, R. W., Matush, L., … Shapiro, S. (2008). Breastfeeding and child cognitive development: New evidence from a large randomized trial. *Archives of General Psychiatry*, *65*(5), 578–584. https://doi.org/10.1001/archpsyc.65.5.578

Kristensen, S., Henriksen, T. B., & Bilenberg, N. (2010). The child behavior checklist for ages 1.5-5 (CBCL 11/2-5): Assessment and analysis of parent- and caregiver-reported problems in a population-based sample of Danish preschool children. *Nordic Journal of Psychiatry*, *64*(3), 203–209. https://doi.org/10.3109/08039480903456595

Kumar, S. A., Franz, M. R., DiLillo, D., & Brock, R. L. (2022). Promoting resilience to depression among couples during pregnancy: The protective functions of intimate relationship satisfaction and self-compassion. *Family Process*, *62*(1), 387–405. https://doi.org/10.1111/famp.12788

Kuruvilla, S., Sadana, R., Montesinos, E. V., Beard, J., Vasdeki, J. F., Carvalho, I. A. De, … Bustreo, F. (2018). A life-course approach to health: Synergy with sustainable development goals. *Bulletin of the World Health Organization*, *96*(1), 42–50. https://doi.org/10.2471/BLT.17.198358

Lacey, R. E., Gondek, D., Smith, B. J., Smith, A. D. A. C., Dunn, E. C., & Sacker, A. (2023). Testing lifecourse theories characterising associations between maternal depression and offspring depression in emerging adulthood: the Avon Longitudinal Study of Parents and Children. *Journal of Child Psychology and Psychiatry*, *64*(8), 1149–1158. https://doi.org/10.1111/jcpp.13699

Lahti-Pulkkinen, M., Girchenko, P., Robinson, R., Lehto, S. M., Toffol, E., Heinonen, K., … Räikkönen, K. (2020). Maternal depression and inflammation during pregnancy. *Psychological Medicine*, *50*(11), 1839–1851. https://doi.org/10.1017/S0033291719001909

Lahti, M., Pesonen, A. K., Räikkönen, K., Heinonen, K., Wahlbeck, K., Kajantie, E., … Eriksson, J. G. (2012). Temporary separation from parents in early childhood and serious personality disorders in adult life. *Journal of Personality Disorders*, *26*(5), 751–762. https://doi.org/10.1521/pedi.2012.26.5.751

Lahti, M., Savolainen, K., Tuovinen, S., Pesonen, A. K., Lahti, J., Heinonen, K., … Räikkönen, K. (2017). Maternal Depressive Symptoms During and After Pregnancy and Psychiatric Problems in Children. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*(1), 30-39.e7. https://doi.org/10.1016/j.jaac.2016.10.007

Lahti, Räikkönen, K., Pesonen, A. -K., Heinonen, K., Kajantie, E., Forsén, T., … Eriksson, J. G. (2010). Prenatal growth, postnatal growth and trait anxiety in late adulthood – the Helsinki Birth Cohort Study. *Acta Psychiatrica Scandinavica*, *121*(3), 227–235. https://doi.org/10.1111/j.1600-0447.2009.01432.x

Lai, M. C., & Huang, L. T. (2011). Effects of early life stress on neuroendocrine and neurobehavior: Mechanisms and implications. *Pediatrics and Neonatology*, *52*(3), 122–129. https://doi.org/10.1016/j.pedneo.2011.03.008

Lampi, K., Sourander, A., Gissler, M., Niemelä, S., Rehnström, K., Pulkkinen, E., … Von Wendt, L. (2010). Brief report: validity of Finnish registry-based diagnoses of autism with the ADI-R. *Acta Paediatrica*, *99*(9), 1425–1428. https://doi.org/10.1111/j.1651-2227.2010.01835.x

Lanoue, M. D., George, B. J., Helitzer, D. L., & Keith, S. W. (2020). Contrasting cumulative risk and multiple individual risk models of the relationship between Adverse Childhood Experiences (ACEs) and adult health outcomes. *BMC Medical Research Methodology*, *20*(1), 239. https://doi.org/10.1186/s12874-020-01120-w

Le Bas, G. A., Youssef, G. J., Macdonald, J. A., Mattick, R., Teague, S. J., Honan, I., … Hutchinson, D. M. (2021). Maternal bonding, negative affect, and infant social-emotional development: A prospective cohort study. *Journal of Affective Disorders*, *281*, 926–934. https://doi.org/10.1016/j.jad.2020.11.031

Le Bas, G. A., Youssef, G. J., Macdonald, J. A., Rossen, L., Teague, S. J., Kothe, E. J., … Hutchinson, D. M. (2020). The role of antenatal and postnatal maternal bonding in infant development: A systematic review and meta-analysis. *Social Development*, *29*(1), 3–20. https://doi.org/10.1111/sode.12392

Leppäkoski, T., Vuorenmaa, M., & Paavilainen, E. (2021). Psychological and physical abuse towards four-year-old children as reported by their parents: A national Finnish survey. *Child Abuse and Neglect*, *118*, 105127. https://doi.org/10.1016/j.chiabu.2021.105127

Lewinn, K. Z., Bush, N. R., Batra, A., Tylavsky, F., & Rehkopf, D. (2020). Identification of Modifiable Social and Behavioral Factors Associated with Childhood Cognitive Performance. *JAMA Pediatrics*, *174*(11), 1063–1072. https://doi.org/10.1001/jamapediatrics.2020.2904

Li, M., D'Arcy, C., & Meng, X. (2016). Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: Systematic review, meta-analysis, and proportional attributable fractions. *Psychological Medicine*, *46*(4), 717–730. https://doi.org/10.1017/S0033291715002743

Li, Muzi, Gao, T., Su, Y., Zhang, Y., Yang, G., D'Arcy, C., & Meng, X. (2023). The Timing Effect of Childhood Maltreatment in Depression: A Systematic Review and meta-Analysis. *Trauma, Violence, and Abuse*, *24*(4), 2560–2580. https://doi.org/10.1177/15248380221102558

Liu, Jiaqi, Deng, J., Zhang, H., & Tang, X. (2023). The relationship between child maltreatment and social anxiety: A meta-analysis. *Journal of Affective Disorders*, *329*, 157–167. https://doi.org/10.1016/j.jad.2023.02.081

Liu, Jiaxuan, Cerutti, J., Lussier, A. A., Zhu, Y., Smith, B. J., Smith, A. D. A. C., & Dunn, E. C.

(2023). Socioeconomic changes predict genome-wide DNA methylation in childhood. *Human Molecular Genetics*, *32*(5), 709–719. https://doi.org/10.1093/hmg/ddac171

Liu, Reed, M., & Girard, T. A. (2017). Advancing resilience: An integrative, multi-system model of resilience. *Personality and Individual Differences*, *111*, 111–118. https://doi.org/10.1016/j.paid.2017.02.007

Lobel, M., Cannella, D. L., Graham, J. E., DeVincent, C., Schneider, J., & Meyer, B. A. (2008). Pregnancy-specific stress, prenatal health behaviors, and birth outcomes. *Health Psychology*, *27*(5), 604–615. https://doi.org/10.1037/a0013242

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*(5), 561–592. https://doi.org/10.1016/S0272-7358(98)00100-7

Luoma, I., Korhonen, M., Puura, K., & Salmelin, R. K. (2019). Maternal loneliness: concurrent and longitudinal associations with depressive symptoms and child adjustment. *Psychology, Health and Medicine*, *24*(6), 667–679. https://doi.org/10.1080/13548506.2018.1554251

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*(6), 434–445. https://doi.org/10.1038/nrn2639

Luthar, S. S., Sawyer, J. A., & Brown, P. J. (2006). Conceptual issues in studies of resilience: Past, present, and future research. *Annals of the New York Academy of Sciences*, *1094*, 105–115. Blackwell Publishing Inc. https://doi.org/10.1196/annals.1376.009

MacKinnon, N., Kingsbury, M., Mahedy, L., Evans, J., & Colman, I. (2018). The Association Between Prenatal Stress and Externalizing Symptoms in Childhood: Evidence From the Avon Longitudinal Study of Parents and Children. *Biological Psychiatry*, *83*(2), 100–108. https://doi.org/10.1016/j.biopsych.2017.07.010

