Substance use in adolescent girls: The interplay of pubertal timing, family and peer influence

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DECLARATION

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ETHICAL STATEMENT

Ethical approval for this doctoral research was obtained from the Avon Longitudinal Study of Parents and Children (ALSPAC) Law and Ethics Committee.

THESIS SUMMARY

Pubertal timing and relationships with parents and peers have each been linked to substance use in adolescent girls. However, to understand the origin of adolescent substance use in relation to these factors, it is important to focus on combined risk effects. As shown in the systematic review (the first part of this PhD project) only a few studies have tested the relationships between these factors in predicting adolescent substance use

The aim of this thesis was to evaluate the main effects of pubertal timing and psycho-social factors (parent-daughter relations and peer deviance) on substance use. A second aim was to examine whether the links between pubertal timing and girl's substance use are indirect via psycho-social factors (mediation) and whether the links between psycho-social factors and substance use differ across pubertal timing groups (moderation).

Girls' data from the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) was analysed. Pubertal timing was assessed yearly between ages 8 and 17, parent-daughter relations and peer deviance at age 15, and alcohol, cigarette and cannabis use at age 16. Additionally, analyses controlled for a set of *a priori* selected confounders.

Late maturing girls had lower levels of cannabis use compared to on-time maturing girls. Late maturing girls had fewer alcohol drinking, cannabis using and delinquent friends than early maturing girls and fewer cannabis using friends than on-time maturing girls. Additionally, late maturing girls' lower levels of alcohol use were partly explained by having fewer cannabis using and delinquent friends.

To conclude, in late adolescence, the combined effects of peer deviance and pubertal timing are more influential than the combined effects of parent-daughter relations and pubertal timing, in predicting adolescent substance use. Collectively, the findings indicate the importance of creating targeted prevention programs that are sensitive to developmental stage in relation to the peer group.

CHAPTER 1: THESIS OVERVIEW

The period of adolescence (10-19 years of age; WHO, 2008) is marked by developmental and social changes in a young person's life (WHO, 2008). Experimentation with substances is common during this period (BMA, 2003; National Center for Health Statistics, 2011). Although the majority of adolescents emerge from this period without any problems, a proportion develops patterns of heavy/problem use associated with future risk of substance use disorder (Lewis et al., 2002). Adolescent-onset substance abuse has been characterised by rapid development of multiple drug dependencies and disruption in brain functioning affecting memory, learning, motivation, judgment and behaviour control (Spear, 2002; Volkow, 2010). Furthermore, early-onset alcohol initiation (before 13 years), specifically, may increase the risk of alcohol abuse and dependence (Spear, 2002), as well as cigarette and drug use (Donovan 2004). Heavy substance use in adolescence has been associated with a variety of adverse psycho-social consequences, including delinquency, hazardous driving, risky sexual behaviour, psychiatric problems and school drop-out (Bava & Tapert, 2010). It is therefore important to understand the factors that put adolescents at increased risk of problem substance use.

Biological and psycho-social processes play a role in the development of substance use/ misuse in adolescence (van den Bree et al., 2004), as adolescents are highly vulnerable to social influences (Volkow, 2010) and have a greater reward sensitivity and proclivity to risk taking than older people. This may be related to changes in the developing brain (Bava & Tapert, 2010); more specifically, adolescent risk-taking behaviour is stimulated by increased activity in the socio-emotional reward system at the beginning of puberty, whereas this increase in activity precedes the maturation of the cognitive control system (Steinberg, 2010). Adolescents who experience multiple risk factors may have an increased chance of engaging in substance misuse (van den Bree & Pickworth, 2005), and the importance of understanding the interplay of such factors with regards to substance use in adolescence has been highlighted (Glaser et al., 2010; Rhodes et al., 2003). One biological factor that has been related to substance use in young people is pubertal development. More specifically, pubertal timing relative to the peer group rather than status *per se*, has been associated with risk of substance misuse (Alsaker, 1996, Buck et al., 2008), with the majority of findings for girls indicating an association between early pubertal timing and increased substance use (Hummel et al., 2013).

With regards to psycho-social factors, considerable research attention has been directed towards links between family functioning and peer behaviour as risk factors for adolescent substance use (van den Bree et al., 2004). The rationale for looking at family functioning with regards to pubertal timing and adolescent substance use was highlighted by Ge et al.'s *contextual amplification theory*. This theory proposes that social processes (e.g., parenting) interact with pubertal transition to increase the risk of adjustment problems (e.g., externalizing problems, substance use; Ge et al., 2002). There is substantial evidence indicating associations between adolescent alcohol, cigarette and drug use and poor family functioning (Celio et al., 2006; Donovan, 2004; Enoch, 2011; Hummel et al., 2013), including aspects of parenting behaviour specifically (e.g., Dishion et al., 2004; Ge et al., 1996; Kaltiala-Heino et al., 2011; Shelton et al., 2008).

The rationale for looking at peer behaviour and adolescent substance use has been highlighted by the *social learning theory*, which proposes that individuals learn to take substances in groups (Bahr et al., 2005). During adolescence, particular research attention is given to peer groups, especially to peers' substance use, due to the importance adolescents place on peers while they strive to achieve autonomy from their parents (Bahr et al., 2005).There is substantial evidence indicating associations between adolescent alcohol, cigarette and drug use and affiliation with deviant peer groups, who are involved in substance misuse and delinquency (e.g., Ali et al., 2011; Branstetter et al., 2011; Cruz et al., 2012; Glaser et al., 2010; Skinner et al., 2009; van den Bree & Pickwoth 2005; van den Bree et al., 2004).

However, the psychosocial development of young people (including their substance use/ misuse) is best understood as the result of the combined effects of individual factors over time (Rutter, 1999, Rutter & Casear, 1991) and would therefore be imperfectly captured by cross-sectional models focussing on main effects only (Cicchetti, 1984; Rutter, 2005; Rutter, 1999). Therefore, as part of this PhD project a systematic review, looking at pubertal timing, family functioning and adolescent substance use, was first undertaken (Hummel et al., 2013). Additionally, two separate studies were conducted with the aim to elucidate the interplay of these factors in relation to increased substance use in adolescence.

The first study focussed on the interplay of pubertal timing and parent-daughter relationship quality (level of parent-daughter communication, conflict and parental monitoring) on substance use (alcohol, cigarette and cannabis) in late adolescent girls while controlling for *a priori* selected confounders.

The second study focussed on the interplay of pubertal timing and peer deviance (number of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends (showing aggression towards people and animals, deliberately destroying others' property, rule breaking, lying and stealing; American Academy of Child and Adolescent Psychiatry (AACAP), 2012) on substance use in late adolescent girls while controlling for *a priori* selected confounders.

With the systematic review I aimed to systematically assess and discuss the literature focussing on pubertal timing, family functioning and adolescent substance use to highlight the findings already reported within this field as well as guide my subsequent research studies. My own studies aimed to investigate how pubertal timing and psycho-social factors, linked to parent-adolescent relationship quality and peer deviance, combine to influence girls' substance use using data from the population-based Avon Longitudinal Study of Parents and Children (ALSPAC).

CHAPTER 2: LITERATURE REVIEW

2.1 Theoretical perspectives on adolescence

The World Health Organization (WHO) identified adolescence as the period from age 10 to 19 years (WHO, 2008). This period is characterised by multiple developmental and social changes in a young person's life (WHO, 2008).

Many theories have considered the period of adolescence. G. Stanley Hall (1844-1924) might be seen as the pioneer of introducing a theory of adolescence. Mainly influenced by Darwin's *evolutionary theory,* Hall theorised adolescence as a period of *Sturm und Drang* (storm and stress) caused by inner conflicts between individual development and evolutionary development of humankind, mirrored in frequent mood swings in the adolescent (Hall, 1904; cited by King, 2004). Anna Freud (1895-1982), who was strongly influenced by her father Sigmund Freud, theorised adolescence to be a period of conflict between the *id* (i.e., sexual appetite introduced by physiological changes during puberty) and society, which dictates that many of these newly experienced urges are undesirable and must therefore be restricted (Freud, 1948; cited by King, 2004). The theory introduced by Hall, and further developed by Anna Freud, emphasised the importance of biological changes in the adolescent. These changes, which start with the onset of puberty, place the adolescent in a conflict between new inner urges (i.e., the newly experienced evolutionary urge to reproduce) and the morals dictated by society. Resolving this conflict is linked to the degree to which the adolescent possesses the cognitive and emotional abilities that allow him to achieve a balance between the new biological urges and social norms. More specifically, the beginning of puberty is marked by increased activity in the socio-emotional reward system, which explains adolescents' readiness to engage in risk-taking behaviour (i.e., responding to their inner urges, such as sex drive). The cognitive and emotional abilities to control behaviour are linked to the cognitive control system, which matures increasingly over the course of adolescence (Steinberg, 2010). Additionally, over the course of growing up adolescents develop cognitive skills (i.e., critical thinking), which allow them to compare the environment they see to their knowledge about it. This means that adolescents entering puberty at an early age might be less well prepared, with regards to cognitive skills (i.e., critical thinking; Kuhn, 1999), and therefore might experience greater inner conflicts than adolescents who enter puberty at a later age, and were therefore able to acquire more of these cognitive skills prior to entering puberty (Freud, 1948; cited by King, 2004).

Kurt Lewin (1890-1947), on the other hand, proposed in his theory of development that adolescence is mainly a period of transition; more specifically, the adolescent has to transition from being a child to being an adult. According to Lewin, the more clear-cut the distinction between childhood and adulthood, the more difficult the transition from the one to the other stage might be for the adolescent. Furthermore, adolescents who enter puberty at an early age might experience a more difficult transition than adolescents entering puberty later (Lewin, 1942; cited by King, 2004). This might be due to the fact that certain forms of childish behaviour might no longer be accepted by the parents (although still age appropriate for the adolescent's young age; for example depending on the parent to arrange his appointments for him, etc.) and certain forms of adult behaviour might not be permitted yet (due to parental restrictions, legal limitations, etc).

Erik Erikson's *theory of identity development* (1950) emphasised the acquisition of a personal identity as the primary task in adolescence. During this period, adolescents might feel confused and therefore need to experiment with different roles and behaviours to acquire a clear sense of themselves and their direction in life. Although parents could provide role models, the adolescent might reject them, as older generations might be seen as inappropriate because they grew up in a different time with different social norms. This renders peers the main source of identity formation in the adolescent's life, highlighting the importance of the peer group during adolescence (Erikson, 1950; cited by King, 2004). Erikson emphasised the importance of successfully acquiring a personal identity at this age. According to Erikson, failure to acquire a personal identity during adolescence will keep the adolescent from developing into an emotionally mature adult and will manifest in the adolescent either developing into a socially disconnected adult or an adult with an exaggerated sense of self-importance (Erikson, 1950; cited by King, 2004). The theory introduced by Erikson highlighted the importance of parental and peer influence during adolescence with regards to adolescent's identity formation. However, as mentioned earlier, during adolescence peer's influence over the adolescent increases while the parent's influence decreases (Kandel, 1980; Kandel & Andrews, 1987).

Although the different theories of adolescence focus on different opposing forces such as personal development versus evolutionary development (Hall, 1904); sexual development versus society (Freud, 1948); childhood behaviour versus adulthood behaviour (Lewin, 1942) and identity versus confusion (Erikson, 1950), the common denominator is a focus on adolescence as a period of physiological change and psychological confusion. However, this psychological confusion has been theorised to originate in different conflicts: Hall and Freud emphasised the conflict being fought between the adolescent's inner urges and society, whereas Lewin and Erikson emphasised that the conflict cannot mainly be due to the growing inner urges of the *id*, but rather to the necessity of the adolescent finding a new place for himself in society and conflicts arising when the adolescent failed to do so (Seiffge-Krenke, 2010). More specifically, different theories have identified different risk factors generating conflicts during adolescence: whereas Hall and Freud emphasised inner urges (i.e., biological factors) Lewin and Erikson focussed on psycho-social factors (with Lewin paying more attention to the family environment and Erikson paying more attention to the peer environment).

2.1.1 Stages of adolescence. To better identify the levels of adolescent development, adolescence is commonly divided into three stages: early adolescence (9 to 13 years of age), mid-adolescence (13 to 15 years of age) and late adolescence (15 to 18 years of age; Pickhardt, 2009; Steinberg & Levine, 1997). Different processes take place during these stages. Early adolescence is marked by increased conflict with parents, increased influence of the peer group and desire for independence (AACAP, 2011). Mid-adolescence is defined by the tendency to distance oneself from the parents, the growing need for independence, and the tendency to increasingly rely on friends, whereby popularity can be an issue (AACAP, 2011). Finally, late adolescence is defined by a firmer sense of identity and increased independence; peer relationships remain important (AACAP, 2011).

2.2 Risk taking in adolescence

In addition to an emerging sense of independence from parents, the adolescent's brain undergoes major developmental changes which are linked to risk taking behaviour and cognitive ability. Steinberg (2010) introduced a model of two neurobiological systems of brain development during adolescence. The interaction of these two systems was theorised to underlie adolescent risk taking behaviour (Steinberg, 2010). The two distinct systems were identified as the "socio-emotional reward system", which is located in the limbic and paralimbic areas of the brain, and the "cognitive control system", which is mainly located in the prefrontal cortex (Steinberg, 2010). According to Steinberg risk taking behaviour in adolescence is stimulated by an immense increase in dopaminergic activity in the socio-emotional reward system around the emergence of puberty.

This increase in hormonal activity precedes the maturation of the cognitive control system as well as the connectivity between the two systems, which gradually unfold over the course of adolescence. The temporal gap between the maturation of the socio-emotional reward system (in early adolescence) and the maturation of the cognitive control system (in late adolescence) defines a period in early and mid-adolescence during which the adolescent is especially prone to engage in risky behaviour (Steinberg, 2010).

In 1991, Jessor introduced a conceptual framework for adolescent risk taking behaviour. This framework proposed that risk behaviours in adolescence were part of the adolescent's choice of lifestyle as these risk behaviours are directly linked to later health and life-compromising outcomes (i.e., limited health, social roles, personal development and preparation for being a functioning adult). Jessor identified three domains of risk behaviour (problem behaviour (i.e., illicit drug use and delinquency), health-related behaviour (i.e., unhealthy eating, alcohol and cigarette use, etc) and school behaviour (i.e., school dropout, truancy; Jessor, 1991)). Furthermore, the conceptual framework identified five separate, albeit related, domains creating a *web of causation* for risk behaviour: biology/genetics (i.e., family history of substance abuse, early pubertal timing), social environment (i.e., low socioeconomic status, ethnic inequality), perceived environment (i.e., conflicts with parents and friends), personality (i.e., low self-esteem, mental disorders) and behaviour (i.e., high levels of substance use, poor school work; Jessor, 1991).

Ponton (1997) stated that risk-taking was functional behaviour in adolescence as adolescents tend to experiment with new behaviours in building their identity. Furthermore, adolescents tend to engage in multiple risk taking behaviours, which suggest they are correlated with each other (Ponton, 1997), a view also held by Jessor (1991). This leads to the conclusion that it is uncommon for adolescents to engage in risk behaviours only in one area of their life, but rather such behaviours occur across different domains, which identifies adolescents as a group prone to engaging in multiple risk behaviours (Leather, 2009). Furthermore, risk behaviours in mid- and late adolescence have been linked to health outcomes not only in adolescence but also in adulthood, whereby socioeconomic factors also should be taken into consideration as adolescents from low socioeconomic backgrounds tend to engage in more risk taking behaviours (Raphael, 2013). This phenomenon was earlier discussed by Lempers and colleagues, who found that the link between low SES and increased adolescent risk taking behaviour was indirect via low levels of parental nurturance and inconsistent parental discipline (Lempers et al., 1989).

Substance use has been identified as one of the main risk taking behaviours during adolescence (British Medical Association (BMA), 2003; National Center for Health Statistics, 2011) with adolescents having a greater tolerance for substances than adults, which may increase their risk of heavy use (Jain & Balhara, 2010). Early-onset alcohol initiation (before 13 years) has been associated with increased risk of development of alcohol abuse and dependence (Spear, 2002), as well as cigarette and drug use (Donovan, 2004). Moreover, adolescent-onset substance abuse is characterised by more rapid development of multiple drug dependencies and more severe psychopathology (Spear, 2002; Volkow, 2010).

2.2.1 Substance use in adolescence. According to early research it is important to investigate substance use in adolescence by looking at the substances separately because of the different health and behavioural outcomes in adolescence and adulthood that are linked to each substance (Newcomb & Bentler, 1988). More specifically, alcohol use is seen as more normative in adolescence, whereas cigarette and cannabis use has been more strongly associated with delinquent behaviour (e.g., being a bully; Radliff et al., 2012). Furthermore, excessive alcohol use (regularly drinking more than the recommended daily limits of 3-4 units for men and 2-3 units for women) has been linked to liver damage, reduced fertility, high blood pressure and increased risk of various cancers and heart disease (National Health Service (NHS), 2012). Cigarette smoking has been linked to more than 50 health conditions (i.e., lung and various other cancers, heart disease; NHS, 2012). Finally, chronic cannabis use impacts on learning and memory where the consequences can last for years when excessive use took place during adolescence, while furthermore there is also an increased risk of heart disease and mental health problems (National Institute on Drug Abuse (NIH), 2012).

Alcohol was reported to be the substance most frequently used amongst adolescents and initiation of alcohol use often takes place at family events (United Nations, 2003). There is a need, therefore, to consider the influence of parents on children's substance use. A report by Battaglia (2009) about the National Survey of American Attitudes on Substance Abuse: Parents and Teens highlighted the importance of parental attitudes towards substance use. It also reported that adolescents who had seen their parents drunk were more than twice as likely to get drunk and three times more likely to smoke cigarettes and use cannabis (Battaglia, 2009). Additionally, this report indicated that adolescents, who thought their fathers approved of their alcohol use, were two and a half times more likely to get drunk compared to adolescents thinking their fathers disapproved (Battaglia, 2009). Five percent of girls aged 12-15 years (9% of boys in the same age range) had their fathers' approval with regard to alcohol use. This percentage increased to 13% for girls aged 16-17 years and to 20% for boys in the same age range (Battaglia, 2009). The report also highlighted the importance of parents' expectations regarding their children's substance use. As part of the survey it was found that nearly all parents said that it was important to them that their adolescents would not use cannabis, however only about 50% of parents believed that their adolescents would never try cannabis. This attitude towards their children's substance use might lead to increased risk of adolescents trying drugs as it was found that adolescents, whose parents thought it very likely that their children would try drugs, were ten times more likely to try cannabis compared to adolescents whose parents thought it unlikely that their children would try drugs (Battaglia, 2009). More specifically, the report concluded that parents' permissive attitudes towards their children's substance use enabled the adolescents to engage in increased alcohol, cigarette and cannabis use (Battaglia, 2009).

It is also important to consider the different aetiologies of alcohol, cigarette and cannabis use. There is considerable evidence to indicate that substance use is influenced by genetic and environmental factors. Genetic factors refer to biological differences that may make someone more or less prone to engage in substance abuse, whereas environmental factors refer to social influences from parents and peers (i.e., impact of parental attitudes towards substance use, peer pressure, etc). Fowler and colleagues (2007) reported that alcohol initiation was mainly explained by environmental influences (74%) compared to genetic influences (26%). Similarly, cigarette initiation was also primarily explained by environmental influences (59%) compared to genetic influences (41%), as was cannabis initiation (65% for environmental influences compared to 35% for genetic influences; Fowler et al., 2007). These percentages highlight the importance of looking at the effect of various domains of environmental factors with regards to adolescent substance initiation as alcohol, cigarette and cannabis initiation were more strongly influenced by environmental factors than genetic factors, which were reported to be more influential on the progression to substance abuse (Fowler et al., 2007). This indicates that environmental interventions may have a greater impact at the initiation stage (e.g., adolescence).

The research conducted for this thesis examines alcohol, cigarette and cannabis use separately. The next section describes prevalence rates as well as prevention and treatment approaches for these substances to provide a full overview of these different substances.

2.2.2 Alcohol use in adolescence. Alcohol is the most frequently used substance during adolescence in both the United Kingdom (British Medical Association (BMA), 2003) and the United States (National Center for Health Statistics, 2011). UK statistics for 2010 showed that among 11–15 year olds in England, 13% had drunk alcohol in the last week (Wright, 2011). The European School Survey Project on Alcohol and other Drugs (ESPAD; Hibell et al., 2011) collected substance use data from 15–16 year-olds in 36 European countries. An average of 87% of students had used alcohol in their lifetime and 57% had used alcohol in the month prior to the survey. In terms of intoxication, which was defined as “staggering when walking, not being able to speak properly, throwing up or not remembering what happened”, 47% of respondents reported having been intoxicated at least once in their lifetime. The UK was amongst the two countries with the highest percentages of students who had been intoxicated ten times or more in their lifetime. Denmark had the highest percentage with 21% followed by the UK with 18%. US statistics indicated that in 2010 15% of 13–14 year olds had used alcohol in the past month.

In the UK over the last 20 years the price of alcohol has been rising at the same rates as other consumer goods, but general income has risen faster. Also, alcohol is sold in supermarkets across the UK (NICE, 2010). These two facts make alcohol an affordable and easily accessible product. Although it is illegal to sell alcohol to minors in the UK, access is still possible via older family members and acquaintances.

The National Treatment Agency (NTA) reported in 2013 that the costs of alcohol-related harm sum to about £3.5 billion a year in England (NTA, 2013). 1.2 million hospital admissions due to alcohol-related causes were reported for 2010/11 and 15,500 people were estimated to have died from alcohol-related causes in 2010 (NTA, 2013). These figures highlight the need to reduce alcohol abuse, especially in young people. High levels of alcohol use in adolescence have been linked to increased risk of developing alcohol dependence in adulthood, drink driving, unsafe sex and abnormalities in the brain development (Australian Drug Foundation (ADF), 2013; Brown & Tapert, 2004; Chambers et al., 2003).

To prevent alcohol-related disorders in the UK several government policy initiatives and public service agreements have been introduced since 2004 some of which focus on adolescent alcohol use prevention e.g.,: "PSA (Public Service Agreement) 14: increase the number of children and young people on the path to success" (2007) and "Youth alcohol action plan" (2008) (NICE, 2010).

2.2.3 Cigarette use in adolescence. UK statistics from 2010 indicated that 5% of the 11-15 year olds were regular smokers (Wright, 2011). The ESPAD report, comparing data of 15-16 year olds from 36 European countries, indicated that an average of 54% of students had smoked cigarettes in their lifetime and 28% reported smoking cigarettes in the month prior to the survey, whereby it was reported that the countries with high lifetime-prevalence rates for having tried smoking cigarettes were likely to have high rates of cigarette smoking during the last 30 days (ESPAD, 2011). US statistics indicated that in 2010 7% of 13-14 year olds had used cigarettes in the past month (National Center for Health Statistics, 2011). Fact sheets by Action on Smoking and Health (ASH) reported in 2013 that the costs of disease related to cigarette smoking range from £2.7 to £5.2 billion a year in England (ASH, 2013). 460,000 hospital admissions among adults older than 35 years of age due to cigarette smoking-related causes were reported for 2010/11 with about 100,000 people having died from these causes in the UK (ASH, 2013). The National Institute for Health and Clinical Excellence (NICE) has placed emphasis on reducing cigarette smoking in adolescents (NICE, 2010), as the addictive nature of nicotine is higher in adolescents than in adults (Karpinski et al., 2010). Furthermore it has been reported that 1 out of 3 young people, who become regular smokers during adolescence, will die of disease related to cigarette smoking (Maine Center for Disease Control and Prevention, 2013). High levels of cigarette smoking in adolescence are associated with a high chance of being a smoker in adulthood, reduced fertility, having multiple sexual partners, delinquent behaviour and increased alcohol and cannabis use (Office of Adolescent Health (OAH), 2013), which highlights the importance of smoking prevention and cessation programs for adolescents.

According to Kring and colleagues (2007) nicotine addiction develops much faster than alcohol addiction. This may mean that if the same amount of people experimented with alcohol and cigarette use, more people would need smoking cessation treatment than alcohol abuse treatment at a later time point (Kring et al., 2007). Smoking cessation programs in adolescence are especially important to prevent negative health outcomes in adulthood as about 90% of adult smokers smoked their first cigarette before age 18 years (Rosen & Sockrider, 2013). In the UK, several smoking cessation treatment possibilities are offered to adults (NICE, 2008). Among the adolescent population, the best success rates of smoking cessation were reported when pharmacotherapy (i.e., nicotine patches, nicotine gums) was combined with counselling (Karpinski et al., 2010).

2.2.4 Cannabis use in adolescence. UK statistics from 2010 indicated that 7% of the 11 to15 year olds had used cannabis in the last month (Wright, 2011). According to the ESPAD report (ESPAD, 2011) 43% of the 15-16 year olds in 36 European countries had used cannabis in their lifetime with 7% having used cannabis in the month prior to the survey. US statistics indicated that in 2010, 7% of the 13-14 year olds had used cannabis in the past month (National Center for Health Statistics, 2011). In the UK cannabis is the most commonly taken illicit drug among adolescents (Maddock & Babbs, 2006), however, as shown in the reported prevalence rates, the use of cannabis is relatively low compared to alcohol and cigarettes. This might be due to the lack of availability or the unwillingness of adolescents to break the law as cannabis use is illegal in the UK, US and most of Europe. Nevertheless, according to the American Academy of Child and Adolescent Psychiatry (AACAP) cannabis use prevalence rates recently reached their highest level in 30 years (AACAP, 2012). Adolescent cannabis use is associated with multiple negative health outcomes including short-term consequences (i.e., problems with concentration and memory, accidents, increased alcohol and cigarette use, risky sexual behaviour, etc.) as well as long-term consequences (i.e., decreased motivation, lower intelligence and mental health problems (whereby it is not always possible to know whether the last two were pre-existing); AACAP, 2012).

In the UK, cannabis misuse treatment is mostly based on psychological therapies: motivational interviewing, cognitive-behavioural therapy and relapse prevention (Maddock & Babbs, 2006). In the US, four strategies of treating cannabis misuse in adolescence have been introduced: the first strategy is a combination of motivational enhancement therapy and cognitive-behavioural therapy, the second strategy consists of generating a family support network for the adolescent cannabis user, the third strategy consists of an adolescent community reinforcement approach providing the user with coping skills, and the fourth and final strategy consists of multidimensional family therapy (Cannabis Youth Treatment Series (CYS), 2001). A study about treatment efficacy by Ramchand and colleagues (2011) reported that the first of these strategies (combination of motivational enhancement therapy and cognitive-behavioural therapy) is as effective as the others and also relatively cost-effective.

2.3 Pubertal timing

Puberty can be defined as the period in adolescence during which the body reaches sexual maturation (Kliegman et al., 2007). This period is based on transition and change in a young person's life as the body develops towards reproductive maturity. Due to these changes experienced by the adolescent, puberty can be a confusing time and has been linked to increased risk of substance use (NHS, 2010). Research on puberty has focussed on two distinct assessments of development: *pubertal status* and *pubertal timing*. Puberty is defined by different stages and pubertal status refers to an adolescent's specific stage of development. The oldest, and one of the most used measures of pubertal status in research studies, is Tanner staging (Marshall & Tanner, 1969, 1970). This method allows for categorisation of the adolescent into one of the five Tanner stages (Stage I representing pre-adolescence and Stage V representing mature physique) based on the adolescent's pubic hair and breast /male genitalia development, whereby body drawings are provided to help identify an adolescent's correct stage. The most reliable assessment is achieved when a General Practitioner or a trained nurse conduct the staging through physical examination; however as this is time- and money-consuming researchers often rely on the parent report or child self-report (Dorn et al., 2003; Owen Blakemore et al., 2009; Turner et al., 1998). Even though Tanner staging is seen as the gold standard for identifying the stage of pubertal development, it still has shortcomings. First, these stages were developed for Caucasian adolescents, which might skew assessment in other ethnic groups. Furthermore, it was based on adolescents with normal body weight; therefore overweight girls are likely to be misclassified as being in a more advanced stage, due to use of pictures of breast development (Blakemore et al., 2010).

In contrast to pubertal status, which refers to the adolescent's stage of pubertal development at a point in time, pubertal timing refers to the onset of the adolescent's development relative to same-age peers. Research on puberty has focussed on off-time versus on-time pubertal development. Off-time development is further subdivided into early pubertal development (or precocious puberty) and late pubertal development (or delayed puberty). In this thesis, consistent with Alsaker, the term *early maturer* will be used for the approximately 10-15% of adolescents who mature early compared to their same-age, same-sex peers and the term *late maturer* for the approximately 10-15% of adolescents who mature late compared to their same-age, same-sex peers (Alsaker, 1996). The age at menarche has been identified as the best marker of female pubertal development (Marshall & Tanner, 1969). According to a girl's age at menarche, she can be categorised into one of the following categories: early pubertal timing (girls who experienced menarche before age 12 years), on-time pubertal timing (girls who experienced menarche between age 12 and 13 years) and late pubertal timing (girls who experienced menarche after age 13 years) (Joinson et al., 2011; Stice et al., 2001; Tam et al., 2006). Evidence shows that not pubertal status *per se*, but rather pubertal timing relative to the peer group (more specifically off-time pubertal timing) represents a risk factor for adolescent substance use (Alsaker, 1996; Buck et al., 2008).

According to Peskin's *early timing hypothesis* early maturers are at increased risk of early substance initiation because they are less well prepared for pubertal change (Peskin, 1973). It has been hypothesised that the higher risk of substance use in early maturing girls is due to their maturational dys-synchrony, which can result in incongruity in the timing of hormonal, physical, psychological and social processes occurring during puberty (Dawes et al., 2000). More specifically, because of their body development an early maturing adolescent may engage in more mature behaviour compared to same-aged peers; however they are less likely to have the maturity of cognitive and emotional control (see section 2.1). Thus, there is dys-synchrony between the mature appearance of the early maturing adolescent's body and their still limited emotional and cognitive resources. This maturational dys-synchrony can increase vulnerability to environmental stressors such as conflict with the parents or peer pressure (Dawes et al., 2000).

Early maturation in girls has been associated with increased alcohol use and abuse (Arim et al., 2011; Bratberg et al., 2007; Costello et al., 2007; Gaudineau et al., 2010; Martin et al., 2002; Patton & Viner, 2007). For example, 40% of early-maturing girls experienced early alcohol initiation (before age 13; Dick et al., 2000), thus increasing the risk of later alcohol dependence (Costello et al., 2007). Early maturation in girls has also been linked to increased risk of cigarette smoking (Arim et al., 2011; Bratberg et al., 2007; Dick et al., 2000; Jean et al., 2011; Patton & Viner, 2007). The need to take into account more complex inter-relationships, when studying the links between pubertal timing and substance misuse is illustrated by a paper by Pedersen and colleagues, who reported that the association between early maturation and cannabis use in girls appeared to be indirect, via delinquency (Pedersen et al., 2001). Two studies, focussing on late pubertal maturation, found that by late adolescence late maturing girls did not differ from on-time and early maturing girls with regards to substance use (Berg-Kelly & Kullander, 1999; Patton & Viner, 2007). These findings would indicate that early maturing girls may no longer be at increased risk of substance use compared to the other maturation groups once they reach late adolescence. I will return to this interesting notion and the implications associated with it later in this dissertation.

For boys, with the exception of one study (Arim et al., 2011) previous research has indicated that early maturation is related to higher levels of substance use in general (Alsaker, 1995; Dick et al., 2001; Downing & Bellis, 2009; Graber et al., 2004; Martin et al., 2002; Michaud et al., 2006) as well as higher levels of alcohol use and abuse (Bratberg et al., 2007; Costello et al., 2007) and cigarette use (Bratberg et al., 2007). Arim and colleagues (2011), however, reported no difference in alcohol and cigarette use between boys who experienced early maturation compared to those who did not. More papers have studied late maturation among boys (*n* = 4) than among girls (*n* = 2), but the findings are inconsistent. Reviews by Alsaker (1996) and Waylen and Wolke (2004) reported higher levels of substance use in late maturing boys compared to on-time maturing boys. In contrast, longitudinal studies by Berg-Kelly & Kullander (1999) and Graber et al. (2004) reported lower levels of substance use in late maturing boys compared to on-time maturing boys in adolescence (whereby specific age cut-offs for on-time and late pubertal timing were not given in all studies). Graber et al. (2004), however, reported that late maturing boys were at greater risk of alcohol abuse in young adulthood, suggesting a catch-up effect. Such findings highlight the value of follow-up studies beyond the adolescent years. Furthermore, substance use patterns in late adolescence have health consequences extending into adulthood (McCambridge et al., 2011; McCarty et al., 2004; Newcomb & Bentler, 1987; Viner & Taylor, 2005) as well as consequences regarding education, work, romantic relationships, and global adaptation in adulthood (Englund et al., 2012). Resolving whether links between early pubertal timing and higher levels of substance involvement extend into late adolescence may have implications for developing practice and policy aimed at prevention (McCarty et al., 2004; Viner & Taylor, 2005). Indeed, identifying the risk factors underlying increased substance use in late adolescence is a potentially important step in preventing substance abuse in adulthood.

