Chapter 1

General Introduction
What makes some children vulnerable to face difficulties and what makes others resilient? Differences between children’s developmental paths are due to a combination of the children’s biological predisposition, the children’s characteristics, and the children’s rearing environment. In other words, child development is affected by multiple influences: biological, psychological, and environmental factors and the interplay between them. The aim of this thesis is to advance our understanding of why some children thrive and others not. It is of global concern to unravel the causes of individual differences in social-emotional and cognitive development in order to reduce the prevalence of childhood problems and its lifelong impact. In sum, we wondered what makes some children vulnerable and others resilient?

Within this overarching question, this thesis focused on two very important, but poorly understood topics: 1) bullying during primary school, and 2) influences of parental age on child development. For bullying, I looked at influences of risk factors on the prevalence of perpetration and victimization as well as at the etiology of different subtypes of perpetration (the ones who bully), victimization (the victims of bullying), and the association between perpetration and victimization. Regarding parental age influences, I gained unique insight into the extent to which a children’s development is influenced by parental age at birth. We focused on the influences of parental age on the children’s socio-emotional and cognitive development.

Research on child development so far has been hampered by the traditional boundaries of the research areas involved. This inspired the formation of the Consortium on Individual Development (CID), which brings together researchers from several Dutch universities from a wide range of behavioral and social science disciplines. Bundling expertise may lead to understanding that goes beyond earlier attempts to understand child development. This consortium includes four different work packages (WP) with large existing and new youth cohorts in the Netherlands to study childhood development, see Figure 1.
The studies reported in this thesis are part of WP3 of this CID consortium, which is about intergenerational transmission. Intergenerational transmission refers to the genetic and environmental transmission of characteristics, skills and traits from parents to their children and creates for example resemblance between siblings. In what follows I will introduce the two topics of this thesis, bullying and parental age at birth of offspring, and the studies within that topic. Bullying is an outcome trait for which I looked at risk factors and familial resemblance. Parental age at birth of offspring is a predictor variable that represents a characteristic of parents which is thought to influence multiple aspects of children’s development.
1. Bullying

Bullying is a widespread phenomenon. It is the most frequent form of abuse encountered by children. Around 40% of the children are victims of bullying; around 30% of the children are perpetrators of bullying (Modecki, Minchin, Harbaugh, Guerra & Runions, 2014) and it is thought that being a victim and being a perpetrator may be associated within the same individual. Bullying has detrimental consequences on both children’s physiological and psychological health. Victims have, for instance, more often internalizing problems and anxiety, or depression disorder, while bullies are more at risk for delinquent behavior (Wolke & Lereya, 2015). These negative health effects persist into adolescence and adulthood. That is, being victimized in school is a risk factor for the manifestation of depression later in life (Wolke & Lereya, 2015). In my PhD I investigated children’s vulnerability of bullying in schools, employing a large sample of twins of the NTR.

1.1 Risk Factors

Factors influencing involvement in bullying range from individual to contextual. Studies so far mostly investigated general factors, that are not specific to twins. These studies showed that boys are more vulnerable to become victims or bullies (e.g., Iossi Silva, Pereira, Mendonça, Nunes & Oliveira, 2013), but they are inconsistent about the effect of age (Moura, Cruz, Quevedo, 2011; Craig et al., 2009). Questions regarding bullying in twins (i.e., twin-specific factors) remain unanswered. For instance, it is unknown what the effects are of having a co-twin (i.e., having close companionship) or sharing a classroom with a close sibling such as a cotwin. The first question is about whether twins - having a co-twin by their side - are at higher, equal, or lower risk than non-twin children (called singletons). So far three studies tried to answer this question for victimization by comparing twins with unrelated singletons (Barness & Boutwell, 2013; Oshima et al., 2010; Weissenberg et al., 2007). Studies should however compare twins with their non-twin siblings to make sure they closely match on important family background factors. The second question is about whether or not twins should share classroom in primary school. This is an important question, also in the light of the policy of many schools to separate twins and not allow them to be in the same classroom.