Macpherson, J. M., Gray, S. R., Ip, P., McCallum, M., Hanlon, P., Welsh, P., … Ho, F. K. (2021). Child maltreatment and incident mental disorders in middle and older ages: a retrospective UK Biobank cohort study. *The Lancet Regional Health - Europe*, *11*. https://doi.org/10.1016/j.lanepe.2021.100224

Madathil, S., Joseph, L., Hardy, R., Rousseau, M.-C., & Nicolau, B. (2018). A Bayesian approach to investigate life course hypotheses involving continuous exposures. *International Journal of Epidemiology*, *47*(5), 1623–1635. https://doi.org/10.1093/ije/dyy107

Madigan, S., Brumariu, L. E., Villani, V., Atkinson, L., & Lyons-Ruth, K. (2016). Representational and questionnaire measures of attachment: A meta-analysis of relations to child internalizing and externalizing problems. *Psychological Bulletin*, *142*(4), 367–399. https://doi.org/10.1037/bul0000029

Madigan, S., Oatley, H., Racine, N., Fearon, R. M. P., Schumacher, L., Akbari, E., … Tarabulsy, G. M. (2018). A Meta-Analysis of Maternal Prenatal Depression and Anxiety on Child Socioemotional Development. *Journal of the American Academy of Child and Adolescent Psychiatry*, *57*(9), 645-657.e8. https://doi.org/10.1016/j.jaac.2018.06.012

Manwell, L. A., Barbic, S. P., Roberts, K., Durisko, Z., Lee, C., Ware, E., & McKenzie, K. (2015). What is mental health? Evidence towards a new definition from a mixed methods multidisciplinary international survey. *BMJ Open*, *5*(6). https://doi.org/10.1136/bmjopen-2014-007079

Manzari, N., Matvienko-Sikar, K., Baldoni, F., O'Keeffe, G. W., & Khashan, A. S. (2019). Prenatal maternal stress and risk of neurodevelopmental disorders in the offspring: a systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology*, *54*(11), 1299–1309. https://doi.org/10.1007/s00127-019-01745-3

Marmot, M., Allen, J., Boyce, T., & Goldblatt, J. M. (2020). *Health equity in England: the Marmot review 10 years on*. London: Institute of Health Equity.

Martín-Gómez, C., Moreno-Peral, P., Bellón, J. A., Conejo-Cerón, S., Campos-Paino, H., Gómez-Gómez, I., … Motrico, E. (2022). Effectiveness of psychological interventions in preventing postpartum depression in non-depressed women: A systematic review and meta-analysis of randomized controlled trials. *Psychological Medicine*, *52*(6), 1001–1013. https://doi.org/10.1017/S0033291722000071

Matvienko-Sikar, K., Flannery, C., Redsell, S., Hayes, C., Kearney, P. M., & Huizink, A. (2021). Effects of interventions for women and their partners to reduce or prevent stress and anxiety: A systematic review. *Women and Birth*, *34*(2), e97–e117. https://doi.org/10.1016/j.wombi.2020.02.010

McGrath, J. J., Al-Hamzawi, A., Alonso, J., Altwaijri, Y., Andrade, L. H., Bromet, E. J., … Zaslavsky, A. M. (2023). Age of onset and cumulative risk of mental disorders: a cross-national analysis of population surveys from 29 countries. *The Lancet Psychiatry*, *10*(9), 668–681. https://doi.org/10.1016/S2215-0366(23)00193-1

McKay, M. T., Cannon, M., Chambers, D., Conroy, R. M., Coughlan, H., Dodd, P., … Clarke, M. C. (2021). Childhood trauma and adult mental disorder: A systematic review and meta-analysis of longitudinal cohort studies. *Acta Psychiatrica Scandinavica*, *143*(3), 189–205. https://doi.org/10.1111/acps.13268

McKay, M. T., Cannon, M., Healy, C., Syer, S., O'Donnell, L., & Clarke, M. C. (2021). A meta-analysis of the relationship between parental death in childhood and subsequent psychiatric disorder. *Acta Psychiatrica Scandinavica*, *143*(6), 472–486. https://doi.org/10.1111/acps.13289

McLaughlin, K. A., Breslau, J., Green, J. G., Lakoma, M. D., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2011). Childhood socio-economic status and the onset, persistence, and severity of DSM-IV mental disorders in a US national sample. *Social Science and Medicine*, *73*(7), 1088–1096. https://doi.org/10.1016/j.socscimed.2011.06.011

McManus, M. A., Khalessi, A. A., Lin, J., Ashraf, J., & Reich, S. M. (2017). Positive feelings during pregnancy, early feeding practices, and infant health. *Pediatrics International : Official Journal of the Japan Pediatric Society*, *59*(5), 593–599. https://doi.org/10.1111/ped.13209

Meaney, M. J. (2018). Perinatal maternal depressive symptoms as an issue for population health. *American Journal of Psychiatry*, *175*(11), 1084–1093. https://doi.org/10.1176/appi.ajp.2018.17091031

Mercan, Y., & Tari Selcuk, K. (2021). Association between postpartum depression level, social support level and breastfeeding attitude and breastfeeding self-efficacy in early postpartum women. *PLOS ONE*, *16*(4), e0249538. https://doi.org/10.1371/journal.pone.0249538

Mesman, J., & Koot, H. M. (2001). Early preschool predictors of preadolescent internalizing and externalizing DSM-IV diagnoses. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*(9), 1029–1036. https://doi.org/10.1097/00004583-200109000-00011

Moeller, J., Ivcevic, Z., Brackett, M. A., & White, A. E. (2018). Mixed emotions: Network analyses

of intra-individual co-occurrences within and across situations. *Emotion*, *18*(8), 1106–1121. https://doi.org/10.1037/emo0000419

Mokdad, A. H., Forouzanfar, M. H., Daoud, F., Mokdad, A. A., El Bcheraoui, C., Moradi-Lakeh, M., … Murray, C. J. L. (2016). Global burden of diseases, injuries, and risk factors for young people's health during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*, *387*, 2383–2401. https://doi.org/10.1016/S0140-6736(16)00648-6

Molyneaux, E., Poston, L., Ashurst-Williams, S., & Howard, L. M. (2014). Obesity and Mental Disorders During Pregnancy and Postpartum. *Obstetrics & Gynecology*, *123*(4), 857–867. https://doi.org/10.1097/AOG.0000000000000170

Mondolin, V., Karlsson, H., Tuulari, J. J., Pelto, J., Karlsson, L., Nordenswan, E., & Kataja, E. L. (2024). Childhood maltreatment, trait resilience and prenatal distress among expecting mothers and fathers in the FinnBrain Birth Cohort Study. *Journal of Affective Disorders*, *344*, 41–47. https://doi.org/10.1016/j.jad.2023.10.026

Monk, C., Lugo-Candelas, C., & Trumpff, C. (2019). Prenatal Developmental Origins of Future Psychopathology: Mechanisms and Pathways. *Annual Review of Clinical Psychology*, *15*(1), 317–344. https://doi.org/10.1146/annurev-clinpsy-050718-095539

Monroe, S. M., & Simons, A. D. (1991). Diathesis-stress theories in the context of life stress research: implications for the depressive disorders. *Psychological Bulletin*, *110*(3), 406–425. https://doi.org/10.1037/0033-2909.110.3.406

Monteiro, F., Fonseca, A., Pereira, M., & Canavarro, M. C. (2021). Is positive mental health and the absence of mental illness the same? Factors associated with flourishing and the absence of depressive symptoms in postpartum women. *Journal of Clinical Psychology*, *77*(3), 629–645. https://doi.org/10.1002/jclp.23081

Na, P. J., Jeste, D. V., & Pietrzak, R. H. (2023). Social Disconnection as a Global Behavioral Epidemic—A Call to Action About a Major Health Risk Factor. *JAMA Psychiatry*, *80*(2), 101–102. https://doi.org/10.1001/jamapsychiatry.2022.4162

Nanni, V., Uher, R., & Danese, A. (2012). Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: A meta-analysis. *American Journal of Psychiatry*, *169*(2), 141–151. https://doi.org/10.1176/appi.ajp.2011.11020335