2.4 Parent-adolescent relationship quality

During adolescence the dynamics change within a family as the adolescent loosens the bond with the parents and gains in autonomy (i.e., seeking the right to make their own decisions about what to wear, how to spend their money, who they spend their time with, etc; Geuzaine et al., 2000). This means that some aspects of family functioning change to accommodate the adolescent's new sense of autonomy (Geuzaine et al., 2000), which is shown in the decrease of parental monitoring and parent-adolescent communication and often also in the increase of parent-adolescent conflict due to the fact that the adolescent as well as the parent need to adjust to this decrease in dependence (Galambos & Almeida, 1992; Molina & Chassin, 1996). However, this does not mean that the parent-adolescent relationship ceases to exist once the child becomes an adolescent, but the effect of the parent-adolescent relationship quality may combine with the effect of peer behaviour to influence adolescents' behaviour (Geuzaine et al., 2000). During adolescence, one important role of the parent is to manage structure and reduce potential negative influences on the adolescent. To be effective in this role parents need to have positive relationships with their adolescents, meaning low levels of conflict and high levels of positive communication (Dishion et al., 2004). Indeed, the parents still exert an influence, whether negative or positive, on the adolescent's choices, including their substance use (Brody & Ge, 2001; Dishion et al., 2004; Kaltiala-Heino et al., 2011) and nurturing family environments, especially family connectedness, can provide protection against negative health outcomes (including substance use; Viner et al., 2012) during this period.

Among family variables, the parent–adolescent relationship in particular has received research attention, with different studies highlighting the importance of looking at parent-adolescent communication, parent-adolescent conflict and parental monitoring (e.g., Shelton et al., 2008; van den Bree, 2005). Parent-adolescent communication refers to the willingness of adolescents to communicate with their parents about events happening in their life. Parent-adolescent conflict refers to the level of discussions between the adolescents and the parents regarding different aspects of the adolescent's life (i.e., spending of money, adolescent's appearance, chores, etc.), whereas parental monitoring refers to the knowledge the parents have about what their adolescent is doing when not at home and with whom the adolescent spends his spare time. Study results indicate that low levels of parent–adolescent communication and low levels of parental monitoring are associated with increased adolescent substance use (Dishion et al., 2004; Kaltiala-Heino et al., 2011). As part of the Edinburgh Study of Youth Transitions and Crime it was reported that parental monitoring, parental communication and levels of parent-adolescent conflict showed the strongest associations, of eight different family functioning factors, with substance use in late adolescence (age 15 and 17 years; McVie & Holmes, 2005). A possible explanation for these findings is that parent–child relationships that are non-supportive or characterised by conflict can undermine adolescents' ability to regulate their behaviour in a goal-orientated way, with low levels of self-regulation associated with greater risk of alcohol use (Brody & Ge, 2001). Adolescents from non-supportive homes may also be more likely to engage with deviant peers to gain social support and a sense of belonging (Weichold & Silbereisen, 2006). It has also been suggested that adolescents use substances as a way to cope with family relationships characterised by hostility and low levels of warmth and affection (Shelton & van den Bree, 2010).

On the other hand, a cross-sectional study by Ge and colleagues (2002) of African American children identified positive parenting as a protective factor in the relationship between early pubertal maturation and affiliation with deviant peers. They reported that early maturing adolescents affiliated with deviant peers less when they received supportive–involved parenting and more when they received harsh–inconsistent parenting. Taken together, although theorists have argued that adolescence represents a period of development when young people seek autonomy from their parents in key aspects of decision making, research consistently highlights links between parent-adolescent relationship quality and adolescent well-being, including levels of substance use.

2.5 Deviant peer behaviour and adolescent well-being

Creating and maintaining relationships with peers is an important developmental task of adolescence. These close relationships allow a strong influence of the peers on the adolescent, which can be either positive or negative (Viner et al., 2012). According to the Oxford Dictionaries deviance is defined as a state not within the standards of social acceptance (Oxford Dictionaries, 2014). With regards to peer deviance this can be seen as associating with peers who engage in high levels of substance use (not within the norms of age appropriateness) or show delinquent behaviour (showing aggression towards people and animals, deliberately destroying others' property, rule breaking, lying and stealing). Associating with prosocial peers is linked to positive health outcomes (functioning as a protective factor against violent and risky sexual behaviour) whereas associating with deviant peers is linked to negative health outcomes (including risky sexual behaviour, violence and substance use; Viner et al., 2012). Two theories have been used to explain the relationship between deviant peer behaviour and adolescent substance use: the *social learning theory* and the *developmental theory*.

Social learning theory was introduced by Albert Bandura in the early 1970s and states that people learn from each other by observing, imitating and modelling behaviour (Bandura, 1971). According to this theory, individuals learn to take substances in groups (Bahr et al., 2005). During adolescence research attention is given to the peer group, especially to peers' substance use, due to the importance adolescents place on peers while they gain autonomy from the parents (Bahr et al., 2005). The importance of focussing on the peer group was also highlighted by Kandel (1980), who reported that although parent-adolescent relationship and peer behaviour both influenced adolescents, peer behaviour might be the stronger influence of the two in relation to adolescents' substance use in late adolescence. This might be due to the adolescent's growing sense of autonomy and independence from the parents.

As adolescents gain autonomy from their parents their peers represent the primary role model for the adolescent's identity formation (see section 2.1). The *developmental theory* poses that during adolescence, parental influence (in terms of forming opinions, beliefs and behaviours) decreases and the influence of the peer group increases. However, this does not mean that the parents' influence on the adolescent completely ceases during adolescence, but rather that there is interplay between both sets of influence, whereby the strength of each changes during the course of adolescence. This change might be due to the adolescent's increasing sense of autonomy from the parents, whereby the peer group increasingly gains influence as the role model for the adolescent's identity formation (Kandel & Andrews, 1987; Wood et al., 2004).

These two theories are important frameworks for this thesis as they both focus on the importance of the peer group in adolescence. While the *developmental theory* focusses on the increasing influence of the peer group during adolescence the *social learning theory* highlights that behaviour is learned by observing, imitating and modelling the ones closest to us. As the peer group gains in influence over the course of adolescence (Kandel & Andrews, 1987; Wood et al., 2004), the adolescent tends to imitate the behaviour of the peers he associates with. More specifically, associating with deviant peers often leads to the adolescent adopting deviant behaviours (including substance use). Additionally, as mentioned in section 2.2, adolescent risk taking behaviour can be explained by the discrepancy in time between the development of the socio-emotional reward system and the cognitive control system. The socio-emotional reward system, which motivates the adolescent to engage in behaviours providing a reward (i.e., fun, popularity within the peer group, etc.), develops in early adolescence while the cognitive control system, which provides the adolescent with the cognitive ability to resist/control rewarding behaviour, develops in late adolescence (Steinberg, 2010). This identifies the time span of early and mid-adolescence as a critical period during which the adolescent is easily influenced by the peer group (Albert & Steinberg, 2011; Steinberg & Monahan, 2007). Moreover, research shows that associating with peers heightens the sensitivity of the socio-emotional reward system and therefore increases the chance of engaging in risk taking behaviours (Chein et al., 2011). This heightened sensitivity is explained by an increasing density of hormone receptors in the brain in the beginning of adolescence (Spear, 2009). Furthermore, a study by Blakemore (2008) showed that adolescents show increased activity in the socio-emotional reward system as a response to social stimuli (i.e., pictures of facial expressions and feedback from peers) compared to children and adults. Given these findings, being aware of the presence of peers might provide enough stimuli to increase activation in the socio-emotional reward system and therefore lead to increased risk taking behaviour in adolescence (Chein et al., 2011).

Among peer deviance factors, the number of substance using peers and delinquent friends have been identified as relevant predictors of substance use in adolescence, with similar effects found for close friends and classmates (Ali et al., 2011), which is worrying for schools and youth groups as this suggests the possibility of deviant behaviour being adopted through “contagion effects”. Research has shown that having many substance using peers is linked to increased levels of adolescent substance use (Ali et al., 2011; Ary et al., 1999; Branstetter et al., 2011; Cruz et al., 2012; Ellickson et al., 2001; Engels & Diehr 2004; Glaser et al., 2010; Kokkevi et al., 2007; Korhonen et al., 2008; Monahan et al., 2009; Urberg & Luo, 2003; Wood et al., 2004), and similarly having delinquent peers has also been related to increased levels of adolescent substance use (Skinner et al., 2009; Westling et al., 2008). These findings support the *social learning theory* and the *developmental theory* as they clearly suggest that peers have an influence on adolescents (as proposed by the *developmental theory)* and that having deviant peers leads the adolescent to engage in deviant behaviour (as proposed by the *social learning theory*).

2.6 Parent-adolescent relationship quality, pubertal timing and adolescent substance use

According to Ge et al.’s *contextual amplification theory*, social processes (e.g., parenting) interact with pubertal transition to increase the risk of adjustment problems (e.g., externalizing problems, substance use; Ge et al., 2002). It has been reported that family functioning and pubertal timing interact to put early maturing adolescents at increased risk of substance use (Ge et al., 2002). Early maturation is argued to curtail the time available to adolescents to acquire and assimilate skills that allow them to adapt successfully to stressful experiences (Ge et al., 2002). Consistent with this interpretation, research shows that the parent–child relationship in the families of early maturing boys and girls is characterised by more conflict and a greater reduction in closeness in the early and mid-adolescent years compared to families with later maturing adolescents (Ge et al., 2002). In this context, early pubertal maturation may be seen as a risk factor for premature disengagement from the family, which is intensified by harsh and inconsistent parenting behaviour and decreased by supportive and involved parenting behaviour (Ge et al., 2002). This theory provides a framework to understand the interplay between pubertal timing and family functioning in the aetiology of substance use.

In light of the evidence reviewed in sections 2.1-2.3, documenting the main effects of parent-adolescent relationship quality and pubertal timing, respectively, I set out to review systematically the literature on the inter-relations between the psychosocial context of family life, pubertal timing and substance use (Hummel et al., 2013). This systematic review is reported in Chapter 3.

If adolescents who experience both poor-quality relationships with their parents and off-time pubertal development are at particularly increased risk of development of substance use disorders, as suggested by the studies in the systematic review (Hummel et al., 2013), this group needs to be a focus of prevention approaches. However, as I will report later, the number of studies undertaken to date is small and many issues (especially, the underlying mechanisms (i.e., mediation, moderation, see section 4.2.1) of these effects and whether additional factors play a role) remain unclear. To my knowledge, no study has focussed on the role of pubertal timing in alcohol, cigarette and cannabis use in adolescence separately as well as on the distinct domains of parent-adolescent communication, parent-adolescent conflict and parental monitoring within a single study. The importance of looking at substances separately is evidenced by the different prevalence rates and aetiologies of the substances (see sections 2.2.1 to 2.2.4), whereas the relevance of focussing on parent-adolescent communication, parent-adolescent conflict and parental monitoring was discussed in section 2.4.

2.7 Peer deviance, pubertal timing and adolescent substance use

Early maturing girls show a frequent pattern of socialising with older peers (Dawes et al., 2000). This might be explained by the *maturation disparity hypothesis* (Ge & Natsuaki, 2009; Moffitt, 1993), which states that girls' changing physical appearance during puberty creates an environment of new social experiences (especially risk taking behaviours such as delinquency and sexual behaviours). Early maturing girls are at higher risk in the context of these experiences, because they have lower levels of emotional and cognitive resources compared to same-aged girls who enter puberty at a later age (Ge et al., 2002). This may lead them to engage in behaviours such as experimental substance use that are age-normative for the peer group, but not for the girls themselves (Stattin & Magnusson, 1990). Marklein and colleagues reported that early maturing girls had more friends using substances than on-time and late maturing girls, which is a possible explanation for early maturing girls' increased substance use (Marklein et al., 2009). It was reported that early maturing boys may not be exposed to equivalent risks because their advanced physical development confers higher status in the peer group, due to their relative better achievements in athletics compared to same-aged peers (Kindlundh et al., 2001).

Negriff and Trickett (2012) reported that the effect of pubertal timing on alcohol and cannabis use at age 13 was mediated by peers' alcohol and cannabis use at age 12 while adjusting for earlier own and peers' alcohol and cannabis use. Marklein and colleagues (2009) looked at the interaction of pubertal timing, peers' cigarette use and girls' alcohol, cigarette and cannabis use in late adolescence but no effects were found. Biehl and colleagues (2007) found that the number of friends who drink alcohol moderated the effect of pubertal timing on alcohol use at age range 12-16 years; that is early maturing girls used more alcohol when they had more friends who drank alcohol.

However, to my knowledge no study has examined the role of pubertal timing in alcohol, cigarette and cannabis use separately with regards to adolescent substance use and the following relevant individual factors of peer deviance (the number of alcohol drinking, cigarette smoking and cannabis using peers as well as having peers with conduct problems) within one study. The importance of including peers' substance use as well as peers' delinquency was highlighted in section 2.5.

2.8 Parent-adolescent relationship quality, peer deviance, pubertal timing and adolescent substance use

Only two studies have focussed on the interplay of parent-adolescent relationship quality, peer deviance and pubertal timing on substance use in adolescence. Westling and colleagues (2008) reported that affiliation with deviant peers mediated the effect of pubertal timing on trying alcohol in mid-adolescence for girls with poor or average parental monitoring compared to high parental monitoring. Similarly, Ge and colleagues (2002) reported that affiliation with deviant peers mediated the effect of pubertal timing on conduct problems in early adolescence for girls and boys experiencing harsh-inconsistent parenting compared to nurturing-involved parenting. Taken together, these studies indicate that there are combined effects of pubertal timing, parent-adolescent relationship quality and peer deviance with positive parent-adolescent relationship qualities acting as a protective factor in the relationship between timing and affiliation with deviant peers. However, with regards to substance use in adolescence only one study (Westling et al., 2008) focussed on these combined effects in predicting adolescent substance use.

Within this chapter I have introduced the individual impacts of pubertal timing, parent-adolescent relationship quality and peer deviance on substance use in adolescence. Additionally, I reviewed studies which focussed on the combined effects of these factors on adolescent substance use. The final paragraph (section 2.8) highlighted that there are only two studies looking at the combined effects of pubertal timing, parent-adolescent relationship quality and peer deviance (Ge et al., 2002; Westling et al., 2008), with only the study by Westling and colleagues (2008) focussing on the interplay of these factors in predicting adolescent substance use. Due to the importance of establishing what the causes of adolescent substance use are, additional research is warranted to disentangle the combined effects of pubertal timing, parent-adolescent relationship quality and peer deviance on substance use in adolescence, and this is what this PhD aims to achieve.

CHAPTER 3: SYSTEMATIC REVIEW OF PUBERTAL TIMING, PARENT-ADOLESCENT RELATIONSHIP AND SUBSTANCE USE IN ADOLESCENCE[1]

This chapter presents the results of a systematic review of research linking pubertal timing, parent-child relationship quality and adolescent substance use. I conducted the systematic search, read and sorted the search results and wrote the systematic review. The review was published with me as the first author in the journal *Addiction* in March 2013. The co-authors were my doctoral supervisors: Dr Katherine Shelton, Dr Jon Heron, Prof. Laurence Moore and Dr Marianne van den Bree. Each provided helpful comments and contributions.

The inclusion of deviant peer factors was decided in the progress of this PhD, therefore, as this systematic review was the first step of the PhD, deviant peer behaviour was not included in this systematic review.

3.1 Rationale for the systematic review

Compared to a narrative review, a systematic review is preferable as it provides a summary of the published reports to answer a specific research question using explicit methods with regards to search, appraisal and reporting of findings (Akobeng, 2005). A meta-analysis takes a systematic review one step further by reanalysing individual studies using established statistical methods (Akobeng, 2005). To conduct a meta-analysis, individual studies need to be pooled quantitatively, which is only possible if similar assessments were used across the studies. However, as parent-child relationship factors

[1] Hummel, A., Shelton, K. H., Heron, J., Moore, L., & van den Bree, M. B. M. (2013). A systematic review of the relationships between family functioning, pubertal timing and substance use in adolescence. *Addiction, 108*(3), 487-496.

and adolescent substance use were differently assessed across most studies, this approach was not possible for this PhD project.

Therefore, I set out to systematically review the literature on the inter-relations between the psychosocial context of family life, pubertal timing and substance use. The systematic review addresses a gap in the literature, because previous reviews have focussed either on the relationship between family functioning and adolescent substance use (Dawes et al., 2000; Donovan, 2004; Enoch, 2011; Henricson & Roker, 2000) or on pubertal timing and adolescent substance use (Celio et al., 2006; Patton & Viner, 2007; Short & Rosenthal, 2008; Waylen & Wolke, 2004), but not on the possible inter-relationships between all three factors. Thus, it remains unclear to what extent the links between family functioning and adolescent substance use may be explained by pubertal timing and vice versa. Elucidating these issues will have important implications for prevention strategies, as groups especially at risk (i.e., early maturing adolescents and high risk family environment) will be identified. Furthermore, with the exception of the reports by Celio and colleagues (2006; which focussed on early pubertal timing as risk factor for aggressive and delinquent behaviour in adolescent girls) and Patton and Viner (2007; which focussed on the link between health and pubertal transition), which took place a number of years ago, previous reviews have been non-systematic.

The systematic review aimed to answer the following research questions:

1. Is early pubertal maturation associated with increased substance use for males and females?

2. Is there a stronger relationship between poor parent-adolescent relationship quality and substance use for early maturing adolescents compared to late maturing adolescents?
3. Does parent-adolescent relationship quality influence pubertal timing and vice versa in the prediction of substance use?

3.2 The systematic search

The systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. The PRISMA statement consists of a 27-item checklist, which gives exact instructions on how to conduct and report the systematic search as a guideline for authors to ensure the highest standards in systematic reviews (Moher et al., 2009). One important part of the PRISMA statement is the instruction of creating a four-phase flow diagram, reporting the exact steps of sorting the results of the systematic search. As specified by the PRISMA statement the search terms (shown in Table 1) and the exclusion criteria for selecting the relevant articles were specified prior to the search. Five exclusion criteria were specified: animal studies, studies based on clinical samples (i.e., off-time pubertal development due to medical conditions), studies with a focus on environmental factors (i.e., off-time pubertal development due to chemical exposure), studies focussing on teenage sexuality/pregnancy and studies based on participants older than 18 years of age. The search was conducted in the data bases Web of Knowledge, PubMed and PsycINFO. In total the search yielded 689 hits (375 hits in Web of Knowledge, 255 hits in PubMed and 59 hits in PsycINFO); an additional hand search of references at google.com yielded another 16 hits. After removing the duplicates 434 articles remained. Screening the titles and abstracts according to the exclusion criteria resulted in removing 362 articles. This step was conducted separately by the first author (Hummel) as well as a second independent researcher. The two researchers had an overall level of agreement of 96%; after a final meeting 100% agreement was achieved. I read the final 72 articles in detail and made final selections according to the exclusion criteria; this resulted in the final inclusion of 58 articles (the four-phase flow diagram reporting the selection process is shown in Figure 1).

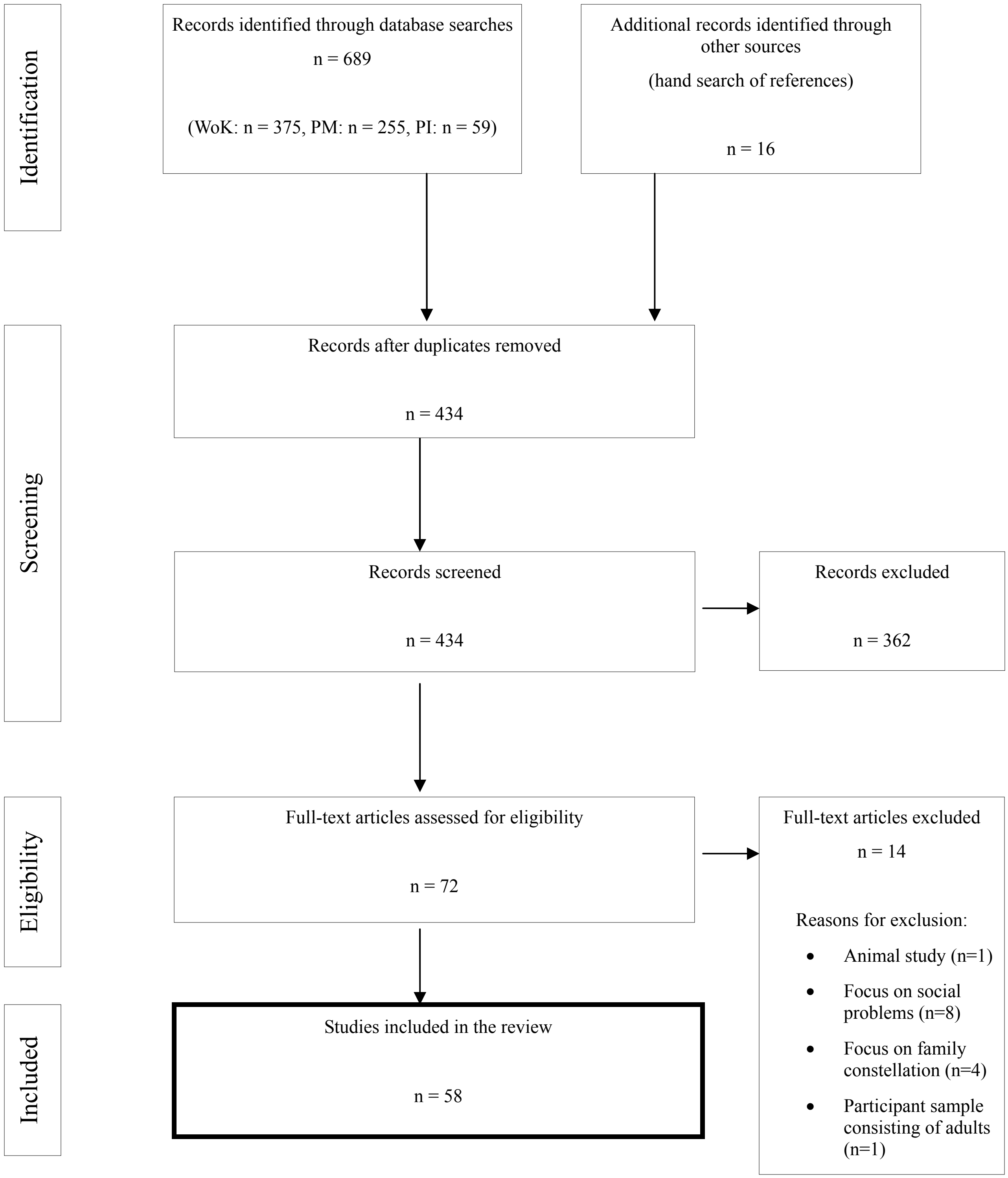
Table 1 Specification of search parameters I

Operator	*Definition*
# 1 Keywords[a]	family OR parent OR sibling[b]
# 2 Keywords[a]	puberty OR menarche
# 3 Keywords[a]	substance OR alcohol OR cigarette OR marijuana OR addiction
# 4 Boolean operator	#1 AND #2 AND #3
# 5 Limits language	English language
# 6 Limits kind of studies	classical article OR comparative study OR evaluation studies OR journal article OR review OR twin study
# 7 Limits subjects of studies	(male OR female) AND (humans) AND (adolescence[c])
# 8 Boolean operator	#4 AND #5 AND #6 AND #7
# 9 Selection	Removal of duplicates and manual exclusion of articles not meeting inclusion criteria

[a]The search also included additional related search terms [e.g., parent, parenting, puberty, pubertal, substance, substance use, substance misuse, substance abuse, etc.].

[b]Although theories on family functioning and substance use in adolescence are primarily based on parenting behaviour, I included the search terms “family”, “parent” and “sibling” to capture as many studies assessing the relationship between family functioning and adolescent substance use as possible.

[c]Based on the definition provided by the World Health Organization referring to those aged between 10 and 19 years (WHO, 2008).



Key: WoK = Web of Knowledge; PM = PubMed; PI = PsycINFO

Figure 1. Selection of research for inclusion I

3.3 Results of the systematic search

Fifty-eight papers were included in the review (references marked with * in the reference list), which could be categorised into four categories: pubertal timing and substance use in adolescence, parent-adolescent relationship quality and substance use in adolescence, pubertal timing and parent-child relationship quality and finally pubertal timing, parent-child relationship quality and substance use in adolescence.

3.3.1 Pubertal timing and substance use in adolescence. The literature I reviewed showed a relationship between pubertal timing and substance use in adolescence, with early maturers being at higher risk of using substances than late maturers (Bratberg et al., 2007; Downing & Bellis, 2009). Most papers on pubertal timing and substance use in adolescence (n = 19) assessed effects separately for males and females, so the findings are summarized accordingly.

3.3.1.1 Pubertal timing and substance use in adolescent girls. All studies reported that early maturing girls had higher levels of substance use than on-time maturing girls (Alsaker, 1995; Copeland et al., 2010; Dawes et al., 2000; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Lanza & Collins, 2002; Michaud et al., 2006; Waylen & Wolke, 2004). A number of studies differentiated between substances such as alcohol, cigarettes and cannabis and also between direct and indirect effects. Early maturation in girls has been linked to increased alcohol use and abuse (Arim et al., 2011; Bratberg et al., 2007; Costello et al., 2007; Gaudineau et al., 2010; Martin et al., 2002; Patton & Viner, 2007). It was found that 40% of early maturing girls experienced early alcohol initiation (before age 13 years; Dick et al., 2000), thus increasing the risk of later alcohol use disorder (Costello et al., 2007). Early maturation in girls has also been linked to increased risk of cigarette smoking (Arim et al., 2011; Bratberg et al., 2007; Dick et al., 2000; Jean et al., 2011; Patton & Viner, 2007). Pedersen and colleagues reported that the association between cannabis use and early maturation in girls appeared indirect via links between pubertal timing and delinquency (Pedersen et al., 2001). Two studies found that late maturing girls were not at increased risk of substance use compared to on-time and early maturing girls (Berg-Kelly & Kullander, 1999; Patton & Viner, 2007).

3.3.1.2 Pubertal timing and substance use in adolescent boys. Fewer papers examined pubertal timing in boys (n = 12), and even fewer compared associations between early and late maturing boys. All except one paper (Arim et al., 2011) indicated that early maturation in boys was related to higher levels of substance use (Alsaker, 1995; Dick et al., 2001; Downing & Bellis, 2009; Graber et al., 2004; Martin et al., 2002; Michaud et al., 2006), higher levels of alcohol use and abuse (Bratberg et al., 2007; Costello et al., 2007) and increased risk of cigarette use (Bratberg et al., 2007). Arim and colleagues (2011), however, reported no significant difference in alcohol and cigarette use between boys who experienced early maturation compared to those who did not. More papers have studied late maturation among boys (n = 4) than among girls (n = 2), but the findings are inconsistent. Reviews by Alsaker (1996) and Waylen and Wolke (2004) reported higher levels of substance use in late maturing boys compared to on-time maturing boys. In contrast, longitudinal studies by Berg-Kelly and Kullander (1999) and Graber and colleagues (2004) found lower levels of substance use in late maturing boys compared to on-time maturing boys. Graber and colleagues (2004), however, reported that late maturing boys were at greater risk of alcohol abuse in young adulthood, suggesting a catch-up effect.

3.3.2 Family functioning and substance use in adolescence. The majority of research investigating the relationship between family functioning and substance use has focussed on parenting and parent–adolescent relationships (n = 7). Studies with adolescent samples have indicated that poor parent-adolescent relationship quality predicted initiation of experimental smoking in girls, but not boys (van den Bree et al., 2004); that negative parenting (low levels of mother–child warmth and high levels of mother–child hostility) was associated with increased cigarette use (Shelton et al., 2008); and that boys and girls who undertook more activities with their mothers were more likely to discontinue regular cannabis use (van den Bree & Pickworth, 2005). Kaltiala-Heino and colleagues (2011) focussed on parental monitoring and substance use in adolescents. Their results showed that alcohol, cigarette and cannabis use among boys and girls was associated with lower levels of parental monitoring. This was also reported by Wang and colleagues, who found lower levels of alcohol and cigarette use among boys and girls experiencing higher levels of parental monitoring (Wang et al., 2011). Belsky and colleagues examined the link between early rearing experiences and adolescents' risk-taking in an all-girl sample (Belsky et al., 2010). They reported that high levels of maternal harshness during childhood were related to higher levels of young people's substance use. Brody and colleagues found that fathers engaging in positive problem-solving and effective arguing were more successful in conveying alcohol-related norms to their adolescents (Brody et al., 2000). All seven of these studies used a longitudinal research design; with findings suggesting that family-related factors pre-date, and may therefore contribute to the initiation and progression of adolescent substance use. A review by Donovan (2004) concluded that high levels of parental support were associated with lower levels of alcohol use, while poor quality parent–adolescent relationship was a risk factor for substance use (Dishion et al., 2004), substance abuse (Henricson & Roker, 2000) and early-onset substance initiation (Enoch, 2011). The findings support the conclusion that poor quality parent–adolescent relationships are associated with increased risk of substance use in adolescence.

3.3.3 Pubertal timing and parent-child relationship quality. I found three studies examining the relation between quality of parenting during childhood and pubertal timing. Belsky and colleagues reported that negative parenting during childhood was associated with earlier maturation in girls. The authors proposed an evolutionary theory of socialisation, stating that girls who are reared in more threatening circumstances (i.e., characterised by greater contextual risk and uncertainty) may mature earlier in order to increase the probability of passing on their genes by having offspring (Belsky et al., 2010). Interestingly, in an earlier longitudinal study, this effect had not been found for boys (Belsky et al., 2007) and it also seemed to be more pronounced for girls who had experienced harsh maternal compared to harsh paternal parenting (Belsky et al., 2010). This was the first report indicating that the quality of maternal versus paternal parenting could have a differential outcome in terms of pubertal development. Where previous studies had assessed paternal parenting behaviour based on mothers' reports, Belsky and colleagues (2007) obtained father self-reports and observed father–child interactions and the rigour of this approach may have contributed to the ability to discriminate between the rearing styles of fathers and mothers. The importance of looking at mothers and fathers separately with regards to parent-child relationship quality was also highlighted by Levin and Currie in 2011. Conversely, positive parenting during childhood, as characterised by high levels of parental support, has been associated with a lower probability of early maturation in both boys and girls (Ellis & Essex, 2007). Findings indicated that for parental supportiveness, in contrast to harsh parenting, the relationship with the father might be related more strongly to pubertal maturation than maternal supportiveness for both girls and boys. This supports Ellis' *paternal investment theory* proposing that girls whose biological fathers were present and involved in their daughters' up-bringing were less likely to experience early pubertal maturation (Ellis, 2004). A cross-sectional study by Ge and colleagues (2002) of African American children identified positive parenting as a protective factor in the relationship between early pubertal maturation and affiliation with deviant peers. They reported that early maturing adolescents affiliated with deviant peers less when they received supportive–involved parenting and more when they received harsh–inconsistent parenting. I found only two studies examining the relation between pubertal development and subsequent parent–adolescent relationship quality. Both of these focussed on puberty, rather than pubertal timing. One longitudinal study compared parent–child relationships prior to puberty and subsequently after the onset of puberty and reported a decrease in conflict about chores, appearance and politeness between adolescent and parent, but an increase in conflict about finances and substance use (Galambos & Almeida, 1992). A longitudinal study by Molina and Chassin (1996) investigated differences between white and Hispanic adolescents in the relationships they had with their parents prior to and during puberty. The results showed that pubertal girls reported an increase in conflict and a decrease in support from their mothers, irrespective of ethnic background. Additionally, white (but not Hispanic) pubertal girls reported a decrease in support from their fathers.

White boys reported a decrease and Hispanic boys an increase in parental support with the onset of puberty. Collectively, findings suggest that parenting behaviour during childhood is associated with pubertal timing, especially in girls. Puberty itself appears to influence the parent–adolescent relationship, with one study suggesting cultural differences. Positive parenting in adolescence also appears to function as a protective factor for deviant-peer affiliation.

3.3.4 Pubertal timing, parent-child relationship quality and substance use in adolescence. Six studies examined links between pubertal timing, family functioning and substance use. Two reviews and one longitudinal study reported that early maturing girls experience higher levels of family conflict and substance use than on-time maturing girls (Celio et al., 2006; Short & Rosenthal, 2008; Westling et al., 2008). None of these reports presented findings indicating whether there was any relationship between family conflict and adolescent substance use or examined the interplay between all three factors. Shelton and van den Bree (2010) found that the across-time association between parent–adolescent relationship quality and cigarette use was stronger for late maturing girls compared to early and on-time maturing girls. No effects were observed for early and late maturing boys in pathways between parent–child relationship quality and substance use. Lynne-Landsman and colleagues (2010) conducted a longitudinal study examining the moderating role of family risk, measured in household resources (parental education and family income), stability of household structure (family structure over time) and household conflict (level of conflict in the household, quality of parent–adolescent relationship and parental substance use) on the association of pubertal timing and substance use at age 14 years. Early maturers in the moderate and high-risk family groups were found to have higher levels of binge drinking, cigarette and marijuana use than early, on-time and late maturers in low risk families. Belsky and colleagues (2010) reported direct effects of harsh maternal parenting during childhood on pubertal timing and on substance use in girls; however, no interaction effects were found between the three factors.