Chapter 2 reports on a study that investigated the prevalence of the active form of bullying (“perpetration”) and the passive form (“victimization”). First, in this chapter I compared the bullying behavior of twins with that of singletons to see, for instance, whether having a cotwin protects children from being bullied. We are the first that will do so with a large sample of twins and their non-twin siblings in order to make sure they closely match on important family-background factors. Importantly, we were the first to compare twins and singletons on the prevalence of perpetration.
Secondly, this chapter describes how the prevalence of perpetration and victimization is influenced by twin-specific (e.g., classroom-sharing) and non-twin specific (e.g., age and gender) factors. Whether or not twins should share a classroom is an important decision for parents of twins who enter primary school. When we know the effect of classroom sharing on bullying, we can give twin parents and teachers advice regarding the placement of twins, since classroom-sharing is a malleable factor.

1.2 Etiology

Even after accounting for general effects, like boys being more involved in bullying than girls, large individual differences remain. So it is not the case that all boys and none of the girls are bullies. Why are some children more likely to be involved in bullying, either as a victim, bully, or both (i.e., bully-victim)? The literature does not include many studies that investigated causes of individual differences.

The genetically-sensitive studies done so far studied mostly victimization (e.g., Silberg et al., 2016). Perpetration, and the association between both, was investigated only once (Ball et al., 2008). Furthermore, almost all studies are based on bullying behavior in general, while we know from earlier studies that bullying behavior comes in different forms, and that each have their own prevalence. Boys and girls are differently involved in these forms: boys are more often involved in physical and verbal bullying, while girls are more often involved in relational bullying (Scheithauer, Hayer, Petermann & Jugert, 2006). Eastman et al. (2018) were the first that investigated the genetic and environmental influences on different forms of victimization. However, this remains unanswered for different types of perpetration and for the overlap between them.

Chapter 3 is about the relative contributions of genetic and environmental influences on different forms of bullying. It is about the question why some children are involved in bullying, either as victims or as perpetrators or even both. Genetic and environmental effects were investigated for general, verbal, physical, and relational bullying, for both the active form (perpetration) and the passive form (victimization). I also looked at the question of their association (representing bully-victims) across these different forms. Information on bullying was obtained from children’s teachers in primary school. The parents in families registered with the Netherlands Twin Register were asked for permission to approach their children’s teachers and if they agreed, the teachers were asked to complete a survey including questions about bullying.
2. **Parental Age**

The influences of advanced parenthood on various severe neurodevelopmental disorders are well established. That is, offspring of older parents are at higher risk for schizophrenia, autism, and Down Syndrome (Merikangas, 2016; 2017; de Kluiver et al. 2017). Consequently, concerns are growing, because the mean age at which people start a family has been growing since the widespread availability of contraception around 1970. While in the Netherlands in 1970 the mean age at first birth was 24.3, nowadays the mean age at first birth is around 30 (CBS, 2019). The important next step in this field is to investigate whether the established adverse effects of advanced parental age on rare disorders extent to milder – but more common – neurodevelopmental problems. This part of this thesis addresses this question, regarding 1) two broad categories of behavioral and emotional problems in children, i.e. internalizing and externalizing problems, and 2) attention problems and cognitive functioning as assessed by psychometric IQ tests and educational attainment (CITO scores). Both projects are unique in that they included and combined data of all four large CID cohorts of WP3, representing a very large sample of children from all across the Netherlands.

The cohorts that are part of CID WP3 are Generation-R (Gen-R), Tracking Adolescents’ Individual Lives Survey (TRAILS), Research on Adolescent Development and Relationships-Young (RADAR-Y), and Netherlands Twin Registry (NTR). Gen-R is conducted by Erasmus University Rotterdam, TRAILS by the University of Groningen, RADAR-Y by Utrecht University, and NTR by the Vrije Universiteit Amsterdam. Gen-R is a prospective study that recruited mothers in the city of Rotterdam during pregnancy. Their partners and their children were also invited to participate. TRAILS recruited their sample in the Northern regions of the Netherlands and RADAR-Y in the province of Utrecht and four large cities in the mid-west part of the Netherlands. NTR recruits new-born twins from all regions in the Netherlands. These CID cohorts follow children in longitudinal studies.