National Scientific Council on the Developing Child. (2004). Young Children Develop in an Environment of Relationships: Working Paper No. 1. Retrieved March 7, 2023, from http://www.developingchild.net

Nazzari, S., Fearon, P., Rice, F., Ciceri, F., Molteni, M., & Frigerio, A. (2020). Neuroendocrine and immune markers of maternal stress during pregnancy and infant cognitive development. *Developmental Psychobiology*, *62*(8), 1100–1110. https://doi.org/10.1002/dev.21967

Nierop, A., Wirtz, P. H., Bratsikas, A., Zimmermann, R., & Ehlert, U. (2008). Stress-buffering effects of psychosocial resources on physiological and psychological stress response in pregnant women. *Biological Psychology*, *78*(3), 261–268. https://doi.org/10.1016/j.biopsycho.2008.03.012

Nijenhuis, E. R. S., Van der Hart, O., & Kruger, K. (2002). The psychometric characteristics of the traumatic experiences checklist (TEC): First findings among psychiatric outpatients. *Clinical Psychology and Psychotherapy*, *9*(3), 200–210. https://doi.org/10.1002/cpp.332

Nishimi, K., Choi, K. W., Davis, K. A., Powers, A., Bradley, B., & Dunn, E. C. (2020). Features of

Childhood Maltreatment and Resilience Capacity in Adulthood: Results from a Large Community-Based Sample. *Journal of Traumatic Stress*, *33*(5), 665–676. https://doi.org/10.1002/jts.22543

Nordentoft, M., Wahlbeck, K., Hällgren, J., Westman, J., Ösby, U., Alinaghizadeh, H., … Laursen, T. M. (2013). Excess Mortality, Causes of Death and Life Expectancy in 270,770 Patients with Recent Onset of Mental Disorders in Denmark, Finland and Sweden. *PLoS ONE*, *8*(1). https://doi.org/10.1371/journal.pone.0055176

Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The Long-Term Health Consequences of Child Physical Abuse, Emotional Abuse, and Neglect: A Systematic Review and Meta-Analysis. *PLoS Medicine*, *9*(11), e1001349. https://doi.org/10.1371/journal.pmed.1001349

O'Connor, T. G., Ciesla, A. A., Sefair, A. V., Thornburg, L. L., Brown, A. S., Glover, V., & O'Donnell, K. J. (2022). Maternal prenatal infection and anxiety predict neurodevelopmental outcomes in middle childhood. *Journal of Psychopathology and Clinical Science*, *131*(4), 422–434. https://doi.org/10.1037/abn0000746

O'Donnell, K. J., Glover, V., Barker, E. D., & O'Connor, T. G. (2014). The persisting effect of maternal mood in pregnancy on childhood psychopathology. *Development and Psychopathology*, *26*(2), 393–403. https://doi.org/10.1017/S0954579414000029

O'Donnell, K. J., & Meaney, M. J. (2017). Fetal origins of mental health: The developmental origins of health and disease hypothesis. *American Journal of Psychiatry*, *174*(4), 319–328. https://doi.org/10.1176/appi.ajp.2016.16020138

O'Donnell, K. J., & Meaney, M. J. (2020). Epigenetics, Development, and Psychopathology. *Annual Review of Clinical Psychology*, *16*(1), 327–350. https://doi.org/10.1146/annurev-clinpsy-050718-095530

OECD. (2010). *The High Cost of Low Educational Performance. The Long-run Economic Impact of Improving PISA Outcomes*.

Office of National Statistics. (2023). Well-being. Retrieved from https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing

Oldehinkel, A. J., & Ormel, J. (2023). Annual Research Review: Stability of psychopathology: lessons learned from longitudinal population surveys. *Journal of Child Psychology and Psychiatry*, *64*(4), 489–502. https://doi.org/10.1111/jcpp.13737

Olino, T. M., Michelini, G., Mennies, R. J., Kotov, R., & Klein, D. N. (2021). Does maternal psychopathology bias reports of offspring symptoms? A study using moderated non-linear factor analysis. *Journal of Child Psychology and Psychiatry*, *62*(10), 1195–1201. https://doi.org/10.1111/jcpp.13394

Orpana, H., Vachon, J., Dykxhoorn, J., McRae, L., & Jayaraman, G. (2016). Monitoring positive mental health and its determinants in Canada: The development of the positive mental health surveillance indicator framework. *Health Promotion and Chronic Disease Prevention in Canada*, *36*(1), 1–10. https://doi.org/10.24095/hpcdp.36.1.01

Orta, O. R., Gelaye, B., Bain, P. A., & Williams, M. A. (2018). The association between maternal cortisol and depression during pregnancy, a systematic review. *Archives of Women's Mental Health*, *21*(1), 43–53. https://doi.org/10.1007/s00737-017-0777-y

Ozbay, F., Johnson, D. C., Dimoulas, E., Morgan, C. A., Charney, D., & Southwick, S. (2007). Social

support and resilience to stress: from neurobiology to clinical practice. *Psychiatry (Edgmont (Pa. : Township))*, *4*(5), 35–40.

Palma-Gudiel, H., Córdova-Palomera, A., Leza, J. C., & Fañanás, L. (2015). Glucocorticoid receptor gene (NR3C1) methylation processes as mediators of early adversity in stress-related disorders causality: A critical review. *Neuroscience and Biobehavioral Reviews*, *55*, 520–535. https://doi.org/10.1016/j.neubiorev.2015.05.016

Palmer, B. W., Jeste, D. V, & Sheikh, J. I. (1997). Anxiety disorders in the elderly: DSM-IV and other barriers to diagnosis and treatment. *Journal of Affective Disorders*, *46*(3), 183–190. https://doi.org/10.1016/s0165-0327(97)00146-8

Parkes, A., & Sweeting, H. (2018). Direct, indirect, and buffering effects of support for mothers on children's socioemotional adjustment. *Journal of Family Psychology*, *32*(7), 894–903. https://doi.org/10.1037/fam0000438

Patel, P., & Oremus, M. (2023). The Association Between Adverse Childhood Experiences and Late-Life Cognition: A Systematic Review of Cross-Sectional and Case-Control Studies. *The Gerontologist*, *63*(6), 1087–1103. https://doi.org/10.1093/geront/gnac041

Pearson, R. M., Bornstein, M. H., Cordero, M., Scerif, G., Mahedy, L., Evans, J., … Stein, A. (2016). Maternal perinatal mental health and offspring academic achievement at age 16: The mediating role of childhood executive function. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *57*(4), 491–501. https://doi.org/10.1111/jcpp.12483

Pearson, R. M., Evans, J., Kounali, D., Lewis, G., Heron, J., Ramchandani, P. G., … Stein, A. (2013). Maternal depression during pregnancy and the postnatal period risks and possible mechanisms for offspring depression at age 18 years. *JAMA Psychiatry*, *70*(12), 1312–1319. https://doi.org/10.1001/jamapsychiatry.2013.2163

Pesonen, A.-K., Lahti, M., Kuusinen, T., Tuovinen, S., Villa, P., Hämäläinen, E., … Räikkönen, K. (2016). Maternal Prenatal Positive Affect, Depressive and Anxiety Symptoms and Birth Outcomes: The PREDO Study. *PloS One*, *11*(2), e0150058. https://doi.org/10.1371/journal.pone.0150058

Pesonen, Räikkönen, K., Heinonen, K., Kajantie, E., Forsén, T., & Eriksson, J. G. (2007). Depressive symptoms in adults separated from their parents as children: A natural experiment during World War II. *American Journal of Epidemiology*, *166*(10), 1126–1133. https://doi.org/10.1093/aje/kwm254

Peverill, M., Dirks, M. A., Narvaja, T., Herts, K. L., Comer, J. S., & McLaughlin, K. A. (2021). Socioeconomic status and child psychopathology in the United States: A meta-analysis of population-based studies. *Clinical Psychology Review*, *83*, 101933. https://doi.org/10.1016/j.cpr.2020.101933

Philipp, J., Ziler, M., Waldherr, K., Truttmnn, S., Dür, W., Karwautz, A. F. K., & Wagner, G. (2018). Prevalence of emotional and behavioral problems and subthreshold psychiatric disorders in austrian adolescents and the need for prevention. *Social Psychiatry and Psychiatric Epidemiology*, *53*(12), 1325–1337. https://doi.org/10.1007/s00127-018-1586-y