3.4 Discussion of the systematic review

I set out to review systematically the published evidence of relationships between parent-adolescent relationship quality, pubertal timing and substance use in adolescence. My first research question was to evaluate the evidence that early maturers are at higher risk of substance use than late maturers. The literature suggested that early maturing girls were at higher risk of substance use compared to on-time and late maturing girls. The literature was less consistent for boys, with some evidence for increased risk of substance use in early maturing boys but varying findings for late maturing boys. My second research question aimed to evaluate the evidence for a stronger relationship between parent-adolescent relationship quality and substance use for early than late maturers. The literature suggested that this may be the case for girls, but was inconclusive for boys. The reasons for the inconsistency in the boys' findings remain unclear. Thirdly, I evaluated the evidence that off-time pubertal maturation predates worsening relations with the parents and subsequent substance use and vice versa. Evidence was found that poor-quality parenting during childhood is associated with early pubertal timing for girls but not for boys, while a single study (Belsky et al., 2007) indicated that this effect may be more pronounced in the context of harsh maternal parenting. Furthermore, puberty itself may also impact upon parent–adolescent relationships, with one study suggesting that these effects may vary between cultures. However, I found no studies examining whether off-time pubertal timing preceded worsening of relationships with the parent. I found two longitudinal studies reporting an interaction between pubertal timing and family functioning with regards to substance use (Lynne-Landsman et al., 2010; Shelton & van den Bree, 2010); however, these findings are mixed, which calls for further longitudinal studies looking at these inter-relationships with regards to their direction over time. However, this review indicates that harsh-inconsistent parenting during childhood is linked to early pubertal maturation, which itself is linked to increased substance use in adolescence. Additionally, supportive-involved parenting in adolescence serves as a protective factor with regards to the association with deviant peers. This highlights the importance of supportive-involved parenting during childhood and adolescence, which supports the *contextual amplification theory* stating that the negative effect of early pubertal maturation on substance use may be reduced in a supportive and involved family environment (Ge et al., 2002).

CHAPTER 4: SYSTEMATIC REVIEW OF PUBERTY, PARENT-ADOLESCENT RELATIONSHIP, PEERS AND ADOLESCENT SUBSTANCE USE

As the systematic review, introduced and discussed in chapter 3, was conducted and published before it was decided to include peers as an additional factor within this PhD project, a second systematic search was conducted, which included peers as an additional factor.

This chapter will report on the systematic search and discuss the findings.

4.1 Rationale for this systematic review

Over the course of this PhD project peers were introduced as an additional factor within the relationship of pubertal timing, parent-adolescent relationship quality and substance use in adolescence. Therefore, the systematic review, which was introduced in chapter 3, provided an incomplete overview of the topic. To offer the full scope of background information for this PhD an additional systematic review was warranted to enlighten the interplay of puberty, parent-adolescent relationship quality and peers with regards to substance use in adolescence. The benefits of a systematic review compared to a regular literature review were already discussed in section 3.1.

4.2 The systematic search

The systematic review was conducted according to the Preferred Items for Systematic reviews and Meta-Analyses (PRISMA) statement (for information see section 3.2). The exclusion criteria were the same as in the earlier systematic review: animal studies, studies based on clinical samples (i.e., off-time pubertal development due to medical conditions), studies with a focus on environmental factors (i.e., off-time pubertal development due to chemical exposure), studies focussing on teenage sexuality/pregnancy and studies based on participants older than 18 years of age. The search terms are presented in Table 2.

The search was conducted in the data bases Web of Science, PubMed and PsycINFO. In total the search yielded 319 hits (231 hits in PsycINFO, 52 hits in PubMed and 36 hits in Web of Science). After removing the duplicates 69 articles remained. Screening the titles and abstracts according to the exclusion criteria resulted in removing 43 articles. The remaining 26 articles were read in detail (the four-phase flow diagram reporting the selection process is shown in Figure 2).

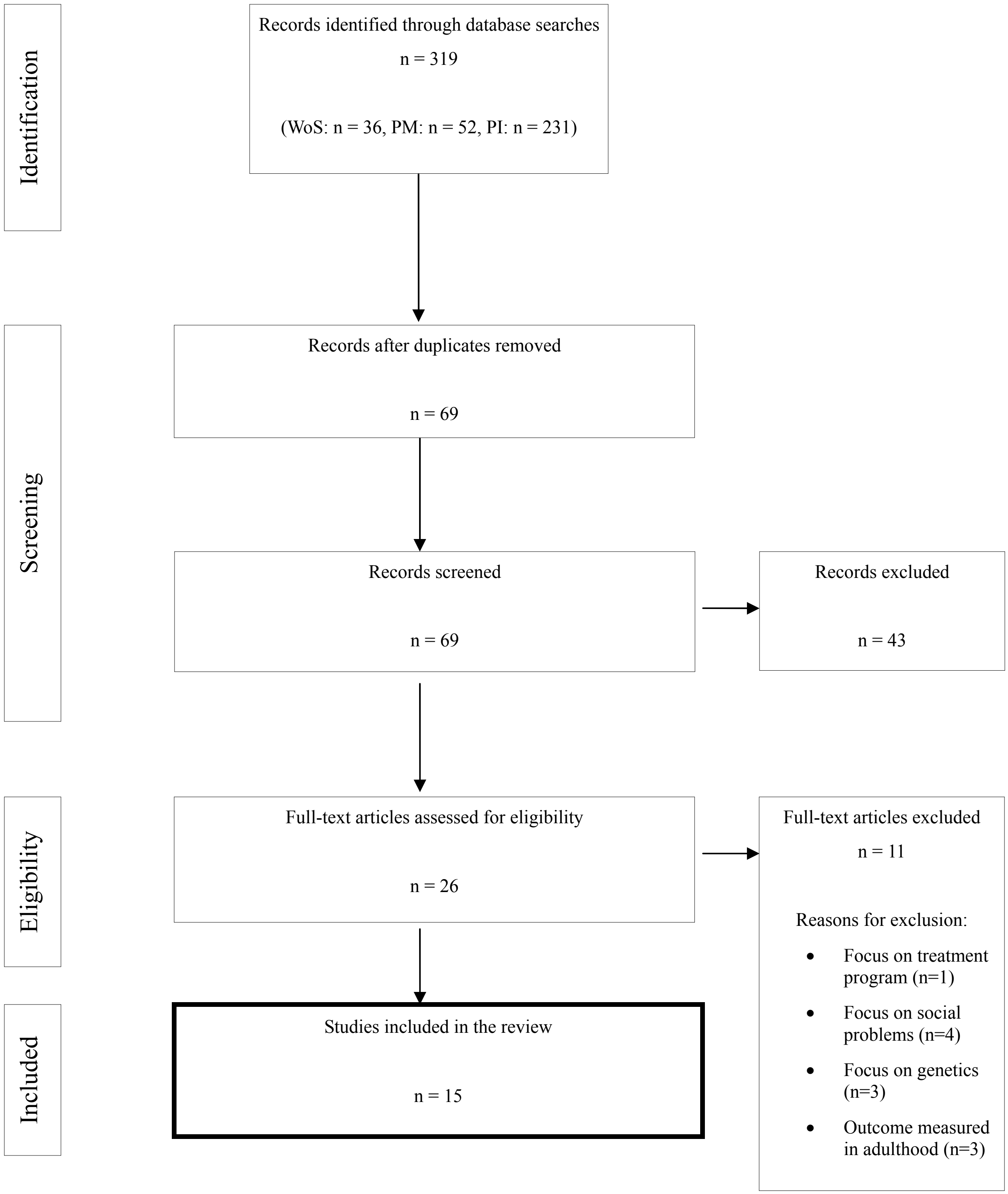
Table 2 Specification of search parameters II

Operator	*Definition*
# 1 Keywords[a]	family OR parent[b]
# 2 Keywords[a]	puberty OR menarche
# 3 Keywords[a]	alcohol OR cigarette OR marijuana OR cannabis
# 4 Keywords[a]	peer OR friend
# 5 Boolean operator	#1 AND #2 AND #3 AND #4
# 6 Limits language	English language
# 7 Limits kind of studies	classical article OR comparative study OR evaluation studies OR journal article OR review OR twin study
# 8 Limits subjects of studies	(male OR female) AND (humans) AND (adolescence[c])
# 9 Boolean operator	#4 AND #5 AND #6 AND #7
# 10 Selection	Removal of duplicates and manual exclusion of articles not meeting inclusion criteria

[a]The search also included additional related search terms [e.g., parent, parenting, puberty, pubertal, friend, friendship, etc.].

[b]Although theories on family functioning and substance use in adolescence are primarily based on parenting behaviour, I included the search terms “family” and “parent” to capture as many studies assessing the relationship between family functioning and adolescent substance use as possible.

[c]Based on the definition provided by the World Health Organization referring to those aged between 10 and 19 years (WHO, 2008).



Key: WoS = Web of Science; PM = PubMed; PI = PsycINFO

Figure 2. Selection of research for inclusion II

4.3 Results of the systematic search

Fifteen papers were included in this review (references are marked with ° in the reference list). These fifteen papers can be categorised into five categories: main effects, interaction of parenting and peer factors, interaction of pubertal timing and peer factors, interaction of pubertal timing and parenting factors, and interaction of pubertal timing, parenting and peer factors.

4.3.1 Main effects. Eight papers reported on the main effects of pubertal timing, parenting and peer factors on substance use in adolescence. It was found that early pubertal timing was linked to earlier alcohol and cigarette initiation (Arim et al., 2011; Dick et al., 2000), higher levels of alcohol, cigarette and cannabis use (Celio et al., 2006; Hummel et al., 2013; Whitesell et al., 2013; Windle et al., 2008) and to a higher likelihood of associating with deviant peers (Kelly et al., 2012). With regards to parenting factors it was reported that lower levels of parent-adolescent relationship quality (e.g., low levels of parental monitoring, low levels of parental warmth and closeness, high levels of parent-child conflict) were linked to higher levels of substance use in adolescence (Hummel et al., 2013; Poikolainen, 2002; Whitesell et al., 2013; Windle et al., 2008). Finally, associating with deviant peers (e.g., having peers using substances without their parents' knowledge) was reported to be linked to higher levels of alcohol, cigarette and cannabis use in adolescence (Poikolainen, 2002; Whitesell et al., 2013; Windle et al., 2008).

4.3.2 Interaction of parenting and peer factors on adolescent substance use. Two studies looked at how parenting and peer factors interact in predicting adolescent substance use. A review by Marschall-Levesque and colleagues in 2014 and a longitudinal study by Dishion and colleagues in 2004 reported that parental monitoring moderated the effect of substance using peers on adolescent substance use. More specifically, having a lot of substance using peers was more strongly linked to high levels of substance use if parental monitoring was low (Dishion et al., 2004; Marschall-Levesque et al., 2014).

4.3.3 Interaction of pubertal timing and peer factors on adolescent substance use. A cross-sectional study by Patton and colleagues in 2004 found that the number of substance using peers mediated the effect of pubertal stage (indicating the process from early to late adolescence) on adolescent substance use. More specifically, the further along in adolescence the adolescent was the more substance using peers did they have and the higher the levels of their own substance use (Patton et al., 2004). Schelleman-Offermans and colleagues reported in their longitudinal study, which was published in 2013, that having a high proportion of substance using peers in the peer group mediated the effect of pubertal timing on the initiation of weekly alcohol use in Dutch adolescents in mid- and late adolescence (Schelleman-Offermans et al., 2013).

4.3.4 Interaction of pubertal timing and parenting factors on adolescent substance use. Waylen and Wolke conducted a review in 2004 and reported that parental monitoring moderated the effect of pubertal timing on anti-social behaviours (including substance use) in adolescent girls. This stated that early maturing girls engaged in higher levels of anti-social behaviours if they experienced low levels of parental monitoring compared to early maturing girls who experienced high levels of parental monitoring (Waylen & Wolke, 2004).

4.3.5 Interaction of pubertal timing, parenting and peer factors on adolescent substance use. Only two studies were identified in the systematic search addressing how pubertal timing, parenting and peer factors interact in predicting adolescent substance use. A longitudinal study by Costello and colleagues reported in 2007 that the highest risk of adolescent alcohol use was found in early maturing boys and girls associating with deviant peers and additionally in early maturing girls experiencing low levels of parental monitoring (Costello et al., 2007). Westling and colleagues reported in their longitudinal study that parental monitoring moderated the effect of pubertal timing on the initiation of alcohol use for boys and girls. They also found that associating with deviant peer mediated the effect of pubertal timing on the initiation of alcohol and cigarette use for girls (Westling et al., 2008).

4.4 Discussion

Only very few studies were found addressing the effect of pubertal timing, parenting and peer factors on adolescent substance use. Furthermore, only two studies looked at the interplay of the three factors in predicting substance use in adolescence. Although the studies were conclusive in general, it is noticeable that there is a shortage of information available on this topic. This warrants for further longitudinal research looking at the interplay of pubertal timing, parenting and peer factors on adolescent substance use to further enlighten this important area of adolescent health.

CHAPTER 5: OVERALL STUDY DESIGN

The preceding chapters introduced and discussed research that has examined links between pubertal timing, parent-adolescent relations, peer deviance and adolescent substance use. This chapter turns to describing the rationale and research design underpinning the empirical work conducted as part of my doctoral candidature.

5.1 Research aims

The aim of the research contained in this thesis is to disentangle the interplay of psycho-social factors associated with substance use in adolescence (i.e., parent-adolescent relationship quality and peer deviance assessed at age 15 years) and pubertal timing to better understand the underlying temporal relationships leading to increased levels of substance use in adolescence (i.e., alcohol, cigarette and cannabis use assessed at age 16 years). Analyses are based on data from the Avon Longitudinal Study of Parents and Children (ALSPAC).

5.2 Theoretical rationale

As mentioned in Chapter 2, the psychosocial development of young people (including their substance use/ misuse) is best understood as the result of the combined effects of individual factors over time (Rutter, 1999, Rutter & Casear, 1991) and would therefore be imperfectly captured by cross-sectional models focussing on main effects only (Cicchetti, 1984; Rutter, 2005; Rutter, 1999). Furthermore, with regards to risk behaviour in adolescence (including adolescent substance use) it has been advocated to focus on combinations of domains that have been identified to cause risk behaviour (Jessor, 1991). Thus only examining the individual effects of pubertal timing, parent-adolescent relationship quality and peer deviance on adolescent substance use would provide an incomplete picture, while a more complete understanding can be obtained from the examination of the possible interplay of these factors in predicting adolescent substance use.

5.2.1 Mediation and moderation models. Mediation and moderation models represent informative ways of specifying the unfolding relationships between risk factors and psychosocial traits, especially when controlling for confounders (e.g., analysis of longitudinal data; Rose et al., 2004). However, when adjusting for confounders it is important to adjust for confounders, which were assessed at an earlier time point than the predictor variable to avoid that the confounders themselves are affected by the predictor variable (Vansteelandt, 2009; Van der Weele, 2009). Mediation analysis permits a test of whether the direct effect of a predictor variable on an outcome variable can be explained by a mediator lying on the pathway between these two variables. I used mediation analysis to explore whether the relationship between early pubertal timing (predictor variable) on increased adolescent substance use (outcome variable) is explained indirectly by mediators in the psycho-social domain (parents-adolescent relationship quality and peer deviance; see Figure 3). Moderation analysis on the other hand allows examination of whether the effect of a predictor variable (in this case parent-adolescent relationship quality or peer deviance) on an outcome variable (adolescent substance use) is different for early, on-time and late maturing adolescents (that is, pubertal timing is the moderator variable; see Figure 4).

Mediation models help to establish whether prevention programs should address the indirect effect rather than the direct effect. More specifically mediation analyses will provide information on how the prevention program will work (MacKinnon, 2011). Moderation analyses, on the other hand, identify the risk group to aim the prevention program at. More specifically, moderation analyses provide information on for which group the prevention program will work (MacKinnon, 2011). Consequently, the findings of such models can contribute to increased understanding and ultimately lead to more effective prevention approaches.

Although early pubertal maturation, poor parent-adolescent relationship quality and affiliation with deviant peers have each been identified as individual risk factors for increased substance use in adolescence, to my knowledge only a handful of studies have examined the links between these factors. Negriff and Trickett (2012) reported that the effect of pubertal timing on alcohol and cannabis use at age 13 years was mediated by peers' alcohol and cannabis use at age 12. That is, early maturers, who subsequently affiliated with alcohol and cannabis using peers at age 12 years, tended to use more alcohol and cannabis at age 13 years. Biehl and colleagues (2007) reported that early maturing girls with more alcohol drinking friends used more alcohol when aged between 12-16 years than early maturing girls with fewer alcohol drinking friends. Marklein and colleagues (2009) hypothesised, that early maturers, who affiliated with cigarette smoking peers, tended to use more alcohol, cigarettes and cannabis than early maturers who affiliated with non-smoking peers. However, they found no evidence that peers' cigarette use moderated the relationship between pubertal timing and girls' alcohol, cigarette and cannabis use in a sample aged 11-17 years. This lack of evidence might be due to their relatively small sample size (N=264 girls). Lynne-Landsman and colleagues (2010) tested for moderation and found that early maturing girls in average and high risk families (based on household resources, conflict and stability of household structure) had higher levels of binge drinking, cigarette and cannabis use at age 14 than early, on-time and late maturing girls in low risk families. Finally, Shelton and van den Bree (2010) reported that pubertal timing moderated the effect of parent-adolescent relationship quality (warmth and closeness) on cigarette use at age range 12-15 years. More specifically the effect of low levels of parent-child warmth and closeness on increased cigarette use was stronger in late maturing girls compared to early and on-time maturing girls.

Taken together, studies have focussed either on the effect of pubertal timing and the family environment on adolescent substance use or on the effect of pubertal timing and the peer environment on adolescent substance use. This does not permit a comparison of the combined effects regarding the family environment with the combined effects regarding the peer environment, as they are mostly based on the analyses of different samples. Additionally, only one study has examined the mediating role of peer deviance on the effect of pubertal timing on substance use (Negriff & Trickett, 2012) and no research appears to have tested the mediating role of the family environment. Two studies have focussed on the moderating role of peer deviance (Biehl et al., 2007; Marklein et al., 2009), and these have reported inconsistent findings. Finally, two studies have focussed on family functioning (Lynne-Landsman et al., 2010; Shelton & van den Bree, 2010), whereby Lynne-Landsmann and colleagues (2010) focussed on the moderating role of low, average and high risk families (based on household resources, conflict and stability of household structure) and Shelton and van den Bree (2010), on the other hand, focussed on the moderating role of pubertal timing. I therefore aimed to contribute to the existing literature by examining the role of parent-adolescent relationship quality and peer deviance in the links between pubertal timing and substance use in girls by exploring the evidence for the two different models of interrelationships explained above (i.e., mediation and moderation). As mentioned above, insight into possible mediation pathways or moderating influences (which indicate higher risks for a specific subgroup) can inform prevention strategies. Discrepancies between previous studies may possibly have arisen due to small sample sizes. The present dissertation is based on a sample larger than has been previously used (Lynne-Landsman et al., 2010; Marklein et al., 2009; Negriff & Trickett, 2012; Shelton & van den Bree, 2010), with the exception of one study (Biehl et al., 2007). Examining mediation and moderation effects within one study combines what so far has only been done in separate studies. This provides results derived from analysing one sample and therefore one does not need to take differences in sample characteristics into account. Additionally, I adjusted all analyses for *a priori* selected confounders (including earlier measures of substance use, parent-child relationship quality and peer behaviour, parental substance use and socioeconomic factors), thus limiting the possibility that these earlier influences explained the effects tested.

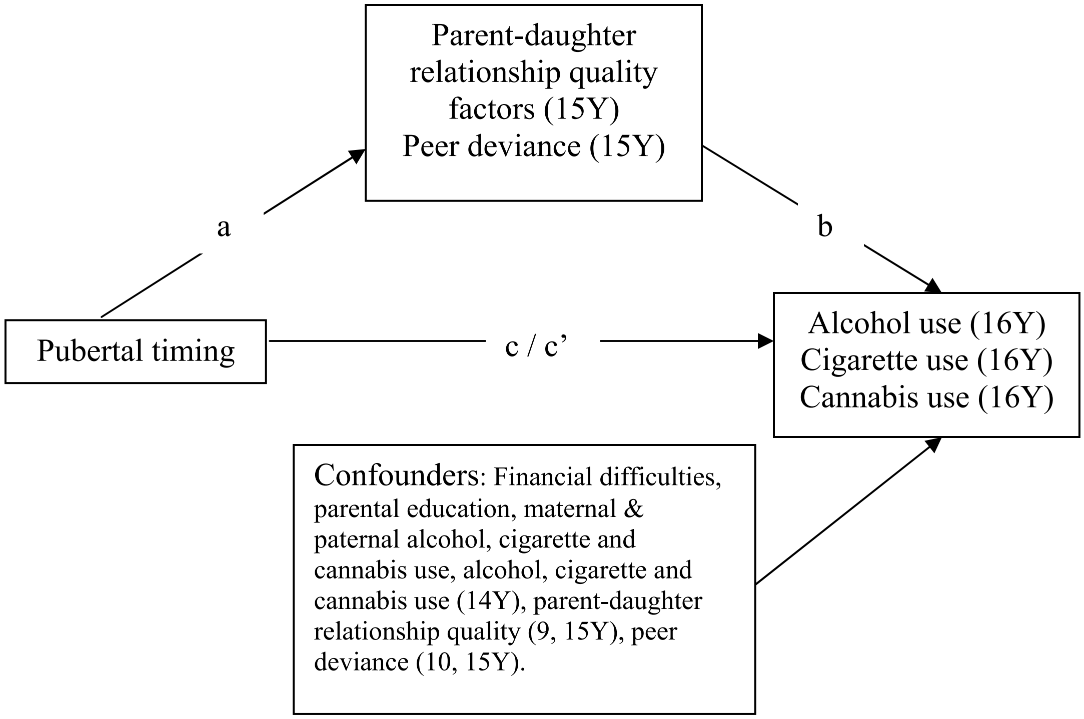


Figure 3. Mediation model

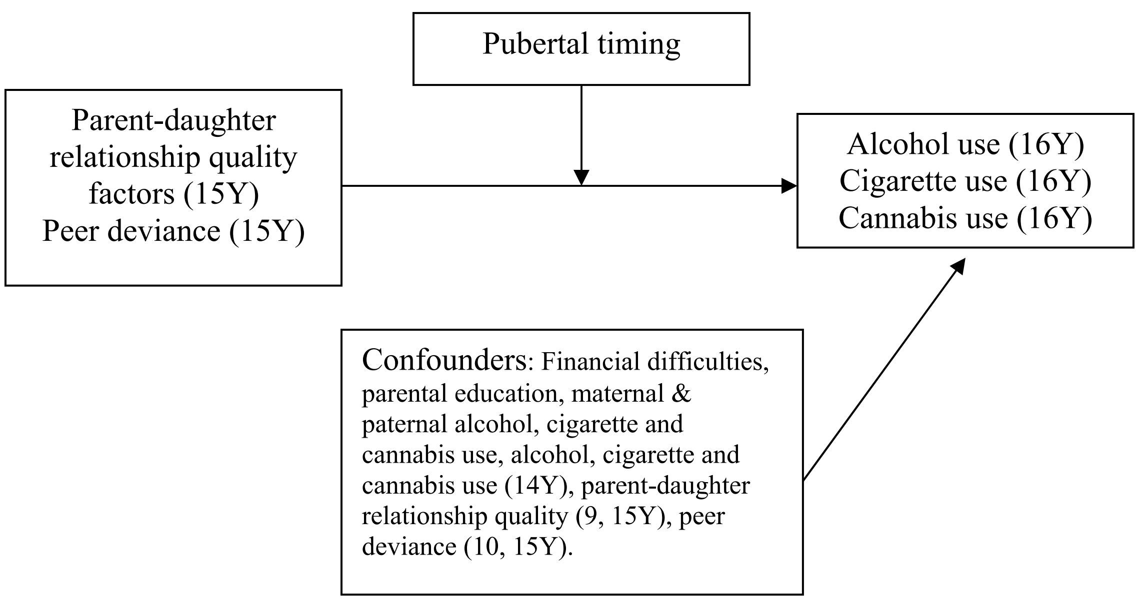


Figure 4. Moderation model

5.3 Analysing an all-female sample

Substance use rates and patterns can differ for males and females. For example, in a number of European countries, young females are now more likely to smoke (Heron et al., 2011; Hibell et al., 2007; MacArthur et al., 2012); however for alcohol use the results are less consistent with more young females having been intoxicated from alcohol than young males (Hibell et al., 2007) (although no sex differences have been reported in the frequency of alcohol consumption (Heron et al., 2012; MacArthur et al., 2012)). These findings have led researchers to call for gender-specific substance research to inform policy and practice (Amos et al., 2012).

Furthermore, the timing and course of pubertal development differs for the sexes (with puberty not being marked by a clear-cut biological event for boys as onset of menarche is for girls and girls generally entering puberty before boys; Ge et al., 2007). Therefore, assessing the pubertal timing of boys needs to be based on reports of the growth of pubic hair and testes (as for example assessed by the method of Tanner staging). However, this measurement has been shown to be fraught with problems because boys, when asked to assess their stage of development, tend to overestimate their own stage of development and therefore provide information which cannot be regarded as valid or reliable.

There is also evidence that family relationships may have a stronger impact on substance use among girls compared to boys (Saraceno et al., 2012; van den Bree et al., 2004). This may be related to findings reporting that girls tend to be more concerned about their social environments (family and peers) than boys (Lager et al., 2012; Tomori et al., 2000; West & Sweeting, 2003). In addition, the relationship between parents and the adolescent has been reported to become more complicated for girls, especially early maturing girls, than for boys (Celio et al., 2006). This may be related to several findings including that the onset of puberty is commonly associated with greater restrictions for girls than boys (Celio et al., 2006). Furthermore, early maturing girls associate more often with older peers than early maturing boys (Dawes et al., 2000), while girls are also more likely to have boyfriends, who are older than themselves (Gowen et al., 2004; Young & d'Arcy, 2005). I therefore decided to focus on girls exclusively in this study.

This chapter outlined the rationale for investigating the combined effects of pubertal timing and parent-adolescent relationship quality on adolescent substance use as well as the combined effects of pubertal timing and peer deviance on substance use in adolescence by conducting mediation and moderation analyses in an all-female sample. My analyses were based on the ALSPAC study, which is described in detail in the next chapter.

CHAPTER 6: STUDY SAMPLE AND VARIABLES

This chapter describes key characteristics of the Avon Longitudinal Study of Parents and Children (ALSPAC) data set, which was used for the empirical studies described in Chapters 7 and 8. Additionally, this chapter provides a detailed description of the study variables.

6.1 Avon Longitudinal Study of Parents and Children (ALSPAC)

6.1.1 History of ALSPAC. The Avon Longitudinal Study of Parents and Children is an ongoing longitudinal birth cohort study having recruited pregnant women with an expected delivery date between 1st April 1991 and 31st of December 1992 residing in three districts of the Avon area in the UK. Eligible women were contacted through media campaigns, staff visiting community locations and handing out "interest cards" at antenatal and maternity health services. This resulted in the recruitment of 14,541 pregnant women. The initial sample consisted of 14,062 live births of which 13,988 children were alive at one year of age (6,747 girls (48%)). These children are now 21 years of age. Since 1991/92 the children's health and development has been followed by collecting genetic and environmental information through questionnaires, focus clinics and lab-based assessments on a yearly basis. By age 17 years, 105 postal questionnaires (19 carer-based questionnaires, 23 child-based questionnaires answered by the carer, 24 child-completed questionnaires, 16 partner-based questionnaires, nine puberty questionnaires and 14 school-based questionnaires) have been sent to the mothers, partners and children. Additionally, from age 7 years all ALSPAC children were invited annually to nine walk-in focus clinics to complete computer tasks, individual interviews and focus groups (ALSPAC, 2012).

6.1.2 ALSPAC representativeness. The ALSPAC sample is representative of the British population as indicated by comparisons with the 1991 census (ALSPAC, 2012). The results of this comparison, which are presented on the ALSPAC website (http://www.bristol.ac.uk/alspac/researchers/resources-available/cohort/represent/) accessed on 09.07.13, are shown in Table 3.

Table 3 Comparison of mothers with < 1-year-old children from UK, Avon or ALSPAC

Socio-economic characteristic	Whole of UK	Avon	ALSPAC
Owner occupier	63.4%	68.7%	79.1%
1+ person/room	30.8%	26.0%	33.5%
Car in household	75.6%	83.7%	90.8%
Married couple	71.8%	71.7%	79.4%
Non-white mother	7.6%	4.1%	2.2%

However, ALSPAC participants completing questionnaires at age 16 years were found to score higher on school performance based on the National Pupil Database (NPD) 'Key Stage 4' (KS4) assessment completed at a mean age of 16 years compared to non-ALSPAC pupils and ALSPAC drop-outs. ALSPAC children completing a questionnaire at age 16 were more likely to be female and less likely to be eligible for free school meals than ALSPAC drop-outs (Boyd et al., 2012). There was a slight decline in mothers' participation during pregnancy and the postnatal period up to 33 months, after which response rates remained consistent at ~70% until the children were 13 years of age (Fraser et al., 2012). These biases might slightly affect the pattern of results of my analyses insofar as the data set includes an overrepresentation of adolescent girls who perform better in school and are from wealthier families compared to the average girl in the UK. This needs to be kept in mind when interpreting the results of this study.

6.1.3 Objectives and advantages of using ALSPAC. The ALSPAC study is one of the largest ongoing population-based birth cohort studies in the UK with detailed and frequent data collection (Boyd et al., 2012; Fraser et al., 2012). Data cohorts comparable to the ALSPAC cohort are the Millennium Cohort Study (MCS) and the Longitudinal Study of Young People in England (LSYPE). The MCS is a longitudinal birth cohort study following about 19,000 children born in the UK (participants in England, Wales, Scotland and Northern Ireland) in 2000/01. Including participants across all four countries is beneficial compared to the participant sample of the ALSPAC, which is reduced to the Avon area. However, the MCS has only collected data at five time points so far (when the children were 9 months, 3, 5, 7 and 11 years of age; Hansen, 2012), which is far less frequent than data collection of the ALSPAC study. The LSYPE started in 2004 with the yearly data collection from about 16,000 children living in England (Centre for Longitudinal Studies, 2014). However, as data collection did not start until the children were 14 years of age; the LSYPE is missing a lot of information about the children's early childhood, which is provided within the ALSPAC study. Therefore, the ALSPAC data set provided the most frequent data collection from birth until late adolescence, which makes it the most beneficial data cohort for my studies.

Data on the "ALSPAC children" has been collected regularly with 68 data collection time points spaced from birth to age 18 years. During infancy (age 4 weeks to 2 years) data collection included four mother- or main carer-completed questionnaires and a subsample of the children born in the last 6 months of the recruitment phase took part in the first "children in focus" assessment clinic. During early childhood (age 2 to 7 years) data collection was based mainly on mother- or main carer-completed questionnaires but also included child-completed questionnaires and again the "children in focus" subsample participated in further assessment clinics. Childhood data collection (age 7 years) included the first focus clinic study assessment in which all participants took part, while furthermore one questionnaire to be completed by the child was also sent to families. During late childhood (age 7 to 13 years) data collection included mother- or main carer-completed questionnaires, child-completed questionnaires and further focus clinics including all participants. During adolescence (age 13 to 16 years) data collection was mainly based on child-completed questionnaires, but also on mother- or main carer-completed questionnaires and focus clinics including all participants. Finally, during transition into adulthood (age 16 to 18 years) data collection was once again mainly based on child-completed questionnaires, but also one mother- or main carer-completed questionnaire and the final focus clinic including all participants (Boyd et al., 2012).

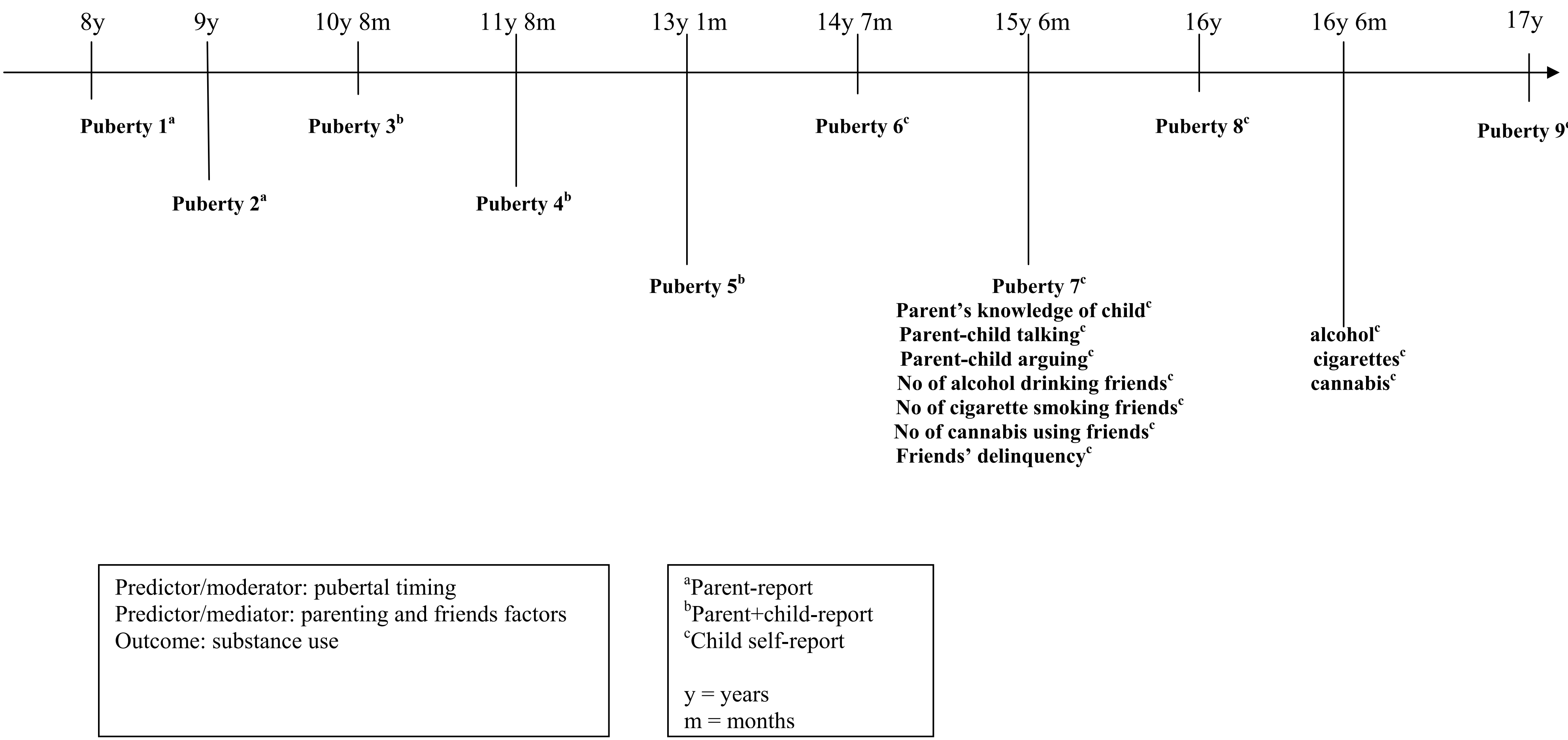


Figure 5. Timeline of main variables

In addition to child data, information was also collected on the ALSPAC mothers and their partners themselves. The mothers completed between one to four questionnaires during pregnancy depending on when during their pregnancy they were recruited. Over a period of 20 years mothers and their partners have been sent 16 questionnaires assessing their health and well-being. These assessments are important because they provide information about factors that can impact upon the children's health and well-being, including socioeconomic status, parents' education, parents' substance use etc.