2.1 **Internalizing and Externalizing Problems**

There is little comprehensive evidence from population-based cohorts on the effect of paternal and maternal age on internalizing and externalizing problem behavior. A number of studies have investigated effects on externalizing problems. While most studies have identified negative associations with maternal age (for a review, see: Tearne, 2015), there are exceptions. For instance, Weiser et al. (2008) found that advanced parental age is associated with poorer social functioning. These prior studies, however, used a wide variety of populations and analytic strategies. In addition, the effects are mostly investigated for mothers’ age, but might be different for fathers’ age, underlining the need to study them separately.
Saha, Barnett, Buka, McGrath (2009) indeed showed different effects for maternal and paternal age. They showed that advanced maternal age was protective against externalizing problems (but associated with an increased risk for internalizing problems), while advanced paternal age was associated with an increase of adverse externalizing problems (and not with internalizing problems). Importantly, prior population-based studies rarely included internalizing problems. There are a few exceptions, but these exceptions require replication in other cohorts (e.g., Orlebeke, Knol, Boomsma & Verhulst, 1998; Tearne, Robinson, Jacoby, Newnham, McLean, 2015). Taken together, there is need for studies that investigate both the paternal and maternal age effects on core dimensions of offspring mental health, including both internalizing and externalizing problems, with the same analytical strategy.

**Chapter 4** is about the parental age effects on externalizing and internalizing problem behavior. Externalizing and internalizing data of participants around age 10-13 years in four population-based cohorts of CID were analyzed. The four cohorts have reports from mothers, fathers, teachers, and the children themselves. As the perception of childhood problems may differ for these different informants for example because of situation-specific problem behavior, we used a multiple informant design in order to get a comprehensive set of outcome measures. The reports from teachers are particularly valuable, because their reports are unlikely to be affected by parental age-related report biases. We tested both linear and non-linear effects, with and without adjusting for child gender and socio-economic status. Due to the previous mixed findings and the availability of a very large sample of children, we used a cross-validation approach. That is, we generated hypotheses based on one random half of the data of each cohort and evaluated these set of hypotheses within the other half of the data. The large datasets of the cohorts were thus of great value. A Bayesian statistical framework was used to investigate the overall support (i.e., of all cohorts together) for each hypothesis about the possible risk of young and older parenthood.
2.2 Attention Problems & Cognitive Functioning

Apart from effects of parental age on internalizing and externalizing problems, we investigated the effects on attention problems and cognitive functioning, which are inversely associated. ADHD is one of the most common neurodevelopmental disorders in childhood (Faraone, Sergeant, Gillberg & Biederman, 2003). All children with ADHD suffer from attention problems. Most studies showed that offspring of younger mothers are more at risk (e.g., Mikkelsen et al., 2016), but this effect is also found for older mothers (e.g., Chudal et al., 2015). Mikkelsen et al. (2016) found no effect for fathers, while D’Onofrio et al. (2014) reported a higher risk for older fathers and Chudal et al. (2015) for younger fathers. The mixed findings for ADHD are mirrored in the literature on effects on offspring’s cognitive functioning. For example, D’Onfrio et al. (2014) showed adverse effects of delayed parenthood, while McGrath et al. (2013) showed adverse effects of young fatherhood as well. The previous mixed findings for ADHD and cognitive functioning might be due to differences between cohorts and analytic strategies. Hence, in this study we combined data of four large cohorts and used the same analytic procedure for each cohort. Again, the dataset was split into a discovery and a replication sample. The age effects for fathers and mothers might differ and might be the reverse from what we would have expected from research about the more severe neurodevelopmental outcomes.

Chapter 5 looks into the effects of parental age on the neurodevelopmental outcomes attention problems and cognitive functioning. For cognitive functioning, we focused on intelligence (psychometric IQ) and educational achievement (as measured by the Dutch CITO test which is completed by the majority of children in the Netherlands). The aim was to clarify whether effects for relatively rare disorders extend to these more common outcomes (i.e., the entire distribution). Again, data of mothers, fathers, teachers and the children themselves were used from the same four large CID cohorts. Paternal and maternal age were separately investigated, both with and without the adjustment of child gender and socio-economic status of the parents. In this chapter, the same analytical method was used as in Chapter 4 to combine the data of the four cohorts in order to investigate the possible risks of young and older parenthood on attention problems, academic achievement and IQ.

A summary of the main results of all four projects and a general discussion can be found in Chapter 6, followed by a Dutch summary in Chapter 7.
References