Phua, D. Y., Kee, M. K. Z. L., Koh, D. X. P., Rifkin-Graboi, A., Daniels, M., Chen, H., … Yeo, G. S. H. (2017). Positive maternal mental health during pregnancy associated with specific forms of adaptive development in early childhood: Evidence from a longitudinal study. *Development and Psychopathology*, *29*(5), 1573–1587. https://doi.org/10.1017/S0954579417001249

Phua, D. Y., Kee, M. Z. L., & Meaney, M. J. (2020). Positive Maternal Mental Health, Parenting, and Child Development. *Biological Psychiatry*, *87*(4), 328–337. https://doi.org/10.1016/j.biopsych.2019.09.028

Pihlakoski, L., Sourander, A., Aromaa, M., Rautava, P., Helenius, H., & Sillanpää, M. (2006). The continuity of psychopathology from early childhood to preadolescence: A prospective cohort study of 3-12-year-old children. *European Child and Adolescent Psychiatry*, *15*(7), 409–417. https://doi.org/10.1007/s00787-006-0548-1

Plana-Ripoll, O., Weye, N., Knudsen, A. K., Hakulinen, C., Madsen, K. B., Christensen, M. K., … McGrath, J. J. (2023). The association between mental disorders and subsequent years of working life: a Danish population-based cohort study. *The Lancet Psychiatry*, *10*(1), 30–39. https://doi.org/10.1016/S2215-0366(22)00376-5

Pluess, M., & Belsky, J. (2011). Prenatal programming of postnatal plasticity? *Development and Psychopathology*, *23*(1), 29–38. https://doi.org/10.1017/S0954579410000623

Pluess, M., & Belsky, J. (2013). Vantage sensitivity: Individual differences in response to positive experiences. *Psychological Bulletin*, *139*(4), 901–916. https://doi.org/10.1037/a0030196

Pluess, M., Wurmser, H., Buske-Kirschbaum, A., Papousek, M., Pirke, K. M., Hellhammer, D., & Bolten, M. (2012). Positive life events predict salivary cortisol in pregnant women. *Psychoneuroendocrinology*, *37*(8), 1336–1340. https://doi.org/10.1016/j.psyneuen.2012.01.006

Power, Atherton, K., Strachan, D. P., Shepherd, P., Fuller, E., Davis, A., … Stansfeld, S. (2007). Life-course influences on health in British adults: effects of socio-economic position in childhood and adulthood. *International Journal of Epidemiology*, *36*(3), 532–539. https://doi.org/10.1093/ije/dyl310

Power, J., van IJzendoorn, M., Lewis, A. J., Chen, W., & Galbally, M. (2021). Maternal perinatal depression and child executive function: A systematic review and meta-analysis. *Journal of Affective Disorders*, *291*, 218–234. https://doi.org/10.1016/j.jad.2021.05.003

Provençal, N., Arloth, J., Cattaneo, A., Anacker, C., Cattane, N., Wiechmann, T., … Binder, E. B. (2020). Glucocorticoid exposure during hippocampal neurogenesis primes future stress response by inducing changes in DNA methylation. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(38), 23280–23285. https://doi.org/10.1073/pnas.1820842116

Public Health Agency of Canada Centre for Surveillance and Applied Research. (2022). Positive Mental Health Indicator Framework Quick Statistics, adults (18 years of age and older), Canada, 2022 Edition. Retrieved from https://health-infobase.canada.ca/positive-mental-health/

Putnam, K., Robertson-Blackmore, E., Sharkey, K., Payne, J., Bergink, V., Munk-Olsen, T., … Meltzer-Brody, S. (2015). Heterogeneity of postpartum depression: A latent class analysis. *The Lancet Psychiatry*, *2*(1), 59–67. https://doi.org/10.1016/S2215-0366(14)00055-8

Pyman, P., Collins, S. E., Muggli, E., Testa, R., & Anderson, P. J. (2021). Cognitive and Behavioural Attention in Children with Low-Moderate and Heavy Doses of Prenatal Alcohol Exposure: a Systematic Review and Meta-analysis. *Neuropsychology Review*, *31*(4), 610–627. https://doi.org/10.1007/s11065-021-09490-8

Racine, N., Devereaux, C., Cooke, J. E., Eirich, R., Zhu, J., & Madigan, S. (2021). Adverse childhood experiences and maternal anxiety and depression: a meta-analysis. *BMC Psychiatry*, *21*(1), 28. https://doi.org/10.1186/s12888-020-03017-w

Racine, N., Plamondon, A., Hentges, R., Tough, S., & Madigan, S. (2019). Dynamic and bidirectional

associations between maternal stress, anxiety, and social support: The critical role of partner and family support. *Journal of Affective Disorders*, *252*, 19–24. https://doi.org/10.1016/j.jad.2019.03.083

Racine, N., Zumwalt, K., McDonald, S., Tough, S., & Madigan, S. (2020). Perinatal depression: The role of maternal adverse childhood experiences and social support. *Journal of Affective Disorders*, *263*, 576–581. https://doi.org/10.1016/j.jad.2019.11.030

Radloff, L. S. (1977). The CES-D Scale. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Räikkönen, K., Lahti, M., Heinonen, K., Pesonen, A. K., Wahlbeck, K., Kajantie, E., … Eriksson, J. G. (2011). Risk of severe mental disorders in adults separated temporarily from their parents in childhood: The Helsinki birth cohort study. *Journal of Psychiatric Research*, *45*(3), 332–338. https://doi.org/10.1016/j.jpsychires.2010.07.003

Raposo, S. M., Mackenzie, C. S., Henriksen, C. A., & Afifi, T. O. (2014). Time does not heal all wounds: Older adults who experienced childhood adversities have higher odds of mood, anxiety, and personality disorders. *American Journal of Geriatric Psychiatry*, *22*(11), 1241–1250. https://doi.org/10.1016/j.jagp.2013.04.009

Rascle, N., & Bruchon-Schweitzer, M. (2005). Short form of Sarason's Social Support Questionnaire: French adaptation and validation. *Psychological Reports*, *97*, 195–202.

Rastad, Z., Golmohammadian, M., Jalali, A., Kaboudi, B., & Kaboudi, M. (2021). Effects of positive psychology interventions on happiness in women with unintended pregnancy: randomized controlled trial. *Heliyon*, *7*(8), e07789. https://doi.org/10.1016/j.heliyon.2021.e07789

Ravesteyn, L. M. V., Berg, M. P. L. Van Den, Hoogendijk, W. J. G., & Kamperman, A. M. (2017). Interventions to treat mental disorders during pregnancy: A systematic review and multiple treatment meta-Analysis. *PLoS ONE*, *12*(3). https://doi.org/10.1371/journal.pone.0173397

Raymond, C., Marin, M. F., Wolosianski, V., Journault, A. A., Longpré, C., Leclaire, S., … Lupien, S. J. (2021). Early childhood adversity and HPA axis activity in adulthood:The importance of considering minimal age at exposure. *Psychoneuroendocrinology*, *124*, 105042. https://doi.org/10.1016/j.psyneuen.2020.105042

Rehm, J., & Shield, K. D. (2019). Global Burden of Disease and the Impact of Mental and Addictive Disorders. *Current Psychiatry Reports*, *21*(2), 1–7. https://doi.org/10.1007/s11920-019-0997-0

Rescorla, L. A. (2005). Assessment of young children using the Achenbach System of Empirically Based Assessment (ASEBA). *Mental Retardation and Developmental Disabilities Research Reviews*, *11*(3), 226–237. https://doi.org/10.1002/mrdd.20071

Robinson, R., Lähdepuro, A., Tuovinen, S., Girchenko, P., Rantalainen, V., Heinonen, K., … Lahti-Pulkkinen, M. (2021). Maternal Hypertensive Pregnancy Disorders and Mental and Behavioral Disorders in the Offspring: a Review. *Current Hypertension Reports*, *23*(5), 1–14. https://doi.org/10.1007/s11906-021-01141-w