6.2 Study variables

The main variables used in this study were parent-daughter relationship quality factors (level of parent-daughter communication, level of parent-daughter conflict and parental monitoring), peer deviance factors (number of alcohol drinking friends, number of cigarette smoking friends, number of cannabis using friends and friends' delinquency), pubertal timing and substance use. A timeline of the outcomes, hypothesised predictors and moderators is shown in Figure 5.

Two different models of the relationships between pubertal timing, substance involvement and psycho-social factors were evaluated (see section 5.2.1): a mediation model (see Figure 3) analysing whether the effect of pubertal timing on adolescent substance use is mediated by parent-daughter relationship quality or by peer deviance; and a moderation model (see Figure 4) analysing whether the effect of parent-daughter relationship quality or peer deviance on adolescent substance use differs for early, on-time and late maturing girls. As the same variables were included in the mediation and the moderation model some specifications are necessary to provide a clear understanding of the analysis. For the mediation models, pubertal timing was the predictor variable and psycho-social factors (parent-daughter relationship quality and peer deviance) were conceptualised as mediators. For the moderation models psycho-social factors (parent-daughter relationship quality and peer deviance) were predictor variables and pubertal timing was the hypothesised moderating variable.

6.2.1 Outcome variables. The outcome measures were alcohol, cigarette and cannabis use in late adolescence (at age 16 years).

6.2.1.1 Alcohol use. Alcohol use was assessed with ten items from the Alcohol Use Disorders Identification Test (AUDIT) questionnaire (Babor et al., 2001) obtained through adolescent self-report via postal questionnaire at the age of 16 years (see Table 4). The internal consistency of these ten items was acceptable ($\alpha = 0.78$). These items were scored and added according to the AUDIT scoring system (Babor et al., 2001) into a single categorical variable with three levels (1 = harmless, 2 = hazardous, 3 = harmful).

Table 4 Items of the AUDIT

	Items
1	How often do you have a drink containing alcohol?
2	How many standard drinks do you have on a typical day when you are drinking?
3	How often do you have six or more standard drinks on one occasion?
4	How often during the last year have you found that you were not able to stop drinking once you had started?
5	How often during the last year have you failed to do what was normally expected of you because of drinking?
6	How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
7	How often during the last year have you had a feeling of guilt or remorse after drinking?
8	How often during the last year have you been unable to remember what happened the night before because you had been drinking?
9	Have you or someone else been injured because of your drinking?
10	Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?

The AUDIT assesses alcohol frequency, quantity and alcohol problem use, therefore this measure combines various aspects of alcohol use. Using the AUDIT criteria (Babor et al., 2001) the information was combined to determine whether a participant engaged in harmless, hazardous or harmful alcohol use. One advantage of using the AUDIT is that it allows for gender specific alcohol use assessment as the categories are based on different cut-offs for boys and girls (Babor et al., 2001). This is important as by drinking the same quantity of alcohol boys may have hazardous alcohol use whereas girls may have harmful alcohol use. Girls are more sensitive to the physiological effects of alcohol than boys due to different organisation of neurotransmitters in the male and female brain, girls' lower body weight and slower alcohol metabolism (Brienza & Stein, 2002). Another advantage of the AUDIT is that it not only identifies harmful alcohol users (drinking alcohol in a quantity that results in physical or psychological harm), but also hazardous alcohol users (drinking alcohol in such a quantity that it places the drinking person at risk of physical or psychological harm), which is not the case in other frequently used screening tools, e.g., in the CAGE questionnaire ("a mnemonic for attempts to cut back on drinking, being annoyed at criticisms about drinking, feeling guilty about drinking, and using alcohol as an eye opener"; Ewing, 1984) or the Michigan Alcoholism Screening Test (MAST; Selzer, 1971). Identifying individuals with harmful versus hazardous alcohol use is important for informing the development of intervention programmes as alcohol users at an earlier stage of alcohol abuse may respond better to treatment (McCusker et al., 2002).

6.2.1.2 Cigarette and cannabis use. Cigarette and cannabis involvement were assessed with two self-report items from the Survey of Drug Use, Smoking and Drinking among Schoolchildren in England questionnaire (Wright, 2011) via postal questionnaire at age 16 years: “Have you ever smoked a cigarette/roll-up”/“Please mark the box which best describes your smoking frequency” and “Have you ever tried cannabis”/“Please mark the box which best describes your cannabis use frequency”. These items were combined into two separate categorical variables with four levels for the cigarette variable (1 = non-smoker, 2 = only ever once or twice, 3 = occasional smoker, 4 = regular smoker) and three levels for the cannabis variable (1 = non-user, 2 = only ever once or twice, 3 = user).

6.2.2 Predictor and mediator variables.

6.2.2.1 Parent-daughter relationship quality. Parent-daughter communication was assessed with two items from the Edinburgh Study of Youth Transitions and Crime questionnaire (ESYTC, 2011; McVie & Holmes, 2005; Smith, 2004) assessed through adolescent self-report at a walk-in focus clinic at the age of 15 years: “How often do you tell your parents about things that happen at school” and “How often do you tell your parents about what you do when you are out”, with the response options for each question being: ‘hardly ever/never’, ‘sometimes’ and ‘often’. The internal consistency of these items was acceptable ($\alpha = 0.75$). The items were summed to create a single categorical variable with three levels (1 = parent and daughter communicate often, 2 = parent and daughter communicate sometimes, 3 = parent and daughter communicate hardly ever/never).

Parent-daughter conflict was assessed with six items from the ESYTC questionnaire (McVie & Holmes, 2005; Smith, 2004) assessed through girl self-report at a walk-in focus clinic at the age of 15 years:

“How often did you argue with your parents about the tidiness of your room”, “How often did you argue with your parents about what you do when you go out”, “How often did you argue with your parents about what time you come home”, “How often did you argue with your parents about who you hang out with”, “How often did you argue with your parents about your clothes and appearance” and “How often did you argue with your parents about other things”, with the response options for each question being: ‘hardly ever/never’, ‘< once a week’, ‘at least once a week’ and ‘most days’. The internal consistency of these items was good ($\alpha = 0.82$). The items were summed to create a single categorical variable with four levels (1 = parent and daughter argue hardly ever/never, 2 = parent and daughter argue less than once a week, 3 = parent and daughter argue at least once a week, 4 = parent and daughter argue most days).

Parent-daughter monitoring Parents’ monitoring of where and with whom their daughter was spending her time when not at home was assessed with four items from the ESYTC questionnaire (McVie & Holmes, 2005; Smith, 2004) assessed through adolescent self-report at a walk-in focus clinic at age 15 years: “When you went out during the last year how often did your parents know where you were going?”, “When you went out during the last year how often did your parents know who you were going out with?”, “When you went out during the last year how often did your parents know what you were doing?” and “When you went out during the last year how often did your parents know what time you would be home?”, with the response options for each question being: ‘never’, ‘sometimes’, ‘usually’ and ‘always’. The internal consistency of these items was good ($\alpha = 0.82$). The items were summed to create a single categorical variable. However, as there were only 4 cases, who reported that their parents never knew where they were, the categories “never” and “sometimes” were combined so that the final variable had three levels (1 = parents always know, 2 = parents usually know, 3 = parents sometimes/never know).

6.2.2.2. Deviant peer behaviour. Number of friends who drink alcohol was assessed with one item from the Edinburgh Study of Youth Transitions and Crime questionnaire (ESYTC, 2011) assessed through girl-report at a walk-in focus clinic at the age of 15 years: “Number of friends that drank alcohol during the last year”. The variable had three categories (1 = none, 2 = one or some, 3 = most or all).

Number of friends who smoke cigarettes was assessed with an item from the ESYTC questionnaire assessed through girl-report at a walk-in focus clinic at the age of 15 years: “Number of friends that smoked cigarettes during the last year”. The variable had three categories (1 = none, 2 = one or some, 3 = most or all).

Number of friends who use illegal drugs was assessed with an item from the ESYTC questionnaire assessed through girl-report at a walk-in focus clinic at age 15 years: “Number of friends that took illegal drugs during the last year. The variable had three categories (1 = none, 2 = one or some, 3 = most or all).

Friends' delinquency was assessed with seventeen yes/no-items from the ESYTC questionnaire (see Table 5) assessed through girl-report at a walk-in focus clinic at age 15 years. The internal consistency of these items was good ($\alpha = 0.87$). The items were summed to create a single binary variable, which was coded: no=0 and yes=1; whereas the yes=1 categorisation was used as soon as the participant had answered any of the seventeen original items with “yes”, which allowed for a very strict measure of whether the peers engaged in delinquent behaviour.

Table 5 ESYTC questions assessing peers' delinquency

	Questions
1	Some of YPs friends were loud, rowdy or unruly in a public place such that people complained or they got into trouble, during the last year
2	Some of YPs friends kicked/punched/attacked someone with the intention of really hurting them, during the last year
3	Some of YPs friends stole money/property that someone was holding, carrying or wearing at the time, during the last year
4	Some of YPs friends hit or picked on someone because of their race or skin colour, during the last year
5	Some of YPs friends stole something from a shop or store, during the last year
6	Some of YPs friends broke into a house or building to steal something, during the last year
7	Some of YPs friends broke into a car/van to steal something, during the last year
8	Some of YPs friends wrote or spray painted on someone's property, during the last year
9	Some of YPs friends damaged someone's property on purpose, during the last year
10	Some of YPs friends set fire or tried to set fire to something on purpose, during the last year
11	Some of YPs friends rode in a stolen car/van/motorbike, during the last year
12	Some of YPs friends skipped or skived off school, during the last year
13	Some of YPs friends travelled on a bus/train without paying enough money or using someone else's pass, during the last year
14	Some of YPs friends sold something that didn't belong to them or they knew was stolen, during the last year
15	Some of YPs friends carried a knife or other weapon for protection or in case it was needed in a fight, during the last year
16	Some of YPs friends sold an illegal drug to someone, during the last year
17	Some of YPs friends hurt or injured an animal or bird on purpose, during the last year

6.2.3 Predictor/moderator variables

6.2.3.1 Pubertal timing: age at menarche. Pubertal timing was derived from the mother-rated questions: "Has your daughter started menarche? [Yes/No]", if yes: "How old was your daughter when she had her first period?" Early postal questionnaires were sent to the mothers for completion (age 9-13 years). Between the ages of 14 and 17 years the postal questionnaires were sent to the study children themselves for completion. As advocated by Joinson and colleagues (2011) I have used the first reported age at onset of menarche to avoid recall bias. The mean age at onset of menarche for the girls in the ALSPAC cohort was 12.3 years (*SD* = 1.29, range: 8-17 years) with eight girls reporting not having started their period by age 17. These girls were classified as late maturers. The average age at menarche in my sample was generally comparable with the reported average age of menarche from the Breakthrough Generation Study (BGS); a cohort study with 81,606 women aged 16-98 years retrospectively reporting their age at menarche, which averaged to 12.7 years (Morris et al., 2010). This slight difference between the average ages at menarche might be due to the fact that the women, who participated in the BGS, had to recall their age at menarche many years after the event, which might have lead to recall bias.

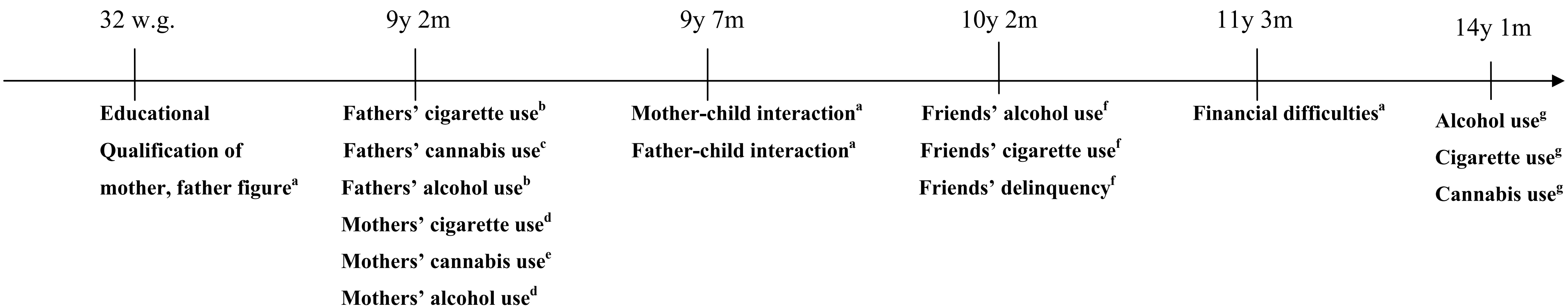
A categorical variable with three levels was derived, where I defined early pubertal timing as occurring before age 12 years (23.1% of the sample, 95% CI: 22%, 24%), on-time between 12 and 13 years (62.6% of the sample, 95% CI: 61%, 64%) and late after age 13 years (14.3% of the sample, 95% CI: 13%, 15%). A similar categorisation has been used in previous studies (Joinson et al., 2011; Stice et al., 2001; Tam et al., 2006).

6.2.4 Confounding variables. Analyses were conducted adjusting for several *a priori* selected confounders, which have been previously reported to be relevant to the relationships of interest. As mentioned in section 2.2.1 environmental factors (such as family, peers and socio-economic factors) are mainly responsible in predicting adolescent substance use (Fowler et al., 2007; van den Bree, 2005). Therefore, it is important to control for environmental factors while looking at the links between psycho-social factors and adolescent substance use. Multiple studies have reported on the association of parental substance abuse and adolescent substance use with findings indicating that adolescents of parents who engage in high levels of substance use tend to use higher levels of substances themselves (i.e., Becklake et al., 2005; Kilpatrick et al., 2000; Li et al., 2002; Meyers & Dick, 2010; Moss et al., 2002; Windle et al., 2008; Wolock & Magura, 1996). Studies have also reported the link between adolescent substance use and socio-economic factors (SES; Hanson & Chen, 2007; Obeidallah et al., 2000; Saraceno et al., 2009; Tifflin et al., 2007; Tjora et al., 2011; Trim & Chassin, 2008), as the studies of this dissertation focussed on the effects of parent-daughter relationship quality and peer deviance on adolescent substance use, it was important to control for SES (i.e., level of parental education and financial difficulties; Sutherland, 2012). Finally, to be able to identify temporal relationships it has been advocated to control for earlier assessments of the variables at interest (Cole & Maxwell, 2003), which were also reported to be linked to substance use in adolescence: earlier substance use (Lansford et al., 2010), pre-adolescent parent-child relationship quality and pre-adolescent peers' behaviour (Oxford et al., 2001). Additionally, family as well as peer factors have been identified as predictors of substance use in adolescence (Barnes et al., 2006); I therefore adjusted for peer factors when examining family relationship factors as the predictor/mediator and vice versa. A timeline of the confounders is shown in Figure 6.

6.2.4.1 Earlier substance use. Girls' earlier substance use was assessed using a self-report questionnaire administered at age 14 years. The information on earlier alcohol use was based on the question, "How old were you when you first had a whole alcoholic drink?" which was assessed via self-report questionnaires in a walk-in focus clinic, whereas information on earlier cigarette and cannabis use was assessed via postal questionnaires. Earlier cigarette use was based on the question "How old were you when you first smoked a cigarette" and earlier cannabis use was based on the question "How old were you when you first tried cannabis". The earlier substance use scores were dichotomised and coded as 0 = did not use substance by age 13 years and 1 = used substance by age 13 years. Age 13 years was used as cut-off as it has been reported that initiating substance use prior to age 13 was linked to increased risk of developing substance abuse later in life (Spear, 2002).

6.2.4.2 Socioeconomic factors. The information on parental education was assessed through mother-report via postal questionnaire during pregnancy. It was based on the questions "Mum's highest educational qualification" and "Father figure's highest educational qualification" and categorised: 0 = none, 1 = CSE, 2 = Vocational, 3 = O Level, 4 = A Level, 5 = Degree.

Financial difficulties were assessed using mother-report via postal questionnaires when the child was 11 years old and based on five questions: "Difficulty I have paying for food at the moment", "Difficulty I have paying for clothing at the moment", "Difficulty I have paying for heating at the moment", "Difficulty I have paying rent/mortgage at the moment" and "Difficulty I have paying for things I need for my children at the moment". The internal consistency of these items was good ($\alpha = 0.85$) and so the items were combined to create a continuous variable with a higher score indicating a higher level of financial difficulties.



[a]Main carer-report
[b]Mother's partner report
[c]Father figure self-report
[d]Father figure's partner-report
[e]Mother self-report
[f]Child's friend-report
[g]Child self-report

w.g. = weeks of gestation
y = years
m = months

Figure 6. Timeline of confounding variables

6.2.4.3 Parents' substance use. Information on mother's alcohol and cigarette use was assessed through father figure-reports about the mother and father figure's alcohol and cigarette use was assessed through mother-reports about the father figure through postal questionnaire when the child was 9 years old. Mothers' alcohol use was based on the question, "Frequency/amount of alcohol wife/partner drinks" and mothers' cigarette use was based on the questions "Number of cigarettes per day father's wife/partner currently smokes on weekdays" and "Number of cigarettes per day father's wife/partner currently smokes on weekend days". Father figure's alcohol use was based on the question "Frequency/amount of alcohol husband/partner drinks" and fathers' cigarette use was based on the questions "Number of cigarettes per day mother's husband/partner currently smokes on weekdays" and "Number of cigarettes per day mother's husband/partner currently smokes on weekend days". Parents' alcohol use was categorised: 0 = never, 1 = very occasionally, 2 = occasionally, 3 = 1-2 glasses a day, 4 = 3+ glasses a day; and parents' cigarette use was categorised: 0 = none, 1 = <10 a day, 2 = 10-19 a day, 3 = >20 a day.

Parents' cannabis use was assessed through self-report through postal questionnaire when the child was 9 years old. Mothers' cannabis use was based on the question "Frequency mother has taken cannabis/marijuana in last 2 years" and father figure's cannabis use was based on the question "Frequency father has taken cannabis/marijuana in last 2 years". Parents' cannabis use was categorised: 0 = not at all, 1 = sometimes, 2 = often, 3 = every day.

6.2.4.4 Earlier parent-child interaction. A variable on mother-child interaction and father figure-child interaction was created by combining 18 mother-report items from a postal questionnaire regarding time spent with the child (see Table 6). ALSPAC adapted these items from the HOME Inventory (Caldwell & Bradley 1984). The internal consistency of the mother-child interaction items and the father figure-child interaction items was good (α= .80 and 0.87, respectively). The items were combined to create two distinct continuous variables with a high score indicating a more positive level of parent-child interaction at age 9 years.

Table 6 HOME Inventory questions assessing parent-child interaction at age 9

	Questions for mother-child interaction	**Questions for father figure-child interaction**
1	Adult female baths or showers child	Adult male baths or showers child
2	Adult female makes things with child	Adult male makes things with child
3	Adult female sings with child	Adult male sings with child
4	Adult female reads to or with child	Adult male reads to or with child
5	Adult female plays with toys with child	Adult male plays with toys with child
6	Adult female cuddles child	Adult male cuddles child
7	Adult female does active play with child	Adult male does active play with child
8	Adult female takes child to park or playground	Adult male takes child to park or playground
9	Adult female puts child to bed	Adult male puts child to bed
10	Adult female takes child swimming, fishing or other activity	Adult male takes child swimming, fishing or similar activity
11	Adult female draws or paints with child	Adult male draws or paints with child
12	Adult female prepares food with child	Adult male prepares food with child
13	Adult female takes child to classes	Adult male takes child to classes
14	Adult female takes child shopping	Adult male takes child shopping
15	Adult female takes child to watch sports/football	Adult male takes child to watch sports/ football
16	Adult female does homework with child	Adult male does homework with child
17	Adult female has conversations with child	Adult male has conversations with child
18	Adult female helps child prepare things for school	Adult male helps child prepare things for school

6.2.4.5 Earlier deviant peer behaviour. Earlier peer substance use behaviour was assessed using girl-report via questionnaire at a walk-in focus clinic with the questions, “Friends drank alcohol” and “Friends smoked cigarettes”. The variables were categorised: 0 = no, 1 = yes. *Earlier peers’ delinquency* was assessed with eight items (see Table 7) through girl-report via questionnaire at the same clinic. The internal consistency of the items was just acceptable (α = 0.63); however, as peer delinquency is not common at the age of 10 years I decided to still include all available information in the variable. The items were combined and dichotomised with the categories: 0 = no, 1 = yes.

Table 7 Items assessing peers’ delinquency at age 10 years

	Questions
1	Any friends skived off school
2	Any friends told off by teacher
3	Any friends destroyed something for fun
4	Any friends set fire to something
5	Any friends stolen something
6	Friends got into fights
7	Friends been cruel to an animal
8	Friends been in trouble with Police

Within this chapter I introduced the longitudinal ALSPAC data set and described which variables were selected for the analyses and how these variables were created. The next chapter provides a detailed description of the empirical analyses.

CHAPTER 7: STATISTICAL ANALYSIS

7.1 Statistical methods

For this study I planned to look at main effects as well as to conduct mediation and moderation analyses to examine the interplay of pubertal timing and psycho-social factors on adolescent substance use. To that end, I used a combination of approaches suitable for ordinal data, which are described below.

7.1.1 Regression model: Ordered logistic regression. As the three outcome variables (alcohol, cigarette and cannabis) were ordinal, ordered logistic regression was the fitting approach to examine main effects. More specifically, ordered logistic regression analysis was used to test the effect of parent-daughter relationship quality and peer deviance (at age 15) and pubertal timing on substance use (at age 16). The benefit of using ordered logistic regression models, compared to transforming the outcome variables into binary variables and using binary regression models is that ordered logistic regression models allow for making full use of the ranked data of the outcome variable (Ananth & Kleinbaum, 1997).

The underlying assumption of ordered logistic regression, called the proportional odds assumption, assumes that the cumulative odds for each predictor variable are the same across all categories of the outcome variable (Ananth & Kleinbaum, 1997; Liu & Koirala, 2013). More specifically, in ordered logistic regression models it is assumed that the coefficients, which describe the effect of the predictor variables on, for example, the lowest category of the outcome variable (i.e., ‘non-smoker’) versus all higher categories of the variable (i.e., smoking as ‘only ever once or twice’, ‘occasional smoker’ and ‘regular smoker’), are the same as those coefficients, which describe the effect of the predictor variables on the lowest and the second lowest category of the outcome variable (i.e., ‘non-smoker’ and smoking ‘only ever once or twice’) versus all other categories of the outcome variable (i.e., ‘occasional smoker’ and ‘regular smoker’) etc. (Kirkwood & Sterne, 2007). If this assumption is met, using ordered logistic regression models is a powerful tool and has the advantage that the results are shown in a single model and are therefore more easily interpretable (Bender, 2000). In Stata 11 for Windows the proportional odds assumption is tested using the *omodel* command, which is based on a likelihood-ratio test (Ordered Logistic Regression, 2012; Williams, 2006).

7.1.2 Data imputation model: Multiple Imputation by Chained Equation. Prospective longitudinal research designs offer the best opportunity to establish the direction of effects operating between variables. However, such studies may face a bias problem due to the loss of participants to study follow-up (also known as data attrition; Carlin et al., 2008). Missing values are therefore common in studies of longitudinal data sets. Certain subgroups have been found to be more likely to drop out of longitudinal studies and this may introduce bias in effect estimation; these subgroups include youths from low socio-economic backgrounds or with high levels of behaviour problems as well as males (Wolke et al., 2009).

The extent to which longitudinal data is biased depends on the causes underlying participant drop-out (Graham, 2009). Three different situations can be distinguished: (1) data missing completely at random (MCAR), (2) data missing at random (MAR) and (3) data missing not at random (MNAR). Rubin (1976) gave the following definitions: MAR is present if missingness depends on the observed data but not on the unobserved data (unobserved due to loss of follow-up); MCAR is present if missingness does not depend on the observed or on the unobserved data; MNAR is present if missingness depends on the unobserved data. If data is not missing completely at random, results of the complete case analysis (analysis of the observed data) may be biased (Sterne et al., 2009). To address this issue imputation of the missing data is advised (Sterne et al., 2009).

7.1.2.1 Characteristics of the Multiple Imputation by Chained Equation model. Various papers have examined which data imputation method is the best to inform researchers about the preferred ways to deal with missing data. Stuart and colleagues compared multiple imputation, single imputation and maximum likelihood approaches. They reported distinct advantages of multiple imputation compared to the other two techniques: compared to multiple imputation single imputation only insufficiently accounts for uncertainty in missing values and maximum likelihood approaches are very complex to implement in complex models (Stuart et al., 2009). Shrive and colleagues (2006) compared six different imputation methods (multiple imputation, single regression, individual mean, overall mean, participant's preceding response and random selection of value). They reported that multiple imputation provided the most valid results in data with 10% missing values and in data with 30% missing values. More specifically, Engels and Diehr (2004) reported that multiple imputation based on the variables, that had been assessed in the participant before their records became incomplete plus any non-missing data present for them in the period after the missing value occurred, was superior to multiple imputation based only on participant's values before the missing value occurred as this provided additional information for the imputation data. Therefore, I conducted multiple imputation, whereby the imputation model included participants' information before and after the missing value.

Multiple imputation was based on the Multiple Imputation by Chained Equation (MICE) approach (Van Buuren et al., 1999) using the *ice* command (Royston, 2009: Royston, 2007; Royston, 2004) in Stata 11 for Windows. Multiple Imputation by Chained Equation is a flexible approach to deal with missing data which has been implemented in available software packages such as Stata (Royston, 2004). MICE allows for uncertainty in missing data by creating multiple data sets with the missing values being replaced by imputed values and appropriately combining results of each data set. Sterne and colleagues stated in 2009 that the process of multiple imputation consisted of two separate stages:

Stage 1: Creation of multiple data sets where the missing values are replaced by imputed values. The imputed values are based on the *Bayesian inference theory*. This theory states that the likelihood that a hypothesis is true (in our case the values of imputed data items) is determined by observed evidence (in our case the values of observed data), which is called the *posterior distribution* of the hypothesis. Therefore, for each variable containing missing data, values are imputed using an equation. This is equivalent to a regression model with the variable with missing values resembling the outcome variable and observed data of other variables resembling predictor variables. More specifically, missing values of a variable will be imputed by using information from observed values of this variable as well as additional other observed variables, which are specified by the researcher based on high likelihood of association with the variable with missing values. The imputation procedure has to be a multiple iterative process, as otherwise it would not fully account for the uncertainty in predicting missing values as it would fail to add appropriate variability into the imputed values. This is important as after all, it is never possible to impute the true values of the missing data.

Stage 2: Standard analyses are used on each data set and the results are combined according to Little and Rubin's theory to get the final estimates and their standard errors (Little & Rubin, 2002; Rubin, 1987). This theory is based on a set of rules called *Rubin's rules*, which calculates a matrix of combined variance and covariance incorporating within-imputation variability (reflecting the uncertainty about the results from each imputed data set) and between-imputation variability (reflecting the uncertainty due to missing values; White et al., 2011).

It has been argued that it is statistically impossible to prove that missing data are MAR (Sterne et al., 2009). Therefore, to avoid bias in imputed data some authors advocate including auxiliary variables in the imputation equation (Graham, 2009). Auxiliary variables are variables which are included in the imputation equation to provide additional information whilst not being included in any subsequent statistical analyses of the imputed data (that is, the statistical analyses that will be conducted to answer research questions, once the imputation process has been completed).

MICE is based on creating multiple imputed data sets, whose estimates will then be combined; a widely debated issue of MICE is the number of imputed data sets ($m > 1$) to be created. Early work advocated that a number of $m = 10$ imputed data sets would be sufficient to achieve reliable results in the imputed data (Schafer & Graham, 2002). However, more recently it has been advocated that the number of imputed data sets should be based on the percentage of missing values. More specifically, with 40% of missing values approximately $m = 40$ imputed data sets should be conducted to achieve reliable imputed data and sufficient power (Graham, 2009; White et al., 2011). However, the percentage of missingness of the main variables of interest is sufficient to take into account; that is, variables which are used as confounders in the later analyses do not have to be considered (Royston, 2004).

With regards to outcome variables two issues should be kept in mind. First, outcome variables need to be included in the imputation equation because of the information they provide for imputing missing values (Sterne et al., 2009; White et al., 2011). Second, when analysing imputed data, it has been advocated that imputed predictor, mediator, moderator and confounding variables should be analysed but unimputed (meaning complete case data only) outcome variables (White et al., 2011). It is important to not include imputed outcome variables in the analyses as they might provide biased estimates (White et al., 2011).

In Stata, MICE was first conducted by using the *mvis* command for multivariate imputations (Royston, 2004) which was later replaced by the *ice* command (Royston, 2009; Royston, 2007; White et al., 2011). To run the *ice* command in Stata, the command needs to be adjusted according to the variables used in the imputation equation. Different regression commands are used to impute different types of variables: to impute normally distributed continuous variables a linear regression model is used, to impute binary variables a logistic regression model is used and to impute ordered categorical variables a multinomial logistic regression model is used (White et al., 2011). Which type of regression model should be used for which variable can be specified with the *cmd()* option of the *ice* command. By including continuous variables, which are not normally distributed due to the concept they are measuring (i.e., financial difficulties, where one would expect that most people do not have financial difficulties), in the imputation equation it is desirable to specify the same non-normal distribution in the imputed continuous variable as in the complete case-based continuous variable. This is achieved by the *match()* option of the *ice* command. When planning to test interaction effects in the imputed data, interaction terms need to be included in the imputation equation to ensure any possible interaction effects are not lost after imputing the data. This is best done by creating interaction terms and including these in the imputation command; furthermore if any of the variables forming the interaction term are categorical, dummy variables need to be created. The interaction terms will then need to be specified in the *ice* command by using the *passive()* option. In addition, it is necessary to specify that the dummy variables are derived from the categorical variable and therefore do not need to be imputed separately. This is specified with the *substitute()* option of the *ice* command. To avoid co-linearity issues, which occur if variables are highly associated with each other, during the imputation process it is possible to specify which variables are used to impute another variable; this is specified by using the *eq()* option of the *ice* command (Royston, 2009; Royston, 2007; Royston, 2004).

7.2 Statistical tests

7.2.1 Quantifying mediation. The test for mediation was conducted by running regression models. The indirect effect of parent-daughter relationship quality and peer deviance on the relationship between pubertal timing and substance use at age 16 years was estimated by assessing the indirect effect of pubertal timing on parent-daughter relationship quality and peer deviance at age 15 years (i.e., path a) as well as the indirect effect of parent-daughter relationship quality and peer deviance at age 15 years on substance use at age 16 years (i.e., path b). As advocated by many researchers (Hayes, 2009; Rucker et al., 2011; Zhao et al., 2010) in more recent years, the theoretical approach of the mediation analysis has moved away from focussing on the total (i.e., path c) and direct effects (i.e., path c') with an increasing attention now focussed on the indirect effects (i.e., path a and b). Additionally, the ratio between the indirect effect and total effect (i.e., $B_{indirect}/B_{total}$), which is used to estimate the extent to which the mediator explains the effect of the predictor on the outcome variable, was calculated.

7.2.2 Tests for moderation. The test for moderation analysis was conducted using ordered logistic regression models. The moderation analysis consists of running the regression model including the predictor variable and the moderation variable separately as well as the interaction term of the two in the regression model. The post-estimation command *testparm* is used to establish the statistical significance of the moderation effect. The *testparm* command is based on the Wald test, which tests the hypothesis that the coefficients of the interaction are equal to zero. If this hypothesis is rejected, sufficient evidence for a moderation effect will be found (Stata, 2012).

7.3 Multiple Imputation by Chained Equation

7.3.1 Identifying the number of imputations. As mentioned in section 7.1.2.1, identifying the number of imputed data sets ($m > 1$) has been widely discussed among statisticians. Earlier work advocated that low numbers of imputed data sets (for example $m = 10$) would be sufficient to receive reliable imputed data (Schafer & Graham, 2002). However, more recent discussions indicate that the number of imputed data sets should be chosen in accordance with the percentage of missing values in the main variables (Graham, 2009; Royston, 2004; White et al., 2011).

Therefore, I calculated the percentage of missing data for the eleven primary study variables: alcohol, cigarette and cannabis use at age 16 years (outcome variables), number of alcohol drinking friends, number of cigarette smoking friends, number of cannabis using friends, friends' delinquency, parent-daughter communication, parent-daughter conflict and parental monitoring all assessed at age 15 years (predictor/mediator variables), and pubertal timing (predictor/moderator variable). The percentage of missing data for these variables is shown in Table 8.

The average percentage of missing data was approximately 60% with pubertal timing showing the lowest percentage of missing data with 41.3%. As advocated by a number of researchers this percentage of missing data requires a minimum of m = 60 imputed data sets (Graham, 2009; White et al., 2011). To ensure that a sufficient number of imputed data sets was conducted I decided to conduct m = 80 imputations; as there is no disadvantage reported of conducting too many imputed data sets, whereas invalid imputed data is created by conducting too few imputed data sets. This means that 80 separate imputed data sets were created and the estimates derived from these were combined during the imputed data analysis.

Table 8 Percentage of missing and observed cases across the primary study variables

	Missing N (%)	**Observed** N (%)
Alcohol use	4148 (61.5%)	2599 (38.5%)
Cigarette use	3896 (57.7%)	2851 (42.3%)
Cannabis use	3889 (57.6%)	2858 (42.4%)
Alcohol drinking friends	4067 (60.3%)	2680 (39.7%)
Cigarette smoking friends	4064 (60.2%)	2683 (39.8%)
Cannabis using friends	4069 (60.3%)	2678 (39.7%)
Delinquent friends	4081 (60.5%)	2666 (39.5%)
Communication	4057 (60.1%)	2690 (39.9%)
Conflict	4059 (60.2%)	2688 (39.8%)
Monitoring	4056 (60.1%)	2691 (39.9%)
Pubertal timing	2787 (41.3%)	3960 (58.7%)

7.3.2 Auxiliary variables. As described in section 7.1.2.1, Graham (2009) advocated the inclusion of auxiliary variables in the imputation equation for additional information to assure the imputed data are not biased. Therefore, 12 auxiliary variables were included in the imputation equation. Five of these were earlier assessments of variables included in the analyses (i.e., financial difficulties, mothers' and father figures' alcohol and cigarette use). Four variables were included due to their theoretical association with information missingness (i.e., weekly family income, crowding index and mothers' and father figures' health). Finally, three variables were included because of their theoretical association with the outcome variables (i.e., friends' level of influence on the child, sensation seeking and conduct problems).

Financial difficulties and partners' alcohol and cigarette use were reported by the mothers, mothers' alcohol use was reported by the partners and mothers' cigarette use was reported by the mothers themselves. All of these variables were assessed via postal questionnaires when the girls were 21 months old.

Mothers' health was reported by the partners and partners' health was reported by the mothers via postal questionnaire when the girls were 21 months old and both had the following categories: 1 = 'always well'; 2 = 'mostly well'; 3 = 'often unwell'; 4 = 'hardly well'. Weekly family income was reported by the mothers when the girls were 35 months old and was categorised 1 = '<£100'; 2 = '£100-199'; 3 = '£200-299'; 4 = '£300-399'; 5 = '>£400'. An index of house crowding, based on the number of people living in the household divided by the number of rooms, was reported by the mothers when the girls were 21 months old (categories: 1 = '< 0.5'; 2 = '0.5-<0.75'; 3 = '0.75-<1'; 4 = '1 or more'). Both were assessed via postal questionnaires.

The level of friends' influence on the girl was reported by the mothers when the girls were age 9 years old. The item was assessed with the question "How much is your child influenced by her/his mates/friends?" and was categorised 1 = 'very strongly', 2 = 'fairly strongly', 3 = 'sometimes', 4 = 'rarely', 5 = 'never'. Level of sensation seeking was reported by the girls at age 11 years at a walk-in focus clinic. I used the score that summed the answers of the 20 items from the Arnett's Inventory of Sensation Seeking (AISS). Level of the girls' conduct problems was reported by the mothers when the girls were 16 years old. It was assessed with 26 items (for example "How often in the last year has your child stolen something from a shop") with the answer categories being: 1 = 'not at all', 2 = 'just once', 3 = '2-5 times', 4 = '6 or more times'. The scores were summed to create a single continuous variable with a higher score indicating a higher level of conduct problems.

7.3.3 The imputation equation. Including as many variables as possible in an imputation model allows providing as much information as possible to impute missing values and is therefore highly beneficial (Sterne et al., 2009). However, using high numbers of variables in an imputation model may also include some potential pitfalls, such as a high possibility of including co-linear variables.

To avoid co-linearity issues two user written programs by Medeiros (2012) have been implemented to be used with the *ice* command in Stata: *pred_eq* and *check_eq*. *Pred-eq* chooses the *n* predictors with the highest absolute of bivariate correlation values to predict a variable with missing values. The equations given by *pred_eq* can then be tested with the command *check_eq*, to check the equations for potential problems which might occur when running the *ice* command (i.e., co-linearity) before they are used with the option *eq()* in the imputation command.

As tests of moderation models were planned, it was necessary to specify interaction terms in the imputation command; as otherwise interaction effects would be attenuated in the imputed data. To create these interaction terms dummy variables of the moderator and predictor variables need to be created, which can then be used to specify interaction terms for the outcome variables. Therefore, dummy variables were created for the following variables: pubertal timing, level of parent-daughter communication, level of parent-daughter conflict, parental monitoring, number of alcohol drinking friends, number of cigarette smoking friends and number of cannabis using friends. Friends' delinquency was also a predictor variable, but as this variable is a binary variable no dummy coding was necessary for this variable. The dummy variables of the moderator and predictor variables were then multiplied with the outcome variables to create the interaction terms.

Additional options of the *ice* command were used in the imputation equation: the *cmd()* option, the *match()* option, the *passive()* option and the *substitute()* option (for detail see section 6.1.2.1).

7.3.4 Testing the imputation model. White and colleagues (2011) introduced a *rule of thumb* to ascertain whether enough imputations have been conducted to assure reproducibility of the analysis. This test is conducted by exploring the Monte Carlo error (defined as the standard deviation across repeated runs of the same imputation procedure with the same data) variability of three quantities:

- "The Monte Carlo error of $\beta^{\wedge}$ is approximately 10% of its standard error"
- "The Monte Carlo error of the test statistic $\beta^{\wedge}/se(\beta^{\wedge})$ is approximately 0.1"
- "The Monte Carlo error of the *p*-value is approximately 0.01 when the true *p*-value is 0.05, and 0.02 when the true *p*-value is 0.1" (White et al., 2011).

To test whether the number of imputed data sets *m*=80 was sufficient to achieve reproducibility of the data, Mote Carlo errors were calculated and compared according to White et al.'s *rule of thumb* (see Tables 9a-9c). The tables present Monte Carlo errors for parent-daughter communication, parent-daughter conflict, parental monitoring and peers' delinquency for *m*=50 and *m*=80 (to check that the estimates of the *m*=80 imputations were improved compared to the *m*=50 imputations) as well as imputed data where all variables (including outcome variables) were imputed *m*=50 for each outcome variable separately. The tables show the best Monte Carlo errors for imputed data with imputed predictor, mediator, moderator and confounding variables with *m*=80 imputations.

Table 9a White et al.'s *rule of thumb* to assess Monte Carlo errors for models with alcohol use as the outcome variable

Variable		Complete cases	N= 2599 (outcome sample)		N= 6747 (imputed sample)
			M=50	M=80	M=50
Communication	Exp(B)	1.19	1.13	1.13	1.04
	B	0.17	0.12	0.12	0.04
	SE(B)	0.08	0.08	0.08	0.06
	p	0.034	0.122	0.102	0.515
	MCerror(B)		0.005*	0.003*	0.005*
	MCerror(t)		0.07*	0.05*	0.09*
	MCerror(p)		0.0158*	0.0104*	0.0561
	FMI		0.219	0.176	0.432
Conflict	Exp(B)	1.32	1.24	1.24	1.10
	B	0.28	0.21	0.22	0.10
	SE(B)	0.07	0.07	0.07	0.04
	p	<0.001	0.001	0.001	0.025
	MCerror(B)		0.005*	0.003*	0.004*
	MCerror(t)		0.10*	0.07*	0.12*
	MCerror(p)		0.0005*	<0.0001*	0.0078*
	FMI		0.249	0.231	0.381
Monitoring	Exp(B)	1.93	1.92	1.94	1.35
	B	0.66	0.65	0.66	0.30
	SE(B)	0.09	0.08	0.09	0.06
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.005*	0.005*	0.005*
	MCerror(t)		0.16	0.17	0.24
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.185	0.258	0.380
Friends' delinquency	Exp(B)	2.62	2.56	2.57	1.59
	B	0.96	0.94	0.94	0.46
	SE(B)	0.14	0.13	0.13	0.08
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.009*	0.007*	0.006*
	MCerror(t)		0.18	0.14*	0.24
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.249	0.228	0.343

Note: * Meets *rule of thumb* of Monte Carlo error (MCerror) (White et al., 2011)

Table 9b White et al.'s *rule of thumb* to assess Monte Carlo errors for models with cigarette use as the outcome variable

Variable		Complete cases	N= 2851 (outcome sample)		N= 6747 (imputed sample)
			M=50	M=80	M=50
Communication	Exp(B)	1.29	1.18	1.19	1.07
	B	0.25	0.17	0.17	0.07
	SE(B)	0.07	0.07	0.07	0.05
	p	0.001	0.024	0.015	0.157
	MCerror(B)		0.005*	0.004*	0.005*
	MCerror(t)		0.10*	0.07*	0.12*
	MCerror(p)		0.006*	0.0029*	0.0357*
	FMI		0.272	0.263	0.421
Conflict	Exp(B)	1.49	1.29	1.35	1.13
	B	0.40	0.26	0.30	0.12
	SE(B)	0.06	0.06	0.06	0.04
	p	<0.001	<0.001	<0.001	0.002
	MCerror(B)		0.004*	0.004*	0.003*
	MCerror(t)		0.15*	0.11*	0.12*
	MCerror(p)		<0.0001*	<0.0001*	0.0012*
	FMI		0.241	0.295	0.372
Monitoring	Exp(B)	1.98	1.65	1.70	1.28
	B	0.68	0.50	0.53	0.24
	SE(B)	0.08	0.08	0.08	0.06
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.005*	0.004*	0.005*
	MCerror(t)		0.14*	0.14*	0.19
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.201	0.249	0.422
Friends' delinquency	Exp(B)	2.36	2.67	2.67	2.09
	B	0.86	0.98	0.98	0.74
	SE(B)	0.11	0.11	0.11	0.10
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.008*	0.006*	0.01*
	MCerror(t)		0.23	0.18	0.48
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.271	0.240	0.668

Note: * Meets *rule of thumb* of Monte Carlo error (MCerror) (White et al., 2011)

Table 9c White et al.'s *rule of thumb* to assess Monte Carlo errors for models with cannabis use as the outcome variable

Variable		Complete cases	N= 2858 (outcome sample)		N= 6747 (imputed sample)
			M=50	M=80	M=50
Communication	Exp(B)	1.15	1.10	1.09	1.02
	B	0.14	0.10	0.09	0.02
	SE(B)	0.09	0.09	0.08	0.05
	p	0.106	0.243	0.294	0.688
	MCerror(B)		0.01*	0.004*	0.004*
	MCerror(t)		0.08*	0.06*	0.08*
	MCerror(p)		0.0321*	0.0265*	0.0561*
	FMI		0.262	0.239	0.298
Conflict	Exp(B)	1.29	1.20	1.25	1.10
	B	0.25	0.18	0.22	0.09
	SE(B)	0.07	0.07	0.07	0.05
	p	<0.001	0.013	0.001	0.060
	MCerror(B)		0.005*	0.004*	0.004*
	MCerror(t)		0.07*	0.07*	0.12*
	MCerror(p)		0.0027*	<0.001*	0.016*
	FMI		0.261	0.237	0.423
Monitoring	Exp(B)	2.34	1.93	1.98	1.42
	B	0.85	0.66	0.68	0.35
	SE(B)	0.09	0.09	0.09	0.06
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.005*	0.004*	0.005*
	MCerror(t)		0.14*	0.16	0.21
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.172	0.213	0.317
Friends' delinquency	Exp(B)	4.10	4.28	4.38	2.70
	B	1.41	1.45	1.48	0.99
	SE(B)	0.17	0.17	0.16	0.15
	p	<0.001	<0.001	<0.001	<0.001
	MCerror(B)		0.01*	0.009*	0.02
	MCerror(t)		0.21	0.15	0.48
	MCerror(p)		<0.0001*	<0.0001*	<0.0001*
	FMI		0.285	0.268	0.745

Note: * Meets *rule of thumb* of Monte Carlo error (MCerror) (White et al., 2011)

Finally, the analysis will be run in the complete case data set as well as in the imputed data set to check that the results are similar.

Within this chapter I described the statistical procedures which I selected to conduct the analyses for this study. In summary, the empirical analyses assessed main effects using ordered logistic regression models, mediation analyses, using multiple regression models, and moderation analyses, using ordered logistic regression models and the post-estimation command *testparm*. Additionally, this chapter has provided a detailed description of the approach taken to handle missing data using multiple imputation. The results of the analyses are reported as two studies in the next two chapters. The first study focusses on the main effects and combined effects of pubertal timing and parent-daughter relationship quality on substance use at age 16 years, while the second one focusses on the main effects and combined effects of pubertal timing and peer deviance on substance use at age 16 years.

CHAPTER 8: PARENT-DAUGHTER RELATIONSHIP QUALITY, PUBERTAL TIMING AND SUBSTANCE USE IN ADOLESCENCE

8.1 Introduction

Experimental substance use is common behaviour in adolescence (British Medical Association (BMA), 2003; National Center for Health Statistics, 2011). Prevalence rates in the UK, Europe and US show that alcohol, cigarettes and cannabis are widely used among adolescents, with numerous consequences for the adolescents' health (see chapter 2). Pubertal timing and social processes play a role in the development of substance use/ misuse in adolescence (Hummel et al., 2013; van den Bree et al., 2004). Adolescents who experience multiple risk factors may be at particularly increased risk of substance misuse (van den Bree & Pickworth, 2005), and the importance of understanding the interplay of key risk factors in relation to substance use in adolescence has been highlighted (Glaser et al., 2010; Rhodes et al., 2003; and section 2.2). In other words, the development of young people (including their substance use) can be best understood by looking at combined effects of individual factors over time rather than focussing on main effects only (Cicchetti, 1984; Rutter, 2005; Rutter, 1999; Rutter & Casear, 1991). As different risk factors are often inter-linked as a result of common underlying variables and processes (Jessor, 1991), it would be disadvantageous to create prevention programs focussing on a single risk factor at a time. Therefore, research into the combined effects of multiple risk factors is warranted as it provides the ground work for creating prevention programs addressing multiple risk factors simultaneously.

As discussed in chapters 2 and 3 early pubertal timing has been linked to increased substance use in adolescent girls, which supports the *early timing hypothesis* proposing that early maturation poses girls at increased risk of adjustment problems compared to girls experiencing on-time and late pubertal maturation (Peskin, 1973). This has been hypothesised to be due to the early maturing girls' limited cognitive and emotional resources to deal with stress and peer pressure compared to on-time and late maturing girls. Early maturing girls may have a disadvantage as these resources develop over the course of adolescence. However, the majority of these findings on early pubertal maturation being linked to negative factors (e.g., increased substance use) was found in samples of girls in early and mid-adolescence (Hummel et al., 2013).

An additional factor linked to adolescent substance use is the parent-adolescent relationship quality with low levels of quality having been associated with increased adolescent substance use (see chapter 2 and 3). To recall, it has been reported that low levels of parent-child communication and parental monitoring and high levels of parent-child conflict specifically are linked to increased levels of adolescent substance use (Dishion et al., 2004; Kaltiala-Heino et al., 2011; McVie & Holmes, 2005). Furthermore, studies have linked the emergence of puberty to decreased levels of parent-adolescent communication and monitoring (Mrug et al., 2008) and increased levels of conflict (Paikoff & Brooks-Gunn, 1991; Wasserman et al., 2012). I found only one study which focussed on the effect of pubertal timing on parent-adolescent relationship quality, and the effects indicated no links for girls (Steinberg, 1987). These findings provide evidence against the *early timing hypothesis*, because the increase in parent-adolescent conflict was reported for all girls at the emergence of puberty regardless of their age at the beginning of puberty. However, they are in support of the *stressful change hypothesis* proposing that it is the pubertal transition itself (regardless of the age at which it is experienced) which is causing behavioural problems (i.e., substance use and delinquent behaviour) in adolescence (Simmons & Blyth, 1987), rather than early pubertal timing.

However, as mentioned above an incomplete picture of the topic is obtained by focussing research on main effects only, therefore it is important to look at the combined effects of pubertal timing and parent-daughter relationship quality with regards to adolescent substance use. Shelton and van den Bree (2010) conducted moderation analyses and reported that the across-time association between low parent–adolescent warmth and closeness and increased cigarette use at age range 12-15 years was stronger for late maturing girls compared to early and on-time maturing girls. Lynne-Landsman and colleagues (2010) also conducted moderation analyses and reported that early maturers in average and high risk families (based on household resources, conflict and stability of household structure) had higher levels of binge drinking, cigarette and cannabis use at age 14 years than early, on-time and late maturing girls in low risk families. However, the number of studies undertaken to date is small and to my knowledge no study has conducted mediation analyses with the aim to investigate evidence for indirect links (via parent-adolescent relationship quality), between pubertal timing and substance use in late adolescence. This approach can represent an important extension, as the literature does indicate evidence of the presence of main effects, that is, longitudinal associations have been reported between pubertal maturation and decreased parent-adolescent relationship quality (e.g., Molina & Chassin, 1996), negative parent-adolescent relationship quality and increased adolescent substance use (e.g., Shelton &

van den Bree, 2010) and early pubertal timing and increased adolescent substance use (e.g., Peskin, 1973). These findings indicate that the effect of early pubertal timing on increased levels of adolescent substance use might be mediated by negative parent-adolescent relationship quality. This chapter addresses this gap in the literature.

8.2 The study

The aim of this study was to test the combined effect of pubertal timing and parent-daughter relationship quality on substance use in adolescent girls by conducting mediation as well as moderation analyses within the ongoing British longitudinal birth cohort ALSPAC study. Both conceptual models (mediation and moderation) have the potential to inform prevention programs with families and young people. If strong and replicated evidence emerges that parent-daughter relationship quality mediates the links between pubertal timing and adolescent substance use, prevention programs can be aimed at decreasing these indirect effects. This could be achieved through family support programs aiming to empower early maturing girls and their parents to better communicate with each other. The moderation models offer insight into whether the effect of poor parent-adolescent relationship quality on increased adolescent substance use is stronger in the context of early compared to on-time and late pubertal timing. Ultimately, positive finding would reveal which subgroups of young people may benefit most from substance use prevention programs.

8.3 Study aims and hypotheses

This study assessed the relationship between parent-daughter relationship quality, pubertal timing and alcohol, cigarette and cannabis use in late adolescence. I decided to use, three separate measures assessing parent-daughter relationship quality (communication, conflict and monitoring) and test effects for girls only while adjusting for *a priori* selected variables (including earlier measures of substance use, early parent-child relationship quality, peer behaviour as well as parental substance use and socioeconomic factors).

The study aimed to examine whether:

1. There is evidence for differences in alcohol, cigarette and cannabis use in late adolescence (age 16 years) for girls who experienced early, on-time or late pubertal timing. I hypothesised that early maturing girls would show higher levels of alcohol, cigarette and cannabis use compared to on-time and late maturing girls;
2. There is evidence that parent-daughter relationship quality at age 15 years is linked to substance use at age 16 years. I hypothesised that poor parent-daughter relationship quality (low levels of parent-daughter communication, high levels of parent-daughter conflict and low parental monitoring) at age 15 years would be linked to increased levels of alcohol, cigarette and cannabis use at age 16 years;
3. Parent-daughter relationship quality mediates the effect of pubertal timing on substance use in late adolescence. I hypothesised that the effect of early pubertal timing on increased substance use would be indirectly explained by poor parent-daughter relationship quality;
4. Pubertal timing moderates the effect of parent-daughter relationship quality on substance use in late adolescence. I hypothesised that the effect of poor parent-daughter relationship quality on increased substance use would be stronger for early compared to on-time and late maturing girls.

8.4 Method

8.4.1 Sample. Data from participants of the Avon Longitudinal Study of Parents and Children (ALSPAC), an ongoing longitudinal cohort study, was analysed. For details on the study sample see section 6.1.

The sample for this study consisted of young girls who were assessed at age 15 years (mean age = 15.5 years, *SD*= 0.3) and 16 years (mean age = 16.7 years, *SD* = 0.2). Questionnaires were sent to 9,994 adolescents and 5,131 (51%) were completed and returned (3,032 questionnaires were answered by girls). Information was provided by girls on their alcohol use (n=2,599), cigarette use (n=2,851) and cannabis use (n=2,858) at age 16 years.

8.4.2 Variables. The outcome variables for this study were alcohol, cigarette and cannabis use, all assessed at age 16 years (for details see section 6.2.1). For the mediation model (see Figure 3) the predictor variable was pubertal timing and the mediator variable was level of parent-daughter communication and conflict as well as level of parental monitoring (for details see section 6.2.2). For the moderation model (see Figure 4) the predictor variables were the three parent-daughter relationship quality variables, whereas the moderator variable was pubertal timing. Both models were adjusted for a set of *a priori* selected variables: socioeconomic status (financial difficulties and parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), earlier substance use (alcohol, cigarette and cannabis use at age 14 years), peer deviance at age 15 years and earlier parent-daughter relationship quality at age 9 years (for details see section 6.2.4).

8.4.3 Statistical analysis. Over time, the ALSPAC sample has experienced somewhat higher attrition rates among less affluent families, ethnic minorities and male participants, a common finding for long-running longitudinal studies (Boyd et al., 2012; Fraser et al., 2012; Perez et al., 2007). Imputed data sets were created using the *ice* package in Stata 11 (Royston, 2007). As advocated by the literature, including imputed outcome data in the analyses may lead to biased estimates (White et al., 2011), therefore I decided to use data sets with imputed predictor, mediator, moderator and confounding variables, but complete case outcome variables, for my analyses of imputed data (for detail on the imputation model see sections 7.1.2 and 7.3).

To check whether similar results are found, the analysis is run in the complete case data as well as in the imputed data.

For descriptive statistics in the complete data χ^2 and ANOVA tests were conducted. As the three outcome variables (alcohol, cigarette and cannabis) are ordinal, ordered logistic regression analysis, which requires the fulfilment of the proportional odds assumption, was used to test hypotheses 1 and 2. In Stata 11 the proportional odds assumption is tested using the *omodel* command, which is based on a likelihood-ratio test (Stata 11; Ordered Logistic Regression, 2012). Running the *omodel* command indicated that the proportional odds assumption was not violated (approximate likelihood-ratio test of proportionality of odds across the alcohol response categories: $\chi^2(3) = 1.18$, $p = .76$; approximate likelihood-ratio test of proportionality of odds across the cigarette response categories: $\chi^2(6) = 10.24$, $p = .12$; approximate likelihood-ratio test of proportionality of odds across the cannabis response categories: $\chi^2(3) =4.96$, $p = .17$).

To test the third hypothesis, mediation analysis (see Figure 3) was conducted using regression models (for details see section 7.2.1). To test the fourth hypothesis, moderation analysis (see Figure 4) was conducted using ordered logistic regression models and the *testparm* command of Stata 11 (for details see section 7.2.2).

8.5 Results for the complete case data

Descriptive statistics are presented in Table 10.

Early maturing girls' father figures smoked more cigarettes than father figures of on-time and late maturing girls. Late maturing girls' mothers used more cannabis than early and on-time maturing girls' mothers. Fewer late maturing girls had drunk alcohol by age 13 years than early and on-time maturing girls. Fewer late maturing girls had smoked cigarettes, or used cannabis, by age 13 years than early and on-time maturing girls. Late maturing girls also had fewer alcohol drinking and cannabis using friends than on-time and early maturing girls at age 15 years, while fewer late maturing girls than early and on-time maturing girls had delinquent friends at age 15 years. Additionally, differences were found between early, on-time and late maturing girls with regards to cigarette and cannabis use at age 16 years, with the highest percentage of non-smokers and non-users being found among the late maturing girls. A closer look at the differences between the three pubertal timing groups with regards to substance use at age 16 years was taken by conducting ordered logistic regression models.

Table 10 Study variable frequencies and means for the three pubertal timing groups

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2 / F, *p*
Parent-daughter relationship quality (predictor / mediator variables)					
Communication					$\chi^2(4)=7.0$ *p*= .14
often	1145 (44%)	253 (46%)	707 (43%)	185 (45%)	
sometimes	1195 (46%)	235 (43%)	783 (48%)	177 (43%)	
hardly ever / never	264 (10%)	63 (11%)	153 (9%)	48 (12%)	

Table 10 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2, ANOVA
Conflict					$\chi^2(4)=12.0$
hardly ever / never	347 (13%)	85 (15%)	203 (12%)	59 (15%)	*p*= .06
< once a week	1529 (59%)	312 (57%)	975 (59%)	242 (59%)	
at least once a week	550 (21%)	105 (19%)	366 (23%)	79 (19%)	
most days	176 (7%)	49 (9%)	98 (6%)	29 (7%)	
Monitoring					$\chi^2(4)=4.3$
always	1421 (55%)	299 (54%)	882 (54%)	240 (58%)	*p*= .36
usually	1055 (40%)	223 (41%)	674 (41%)	158 (38%)	
sometimes / never	130 (5%)	29 (5%)	87 (5%)	14 (4%)	
Adolescent substance use (outcome variables)					
Alcohol					$\chi^2(4)=7.1$
harmless	1554 (63%)	348 (65%)	955 (61%)	251 (67%)	*p*= .13
hazardous	579 (23%)	124 (23%)	377 (24%)	78 (21%)	
harmful	347 (14%)	67 (12%)	236 (15%)	44 (12%)	
Cigarette					$\chi^2(6)=16.6$
non-smoker	1269 (47%)	268 (45%)	785 (46%)	216 (52%)	*p*= .01
only ever once or twice	811 (29%)	161 (27%)	527 (31%)	123 (30%)	
occasional smoker	236 (9%)	57 (10%)	147 (9%)	32 (8%)	
regular smoker	399 (15%)	107 (18%)	250 (14%)	42 (10%)	
Cannabis					$\chi^2(4)=14.3$
non-user	1926 (71%)	420 (71%)	1185 (69%)	321 (78%)	*p*= .006
only ever once or twice	551 (20%)	115 (19%)	373 (22%)	63 (15%)	
user	245 (9%)	59 (10%)	159 (9%)	27 (7%)	
Confounders					
Financial difficulties					F(2)=0.91,
Range (5-20)	3502 (18.7)	692 (18.6)	1966 (18.7)	447 (18.7)	*p*=.40
Mother's alcohol use					$\chi^2(8)=14.3$
never	107 (7%)	20 (6%)	65 (7%)	22 (9%)	*p*= .07
very occasionally	388 (26%)	98 (30%)	241 (26%)	49 (21%)	
occasionally	635 (42%)	126 (38%)	409 (43%)	100 (42%)	
1-2 glasses a day	321 (21%)	72 (22%)	188 (20%)	61 (26%)	
3+ glasses a day	55 (4%)	12 (4%)	39 (4%)	4 (2%)	
Father figure's alcohol use					$\chi^2(8)=10.2$ *p*= .25
never	134 (5%)	26 (4%)	90 (4%)	18 (4%)	
very occasionally	573 (20%)	131 (20%)	366 (20%)	76 (18%)	
occasionally	1164 (40%)	284 (44%)	718 (40%)	162 (38%)	
1-2 glasses a day	774 (27%)	159 (24%)	487 (27%)	128 (30%)	
3+ glasses a day	255 (8%)	52 (8%)	157 (9%)	46 (10%)	

Table 10 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2, ANOVA
Mother's cigarette use					$\chi^2(6)=4.13$ $p= .66$
none	1259 (86%)	273 (85%)	797 (87%)	189 (85%)	
< 10 a day	48 (3%)	11 (3%)	27 (3%)	10 (5%)	
10-19 a day	38 (3%)	6 (2%)	25 (3%)	7 (3%)	
> 20 a day	115 (8%)	31 (10%)	67 (7%)	17 (7%)	
Father figure's cigarette use					$\chi^2(6)=27.58$ $p<.001$
none	2219 (80%)	458 (73%)	1436 (82%)	325 (80%)	
< 10 a day	67 (2%)	17 (3%)	34 (2%)	16 (4%)	
10-19 a day	74 (3%)	19 (3%)	45 (2%)	10 (3%)	
> 20 a day	433 (15%)	133 (21%)	243 (14%)	57 (13%)	
Mother's cannabis use					$\chi^2(6)=13.19$ $p=.04$
not at all	3033 (96%)	685 (96%)	1908 (96%)	440 (94%)	
sometimes	108 (2.6%)	16 (2%)	71 (2.7%)	21 (5.4%)	
often	23 (1%)	10 (1%)	11 (1%)	2 (0.4%)	
every day	12 (0.4%)	5 (1%)	6 (0.3%)	1 (0.2%)	
Father figure's cannabis use					$\chi^2(6)=3.54$ $p=.74$
not at all	1434 (93%)	316 (94%)	897 (92%)	221 (92%)	
sometimes	73 (5%)	13 (4%)	45 (5%)	15 (6%)	
often	19 (1%)	2 (1%)	14 (2%)	3 (1%)	
every day	10 (1%)	2 (1%)	7 (1%)	1 (1%)	
Earlier alcohol use					$\chi^2(2)=7.13$
did not have whole drink before age 13	536 (37%)	118 (34%)	339 (37%)	79 (46%)	$p= .03$
had whole drink before age 13	896 (63%)	226 (66%)	578 (63%)	92 (54%)	
Earlier cigarette use					$\chi^2(2)=8.20$
did not smoke at age 13	2157 (73%)	467 (72%)	1346 (72%)	344 (79%)	$p= .02$
smoked at age 13	792 (27%)	184 (28%)	515 (28%)	93 (21%)	
Earlier cannabis use					$\chi^2(2)=11.64$
did not use at age 13	2770 (94%)	599 (92%)	1746 (94%)	425 (97%)	$p= .003$
used at age 13	177 (6%)	50 (8%)	115 (6%)	12 (3%)	
Mother-child interaction					$F(2)=2.43$, $p=.09$
Range (17-56)	3508 (38.0)	687 (38.0)	1904 (38.0)	427 (38.6)	

Table 10 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2, ANOVA
Father figure-child interaction					F(2)=0.06, *p*=.95
Range (18-84)	3512 (44.0)	698 (44.0)	1899 (44.1)	438 (44.2)	
Number of alcohol drinking friends					χ^2(4)=11.56, *p*=.02
none	70 (3%)	18 (3%)	37 (2%)	15 (4%)	
one or some	724 (28%)	132 (24%)	461 (28%)	131 (32%)	
most or all	1803 (69%)	400 (73%)	1142 (70%)	261 (64%)	
Number of cigarette smoking friends					χ^2(4)=1.31, *p*=.86
none	414 (16%)	84 (15%)	261 (16%)	69 (17%)	
one or some	1488 (57%)	309 (56%)	945 (58%)	234 (57%)	
most or all	698 (27%)	157 (29%)	435 (26%)	106 (26%)	
Number of cannabis using friends					χ^2(4)=19.94, *p*=.001
none	1174 (45%)	227 (41%)	723 (44%)	224 (55%)	
one or some	1150 (44%)	258 (47%)	746 (46%)	146 (36%)	
most or all	271 (11%)	64 (12%)	168 (10%)	39 (9%)	
Having delinquent friends					χ^2(2)=14.16, *p*=.001
no	597 (23%)	102 (19%)	377 (23%)	118 (29%)	
yes	1986 (77%)	446 (81%)	1251 (77%)	289 (71%)	

To test the first hypothesis, ordered logistic regression models were conducted unadjusted as well as adjusted for confounders (financial difficulties, parental education, maternal and father figure alcohol, cigarette and cannabis use, girls' own earlier alcohol, cigarette and cannabis use) to assess whether there were differences in substance use between the three pubertal timing groups (see Table 11). The results showed that late maturing girls drank less alcohol at age 16 years than on-time maturing girls (OR = 0.76), but after adjusting for confounders (i.e., after adjusting for girls' own earlier alcohol use), this effect disappeared. Late maturing girls smoked fewer cigarettes than early (OR = 0.68) and on-time maturing (OR = 0.76) girls at age 16 years, but after adjusting for confounders, these odds ratios were increased to OR = 0.94 in both cases. Additionally, late maturing girls used less cannabis than early (OR = 0.67) and on-time (OR = 0.63) maturing girls at age 16 years; but after adjusting for confounders, the odds ratios were increased to OR = 0.72 and OR = 0.65 respectively.

Having a closer look at the confounders showed that maternal alcohol use (OR=1.43, 95% CI: 1.10, 1.88) and girls' own earlier alcohol use (OR=1.60, 95% CI: 1.06, 2.40) predicted alcohol use at age 16 years. Maternal cigarette use (OR=1.34, 95% CI: 1.12, 1.60) and girls' own earlier cigarette use (OR=7.12, 95% CI: 5.20, 9.75) predicted cigarette use at age 16 years. Father figure cannabis use (OR=2.61, 95% CI: 1.62, 4.20) and girls' own earlier cannabis use (OR=8.33, 95% CI: 4.90, 14.16) predicted cannabis use at age 16 years.