Robinson, R., Lahti-Pulkkinen, M., Heinonen, K., Reynolds, R. M., & Räikkönen, K. (2019). Fetal programming of neuropsychiatric disorders by maternal pregnancy depression: a systematic mini review. *Pediatric Research*, *85*(2), 134–145. https://doi.org/10.1038/s41390-018-0173-y

Roddy Mitchell, A., Gordon, H., Lindquist, A., Walker, S. P., Homer, C. S. E., Middleton, A., … Hastie, R. (2023). Prevalence of Perinatal Depression in Low- and Middle-Income Countries. *JAMA Psychiatry*, *80*(5), 425–431. https://doi.org/10.1001/jamapsychiatry.2023.0069

Rodriguez-Ayllon, M., Acosta-Manzano, P., Coll-Risco, I., Romero-Gallardo, L., Borges-Cosic, M., Estévez-López, F., & Aparicio, V. A. (2021). Associations of physical activity, sedentary time, and physical fitness with mental health during pregnancy: The GESTAFIT project. *Journal of Sport and Health Science*, *10*(3), 379–386. https://doi.org/10.1016/j.jshs.2019.04.003

Rogers, A., Obst, S., Teague, S. J., Rossen, L., Spry, E. A., MacDonald, J. A., … Hutchinson, D. (2020). Association between Maternal Perinatal Depression and Anxiety and Child and Adolescent Development: A Meta-analysis. *JAMA Pediatrics*, *174*(11), 1082–1092. https://doi.org/10.1001/jamapediatrics.2020.2910

Ronfani, L., Vecchi Brumatti, L., Mariuz, M., Tognin, V., Bin, M., Ferluga, V., … Barbone, F. (2015). The complex interaction between home environment, socioeconomic status, maternal IQ and early child neurocognitive development: A multivariate analysis of data collected in a newborn cohort study. *PLoS ONE*, *10*(5). https://doi.org/10.1371/journal.pone.0127052

Ross, K. M., Miller, G., Qadir, S., Keenan-Devlin, L., Leigh, A. K. K., & Borders, A. (2017). Close relationship qualities and maternal peripheral inflammation during pregnancy. *Psychoneuroendocrinology*, *77*, 252–260. https://doi.org/10.1016/j.psyneuen.2017.01.003

Rusby, J. S. M., & Tasker, F. (2009). Long-term effects of the British evacuation of children during World War 2 on their adult mental health. *Aging and Mental Health*, *13*(3), 391–404. https://doi.org/10.1080/13607860902867750

Rutter, M. (1987). Psychosocial resilience and protective mechanisms. *American Journal of Orthopsychiatry*, *57*(3), 316–331. https://doi.org/10.1111/j.1939-0025.1987.tb03541.x

Rutter, M. (2006). Implications of Resilience Concepts for Scientific Understanding. *Annals of the New York Academy of Sciences*, *1094*(1), 1–12. https://doi.org/10.1196/annals.1376.002

Rutter, M. (2012). Resilience as a dynamic concept. *Development and Psychopathology*, *24*(2), 335–344. https://doi.org/10.1017/S0954579412000028

Ryan, R. M., & Deci, E. L. (2001). On happiness and human potentials: A review of research on hedonic and eudaimonic well-being. *Annual Review of Psychology*, *52*, 141–166. https://doi.org/10.1146/annurev.psych.52.1.141

Ryff, C. D., Dienberg Love, G., Urry, H. L., Muller, D., Rosenkranz, M. A., Friedman, E. M., … Singer, B. (2006). Psychological Well-Being and Ill-Being: Do They Have Distinct or Mirrored Biological Correlates? *Psychotherapy and Psychosomatics*, *75*(2), 85–95. https://doi.org/10.1159/000090892

Sachs-Ericsson, N., Gayman, M. D., Kendall-Tackett, K., Lloyd, D. A., Medley, A., Collins, N., … Sawyer, K. (2010). The long-term impact of childhood abuse on internalizing disorders among older adults: The moderating role of self-esteem. *Aging and Mental Health*, *14*(4), 489–501. https://doi.org/10.1080/13607860903191382

Sahle, B. W., Reavley, N. J., Li, W., Morgan, A. J., Yap, M. B. H., Reupert, A., & Jorm, A. F. (2022). The association between adverse childhood experiences and common mental disorders and suicidality: an umbrella review of systematic reviews and meta-analyses. *European Child and Adolescent Psychiatry*, *31*(10), 1489–1499. https://doi.org/10.1007/s00787-021-01745-2

Sallis, H., Szekely, E., Neumann, A., Jolicoeur-Martineau, A., van IJzendoorn, M., Hillegers, M., … Evans, J. (2019). General psychopathology, internalising and externalising in children and functional outcomes in late adolescence. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *60*(11), 1183–1190. https://doi.org/10.1111/jcpp.13067

Sands, A., Thompson, E. J., & Gaysina, D. (2017). Long-term influences of parental divorce on offspring affective disorders: A systematic review and meta-analysis. *Journal of Affective Disorders*, *218*, 105–114. https://doi.org/10.1016/j.jad.2017.04.015

Santos, M. A., Jardim, G. B., Ranjbar, S., Gholam, M., Schuster, J. P., Gomes, I., & von Gunten, A. (2023). Childhood maltreatment and late-life generalized anxiety disorder: Are personality and attachment characteristics mediators? *Journal of Affective Disorders Reports*, *12*, 100514. https://doi.org/10.1016/j.jadr.2023.100514

Sarason, I. G., Sarason, B. R., Shearin, E. N., & Pierce, G. R. (1987). A Brief Measure of Social Support: Practical and Theoretical Implications. *Journal of Social and Personal Relationships*, *4*(4), 497–510. https://doi.org/10.1177/0265407587044007

Savolainen, K., Eriksson, J. G., Kananen, L., Kajantie, E., Pesonen, A. K., Heinonen, K., & Räikkönen, K. (2014). Associations between early life stress, self-reported traumatic experiences across the lifespan and leukocyte telomere length in elderly adults. *Biological Psychology*, *97*(1), 35–42. https://doi.org/10.1016/j.biopsycho.2014.02.002

Savolainen, K., Räikkönen, K., Kananen, L., Kajantie, E., Hovatta, I., Lahti, M., … Eriksson, J. G. (2012). History of mental disorders and leukocyte telomere length in late adulthood: The Helsinki Birth Cohort Study (HBCS). *Journal of Psychiatric Research*, *46*(10), 1346–1353. https://doi.org/10.1016/j.jpsychires.2012.07.005

Scarlett, H., Moirangthem, S., & van der Waerden, J. (2023, August 4). The impact of paternal mental illness on child development: an umbrella review of systematic reviews and meta-analyses. *European Child and Adolescent Psychiatry*, Vol. 1, p. 3. Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s00787-023-02261-1

Schaefer, J. D., Cheng, T. W., & Dunn, E. C. (2022). Sensitive periods in development and risk for psychiatric disorders and related endpoints: a systematic review of child maltreatment findings. *The Lancet Psychiatry*, *9*(12), 978–991. https://doi.org/10.1016/S2215-0366(22)00362-5

Schonewille, N. N., Rijkers, N., Berenschot, A., Lijmer, J. G., van den Heuvel, O. A., & Broekman, B. F. P. (2022). Psychiatric vulnerability and the risk for unintended pregnancies, a systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, *22*(1), 153. https://doi.org/10.1186/s12884-022-04452-1

Schumacher, S. (2012). Psychometric Characteristics of the German adaptation of the Traumatic Experiences Checklist (TEC). *Psychological Trauma: Theory, Research, Practice, and Policy*, *4*, 338–346. https://doi.org/10.1037/a0024044

Scott, K. M., McLaughlin, K. A., Smith, D. A. R., & Ellis, P. M. (2012). Childhood maltreatment and DSM-IV adult mental disorders: Comparison of prospective and retrospective findings. *British Journal of Psychiatry*, *200*(6), 469–475. https://doi.org/10.1192/bjp.bp.111.103267

Shevlin, M., McElroy, E., & Murphy, J. (2017). Homotypic and heterotypic psychopathological continuity: a child cohort study. *Social Psychiatry and Psychiatric Epidemiology*, *52*(9), 1135–1145. https://doi.org/10.1007/s00127-017-1396-7