Table 11 Regression analysis of pubertal timing on substance use

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Alcohol outcome	*Pubertal timing*		
	On-time versus early	0.85 [0.69, 1.03]	0.79 [0.50, 1.24]
	On-time versus late	0.76 [0.60, 0.96]	1.33 [0.73, 2.42]
	Early versus late	0.89 [0.68, 1.18]	1.69 [0.86, 3.31]
		$\chi^2(2)$= 6.97, *p* = .03	$\chi^2(2)$ = 2.42, *p* = .30
Cigarette outcome	*Pubertal timing*		
	On-time versus early	1.12 [0.94, 1.33]	1.01 [0.73, 1.38]
	On-time versus late	0.76 [0.62, 0.93]	0.94 [0.65, 1.37]
	Early versus late	0.68 [0.54, 0.86]	0.94 [0.61, 1.45]
		$\chi^2(2)$ = 10.77, *p* = .005	$\chi^2(2)$ = 0.10, *p* = .95
Cannabis outcome	*Pubertal timing*		
	On-time versus early	0.94 [0.77, 1.15]	0.90 [0.63, 1.29]
	On-time versus late	0.63 [0.49, 0.81]	0.65 [0.42, 1.01]
	Early versus late	0.67 [0.50, 0.90]	0.72 [0.43, 1.21]
		$\chi^2(2)$= 13.53, *p* = .001	$\chi^2(2)$ = 3.69, *p* = .16

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), and substance use at age 14 years

Ordered logistic regression was conducted to assess whether there were differences in the level of parent-daughter communication; level of parent-daughter conflict and level of parental monitoring between the pubertal timing groups unadjusted as well as adjusted for confounders (financial difficulties, parental education, maternal and paternal alcohol, cigarette and cannabis use, earlier alcohol, cigarette and cannabis use, mother-child interaction and father figure-child interaction at age 9 years; see Table 12).

Table 12 Regression analysis of pubertal timing on parent-daughter relationship quality

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Parent-daughter communication	*Pubertal timing*		
	On-time versus early	0.95 [0.79, 1.14]	1.06 [0.68, 1.65]
	On-time versus late	0.98 [0.80, 1.21]	1.81 [0.99, 3.25]
	Early versus late	1.03 [0.81, 1.32]	1.72 [0.89, 3.29]
		$\chi^2(2)= 0.31$, $p = .86$	$\chi^2(2)= 4.02$, $p = .13$
Parent-daughter conflict	*Pubertal timing*		
	On-time versus early	0.94 [0.78, 1.14]	0.99 [0.63, 1.55]
	On-time versus late	0.90 [0.73, 1.12]	1.20 [0.67, 2.15]
	Early versus late	0.96 [0.75, 1.24]	1.22 [0.64, 2.34]
		$\chi^2(2)= 1.09$, $p = .58$	$\chi^2(2)= 0.44$, $p = .80$
Parental monitoring	*Pubertal timing*		
	On-time versus early	0.98 [0.81, 1.18]	0.98 [0.62, 1.54]
	On-time versus late	0.82 [0.66, 1.01]	1.00 [0.55, 1.82]
	Early versus late	0.83 [0.65, 1.07]	1.02 [0.53, 1.97]
		$\chi^2(2)= 3.51$, $p = .17$	$\chi^2(2)= 0.01$, $p = .99$

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), substance use at age 14 years and parent-child interaction at age 9 years

No differences in parent-daughter relationship quality across the three pubertal timing groups were found. Having a closer look at the confounders showed that financial difficulties (OR=0.87, 95% CI: 0.78, 0.97) and parental education (OR=1.26, 95% CI: 1.02, 1.55) predicted parent-daughter communication at age 15 years. Financial difficulties (OR=0.88, 95% CI: 0.80, 0.98) predicted parent-daughter conflict at age 15 years. Financial difficulties (OR=0.89, 95% CI: 0.80, 0.99) and earlier alcohol use (OR=1.63, 95% CI: 1.10, 2.42) predicted parental monitoring at age 15 years.

To test the second hypothesis, ordered logistic regression models were conducted to evaluate the effect of parent-daughter relationship quality (level of parent-daughter communication, parent-daughter conflict and parental monitoring) at age 15 years on substance use (alcohol, cigarette and cannabis use) at age 16 years (see Table 13).

Table 13 Regression analysis of parent-daughter relationship quality on girls' substance use

Outcome	Predictor	Unadjusted for confounders		Adjusted for confounders[1]	
		$\chi^2(1)$, p	OR [95% CI]	$\chi^2(1)$, p	OR [95% CI]
Alcohol	Parent-daughter communication	51.61, <.001	1.68 [1.46, 1.94]	9.45, .002	1.66 [1.20, 2.29]
	Parent-daughter conflict	70.67, <.001	1.70 [1.51, 1.93]	10.94, .001	1.69 [1.24, 2.30]
	Parental monitoring	139.23, <.001	2.60 [2.22, 3.05]	19.12, <.001	2.43 [1.63, 3.61]
Cigarettes	Parent-daughter communication	94.11, <.001	1.89 [1.66, 2.15]	15.03, <.001	1.61 [1.27, 2.06]
	Parent-daughter conflict	133.20, <.001	1.96 [1.75, 2.20]	2.70, .10	1.21 [0.96, 1.52]
	Parental monitoring	193.83, <.001	2.82 [2.44, 3.27]	11.46, .001	1.65 [1.24, 2.21]
Cannabis	Parent-daughter communication	55.43, <.001	1.74 [1.51, 2.02]	12.23, .001	1.63 [1.24, 2.15]
	Parent-daughter conflict	75.90, <.001	1.77 [1.55, 2.01]	2.26, .13	1.22 [0.94, 1.59]
	Parental monitoring	192.62, <.001	3.20 [2.72, 3.77]	34.83, <.001	2.72 [1.95, 3.79]

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 15 years (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-child interaction at age 9 years (mother-child interaction and father figure-child interaction)

Parent-daughter communication predicted alcohol, cigarette and cannabis use in the unadjusted as well as the adjusted models. Parent-daughter conflict predicted alcohol, cigarette and cannabis use in the unadjusted models; however the effect remained only for alcohol use after adjusting for confounders. More specifically, the odds ratio of predicting cigarette use at age 16 years by parent-daughter conflict at age 15 years were decreased from OR = 1.96 to OR = 1.21 after adjusting for confounders. The odds ratio of predicting cannabis use at age 16 years by parent-daughter conflict at age 15 years was reduced from OR = 1.77 to OR = 1.22 after adjusting for confounders. Parental monitoring predicted alcohol, cigarette and cannabis use in the unadjusted as well as the adjusted models. Additionally, parental monitoring was found to be the strongest predictor of substance use of the three parent-daughter relationship quality factors.

To test the third hypothesis, regression models were conducted unadjusted as well as adjusted for confounders. The results of the mediation analysis are shown in Table 14. The results showed that neither level of communication, nor conflict or level of parental monitoring (all assessed at age 15 years) mediated the effect of pubertal timing on alcohol, cigarette or cannabis use at age 16 years. These results were consistent in the unadjusted as well as the adjusted analyses.

Table 14 Mediation by parent-daughter relationship quality of the association between pubertal timing and substance use unadjusted and adjusted[1] for confounders.

Predictor	**Outcome**	**Mediator**	**Estimates Total effect c (95% CI)**	**Estimates Indirect effect ab (95% CI)**	**Estimates Direct effect c' (95% CI)**
Pubertal timing	Alcohol use	Communication Unadjusted	-0.01 (-.06, .04)	0.002 (-.01, .01)	0.003 (-.05, .06)
		Communication Adjusted[1]	0.09 (-.04, .22)	0.01 (-.01, .04)	0.09 (-.04, .21)
		Conflict Unadjusted	-0.01 (-.06, .04)	-0.002 (-.01,.01)	0.0003 (-.05, .05)
		Conflict Adjusted[1]	0.09 (-.04, .22)	0.004 (-.02, .03)	0.09 (-.04, .22)
		Monitoring Unadjusted	-0.01 (-.06, .04)	-0.01 (-.02, .003)	0.01 (-.04, .06)
		Monitoring Adjusted[1]	0.09 (-.04, .22)	0.004 (-.04, .05)	0.09 (-.03, .22)
Pubertal timing	Cigarette use	Communication Unadjusted	-0.12 (-.19, -.05)	0.003 (-.01, .02)	-0.12 (-.20, -.05)
		Communication Adjusted[1]	-0.04 (-.14, .06)	0.02 (-.002, .04)	-0.05 (-.15, .06)
		Conflict Unadjusted	-0.12 (-.19, -.05)	-0.004 (-.02, .01)	-0.13 (-.20, -.05)
		Conflict Adjusted[1]	-0.04 (-.14, .06)	0.001 (-.01, .02)	-0.03 (-.14, .08)
		Monitoring Unadjusted	-0.12 (-.19, -.05)	-0.02 (-.01, .005)	-0.11 (-.18, -.04)
		Monitoring Adjusted[1]	-0.04 (-.14, .06)	0.004 (-.02, .03)	-0.03 (-.14, .07)

Table 14 continued

Predictor	Outcome	Mediator	Estimates Total effect c (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Direct effect c' (95% CI)
Pubertal timing	Cannabis use	Communication Unadjusted	-0.05 (-.09, -.01)	0.002 (-.005, .009)	-0.06 (-.10, -.01)
		Communication Adjusted[1]	-0.02 (-.08, .04)	0.008 (-.007, .02)	-0.05 (-.12, .02)
		Conflict Unadjusted	-0.05 (-.09, -.01)	-0.002 (-.008, .005)	-0.06 (-.10, -.01)
		Conflict Adjusted[1]	-0.02 (-.08, .04)	-0.001 (-.01, .008)	-0.04 (-.11, .03)
		Monitoring Unadjusted	-0.05 (-.09, -.01)	-0.01 (-.02, .01)	-0.05 (-.09, -.01)
		Monitoring Adjusted[1]	-0.02 (-.08, .04)	-0.004 (-.03, .02)	-0.04 (-.10, .02)

[1] Adjusted for: financial difficulties, parental education, parents' substance use, substance use at age 14 years, mother-child interaction at age 9 years, father figure-child interaction at age 9 years and peer behaviour at age 15 years

To test the fourth hypothesis, ordered logistic regression models were conducted and the post-estimation command *testparm* was used to test for moderation (for detail see section 6.2.2). Unadjusted results of the moderation analysis are shown in Table 15 and adjusted results in Table 16.

No moderation effects were found.

Table 15 Moderation by pubertal timing of the relationship between parent-daughter relationship quality and substance use

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Alcohol	Pubertal timing	2.79	.25
Parent-daughter conflict			5.72	.06
Parental monitoring			3.10	.21
Parent-daughter communication	Cigarettes	Pubertal timing	1.12	.57
Parent-daughter conflict			0.84	.66
Parental monitoring			1.33	.51
Parent-daughter communication	Cannabis	Pubertal timing	1.09	.58
Parent-daughter conflict			0.15	.93
Parental monitoring			1.36	.51

Table 16 Adjusted moderation by pubertal timing of the relationship between parent-daughter relationship quality and substance use

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Alcohol	Pubertal timing	0.29	.86
Parent-daughter conflict			1.00	.61
Parental monitoring			0.74	.69
Parent-daughter communication	Cigarettes	Pubertal timing	1.18	.55
Parent-daughter conflict			0.57	.75
Parental monitoring			4.33	.11

Table 16 continued

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Cannabis	Pubertal timing	0.22	.89
Parent-daughter conflict			1.86	.39
Parental monitoring			2.98	.23

Adjusted for: financial difficulties, parental education, maternal and father figure alcohol, cigarette and cannabis use, earlier alcohol, cigarette and cannabis use at age 14 years, earlier mother-child interaction, father figure-child interaction at age 9 years and peer deviance at age 15 years

To summarise, I obtained the following main findings for complete cases: (1) Late maturing girls drank less alcohol, at age 16 years than on-time maturing girls, but no difference between the pubertal timing groups was found after adjusting for confounders; (2) Late maturing girls smoked fewer cigarettes and used less cannabis than early and on-time maturing girls, but no difference between the pubertal timing groups was found after adjusting for confounders; (3) Lower levels of parent-daughter communication at age 15 years were linked to higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted and adjusted models; (4) Higher levels of parent-daughter conflict at age 15 years were linked to higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted models, however the effect remained only for alcohol use after adjusting for confounders; (5) Lower levels of parental monitoring at age 15 years were linked to higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted and adjusted models; and (6) no combined effects (mediation nor moderation) of pubertal timing and parent-daughter relationship quality on substance use at age 16 years were found.

8.6 Results for the imputed data

Due to the relatively high rates of data attrition (see Table 8) multiple imputation was conducted to impute the missing values (see chapter 7). This section presents the results of analysis based on imputed data. To test the first hypothesis, ordered logistic regression models were conducted unadjusted as well as adjusted for confounders for each of the eighty imputed data sets and the estimates of each imputed data set were combined using Rubin's rule (see section 6.1.2.1). Ordered logistic regression was conducted to test whether there were differences in substance use between the pubertal timing groups in the imputed data and the results are shown in Table 17.

Table 17 Imputed regression analysis of pubertal timing on substance use

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Alcohol outcome	*Pubertal timing*		
	On-time versus early	0.86 [0.71, 1.05]	0.85 [0.70, 1.04]
	On-time versus late	0.76 [0.60, 0.96]	0.76 [0.60, 0.96]
	Early versus late	0.88 [0.67, 1.16]	0.89 [0.67, 1.17]
		$\chi^2(2)= 6.33$, $p = .04$	$\chi^2(2) = 6.45$, $p = .04$
Cigarette outcome	*Pubertal timing*		
	On-time versus early	1.12 [0.94, 1.33]	1.05 [0.87, 1.26]
	On-time versus late	0.76 [0.63, 0.94]	0.88 [0.71, 1.09]
	Early versus late	0.68 [0.54, 0.87]	0.84 [0.66, 1.09]
		$\chi^2(2) = 10.26$, $p = .006$	$\chi^2(2) = 1.84$, $p = .40$
Cannabis outcome	*Pubertal timing*		
	On-time versus early	0.95 [0.77, 1.16]	0.88 [0.71, 1.09]
	On-time versus late	0.64 [0.50, 0.82]	0.68 [0.52, 0.88]
	Early versus late	0.67 [0.51, 0.82]	0.77 [0.57, 1.04]
		$\chi^2(2)= 12.19$, $p = .002$	$\chi^2(2) = 8.95$, $p = .01$

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), and substance use at age 14 years

The results show that late maturing girls drank less alcohol at age 16 years than on-time maturing girls (OR = 0.76) and the odds ratio remained constant after taking the confounding variables into account. Late maturing girls also used fewer cigarettes than early (OR = 0.68) and on-time (OR = 0.76) maturing girls but after adjusting for confounders the odds ratio of the late maturing girls compared to the early maturing girls was increased to OR = 0.84 and the odds ratio of the late maturing girls compared to the on-time maturing girls was increased to OR = 0.88. Late maturing girls were also found to use less cannabis than early (OR = 0.67) and on-time maturing girls (OR = 0.64), but after adjustment for confounders the odds ratio of the late maturing girls compared to the early maturing girls was increased significantly to OR = 0.77 and the odds ratio of the late maturing girls compared to the on-time maturing girls was increased to OR = 0.68. The following confounders were identified as contributing to the relationship between pubertal timing and substance use at age 16 years: maternal alcohol use (OR=1.14, 95% CI: 1.01, 1.29), father figure alcohol use (OR=1.12, 95% CI:1.01, 1.25) and girls' own earlier alcohol use (OR=1.54, 95% CI: 1.21, 1.97) predicted alcohol use at age 16 years; maternal cigarette use (OR=1.14, 95% CI: 1.03, 1.25), father figure cigarette use (OR=1.13, 95% CI: 1.05, 1.22) and girls' own earlier cigarette use (OR=7.20, 95% CI: 5.99, 8.64) predicted cigarette use at age 16 years; financial difficulties (OR=0.96, 95% CI: 0.92, 1.00), parental education (OR=1.10, 95% CI: 1.02, 1.18), maternal cannabis use (OR=2.21, 95% CI: 1.45, 3.37) and girls' own earlier cannabis use (OR=8.79, 95% CI: 6.31, 12.25) predicted cannabis use at age 16 years.

The effects of pubertal timing on parent-daughter relationship quality conducted on imputed data unadjusted as well as adjusted for confounders (financial difficulties, parental education, maternal and father figure alcohol, cigarette and cannabis use, earlier alcohol, cigarette and cannabis use, mother-child interaction and father figure-child interaction at age 9 years) are shown in Table 18. No differences in level of parent-daughter communication, parent-daughter conflict and parental monitoring across the three pubertal timing groups were found in the unadjusted as well as the adjusted models. With regards to confounders it was found that girls' own earlier alcohol use (OR=1.16, 95% CI: 1.02, 1.32) and father figure-child interaction (OR=0.98, 95% CI: 0.97, 0.99) predicted parental monitoring at age 15 years.

Table 18 Imputed regression analysis of pubertal timing on parent-daughter relationship quality

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Parent-daughter communication	*Pubertal timing*		
	On-time versus early	0.97 [0.84, 1.12]	0.97 [0.84, 1.12]
	On-time versus late	1.00 [0.85, 1.18]	1.00 [0.85, 1.18]
	Early versus late	1.03 [0.85, 1.25]	1.03 [0.85, 1.25]
		$\chi^2(2)= 0.26$, $p = .88$	$\chi^2(2)= 0.29$, $p = .86$
Parent-daughter conflict	*Pubertal timing*		
	On-time versus early	0.98 [0.84, 1.14]	0.97 [0.83, 1.13]
	On-time versus late	0.96 [0.80, 1.16]	0.96 [0.80, 1.16]
	Early versus late	0.98 [0.78, 1.24]	0.99 [0.78, 1.26]
		$\chi^2(2)= 1.02$, $p = .60$	$\chi^2(2)= 0.98$, $p = .61$
Parental monitoring	*Pubertal timing*		
	On-time versus early	1.00 [0.86, 1.15]	0.99 [0.86, 1.14]
	On-time versus late	0.91 [0.76, 1.08]	0.91 [0.76, 1.08]
	Early versus late	0.91 [0.75, 1.11]	0.92 [0.75, 1.12]
		$\chi^2(2)= 3.32$, $p = .19$	$\chi^2(2)= 3.35$, $p = .19$

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), substance use at age 14 years and parent-child interaction at age 9 years

For the second hypothesis, ordered logistic regression models were conducted to test the effect of parent-daughter relationship quality (level of parent-daughter communication, level of parent-daughter conflict, parental monitoring) at age 15 years on substance use (alcohol, cigarette and cannabis use) at age 16 years in the imputed data (see Table 19). It was found that parent-daughter communication predicted alcohol, cigarette and cannabis use in the unadjusted and the adjusted models. Specifically, lower levels of parent-daughter communication were linked to higher levels of alcohol, cigarette and cannabis use. Parent-daughter conflict predicted alcohol, cigarette and cannabis use in the unadjusted and adjusted models: higher levels of parent-daughter conflict were linked to higher levels of alcohol, cigarette and cannabis use. Parental monitoring predicted alcohol, cigarette and cannabis use in the unadjusted as well as the adjusted models: less parental monitoring was linked to higher levels of alcohol, cigarette and cannabis use. Additionally, it was found that the effects were largest for parental monitoring.

Table 19 Imputed regression analysis of parent-daughter relationship quality on substance use

Outcome	Predictor	Unadjusted for confounders		Adjusted for confounders[1]	
		$X^2(1)$, *p*	OR [95% CI]	$X^2(1)$, *p*	OR [95% CI]
Alcohol	Parent-daughter communication	52.08, <.001	1.56 [1.36, 1.78]	75.63, <.001	1.34 [1.17, 1.54]
	Parent-daughter conflict	71.89, <.001	1.55 [1.38, 1.75]	77.22, <.001	1.33 [1.18, 1.52]
	Parental monitoring	144.06, <.001	2.41 [2.06, 2.82]	85.87, <.001	1.83 [1.55, 2.17]
Cigarettes	Parent-daughter communication	95.70, <.001	1.61 [1.43, 1.82]	299.94, <.001	1.31 [1.15, 1.50]
	Parent-daughter conflict	137.85, <.001	1.68 [1.50, 1.88]	286.83, <.001	1.34 [1.19, 1.51]
	Parental monitoring	200.73, <.001	2.25 [1.96, 2.58]	296.35, <.001	1.49 [1.29, 1.74]

Table 19 continued

Outcome	Predictor	Unadjusted for confounders		Adjusted for confounders[1]	
		$X^2(1)$, *p*	OR [95% CI]	$X^2(1)$, *p*	OR [95% CI]
Cannabis	Parent-daughter communication	55.73, <.001	1.54 [1.34, 1.77]	266.21, <.001	1.25 [1.07, 1.46]
	Parent-daughter conflict	76.91, <.001	1.59 [1.41, 1.79]	255.85, <.001	1.27 [1.11, 1.45]
	Parental monitoring	202.21, <.001	2.49 [2.14, 2.90]	290.24, <.001	1.65 [1.39, 1.97]

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 15 years (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 9 years (mother-child interaction and father figure-child interaction)

To test the third hypothesis, regression models were conducted unadjusted as well as adjusted for confounders (financial difficulties, parental education, maternal and father figure alcohol, cigarette and cannabis use, earlier alcohol, cigarette and cannabis use (at age 14 years), earlier mother-child interaction, father figure-child interaction (at age 9 years) and peer deviance (at age 15 years) in the imputed data. The mediation analysis is shown in Table 20. There was no evidence that parent-daughter relationship quality at age 15 years (level of parent-daughter communication, level of parent-daughter conflict and parental monitoring) mediated the effect of pubertal timing on substance use at age 16 in the unadjusted or the adjusted models.

Table 20 Imputed mediation by parent-daughter relationship quality of the association between pubertal timing and substance use unadjusted and adjusted[1] for confounders

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
Pubertal timing	Alcohol	Communication Unadjusted	-0.01 (-.06, .04)	0.002 (-.005, .008)	-0.01 (-.06, .04)
		Communication Adjusted[1]	0.01 (-.03, .06)	0.001 (-.003, .005)	0.01 (-.03, .06)
		Conflict Unadjusted	-0.01 (-.06, .03)	0.002 (-.008, .01)	-0.01 (-.06, .04)
		Conflict Adjusted[1]	0.01 (-.04, .05)	0.003 (-.003, .009)	0.01 (-.03, .06)
		Monitoring Unadjusted	-0.01 (-.05, .04)	-0.003 (-.02, .01)	-0.01 (-.06, .04)
		Monitoring Adjusted[1]	0.01 (-.03, .06)	-0.0002 (-.009, .008)	0.01 (-.03, .06)
	Cigarettes	Communication Unadjusted	-0.12 (-.18, -.05)	0.003 (-.01, .01)	-0.12 (-.18, -.05)
		Communication Adjusted[1]	-0.05 (-.11, .01)	0.002 (-.002, .007)	-0.06 (-.1, -.01)
		Conflict Unadjusted	-0.12 (-.18, -.05)	0.003 (-.02, .02)	-0.12 (-.18, -.05)
		Conflict Adjusted[1]	-0.05 (-.10, .01)	0.004 (-.004, .01)	-0.04 (-.10, .01)
		Monitoring Unadjusted	-0.11 (-.18, -.05)	-0.005 (-.02, .01)	-0.12 (-.18, -.05)
		Monitoring Adjusted[1]	-0.04 (-.10, .01)	0.002 (-.01, .01)	-0.04 (-.10, .01)

Table 20 continued

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
Pubertal timing	Cannabis	Communication Unadjusted	-0.05 (-.09, -.01)	0.001 (-.004, .007)	-0.05 (-.09, -.01)
		Communication Adjusted[1]	-0.01 (-.05, .02)	0.001 (-.001, .004)	-0.01 (-.05, .02)
		Conflict Unadjusted	-0.05 (-.09, -.01)	0.0007 (-.008, .009)	-0.05 (-.09, -.01)
		Conflict Adjusted[1]	-0.01 (-.05, .02)	0.001 (-.002, .005)	-0.01 (-.05, .02)
		Monitoring Unadjusted	-0.03 (-.07, .01)	-0.003 (-.01, .008)	-0.05 (-.09, -.01)
		Monitoring Adjusted[1]	-0.01 (-.05, .02)	0.0005 (-.005, .006)	-0.01 (-.05, .02)

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 15 years (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 9 years (mother-child interaction and father figure-child interaction)

To test the fourth hypothesis, ordered logistic regression models were conducted in the imputed data and then the post-estimation command *testparm* was used to test for moderation. Analysis was run unadjusted as well as adjusted for confounders. Unadjusted results of the moderation analysis for the imputed data are shown in Table 21.

Table 21 Imputed moderation by pubertal timing of the relationship between parent-daughter relationship quality and substance use

Predictor	**Outcome**	**Moderator**	**Wald $\chi^2(2)$**	***p***
Parent-daughter communication	Alcohol	Pubertal timing	2.33	.31
Parent-daughter conflict			2.58	.28
Parental monitoring			1.57	.46

Table 21 continued

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Cigarettes	Pubertal timing	1.01	.60
Parent-daughter conflict			0.80	.67
Parental monitoring			0.60	.74
Parent-daughter communication	Cannabis	Pubertal timing	0.84	.66
Parent-daughter conflict			0.05	.97
Parental monitoring			0.53	.77

No evidence was found that the effect of parent-daughter relationship quality (level of parent-daughter communication, parent-daughter conflict and parental monitoring) at age 15 years on substance use (alcohol, cigarette and cannabis use) at age 16 years differed for early, on-time and late maturing girls. Adjusted moderation analysis in the imputed data is shown in Table 22. No evidence for the effect of parent-daughter relationship quality (level of parent-daughter communication, level of parent-daughter conflict and parental monitoring) at age 15 years on substance use (alcohol, cigarette and cannabis use) at age 16 years being different across early, on-time and late maturing girls was found in the adjusted models.

Table 22 Imputed moderation by pubertal timing of the relationship between parent-daughter relationship quality and substance use adjusted for confounders.[1]

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Alcohol	Pubertal timing	1.18	.55
Parent-daughter conflict			3.87	.14
Parental monitoring			0.86	.65

Table 22 continued

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Parent-daughter communication	Cigarettes	Pubertal timing	0.83	.66
Parent-daughter conflict			2.10	.35
Parental monitoring			0.31	.86
Parent-daughter communication	Cannabis	Pubertal timing	0.11	.95
Parent-daughter conflict			0.34	.84
Parental monitoring			0.13	.94

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 15 years (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 9 years (mother-child interaction and father figure-child interaction)

The key findings of these analyses were: (1) Late maturing girls drank less alcohol at age 16 years than on-time maturing girls in the unadjusted model. This effect remained after adjusting for confounders; (2) Late maturing girls smoked fewer cigarettes at age 16 years than early and on-time maturing girls in the unadjusted model. This effect disappeared after adjusting for confounders; (3) Late maturing girls used less cannabis at age 16 years than early and on-time maturing girls in the unadjusted model. After adjusting for confounders late maturing girls use less cannabis than on-time maturing girls; (4) Lower levels of parent-daughter communication at age 15 years predicted higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted and adjusted models; (5) Higher levels of parent-daughter conflict at age 15 years predicted higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted and adjusted models; (6) Lower levels of parental monitoring at age 15 years predicted higher levels of alcohol, cigarette and cannabis use at age 16 in the unadjusted and adjusted models; (7) No evidence for combined effects (neither mediation nor moderation) of pubertal timing and parent-daughter relationship quality at age 15 years on substance use at age 16 years was found.

8.7 Comparison of complete case and imputed results

This section is aimed to provide a better overview of the results of the complete case analysis and the imputed analysis (significant effects are represented by hollow data points).

Figures 7-9 show the effects of pubertal timing on alcohol, cigarette and cannabis use in the complete case analysis unadjusted for confounders, complete case analysis adjusted for confounders, imputed analysis unadjusted for confounders and imputed analysis adjusted for confounders.

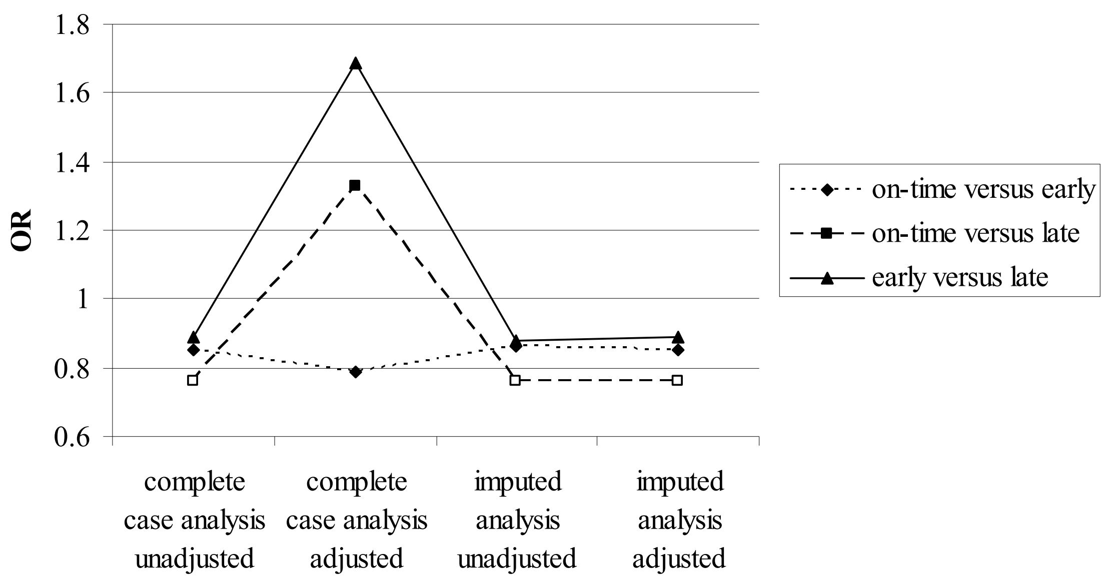


Figure 7. The effects of pubertal timing on alcohol use

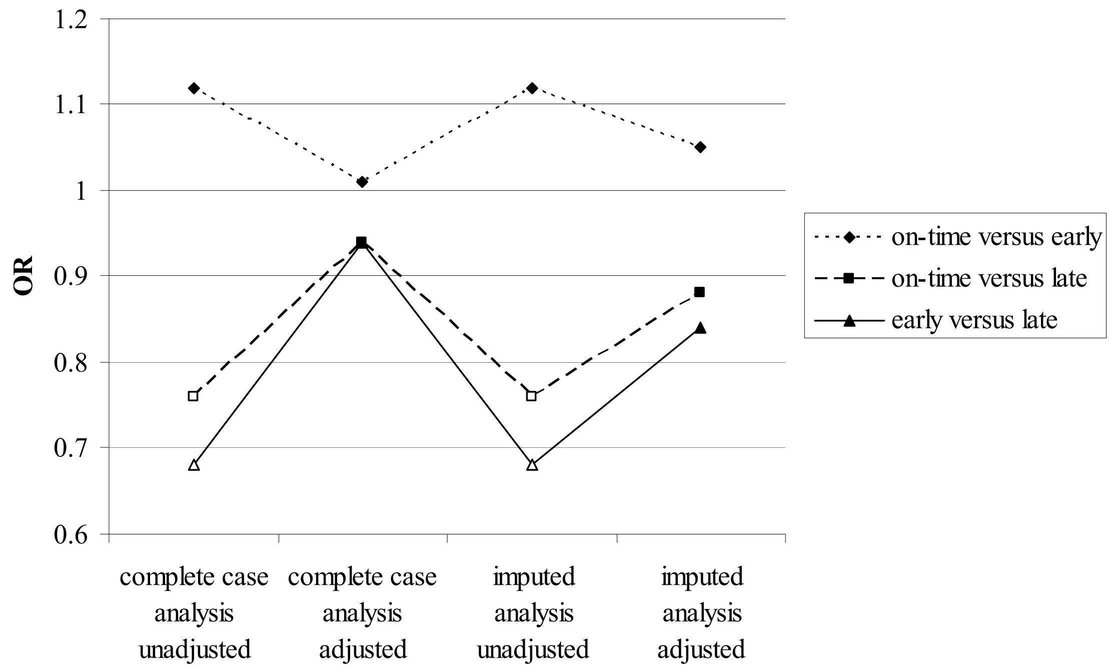


Figure 8. The effects of pubertal timing on cigarette use

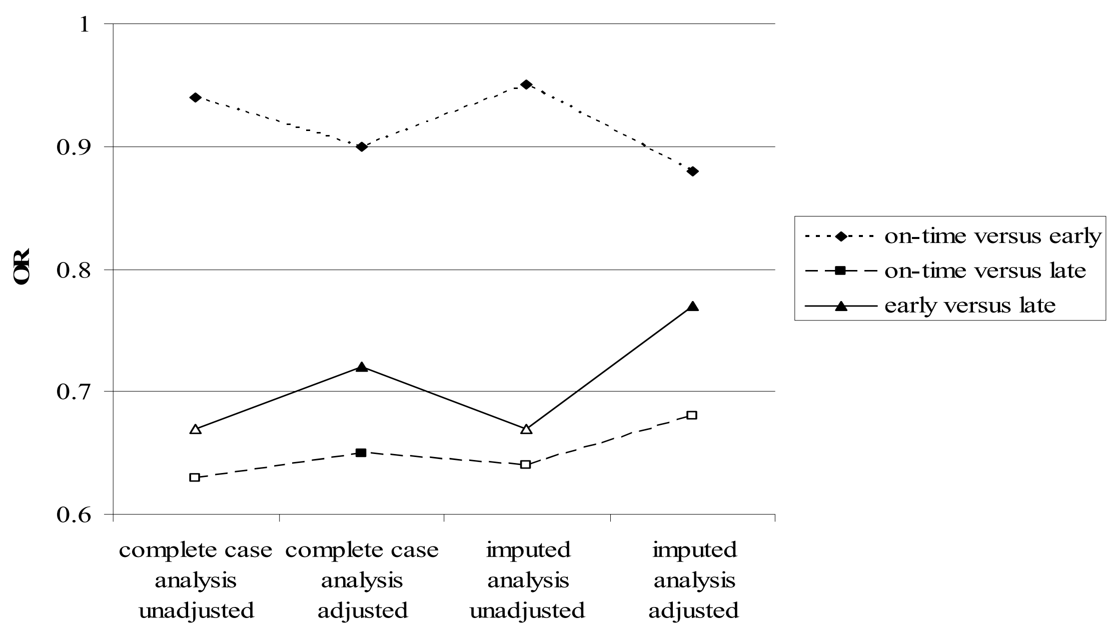


Figure 9. The effects of pubertal timing on cannabis use

Figures 10-12 show the effects of pubertal timing on the parent-daughter relationship quality.

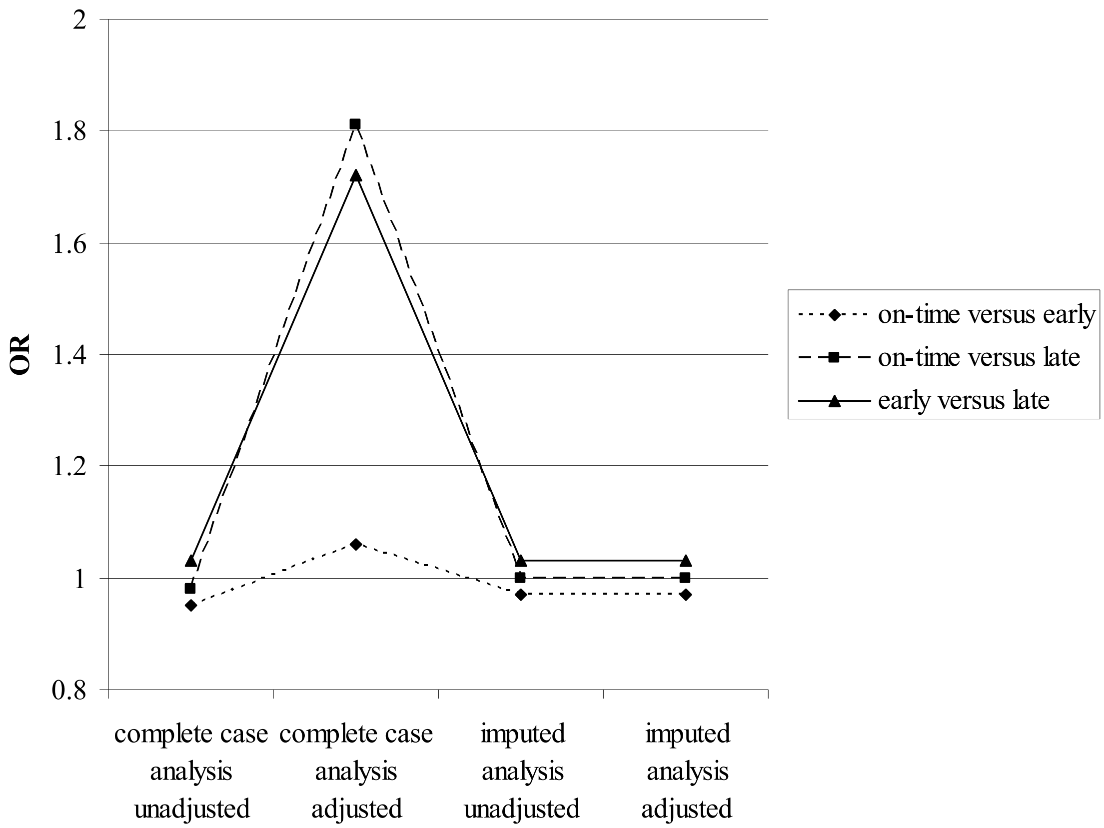


Figure 10. The effects of pubertal timing on parent-daughter communication

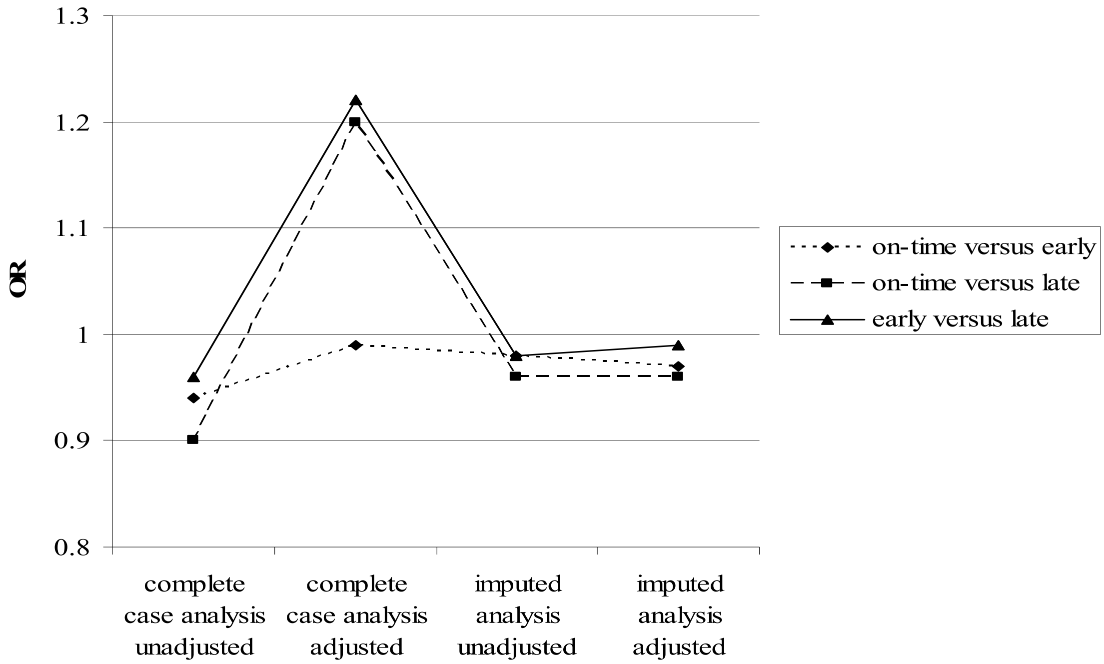


Figure 11. The effects of pubertal timing on parent-daughter conflict

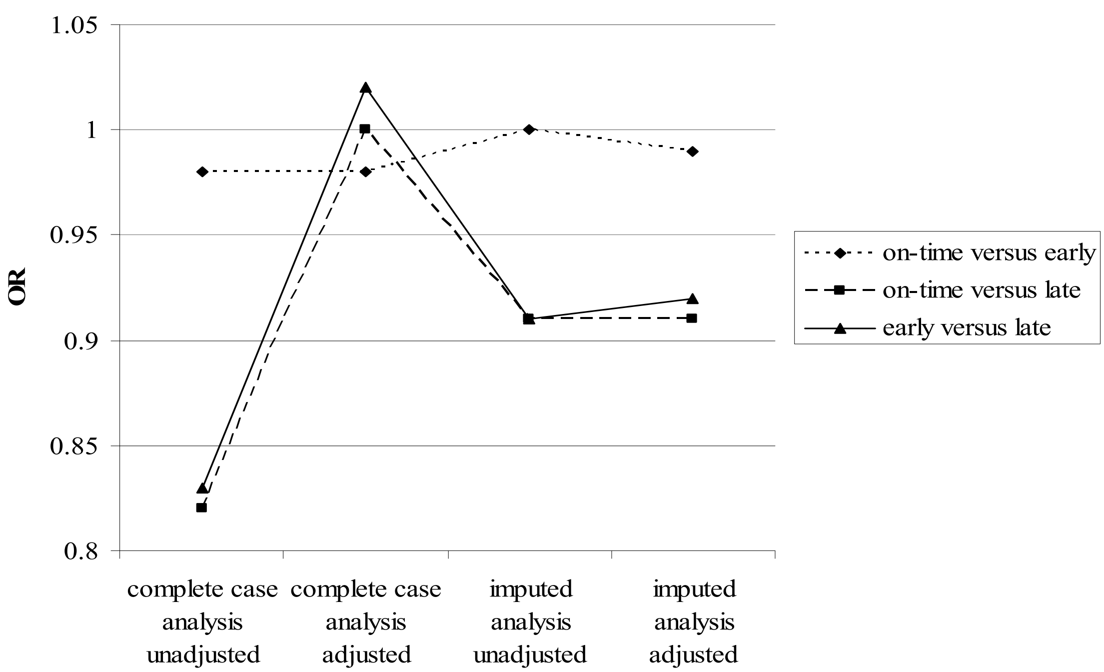


Figure 12. The effects of pubertal timing on parental monitoring

Figures 13-15 show the effects of parent-daughter relationship quality on substance use.

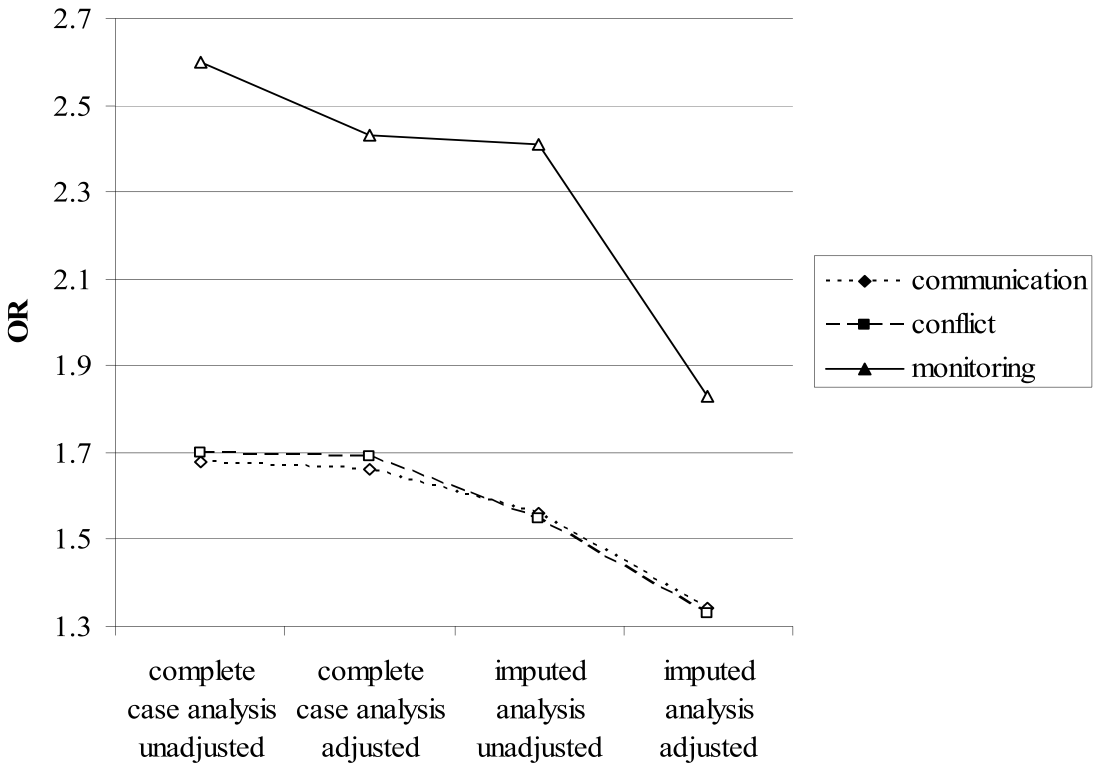


Figure 13. The effects of parent-daughter relationship quality on alcohol use

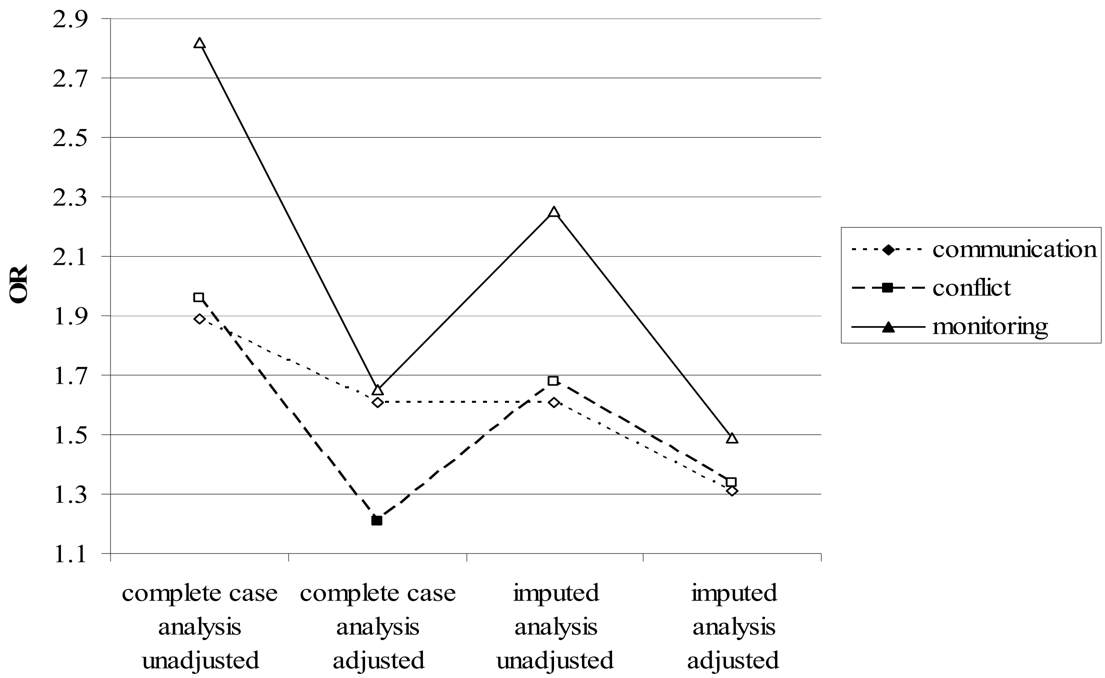


Figure 14. The effects of parent-daughter relationship quality on cigarette use

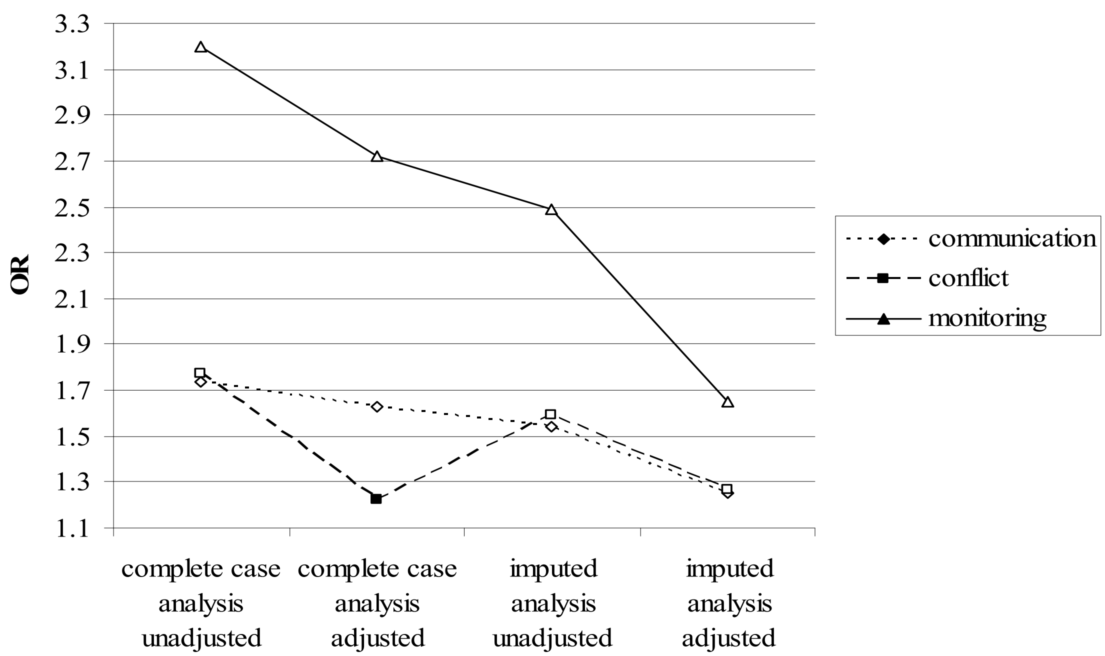


Figure 15. The effects of parent-daughter relationship quality on cannabis use

8.8 Discussion

Few studies have tested the hypothesis that pubertal timing combines with parent-adolescent relationship quality to influence adjustment in adolescence. The present study examined, in a large population based sample, the possible impact of pubertal timing on the longitudinal link between parent-daughter relationship quality and girls' substance use.

8.8.1 Interplay of parent-daughter relationship quality and pubertal timing on substance use. I examined whether specific aspects of parent-daughter relationship quality (communication, conflict and parental monitoring at age 15) combined with pubertal timing to increase risk of substance use in girls, while adjusting for potentially confounding factors.

8.8.1.1 Mediation analysis. There was no evidence that the effect of pubertal timing on substance use at age 16 was mediated by parent-adolescent relationship quality at age 15.

8.8.1.2 Moderation analysis. There was no evidence that the effect of parent-daughter relationship quality on substance use in late adolescence differed for early, on-time and late maturing girls. It is still possible, that such links are present for substance use assessed at an earlier age. This has been previously reported to be the case by Shelton & van den Bree (2010). However, because data on parent-child relationship quality at an earlier age of adolescence is not available in ALSPAC, I could not examine whether such links were present in early or mid-adolescence.

My results are discrepant with previous research by Shelton and van den Bree (2010), who reported a moderating effect of pubertal timing on the relationship between parent-adolescent relationship quality and cigarette use in adolescence, with a stronger effect in late maturing girls than in early and on-time maturing girls. Lynne-Landsman and colleagues (2010) also reported higher levels of binge drinking, cigarette and cannabis use in early maturers in average and high-risk family groups (based on household resources, conflict and stability of household structure) compared to early, on-time and late maturers in low risk families. The discrepancy might be due to differences in sample characteristics (sample size, age, nationality), measurement (e.g., pubertal timing, measures of parent-adolescent relationship quality) and differences in adjustment for confounders. The samples in the studies by Lynne-Landsman and colleagues (2010) and Shelton & van den Bree (2010) were both based on longitudinal studies in the United States and used outcome measures assessed in mid-adolescence, in contrast to my study, which analysed data from a British longitudinal study and used outcome measures assessed in late adolescence. Additionally, the sample size of my study was larger compared to the earlier two studies (Lynne-Landsman et al., 2010; Selton & van den Bree, 2010). Pubertal timing was assessed by child self-report in the study by Shelton and van den Bree (2010) and by mother-report in the study by Lynne-Landsman and colleagues (2010), my study, however used mother-reports as well as girl self-reports to assess pubertal timing. With regards to family functioning Lynne-Landsman and colleagues (2010) focussed on family risk (based on household resources, conflict and stability of household structure), Shelton and van den Bree (2010) focussed on parent-adolescent relationship quality (based on levels of warmth and closeness), whereas my study focussed on parent-adolescent relationship quality based on level of parent-daughter communication, conflict and parental monitoring. Finally, Shelton and van den

Bree (2010) did not adjust for confounders and Lynne-Landsman and colleagues (2010) only adjusted for gender, cohort and ethnicity factors.

8.8.1.3 Interpretation of the findings. There was no evidence in my study for links between early pubertal timing and increased substance involvement in late adolescence (age 15-18 years). This stands in contrast with studies focussing on girls' substance use in early/mid-adolescence (age 9-15 years; Berg-Kelly & Kullander, 1999; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006), but concurs with several (Al-Sahab et al., 2012; Kaltiala-Heino et al., 2011; Marklein et al., 2009), but not all (Bratberg et al., 2007) studies in which girls' substance use was assessed in late adolescence. My findings, however, differed across the three substances, suggesting that by the time girls reach late adolescence (age 16 years) there are differences in alcohol, cigarette and cannabis use across the three pubertal timing groups. That said, after adjusting for confounders, the only remaining difference was that late maturing girls used less alcohol and cannabis than on-time maturing girls. These findings suggest that by the time girls reach late adolescence on-time maturing girls have caught up with early maturing girls in their levels of alcohol, cigarette and cannabis use and late maturing girls have caught up with regards to cigarette use, a finding consistent with three earlier studies (Al-Sahab et al., 2012; Kaltiala-Heino et al., 2011; Marklein et al., 2009).

Some of the results provide support for the *early timing hypothesis* (Peskin, 1973) and the *maturation disparity hypothesis* (see Ge & Natsuaki, 2009). These perspectives propose that early maturing girls are at higher risk of increased substance use because they have fewer cognitive resources to deal with social expectations placed on them commensurate with their mature appearance, compared to girls who mature at a later age (Ge et al., 2002). By the time girls reach late adolescence, their ability to cope with such social expectations may have developed and the adults' expectations may have adjusted to more age appropriate expectations. This, in turn, may attenuate a consistent increase in substance use.

It was also found that lower levels of parent-daughter relationship quality at age 15 years predicted higher levels of substance use at age 16 years. This concurs with previous research (e.g., Dishion et al., 2004; Kaltiala-Heino et al., 2011). A possible explanation of this effect was previously offered by Shelton and colleagues (2008), who proposed that increased substance use of adolescents living in households with poor family functioning, might be seen as a way to cope with lack of emotional and social nurturance at home.

8.8.1.4 Summary. No evidence was found that the effect of pubertal timing on substance use at age 16 years was explained by parent-daughter relationship quality at age 15 years and there was no evidence that the effect of parent-daughter relationship quality at age 15 years on substance use at age 16 years differed for early, on-time and late maturing girls. The only difference between the three pubertal timing groups in levels of substance use was that late maturing girls drank less alcohol and used less cannabis at age 16 years than on-time maturing girls.

CHAPTER 9: PEERS, PUBERTAL TIMING AND SUBSTANCE USE IN ADOLESCENCE

9.1 Introduction

Chapter 8 presented results testing the combined effects of pubertal timing and parent-daughter relationship quality at age 15 years on substance use at age 16 years. Among social factors, parent-daughter relationship quality and peer deviance have been given most research attention (van den Bree et al., 2004), with findings indicating affiliation with deviant peer groups (involved in substance misuse and delinquency) being linked to increased adolescent substance use (Ali et al., 2011; Branstetter et al., 2011; Cruz et al., 2012; Ellickson et al., 2001; Engels & Diehr 2004; Glaser et al., 2010; Kokkevi et al., 2007; Korhonen et al., 2008; Skinner et al., 2009; Westling et al., 2008; Wood et al., 2004; and section 2.5).

Pubertal timing has also been identified as an important factor with regards to adolescent substance use with early pubertal timing being associated with increased levels of substance use in adolescence (see section 2.3; Hummel et al., 2013). Only a few studies have looked at the combined effect of pubertal timing and peer deviance on adolescent substance use (see section 2.7). However, as described in section 8.1 there is a strong rationale for focussing research on the combined effects of risk factors rather than focussing on main effects exclusively. As mentioned in section 5.3 early maturing girls tend to have older peers than is the case for same-aged girls and boys (Dawes et al., 2000); often due to the fact that these girls become involved in a romantic relationship with an older boyfriend (Gowen et al., 2004; Young & d'Arcy, 2005). This association with older peers often places early maturing girls at risk of increased substance use (Dawes et al., 2000). The underlying mechanisms of this increased risk are explained by Erikson's *developmental theory* (proposing that during adolescence the influence of peers over the adolescent increases), Bandura's *social learning theory* (proposing that behaviour is learned by observing and imitating the ones closest to oneself, which during adolescence are the members of the peer group, therefore affiliation with deviant peers is linked to increased substance use) and Moffitt's *maturation disparity hypothesis* (proposing that early maturing girls are at increased risk of affiliating with deviant peers; for more detail see sections 2.5 and 2.7).

With regards to combined effects Negriff and Trickett (2012) reported that the effect of pubertal timing on alcohol and cannabis use at age 13 years was mediated by peers' alcohol and cannabis use at age 12 years. Biehl and colleagues (2007) reported that early maturing girls with more alcohol drinking friends used more alcohol when aged between 12-16 years than early maturing girls with fewer alcohol drinking friends. Marklein and colleagues (2009) examined the interaction of pubertal timing and peers' cigarette use on girls' alcohol, cigarette and cannabis use at age range 11-17 years, but did not find any effects. This lack of evidence might be due to their small sample size (N=264 girls). However, the number of studies undertaken to date is small and many things remain unclear. Especially, it is unclear whether these combined effects of pubertal timing and peer deviance on adolescent substance use are still found in late adolescence; when the adolescent's identity formation comes close to being completed.

9.2 The study

The aim of this study was to test the combined effect of pubertal timing and peer deviance on substance use in late adolescence by conducting mediation as well as moderation analyses using the ALSPAC data set. Both conceptual models (mediation and moderation) have the potential to inform work with young people and their peers. If peer deviance was found to mediate links between pubertal timing and adolescent substance use, prevention programs could be aimed at decreasing adolescent substance use in early maturing girls by reducing the association of early pubertal timing with increased levels of peer deviance. This could be done by introducing prevention programs aiming to empower early maturing girls to resist peer pressure.

The moderation model offers insight into whether the effect of increased levels of peer deviance on adolescent substance use is stronger in the context of early compared to on-time and late pubertal timing. Such a finding would point to the subgroup of girls who may benefit most from substance use prevention programs.

9.3 Study aims and hypotheses

This study assessed the relationship between peer deviance, pubertal timing and alcohol, cigarette and cannabis use in late adolescence. Four distinct measures of peer deviance were used (number of alcohol drinking peers, cigarette smoking peers, cannabis using peers and peers' delinquency, whose relevance has been discussed in section 2.5) and I adjusting for *a priori* selected variables (including financial difficulties, parental education, parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 10 years (having alcohol and cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years; to recall the rationale for adjusting for these confounders please see section 6.2.4).

The study aimed to examine whether:

1. There is evidence that pubertal timing is linked to peer deviance at age 15 years. I hypothesised that early maturing girls had more alcohol drinking, cigarette smoking and cannabis using friends than on-time and late maturing girls and also that the likelihood of having delinquent friends at age 15 years was higher for early maturing girls than for on-time and late maturing girls.
2. There is evidence that peer deviance at age 15 years is linked to substance use at age 16 years. I hypothesised that increased levels of peer deviance (high numbers of alcohol drinking friends, cigarette smoking friends, cannabis using friends and having delinquent friends) at age 15 years would be linked to increased levels of alcohol, cigarette and cannabis use at age 16 years;
3. Peer deviance mediates the effect of pubertal timing on substance use in late adolescence. I hypothesised that the effect of early pubertal timing on increased substance use would be explained indirectly by increased levels of peer deviance;
4. Pubertal timing moderates the effect of peer deviance on substance use in late adolescence. I hypothesised that the effect of increased levels of peer deviance on increased substance use would be stronger for early than on-time and late maturing girls.

9.4 Method

9.4.1 Sample. The sample for this study was the same as in the last study. Therefore see section 8.4.1 for description.

9.4.2 Variables. The outcome variables for this study were alcohol, cigarette and cannabis use, all assessed at age 16 years (for details see section 6.2.1). For the mediation model (see Figure 3) the predictor variable was pubertal timing and the mediator variables were number of alcohol drinking friends, number of cigarette smoking friends, number of cannabis using friends and having delinquent friends (for details see section 6.2.2). For the moderation model (see Figure 4) the predictor variables were the number of alcohol drinking friends, number of cigarette smoking friends, number of cannabis using friends and having delinquent friends; whereas the moderator variable was pubertal timing. Both models were adjusted for a set of *a priori* selected variables.

9.4.3 Statistical analysis. Over time, the ALSPAC sample has experienced somewhat higher attrition rates among less affluent families, ethnic minorities and male participants, a common finding for long-running longitudinal studies (Boyd et al., 2012; Fraser et al., 2012; Perez et al., 2007). To address this issue imputed data sets were created using the *ice* package in Stata 11 (Royston, 2007). As mentioned in section 8.4.3 I used data sets with imputed predictor, mediator, moderator and confounding variables, but complete case outcome variables, for my analyses of imputed data (for detail on the imputation model see sections 7.1.2 and 7.3).
The analyses were run in complete case and imputed data.

For descriptive statistics in the complete data χ^2 and ANOVA tests were conducted. As the three outcome variables (alcohol, cigarette and cannabis) are ordinal, ordered logistic regression analysis, which requires the fulfilment of the proportional odds assumption, was used to test hypotheses 1 and 2. In Stata 11 the proportional odds assumption is tested using the *omodel* command, which is based on a likelihood-ratio test

(Stata 11; Ordered Logistic Regression, 2012). Running the *omodel* command indicated that the proportional odds assumption was not violated (approximate likelihood-ratio test of proportionality of odds across the alcohol response categories: $\chi^2(4) = 0.41$, $p = .98$; approximate likelihood-ratio test of proportionality of odds across the cigarette response categories: $\chi^2(8) = 9.63$, $p = .14$; approximate likelihood-ratio test of proportionality of odds across the cannabis response categories: $\chi^2(4) = 2.77$, $p = .60$).

To test the third hypothesis, mediation analysis (see Figure 3) was conducted using regression models (for details see section 7.2.1). To test the fourth hypothesis, moderation analysis (see Figure 4) was conducted using ordered logistic regression models and the *testparm* command of Stata 11 (for details see section 7.2.2).

9.5 Results for the complete case data.

Although the descriptive statistics were almost identical to Table 9, the descriptive statistics of this study are presented in Table 23 to provide a complete introduction into this analysis.