Shin, E. K., Lewinn, K., Bush, N., Tylavsky, F. A., Davis, R. L., & Shaban-Nejad, A. (2019). Association of Maternal Social Relationships with Cognitive Development in Early Childhood. *JAMA Network Open*, *2*(1), 186963. https://doi.org/10.1001/jamanetworkopen.2018.6963

Silberman, D. M., Acosta, G. B., & Zorrilla Zubilete, M. A. (2016). Long-term effects of early life stress exposure: Role of epigenetic mechanisms. *Pharmacological Research*, *109*, 64–73.

https://doi.org/10.1016/j.phrs.2015.12.033

Slagt, M., Dubas, J. S., Deković, M., & van Aken, M. A. G. (2016). Differences in sensitivity to parenting depending on child temperament: A meta-analysis. *Psychological Bulletin*, *142*(10), 1068–1110. https://doi.org/10.1037/bul0000061

Smeeth, D., Beck, S., Karam, E. G., & Pluess, M. (2021). The role of epigenetics in psychological resilience. *The Lancet Psychiatry*, *8*(7), 620–629. https://doi.org/10.1016/S2215-0366(20)30515-0

Smith, A. D. A. C., Hardy, R., Heron, J., Joinson, C. J., Lawlor, D. A., Macdonald-Wallis, C., & Tilling, K. (2016). A structured approach to hypotheses involving continuous exposures over the life course. *International Journal of Epidemiology*, *45*(4), 1271–1279. https://doi.org/10.1093/ije/dyw164

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., … Fusar-Poli, P. (2022). Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*, *27*, 281–295. https://doi.org/10.1038/s41380-021-01161-7

Sourander, A., Lempinen, L., & Brunstein Klomek, A. (2016). Changes in Mental Health, Bullying Behavior, and Service Use Among Eight-Year-Old Children Over 24 Years. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(8), 717-725.e2. https://doi.org/10.1016/j.jaac.2016.05.018

Southwick, S. M., Vythilingam, M., & Charney, D. S. (2005). The psychobiology of depression and resilience to stress: Implications for prevention and treatment. *Annual Review of Clinical Psychology*, *1*, 255–291. https://doi.org/10.1146/annurev.clinpsy.1.102803.143948

Spann, M. N., Bansal, R., Hao, X., Rosen, T. S., & Peterson, B. S. (2020). Prenatal socioeconomic status and social support are associated with neonatal brain morphology, toddler language and psychiatric symptoms. *Child Neuropsychology*, *26*(2), 170–188. https://doi.org/10.1080/09297049.2019.1648641

Spinhoven, P., Elzinga, B. M., Hovens, J. G. F. M., Roelofs, K., Zitman, F. G., Van Oppen, P., & Penninx, B. W. J. H. (2010). The specificity of childhood adversities and negative life events across the life span to anxiety and depressive disorders. *Journal of Affective Disorders*, *126*(1–2), 103–112. https://doi.org/10.1016/j.jad.2010.02.132

Spira, A. P., Stone, K., Beaudreau, S. A., Ancoli-Israel, S., & Yaffe, K. (2009). Anxiety symptoms and objectively measured sleep quality in older women. *American Journal of Geriatric Psychiatry*, *17*(2), 136–143. https://doi.org/10.1097/JGP.0b013e3181871345

Sprooten, E., Rasgon, A., Goodman, M., Carlin, A., Leibu, E., Lee, W. H., & Frangou, S. (2017). Addressing reverse inference in psychiatric neuroimaging: Meta-analyses of task-related brain activation in common mental disorders. *Human Brain Mapping*, *38*(4), 1846–1864. https://doi.org/10.1002/hbm.23486

Spruit, A., Goos, L., Weenink, N., Rodenburg, R., Niemeyer, H., Stams, G. J., & Colonnesi, C. (2020). The Relation Between Attachment and Depression in Children and Adolescents: A Multilevel Meta-Analysis. *Clinical Child and Family Psychology Review*, *23*(1), 54–69. https://doi.org/10.1007/s10567-019-00299-9

Spry, E. A., Aarsman, S. R., Youssef, G. J., Patton, G. C., Macdonald, J. A., Sanson, A., … Olsson, C. A. (2020). Maternal and paternal depression and anxiety and offspring infant negative

affectivity: A systematic review and meta-analysis. *Developmental Review*, *58*, 100934. https://doi.org/10.1016/j.dr.2020.100934

Stansfeld, S. A., Clark, C., Rodgers, B., Caldwell, T., & Power, C. (2011). Repeated exposure to socioeconomic disadvantage and health selection as life course pathways to mid-life depressive and anxiety disorders. *Social Psychiatry and Psychiatric Epidemiology*, *46*(7), 549–558. https://doi.org/10.1007/s00127-010-0221-3

Steer, R. A., Ranieri, W. F., Beck, A. T., & Clark, D. A. (1993). Further evidence for the validity of the beck anxiety inventory with psychiatric outpatients. *Journal of Anxiety Disorders*, *7*(3), 195–205. https://doi.org/10.1016/0887-6185(93)90002-3

Stein, A., Pearson, R. M., Goodman, S. H., Rapa, E., Rahman, A., McCallum, M., … Pariante, C. M. (2014). Effects of perinatal mental disorders on the fetus and child. *The Lancet*, *384*(9956), 1800–1819. https://doi.org/10.1016/S0140-6736(14)61277-0

Steptoe, A., O'Donnell, K., Badrick, E., Kumari, M., & Marmot, M. (2007). Neuroendocrine and Inflammatory Factors Associated with Positive Affect in Healthy Men and Women: The Whitehall II Study. *American Journal of Epidemiology*, *167*(1), 96–102. https://doi.org/10.1093/aje/kwm252

Stoltenborgh, M., Bakermans-Kranenburg, M. J., Alink, L. R. A., & van IJzendoorn, M. H. (2015). The Prevalence of Child Maltreatment across the Globe: Review of a Series of Meta-Analyses. *Child Abuse Review*, *24*(1), 37–50. https://doi.org/10.1002/car.2353

Su, Y., D'Arcy, C., Yuan, S., & Meng, X. (2019, June 1). How does childhood maltreatment influence ensuing cognitive functioning among people with the exposure of childhood maltreatment? A systematic review of prospective cohort studies. *Journal of Affective Disorders*, Vol. 252, pp. 278–293. Elsevier B.V. https://doi.org/10.1016/j.jad.2019.04.026

Suarez, A., Lahti, J., Czamara, D., Lahti-Pulkkinen, M., Knight, A. K., Girchenko, P., … Raikkonen, K. (2018). The Epigenetic Clock at Birth: Associations With Maternal Antenatal Depression and Child Psychiatric Problems. *Journal of the American Academy of Child and Adolescent Psychiatry*, *57*(5), 321-328.e2. https://doi.org/S0890-8567(18)30107-2 [pii]

Sund, R. (2012). Quality of the Finnish Hospital Discharge Register: A systematic review. *Scandinavian Journal of Public Health*, *40*(6), 505–515. https://doi.org/10.1177/1403494812456637

Tani, Y., Fujiwara, T., Kondo, N., Noma, H., Sasaki, Y., & Kondo, K. (2016). Childhood Socioeconomic Status and Onset of Depression among Japanese Older Adults: The JAGES Prospective Cohort Study. *American Journal of Geriatric Psychiatry*, *24*(9), 717–726. https://doi.org/10.1016/j.jagp.2016.06.001

Tarabulsy, G. M., Pearson, J., Vaillancourt-Morel, M.-P., Bussières, E.-L., Madigan, S., Lemelin, J.-P., … Royer, F. (2014). Meta-Analytic Findings of the Relation Between Maternal Prenatal Stress and Anxiety and Child Cognitive Outcome. *Journal of Developmental & Behavioral Pediatrics*, *35*(1), 38–43. https://doi.org/10.1097/DBP.0000000000000003

Taylor, B. L., Cavanagh, K., & Strauss, C. (2016). The effectiveness of mindfulness-based interventions in the perinatal period: A systematic review and meta-analysis. *PLoS ONE*, *11*(5), 155720. https://doi.org/10.1371/journal.pone.0155720

Thomson, R. M., Allely, C. S., Purves, D., Puckering, C., McConnachie, A., Johnson, P. C. D., … Wilson, P. (2014). Predictors of positive and negative parenting behaviours: Evidence from the

ALSPAC cohort. *BMC Pediatrics*, *14*(1), 1–10. https://doi.org/10.1186/1471-2431-14-247

Tooley, U. A., Bassett, D. S., & Mackey, A. P. (2021). Environmental influences on the pace of brain development. *Nature Reviews Neuroscience*, *22*(6), 372–384. https://doi.org/10.1038/s41583-021-00457-5

Tracy, M., Salo, M., & Appleton, A. A. (2018). The mitigating effects of maternal social support and paternal involvement on the intergenerational transmission of violence. *Child Abuse and Neglect*, *78*, 46–59. https://doi.org/10.1016/j.chiabu.2017.09.023

Trombetta, T., Giordano, M., Santoniccolo, F., Vismara, L., Della Vedova, A. M., & Rollè, L. (2021). Pre-natal Attachment and Parent-To-Infant Attachment: A Systematic Review. *Frontiers in Psychology*, *12*, 620942. https://doi.org/10.3389/fpsyg.2021.620942

Trompetter, H. R., de Kleine, E., & Bohlmeijer, E. T. (2017). Why Does Positive Mental Health Buffer Against Psychopathology? An Exploratory Study on Self-Compassion as a Resilience Mechanism and Adaptive Emotion Regulation Strategy. *Cognitive Therapy and Research*, *41*(3), 459–468. https://doi.org/10.1007/s10608-016-9774-0

Tugade, M. M., & Fredrickson, B. L. (2004). Resilient Individuals Use Positive Emotions to Bounce Back From Negative Emotional Experiences. *Journal of Personality and Social Psychology*, *86*(2), 320–333. https://doi.org/10.1037/0022-3514.86.2.320

Tuovinen, S., Lahti-Pulkkinen, M., Girchenko, P., Lipsanen, J., Lahti, J., Heinonen, K., … Räikkönen, K. (2018). Maternal depressive symptoms during and after pregnancy and child developmental milestones. *Depression and Anxiety*, *35*(8), 732–741. https://doi.org/10.1002/da.22756

Turecki, G., & Meaney, M. J. (2016). Effects of the Social Environment and Stress on Glucocorticoid Receptor Gene Methylation: A Systematic Review. *Biological Psychiatry*, *79*(2), 87–96. https://doi.org/10.1016/j.biopsych.2014.11.022

Tyrka, A. R., Ridout, K. K., & Parade, S. H. (2016). Childhood adversity and epigenetic regulation of glucocorticoid signaling genes: Associations in children and adults. *Development and Psychopathology*, *28*(4), 1319–1331. https://doi.org/10.1017/S0954579416000870

Ungar, M., Hadfield, K., Bush, N., Quesnel-Vallée, A., & Pekelny, I. (2019). Resilience to prenatal stress. In *Pathways and Barriers to Parenthood: Existential Concerns Regarding Fertility, Pregnancy, and Early Parenthood* (pp. 127–153). Springer International Publishing. https://doi.org/10.1007/978-3-030-24864-2_8

Van Den Bergh, B. R. H. (2011). Developmental programming of early brain and behaviour development and mental health: a conceptual framework. *Developmental Medicine and Child Neurology*, *53*(Suppl.4), 19–23. https://doi.org/10.1111/j.1469-8749.2011.04057.x

Van den Bergh, B. R. H., van den Heuvel, M. I., Lahti, M., Braeken, M., de Rooij, S. R., Entringer, S., … Schwab, M. (2020). Prenatal developmental origins of behavior and mental health: The influence of maternal stress in pregnancy. *Neuroscience and Biobehavioral Reviews*, *117*, 26–64. https://doi.org/10.1016/j.neubiorev.2017.07.003

van den Heuvel, M. I., Johannes, M. A., Henrichs, J., & Van den Bergh, B. R. H. (2015). Maternal mindfulness during pregnancy and infant socio-emotional development and temperament: The mediating role of maternal anxiety. *Early Human Development*, *91*(2), 103–108. https://doi.org/10.1016/j.earlhumdev.2014.12.003

van der Put, C. E., Assink, M., Gubbels, J., & Boekhout van Solinge, N. F. (2018). Identifying

Effective Components of Child Maltreatment Interventions: A Meta-analysis. *Clinical Child and Family Psychology Review*, *21*(2), 171–202. https://doi.org/10.1007/s10567-017-0250-5

van der Waerden, J., Bernard, J. Y., De Agostini, M., Saurel-Cubizolles, M.-J., Peyre, H., Heude, B., & Melchior, M. (2017). Persistent maternal depressive symptoms trajectories influence children's IQ: The EDEN mother-child cohort. *Depression and Anxiety*, *34*(2), 105–117. https://doi.org/10.1002/da.22552

van Heijningen, C. J. M., van Berkel, S. R., Rosinda, S. J., Penninx, B. W. J. H., Alink, L. R. A., & Elzinga, B. M. (2023). Long-term effects of experiencing childhood parental death on mental and physical health: A NESDA study. *Stress and Health*. https://doi.org/10.1002/smi.3322

van IJzendoorn, M. H., Bakermans-Kranenburg, M. J., Coughlan, B., & Reijman, S. (2020). Annual Research Review: Umbrella synthesis of meta-analyses on child maltreatment antecedents and interventions: differential susceptibility perspective on risk and resilience. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *61*(3), 272–290. https://doi.org/10.1111/jcpp.13147

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., … Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective-and cross-sectional cohort studies. *Schizophrenia Bulletin*, *38*(4), 661–671. https://doi.org/10.1093/schbul/sbs050

Varin, M., Palladino, E., Orpana, H. M., Wong, S. L., Gheorghe, M., Lary, T., & Baker, M. M. (2020). Prevalence of Positive Mental Health and Associated Factors Among Postpartum Women in Canada: Findings from a National Cross-Sectional Survey. *Maternal and Child Health Journal*, *24*(6), 759–767. https://doi.org/10.1007/s10995-020-02920-8

Verner, G., Epel, E., Lahti-Pulkkinen, M., Kajantie, E., Buss, C., Lin, J., … Entringer, S. (2021). Maternal Psychological Resilience During Pregnancy and Newborn Telomere Length: A Prospective Study. *American Journal of Psychiatry*, *178*, 183–192. https://doi.org/10.1176/appi.ajp.2020.19101003

Vilagut, G., Forero, C. G., Barbaglia, G., & Alonso, J. (2016). Screening for depression in the general population with the center for epidemiologic studies depression (CES-D): A systematic review with meta-analysis. *PLoS ONE*, *11*(5). https://doi.org/10.1371/journal.pone.0155431

Voellmin, A., Entringer, S., Moog, N., Wadhwa, P. D., & Buss, C. (2013). Maternal positive affect over the course of pregnancy is associated with the length of gestation and reduced risk of preterm delivery. *Journal of Psychosomatic Research*, *75*(4), 336–340. https://doi.org/10.1016/j.jpsychores.2013.06.031

Vos, T., Abajobir, A. A., Abbafati, C., Abbas, K. M., Abate, K. H., Abd-Allah, F., … Murray, C. J. L. (2017). Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, *390*, 1211–1259. https://doi.org/10.1016/S0140-6736(17)32154-2

Wadji, D. L., Tandon, T., Ketcha Wanda, G. J. M., Wicky, C., Dentz, A., Hasler, G., … Martin-Soelch, C. (2021). Child maltreatment and NR3C1 exon 1F methylation, link with deregulated hypothalamus-pituitary-adrenal axis and psychopathology: A systematic review. *Child Abuse and Neglect*, *122*, 105304. https://doi.org/10.1016/j.chiabu.2021.105304

Walker, A. L., Witteveen, A. B., Otten, R. H. J., Verhoeven, C. J., Henrichs, J., & de Jonge, A. (2022). Resilience-enhancing interventions for antepartum depressive symptoms: systematic review.

BJPsych Open, *8*(3), e89. https://doi.org/10.1192/bjo.2022.60

Wallwiener, S., Goetz, M., Lanfer, A., Gillessen, A., Suling, M., Feisst, M., … Wallwiener, M. (2019). Epidemiology of mental disorders during pregnancy and link to birth outcome: a large-scale retrospective observational database study including 38,000 pregnancies. *Archives of Gynecology and Obstetrics*, *299*(3), 755–763. https://doi.org/10.1007/s00404-019-05075-2

Walsh, K., McCormack, C. A., Webster, R., Pinto, A., Lee, S., Feng, T., … Monk, C. (2019). Maternal prenatal stress phenotypes associate with fetal neurodevelopment and birth outcomes. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(48), 23996–24005. https://doi.org/10.1073/pnas.1905890116

Wang, Y., Chen, X., Zhou, K., & Zhang, H. (2023). A Meta-Analysis of the Effects of Childhood Maltreatment on Elderly Depression. *Trauma, Violence, and Abuse*, *24*(3), 1593–1607. https://doi.org/10.1177/15248380211073838

Warrier, V., Kwong, A. S. F., Luo, M., Dalvie, S., Croft, J., Sallis, H. M., … Cecil, C. A. M. (2021). Gene–environment correlations and causal effects of childhood maltreatment on physical and mental health: a genetically informed approach. *The Lancet Psychiatry*, *8*(5), 373–386. https://doi.org/10.1016/S2215-0366(20)30569-1

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and Validation of Brief Measures of Positive and Negative Affect: The PANAS Scales. *Journal of Personality and Social Psychology*, *54*(6), 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063

Wechsler, D. (2010). *WISC-IV - Wechsler Intelligence Scale for Children - IV*. Helsinki: Psykologien Kustannus Oy.

Wechsler, D., Golombok, S., & Rust, J. (1992). WISC-III UK Wechsler intelligence scale for children: UK manual. *Sidcup, UK: The Psychological Corporation*.

Weeks, M., Wild, T. C., Ploubidis, G. B., Naicker, K., Cairney, J., North, C. R., & Colman, I. (2014). Childhood cognitive ability and its relationship with anxiety and depression in adolescence. *Journal of Affective Disorders*, *152–154*(1), 139–145. https://doi.org/10.1016/j.jad.2013.08.019

Wei, Q., Zou, J., Ma, X., Xiao, X., Zhang, Y., & Shi, H. (2023). Prospective associations between various prenatal exposures to maternal psychological stress and neurodevelopment in children within 24 months after birth. *Journal of Affective Disorders*, *327*, 101–110. https://doi.org/10.1016/j.jad.2023.01.103

Weiss, A., Baselmans, B. M. L., Hofer, E., Yang, J., Okbay, A., Lind, P. A., … Luciano, M. (2016). Personality polygenes, positive affect, and life satisfaction. *Twin Research and Human Genetics*, *19*(5), 407–417. https://doi.org/10.1017/thg.2016.65

Westerhof, G. J., & Keyes, C. L. M. (2010). Mental illness and mental health: The two continua model across the lifespan. *Journal of Adult Development*, *17*(2), 110–119. https://doi.org/10.1007/s10804-009-9082-y

Wolke, D., Waylen, A., Samara, M., Steer, C., Goodman, R., Ford, T., & Lamberts, K. (2009). Selective drop-out in longitudinal studies and non-biased prediction of behaviour disorders. *British Journal of Psychiatry*, *195*(3), 249–256. https://doi.org/10.1192/bjp.bp.108.053751

Woodard, K., & Pollak, S. D. (2020). Is there evidence for sensitive periods in emotional development? *Current Opinion in Behavioral Sciences*, *36*, 1–6. https://doi.org/10.1016/j.cobeha.2020.05.004

World Health Organization. (2004). *Promoting mental health : Concepts, emerging evidence, practice : Summary report / a report from the World Health Organization, Department of Mental Health and Substance Abuse*. Geneva.

World Health Organization. (2018). *INSPIRE Handbook: action for implementing the seven strategies for ending violence against children*. Geneva.

World Health Organization. (2019). International Classification of Diseases, Eleventh Revision (ICD-11). Retrieved from https://icd.who.int/browse11

World Health Organization. (2022). *World Mental Health Report: Transforming mental health for all*. Geneva: World Health Organization.

Wraw, C., Deary, I. J., Der, G., & Gale, C. R. (2016). Intelligence in youth and mental health at age 50. *Intelligence*, *58*, 69–79. https://doi.org/10.1016/j.intell.2016.06.005

Wraw, C., Deary, I. J., Gale, C. R., & Der, G. (2015). Intelligence in youth and health at age 50. *Intelligence*, *53*, 23–32. https://doi.org/10.1016/j.intell.2015.08.001

Wulff, V., Hepp, P., Wolf, O. T., Balan, P., Hagenbeck, C., Fehm, T., & Schaal, N. K. (2021). The effects of a music and singing intervention during pregnancy on maternal well-being and mother–infant bonding: a randomised, controlled study. *Archives of Gynecology and Obstetrics*, *303*(1), 69–83. https://doi.org/10.1007/s00404-020-05727-8

Yancura, L. A., & Aldwin, C. M. (2009). Stability and Change in Retrospective Reports of Childhood Experiences Over a 5-Year Period: Findings from the Davis Longitudinal Study. *Psychology and Aging*, *24*(3), 715–721. https://doi.org/10.1037/a0016203

Yang, C., Chen, P., Xie, J., He, Y., Wang, Y., & Yang, X. (2021). Childhood Socioeconomic Status and Depressive Symptoms of Young Adults: Mediating Role of Childhood Trauma. *Frontiers in Psychiatry*, *12*. https://doi.org/10.3389/fpsyt.2021.706559

Yang, G., Cao, X., Li, X., Zhang, J., Ma, C., Zhang, N., … Liu, Z. (2022). Association of Unhealthy Lifestyle and Childhood Adversity with Acceleration of Aging among UK Biobank Participants. *JAMA Network Open*, *5*(9), E2230690. https://doi.org/10.1001/jamanetworkopen.2022.30690

Yang, Hu, Y., Silventoinen, K., & Martikainen, P. (2020). Childhood adversity and depressive symptoms among middle-aged and older Chinese: results from China health and retirement longitudinal study. *Aging and Mental Health*, *24*(6), 923–931. https://doi.org/10.1080/13607863.2019.1569589

Yazawa, A., Shiba, K., Inoue, Y., Okuzono, S. S., Inoue, K., Kondo, N., … Kawachi, I. (2022). Early childhood adversity and late-life depressive symptoms: unpacking mediation and interaction by adult socioeconomic status. *Social Psychiatry and Psychiatric Epidemiology*, *57*(6), 1147–1156. https://doi.org/10.1007/s00127-022-02241-x

Yochim, B. P., Mueller, A. E., & Segal, D. L. (2013). Late life anxiety is associated with decreased memory and executive functioning in community dwelling older adults. *Journal of Anxiety Disorders*, *27*(6), 567–575. https://doi.org/10.1016/j.janxdis.2012.10.010

Zhu, J. H., Bo, H. H., Liu, B. P., & Jia, C. X. (2023). The associations between DNA methylation and depression: A systematic review and meta-analysis. *Journal of Affective Disorders*, *327*, 439–450. https://doi.org/10.1016/j.jad.2023.01.079

Zimmerman, M. A., Stoddard, S. A., Eisman, A. B., Caldwell, C. H., Aiyer, S. M., & Miller, A. (2013). Adolescent Resilience: Promotive Factors That Inform Prevention. *Child Development*

Perspectives, *7*(4), 215–220. https://doi.org/10.1111/cdep.12042

Zorn, J. V., Schür, R. R., Boks, M. P., Kahn, R. S., Joëls, M., & Vinkers, C. H. (2017). Cortisol stress reactivity across psychiatric disorders: A systematic review and meta-analysis. *Psychoneuroendocrinology*, *77*, 25–36. https://doi.org/10.1016/j.psyneuen.2016.11.036

Zuber, S., Bechtiger, L., Bodelet, J. S., Golin, M., Heumann, J., Kim, J. H., … Hofer, S. M. (2023). An integrative approach for the analysis of risk and health across the life course: challenges, innovations, and opportunities for life course research. *Discover Social Science and Health*, *3*(1), 14. https://doi.org/10.1007/s44155-023-00044-2

Appendix I: Original publications