Table 23 Study variable frequencies and means for the three pubertal timing groups

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2 / F, p
Peer deviance (predictor / mediator variables)					
Number of alcohol drinking friends					$\chi^2(4)=11.56$, $p=.02$
none	70 (3%)	18 (3%)	37 (2%)	15 (4%)	
one or some	724 (28%)	132 (24%)	461 (28%)	131 (32%)	
most or all	1803 (69%)	400 (73%)	1142 (70%)	261 (64%)	

Table 23 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2 / F, *p*
Number of cigarette smoking friends					$\chi^2(4)=1.31$, $p=.86$
none	414 (16%)	84 (15%)	261 (16%)	69 (17%)	
one or some	1488 (57%)	309 (56%)	945 (58%)	234 (57%)	
most or all	698 (27%)	157 (29%)	435 (26%)	106 (26%)	
Number of cannabis using friends					$\chi^2(4)=19.94$, $p=.001$
none	1174 (45%)	227 (41%)	723 (44%)	224 (55%)	
one or some	1150 (44%)	258 (47%)	746 (46%)	146 (36%)	
most or all	271 (11%)	64 (12%)	168 (10%)	39 (9%)	
Having delinquent friends					$\chi^2(2)=14.16$, $p=.001$
no	597 (23%)	102 (19%)	377 (23%)	118 (29%)	
yes	1986 (77%)	446 (81%)	1251 (77%)	289 (71%)	
Adolescent substance use (outcome variables)					
Alcohol					$\chi^2(4)=7.1$
harmless	1554 (63%)	348 (65%)	955 (61%)	251 (67%)	$p= .13$
hazardous	579 (23%)	124 (23%)	377 (24%)	78 (21%)	
harmful	347 (14%)	67 (12%)	236 (15%)	44 (12%)	
Cigarette					$\chi^2(6)=16.6$
non-smoker	1269 (47%)	268 (45%)	785 (46%)	216 (52%)	$p= .01$
only ever once or twice	811 (30%)	161 (27%)	527 (31%)	123 (30%)	
occasional smoker	236 (9%)	57 (10%)	147 (9%)	32 (8%)	
regular smoker	399 (14%)	107 (18%)	250 (14%)	42 (10%)	
Cannabis					$\chi^2(4)=14.3$
non-user	1926 (71%)	420 (71%)	1185 (69%)	321 (78%)	$p= .006$
only ever once or twice	551 (20%)	115 (19%)	373 (22%)	63 (15%)	
user	245 (9%)	59 (10%)	159 (9%)	27 (7%)	
Confounders					
Financial difficulties					F(2)=0.91,
Range (5-20)	3502 (18.7)	692 (18.6)	1966 (18.7)	447 (18.7)	$p=.40$
Mother's alcohol use					$\chi^2(8)=14.3$
never	107 (7%)	20 (6%)	65 (7%)	22 (9%)	$p= .07$
very occasionally	388 (26%)	98 (30%)	241 (26%)	49 (21%)	
occasionally	635 (42%)	126 (38%)	409 (43%)	100 (42%)	
1-2 glasses a day	321 (21%)	72 (22%)	188 (20%)	61 (26%)	
3+ glasses a day	55 (4%)	12 (4%)	39 (4%)	4 (2%)	
Father figure's alcohol use					$\chi^2(8)=10.2$, $p= .25$
never	134 (5%)	26 (4%)	90 (5%)	18 (4%)	
very occasionally	573 (20%)	131 (20%)	366 (20%)	76 (18%)	
occasionally	1164 (40%)	284 (44%)	718 (39%)	162 (38%)	
1-2 glasses a day	774 (27%)	159 (24%)	487 (27%)	128 (30%)	
3+ glasses a day	255 (8%)	52 (8%)	157 (9%)	46 (10%)	

Table 23 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2, ANOVA
Mother's cigarette use					$\chi^2(6)=4.13$ $p= .66$
none	1259 (86%)	273 (85%)	797 (87%)	189 (85%)	
< 10 a day	48 (3%)	11 (3%)	27 (3%)	10 (4%)	
10-19 a day	38 (3%)	6 (2%)	25 (3%)	7 (3%)	
> 20 a day	115 (8%)	31 (10%)	67 (7%)	17 (8%)	
Father figure's cigarette use					$\chi^2(6)=27.58$ $p<.001$
none	2219 (79%)	458 (73%)	1436 (82%)	325 (80%)	
< 10 a day	67 (2%)	17 (3%)	34 (2%)	16 (4%)	
10-19 a day	74 (3%)	19 (3%)	45 (3 %)	10 (2%)	
> 20 a day	433 (16%)	133 (21%)	243 (13%)	57 (14%)	
Mother's cannabis use					$\chi^2(6)=13.19$ $p=.04$
not at all	3033 (95%)	685 (96%)	1908 (96%)	440 (94%)	
sometimes	108 (3.6%)	16 (2%)	71 (3.7%)	21 (5.4%)	
often	23 (1%)	10 (1%)	11 (1%)	2 (0.4%)	
every day	12 (0.4%)	5 (1%)	6 (0.3%)	1 (0.2%)	
Father figure's cannabis use					$\chi^2(6)=3.54$ $p=.74$
not at all	1434 (93%)	316 (95%)	897 (93%)	221 (92%)	
sometimes	73 (5%)	13 (3%)	45 (5%)	15 (6%)	
often	19 (1%)	2 (1%)	14 (1%)	3 (1.6%)	
every day	10 (1%)	2 (1%)	7 (1%)	1 (0.4%)	
Earlier alcohol use					$\chi^2(2)=7.13$
did not have whole drink before age 13	536 (37%)	118 (34%)	339 (37%)	79 (46%)	$p= .03$
had whole drink before age 13	896 (63%)	226 (66%)	578 (63%)	92 (54%)	
Earlier cigarette use					$\chi^2(2)=8.20$
did not smoke at age 13	2157 (73%)	467 (72%)	1346 (72%)	344 (79%)	$p= .02$
smoked at age 13	792 (27%)	184 (28%)	515 (28%)	93 (21%)	
Earlier cannabis use					$\chi^2(2)=11.64$
did not use at age 13	2770 (94%)	599 (92%)	1746 (94%)	425 (97%)	$p= .003$
used at age 13	177 (6%)	50 (8%)	115 (6%)	12 (3%)	
Communication					$\chi^2(4)=7.0$ $p= .14$
often	1145 (44%)	253 (46%)	707 (43%)	185 (45%)	
sometimes	1195 (46%)	235 (43%)	783 (48%)	177 (43%)	
hardly ever / never	264 (10%)	63 (11%)	153 (9%)	48 (12%)	

Table 23 continued

	N (%, mean)	Early n (%, mean)	On-time n (%, mean)	Late n (%, mean)	χ^2, ANOVA
Conflict					$\chi^2(4)=12.0$ $p= .06$
hardly ever / never	347 (13%)	85 (15%)	203 (12%)	59 (15%)	
< once a week	1529 (59%)	312 (57%)	975 (59%)	242 (59%)	
at least once a week	550 (21%)	105 (19%)	366 (23%)	79 (19%)	
most days	176 (7%)	49 (9%)	98 (6%)	29 (7%)	
Monitoring					$\chi^2(4)=4.3$ $p= .36$
always	1421 (54%)	299 (54%)	882 (54%)	240 (58%)	
usually	1055 (41%)	223 (41%)	674 (41%)	158 (38%)	
sometimes / never	130 (5%)	29 (5%)	87 (5%)	14 (4%)	
Having alcohol drinking friends at age 10					$\chi^2(2)=2.05$ $p= .36$
no	2865 (97%)	631 (96%)	1810 (96%)	424 (98%)	
yes	102 (3%)	25 (4%)	67 (4%)	10 (2%)	
Having cigarette smoking friends at age 10					$\chi^2(2)=2.20$ $p= .33$
no	2834 (94%)	617 (93%)	1813 (94%)	404 (93%)	
yes	192 (6%)	46 (7%)	113 (6%)	33 (7%)	
Having delinquent friends at age 10					$\chi^2(2)=0.58$ $p= .75$
no	422 (14%)	87 (14%)	269 (14%)	66 (15%)	
yes	2495 (86%)	543 (86%)	1592 (86%)	360 (85%)	

Early maturing girls' father figures smoked more cigarettes than father figures of on-time and late maturing girls. Late maturing girls' mothers used more cannabis than early and on-time maturing girls' mothers. Fewer late maturing girls had drunk alcohol before age 13 years than early and on-time maturing girls. Fewer late maturing girls had smoked cigarettes by age 13 years than early and on-time maturing girls. Fewer late maturing girls had used cannabis by age 13 years than early and on-time maturing girls. Differences were found between early, on-time and late maturing girls with regards to cigarette and cannabis use at age 16 years, with the highest percentage of non-smokers and non-users being found among the late maturing girls.

To take a closer look at the differences in peer deviance across the three pubertal timing groups and to address the first hypothesis ordered logistic regression models were run (see Table 24).

Table 24 Regression analysis of pubertal timing on peer deviance

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Number of alcohol drinking friends	*Pubertal timing*		
	On-time versus early	1.14 [0.92, 1.41]	1.35 [0.73, 2.48]
	On-time versus late	0.77 [0.62, 0.97]	0.93 [0.44, 1.96]
	Early versus late	0.68 [0.51, 0.89]	0.69 [0.29, 1.61]
		$\chi^2(2)$= 8.11, p = .02	$\chi^2(2)$= 1.10, p = .58
Number of cigarette smoking friends	*Pubertal timing*		
	On-time versus early	1.09 [0.90, 1.31]	1.36 [0.95, 1.94]
	On-time versus late	0.96 [0.77, 1.18]	1.02 [0.69, 1.53]
	Early versus late	0.88 [0.68, 1.13]	0.75 [0.47, 1.21]
		$\chi^2(2)$= 1.15, p = .58	$\chi^2(2)$= 3.31, p = .19
Number of cannabis using friends	*Pubertal timing*		
	On-time versus early	1.13 [0.94, 1.36]	1.34 [0.96, 1.86]
	On-time versus late	0.69 [0.56, 0.85]	0.98 [0.54, 1.78]
	Early versus late	0.61 [0.47, 0.78]	0.66 [0.35, 1.27]
		$\chi^2(2)$= 16.32, p < .001	$\chi^2(2)$= 3.39, p = .18
Having delinquent friends	*Pubertal timing*		
	On-time versus early	1.32 [1.03, 1.68]	1.28 [0.66, 2.49]
	On-time versus late	0.74 [0.58, 0.94]	1.06 [0.45, 2.48]
	Early versus late	0.56 [0.41, 0.76]	0.83 [0.32, 2.14]
		$\chi^2(2)$= 14.03, p = .001	$\chi^2(2)$= 0.50, p = .78

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), substance use at age 14 years and peer behaviour at age 10 years.

Late maturing girls had fewer alcohol drinking friends at age 15 years than early (OR = 0.68) and on-time maturing girls (OR = 0.77) in the unadjusted models. Late maturing girls had fewer cannabis using friends at age 15 years than early (OR = 0.61) and on-time maturing girls (OR = 0.69). Early maturing girls had more delinquent friends at age 15 years than on-time maturing girls (OR = 1.31); and late maturing girls had fewer delinquent friends at age 15 years than early (OR = 0.56) and on-time maturing girls (OR = 0.74). However, after adjusting for confounders none of these effects remained. Inspection of the results for the hypothesised confounders showed that parental education (OR=1.16, 95% CI: 1.00, 1.35), father figure cannabis use (OR=1.73, 95% CI: 1.07, 2.78) and girls' own earlier cannabis use (OR=7.41, 95% CI: 4.12, 13.32) predicted the number of cannabis using friends at age 15 years. Financial difficulties (OR=1.10, 95% CI: 1.02, 1.18), father figure cigarette use (OR=1.25, 95% CI: 1.05, 1.48) and girls' own earlier cigarette use (OR=4.51, 95% CI: 3.15, 6.46) predicted the number of cigarette smoking friends at age 15 years.

To test the second hypothesis, ordered logistic regression models were used in the complete data to test whether peer behaviour at age 15 years predicted substance use at age 16 years. Results of the unadjusted models and the adjusted models are shown in Table 25.

It was found that higher numbers of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends at age 15 years were linked to higher levels of alcohol, cigarette and cannabis use at age 16 years in the unadjusted models. After adjusting for confounders it was found that most of these effects remained, that is, high numbers of alcohol drinking and cannabis using friends at age 15 years were linked to increased alcohol use at age 16 years. With regards to cigarette and cannabis use at age 16 years, after adjusting for confounders, it was found that higher numbers of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends at age 15 years were linked to increased cigarette and cannabis use at age 16 years.

Table 25 Regression analysis of peer deviance on substance use

Outcome	Predictor	Unadjusted		Adjusted for confounders [1]	
		$X^2(1)$, *p*	OR [95% CI]	$X^2(1)$, *p*	OR [95% CI].
Alcohol	Number of alcohol drinking friends	121.95, <.001	3.59 [2.86, 4.51]	6.56, .01	2.40 [1.30, 4.44]
	Number of cigarette smoking friends	134.03, <.001	2.56 [2.18, 3.00]	1.57, .21	1.42 [0.98, 2.05]
	Number of cannabis using friends	160.86, <.001	2.61 [2.25, 3.02]	7.41, .01	1.77 [1.25, 2.49]
	Friends' delinquency	90.37, <.001	3.61 [2.77, 4.70]	0.95, .33	1.35 [0.74, 2.48]
Cigarettes	Number of alcohol drinking friends	163.04, <.001	3.19 [2.67, 3.81]	38.88, <.001	2.78 [1.99, 3.87]
	Number of cigarette smoking friends	320.32, <.001	3.97 [3.41, 4.62]	59.54, <.001	3.14 [2.38, 4.15]
	Number of cannabis using friends	311.08, <.001	3.43 [2.99, 3.93]	45.34, <.001	2.46 [1.91, 3.18]
	Friends' delinquency	123.52, <.001	3.27 [2.65, 4.03]	15.84, <.001	2.28 [1.55, 3.36]
Cannabis	Number of alcohol drinking friends	125.50, <.001	4.25 [3.30, 5.48]	29.56, <.001	3.69 [2.32, 5.88]
	Number of cigarette smoking friends	217.44, <.001	3.70 [3.11, 4.41]	44.34, <.001	3.03 [2.21, 4.15]
	Number of cannabis using friends	364.22, <.001	5.39 [4.53, 6.40]	82.73, <.001	4.49 [3.27, 6.16]
	Friends' delinquency	110.18, <.001	5.74 [4.14, 7.96]	21.08, <.001	3.86 [2.16, 6.91]

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance 10 years (having alcohol and cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

To test the third hypothesis, regression models were conducted unadjusted as well as adjusted for confounders. The mediation analysis is shown in Table 26.

Table 26 Mediation by peer deviance of the association between pubertal timing and substance use unadjusted and adjusted[1] for confounders

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
Pubertal timing	Alcohol	Number of alcohol drinking friends Unadjusted	0.02 (-.03, .07)	-0.01 (-.03, -.004)	-0.01 (-.06, .04)
		Number of alcohol drinking friends Adjusted[1]	0.11 (-.01, .23)	-0.003 (-.03, .02)	0.10 (-.02, .22)
		Number of cigarette smoking friends Unadjusted	0.01 (-.04, .06)	-0.006 (-.02, .006)	-0.01 (-.06, .04)
		Number of cigarette smoking friends Adjusted[1]	0.12 (-.02, .24)	-0.01 (-.04, .01)	0.10 (-.02, .22)
		Number of cannabis using friends Unadjusted	0.02 (-.03, .07)	-0.02 (-.04, -.01)	-0.01 (-.06, .04)
		Number of cannabis using friends Adjusted[1]	0.11 (-.01, .23)	-0.01 (-.05, -.01)	0.09 (-.03, .21)
		Friends' delinquency Unadjusted	0.02 (-.03, .07)	-0.02 (-.03, -.01)	-0.01 (-.06, .04)
		Friends' delinquency Adjusted[1]	0.12 (-.02,.25)	-0.005 (-.02, -.01)	0.10 (-.02, .22)
	Cigarettes	Number of alcohol drinking friends Unadjusted	-0.10 (-.17, -.02)	-0.02 (-.04,- .006)	-0.12 (-.19, -.05)
		Number of alcohol drinking friends Adjusted[1]	0.01 (-.10, .11)	-0.02 (-.05, .0005)	-0.03 (-.13, .08)
		Number of cigarette smoking friends Unadjusted	-0.11 (-.18, -.05)	-0.01 (-.04, .01)	-0.12 (-.19, -.05)
		Number of cigarette smoking friends Adjusted[1]	-0.01 (-.12, .09)	-0.01 (-.05, .03)	-0.02 (-.13, .08)
		Number of cannabis using friends Unadjusted	-0.08 (-.15, -.01)	-0.05 (-.07, -.02)	-0.12 (-.19, -.05)
		Number of cannabis using friends Adjusted[1]	-0.02 (-.12, .09)	-0.01 (-.05, .03)	-0.03 (-.13, .08)
		Friends' delinquency Unadjusted	-0.09 (-.17, -.02)	-0.03 (-.04, -.02)	-0.12 (-.19, -.05)
		Friends' delinquency Adjusted[1]	-0.02 (-.13, .09)	-0.004 (-.03, .02)	-0.02 (-.13, .09)

Table 26 continued

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
		Number of alcohol drinking friends Unadjusted	-0.04 (-.09, .002)	-0.01 (-.02, -.004)	-0.05 (-.09, -.01)
		Number of alcohol drinking friends Adjusted[1]	-0.01 (-.07, .06)	-0.02 (-.04, .003)	-0.01 (-.07, .06)
		Number of cigarette smoking friends Unadjusted	-0.05 (-.09, -.01)	-0.007 (-.02, .007)	-0.05 (-.09, -.01)
	Cannabis	Number of cigarette smoking friends Adjusted[1]	-0.01 (-.08, .05)	-0.02 (-.04, .003)	-0.01 (-.07, .05)
		Number of cannabis using friends Unadjusted	-0.03 (-.07, .01)	-0.03 (-.05, -.01)	-0.05 (-.09, -.01)
		Number of cannabis using friends Adjusted[1]	0.002 (-.06, .06)	-0.03 (-.06, .009)	-0.01 (-.07, .06)
		Friends' delinquency Unadjusted	-0.04 (-.08, .01)	-0.02 (-.03, -.01)	-0.05 (-.09, -.01)
		Friends' delinquency Adjusted[1]	-0.03 (-.09, .04)	-0.008 (-.02, .002)	-0.01 (-.07, .06)

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer behaviour at age 10 years (having alcohol, cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

"Indirect-only mediation", meaning there is no evidence for the predictor affecting the outcome while there is evidence for the predictor affecting the mediator and the mediator affecting the outcome (Hayes, 2009; Zhao et al., 2010), was found. More specifically, early pubertal timing was associated with having more alcohol drinking friends at age 15 years, which itself was linked to increased alcohol use at age 16 years. Additionally, early pubertal timing was linked to having more cannabis using friends at age 15 years, which itself was linked to increased alcohol use at age 16 years; and early pubertal timing was also linked to having delinquent friends at age 15 years, which itself was linked to increased alcohol use at age 16 years.

Partial mediation, meaning the effect of the predictor on the outcome remains after including the mediator in the model (MacKinnon, 2008), was found. Late pubertal timing was linked to having fewer alcohol drinking friends at age 15 years (B = -0.04; 95% CI: -0.08, -0.01) and having more alcohol drinking friends at age 15 years was linked to increased cigarette use at age 16 years (B = 0.51; 95% CI: 0.43, 0.60) with 17% of the effect of pubertal timing on cigarette use at age 16 years partially explained by the number of alcohol drinking friends at age 15 years.

Late pubertal timing was linked to having fewer cannabis using friends at age 15 years (B = -0.07; 95% CI: -0.12, -0.03) and having more cannabis using friends at age 15 years was linked to increased cigarette use at age 16 years (B = 0.65; 95% CI: 0.58, 0.71) with 38% of the effect of pubertal timing on cigarette use at age 16 years being partially explained by the number of cannabis using friends. Late pubertal timing was linked to a lower chance of having delinquent friends at age 15 years (B = -0.05; 95% CI: -0.08, -0.02) and having delinquent friends was linked to increased cigarette use at age 16 years (B = 0.58; 95% CI: 0.48, 0.68) with 24 % of the effect of pubertal timing on cigarette use at age 16 years being partially explained by having delinquent friends.

Complete mediation, meaning the effect of the predictor on the outcome is significantly reduced after including the mediator in the model (MacKinnon, 2008), was found. Late pubertal timing was linked to having fewer alcohol drinking friends at age 15 years (B = -0.04; 95% CI: -0.08, -0.01) and having more alcohol drinking friends at age 15 years was linked to increased cannabis use at age 16 years (B = 0.30; 95% CI: 0.25, 0.35) with 24 % of the effect of pubertal timing on cannabis use at age 16 years being explained by the number of alcohol drinking friends at age 15 years. Late pubertal timing was linked to having fewer cannabis using friends at age 15 years (B = -0.07; 95% CI: -0.12, -0.03) and having more cannabis using friends at age 15 years was linked to increased cannabis use at age 16 (B = 0.45; 95% CI: 0.41, 0.49) with 63% of the effect of pubertal timing on cannabis use at age 16 years being explained by the number of cannabis using friends at age 15 years. Late pubertal timing was linked to a lower chance of having delinquent friends at age 15 years (B = -0.05; 95% CI: -0.08, -0.02) and having delinquent friends at age 15 years was linked to increased cannabis use at age 16 years (B = 0.36; 95% CI: 0.29, 0.42) with 36% of the effect of pubertal timing on cannabis use at age 16 years being explained by having delinquent friends at age 15 years.

However, after adjusting for confounders the only mediation effects found were "indirect-only mediation" effects. Early pubertal timing was linked to having more cannabis friends at age 15 years, which itself was linked to increased alcohol use at age 16 years (Figure 16). Additionally, early pubertal timing was linked to having delinquent friends at age 15 years, which itself was linked to increased alcohol use at age 16 years (Figure 17).

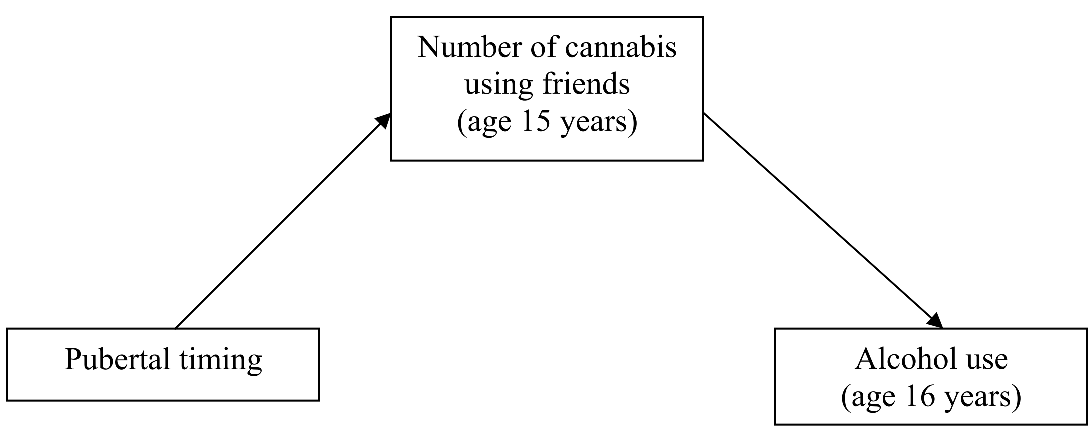


Figure 16. Indirect-only mediation by cannabis using friends

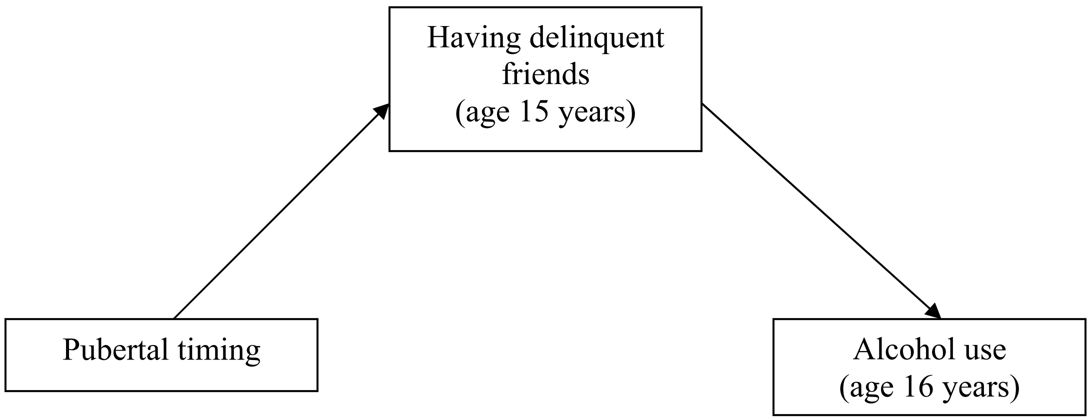


Figure 17. Indirect-only mediation by having delinquent friends

To test the fourth hypothesis, ordered logistic regression models were conducted and then the post-estimation command *testparm* was used to test for moderation (for detail see section 7.2.2). Analyses were conducted unadjusted and adjusted for confounders. The unadjusted results of the moderation analysis are shown in Table 27.

Table 27 Moderation by pubertal timing of the relationship between peer deviance and substance use

Predictor	**Outcome**	**Moderator**	**Wald $\chi^2(2)$**	***p***
Number of alcohol drinking friends	Alcohol	Pubertal timing	14.98	<.001
Separate group analysis of the effect of the number of alcohol drinking friends on alcohol use: Early maturing girls (OR=1.70, 95% CI: 1.10, 2.64), on-time maturing girls (OR=4.05, 95% CI: 3.03, 5.43) and late maturing girls (OR=6.19, 95% CI: 3.22, 11.88)				

Table 27 continued

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Number of cigarette smoking friends	Alcohol	Pubertal timing	3.64	.16
Number of cannabis using friends			1.02	.60
Friends' delinquency			3.34	.19
Number of alcohol drinking friends	Cigarettes	Pubertal timing	2.23	.33
Number of cigarette smoking friends			0.83	.66
Number of cannabis using friends			0.02	.99
Friends' delinquency			1.26	.53
Number of alcohol drinking friends	Cannabis	Pubertal timing	4.13	.13
Number of cigarette smoking friends			3.08	.21
Number of cannabis using friends			0.85	.65
Friends' delinquency			4.38	.11

Evidence was found for pubertal timing moderating the effect of the number of alcohol drinking friends at age 15 years on alcohol use at age 16 years in the unadjusted model. However, the separate group analysis showed that the effect of alcohol drinking friends at age 15 years on alcohol use at age 16 years was significant for early, on-time and late maturing girls, whereas the effect was stronger for on-time and late maturing girls compared to early maturing girls.

Moderation analysis after adjusting for confounders is shown in Table 28. After adjusting for confounders no evidence was found for pubertal timing moderating the effect of peer deviance at age 15 years on substance use at age 16 years.

Table 28 Moderation by pubertal timing of the relationship between peer deviance and substance use adjusted for confounders.[1]

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Number of alcohol drinking friends	Alcohol	Pubertal timing	0.39	.82
Number of cigarette smoking friends			1.91	.38
Number of cannabis using friends			0.04	.98
Friends' delinquency			2.62	.27
Number of alcohol drinking friends	Cigarettes	Pubertal timing	0.06	.97
Number of cigarette smoking friends			4.34	.11
Number of cannabis using friends			4.59	.10
Friends' delinquency			3.47	.18
Number of alcohol drinking friends	Cannabis	Pubertal timing	0.14	.93
Number of cigarette smoking friends			3.69	.16
Number of cannabis using friends			1.59	.45
Friends' delinquency			1.09	.58

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 10 years (having alcohol and cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

In summary, the results of the complete case analysis indicated that: (1) late maturing girls had fewer alcohol drinking friends at age 15 years than early and on-time maturing girls; however, this effect disappeared after adjusting for confounders; (2) Late maturing girls had fewer cannabis using friends at age 15 years than early and on-time maturing girls; this effect disappeared after adjusting for confounders; (3) More early maturing girls had delinquent friends at age 15 years than on-time maturing girls and fewer late maturing girls had delinquent friends at age 15 years than early and on-time maturing girls; however these effects disappeared after adjusting for confounders; (4)

After adjusting for confounders, higher numbers of alcohol drinking friends and higher numbers of cannabis using friends at age 15 years predicted increased alcohol use at age 16 years; (5) After adjusting for confounders higher numbers of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends at age 15 years predicted increased cigarette and cannabis use at age 16 years; (6) After adjusting for confounders, the number of cannabis using friends and having delinquent friends at age 15 years mediated the effect of pubertal timing on alcohol use at age 16 years; (7) Pubertal timing moderated the effect of the number of alcohol drinking friends at age 15 years on alcohol use at age 16 years; however, the effect disappeared after adjusting for confounders.

9.6 Results for the imputed data

Due to the relatively high rates of data attrition (see Table 8) multiple imputation was conducted to impute the missing values (see chapter 7). Analyses were conducted unadjusted and adjusted for confounders as described for the complete case data analysis. The first hypothesis was tested using ordered logistic regression. The results of the analysis are shown in Table 29.

Table 29 Imputed regression analysis of pubertal timing on peer deviance

Outcome	Predictor	Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Number of alcohol drinking friends	*Pubertal timing*		
	On-time versus early	1.09 [0.93, 1.27]	1.09 [0.93, 1.27]
	On-time versus late	0.84 [0.69, 1.01]	0.84 [0.70, 1.01]
	Early versus late	0.77 [0.62, 0.96]	0.77 [0.62, 0.96]
		$\chi^2(2)$= 7.90, *p* = .02	$\chi^2(2)$ = 7.60, *p* = .02

Table 29 continued

Outcome	Predictor	Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[1] OR [95% CI.]
Number of cigarette smoking friends	*Pubertal timing*		
	On-time versus early	1.09 [0.94, 1.26]	1.07 [0.93, 1.24]
	On-time versus late	0.92 [0.77, 1.09]	0.96 [0.80, 1.14]
	Early versus late	0.84 [0.68, 1.05]	0.89 [0.72, 1.11]
		$\chi^2(2) = 1.20$, $p = .55$	$\chi^2(2) = 0.05$, $p = .97$
Number of cannabis using friends	*Pubertal timing*		
	On-time versus early	1.09 [0.94, 1.25]	1.07 [0.93, 1.24]
	On-time versus late	0.80 [0.67, 0.95]	0.82 [0.69, 0.97]
	Early versus late	0.74 [0.60, 0.91]	0.76 [0.62, 0.94]
		$\chi^2(2)= 15.81$, $p < .001$	$\chi^2(2) = 12.89$, $p = .002$
Friends' conduct problems	*Pubertal timing*		
	On-time versus early	1.14 [0.95, 1.36]	1.13 [0.94, 1.35]
	On-time versus late	0.84 [0.68, 1.03]	0.85 [0.69, 1.04]
	Early versus late	0.74 [0.59, 0.93]	0.75 [0.59, 0.95]
		$\chi^2(2)= 14.23$, $p < .001$	$\chi^2(2)= 12.88$, $p = .002$

[1] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure use), substance use at age 14 years and parent-child interaction at age 9 years

Late maturing girls had fewer alcohol drinking friends (OR = 0.77) and delinquent friends (OR = 0.74) than early maturing girls. They also had fewer cannabis using friends than early (OR = 0.74) and on-time (OR = 0.80) maturing girls. The odds ratios were not significantly altered after adjusting for confounding variables. Taking a closer look at the confounders showed that girls' own alcohol use at age 14 years (OR=1.24; 95% CI: 1.04, 1.49) predicted the number of alcohol drinking friends at age 15 years; girls' own cigarette use at age 14 (OR=3.10; 95% CI: 2.61, 3.67) predicted the number of cigarette smoking friends at age 15 years; girls' own cannabis use at age 14 years (OR=3.98; 95% CI: 2.97, 5.33) predicted the number of cannabis using friends at age 15 years and girls' own alcohol use at age 14 years (OR=1.24; 95% CI: 1.04, 1.49) predicted having delinquent friends at age 15 years.

Ordered logistic regression was conducted to test whether peer deviance (number of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends) at age 15 years predicted substance use (alcohol, cigarette and cannabis use) at age 16 years (Hypothesis 2). Results of the unadjusted and adjusted models in imputed data are shown in Table 30.

Table 30 Imputed regression analysis of peer deviance on substance use

Outcome	Predictor	Unadjusted for confounders		Adjusted for confounders [1]	
		$X^2(1)$, p	OR [95% CI]	$X^2(1)$, p	OR [95% CI]
Alcohol	Number of alcohol drinking friends	148.62, <.001	3.53 [2.79, 4.46]	68.67, <.001	3.02 [2.37, 3.87]
	Number of cigarette smoking friends	144.87, <.001	2.45 [2.10, 2.84]	65.83, <.001	2.09 [1.78, 2.45]
	Number of cannabis using friends	168.61, <.001	2.50 [2.18, 2.87]	70.39, <.001	2.10 [1.81, 2.43]
	Friends' delinquency	107.40, <.001	3.21 [2.51, 4.11]	59.53, <.001	2.53 [1.96, 3.28]
Cigarettes	Number of alcohol drinking friends	185.28, <.001	3.05 [2.55, 3.65]	245.60, <.001	2.41 [1.99, 2.92]
	Number of cigarette smoking friends	364.94, <.001	3.98 [3.44, 4.61]	274.53, <.001	2.86 [2.44, 3.34]
	Number of cannabis using friends	330.04, <.001	3.42 [2.99, 3.91]	251.04, <.001	2.47 [2.14, 2.85]
	Friends' delinquency	134.85, <.001	3.23 [2.65, 3.94]	203.41, <.001	2.28 [1.85, 2.82]

Table 30 continued

Outcome	Predictor	Unadjusted for confounders		Adjusted for confounders [1]	
		$X^2(1)$, *p*	OR [95% CI]	$X^2(1)$, *p*	OR [95% CI]
Cannabis	Number of alcohol drinking friends	167.63, <.001	3.96 [3.08, 5.08]	215.98, <.001	3.17 [2.46, 4.09]
	Number of cigarette smoking friends	248.92, <.001	3.59 [3.02, 4.28]	230.46, <.001	2.91 [2.40, 3.52]
	Number of cannabis using friends	435.48, <.001	5.25 [4.45, 6.21]	272.77, <.001	4.16 [3.49, 4.98]
	Friends' delinquency	155.51, <.001	5.35 [3.92, 7.29]	182.46, <.001	3.93 [2.84, 5.44]

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 10 years (having alcohol drinking, cigarette smoking and delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

Having substance using and delinquent friends at age 15 years was associated with increased alcohol, cigarettes and cannabis the adolescent girls used at age 16 years. These findings remained consistent after adjusting for confounders.

To test the third hypothesis, regression models were run to test whether peer deviance at age 15 years mediated the effect of pubertal timing on substance use at age 16 years. The results of the imputed mediation analysis unadjusted as well as adjusted for confounders are shown in Table 31.

Table 31 Imputed mediation by peer deviance of the association between pubertal timing and substance use unadjusted and adjusted[1] for confounders.

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
Pubertal timing	Alcohol	Number of alcohol drinking friends Unadjusted	0.003 (-.04, .05)	-0.01 (-.03, .0002)	-0.01 (-.06, .04)
		Number of alcohol drinking friends Adjusted[1]	0.003 (-.04, .05)	-0.01 (-.02, .0001)	-0.01 (-.05, .04)
		Number of cigarette smoking friends Unadjusted	-0.004 (-.05, .04)	-0.006 (-.02, .006)	-0.01 (-.06, .04)
		Number of cigarette smoking friends Adjusted[1]	-0.003 (-.05, .04)	-0.005 (-.01, .004)	-0.01 (-.05, .04)
		Number of cannabis using friends Unadjusted	0.01 (-.04, .05)	-0.02 (-.03, -.004)	-0.01 (-.06, .04)
		Number of cannabis using friends Adjusted[1]	0.004 (-.04, .05)	-0.01 (-.02, -.003)	-0.01 (-.05, .04)
		Friends' delinquency Unadjusted	0.001 (-.05, .05)	-0.01 (-.02, -.003)	-0.01 (-.06, .04)
		Friends' delinquency Adjusted[1]	0.001 (-.05, .05)	-0.008 (-.02, -.002)	-0.01 (-.05, .04)
	Cigarettes	Number of alcohol drinking friends Unadjusted	-0.10 (-.16, -.03)	-0.02 (-.04, -.004)	-0.12 (-.18, -.05)
		Number of alcohol drinking friends Adjusted[1]	-0.06 (-.12, .03)	-0.01 (-.02, .003)	-0.06 (-.12, .02)
		Number of cigarette smoking friends Unadjusted	-0.10 (-.17, -.04)	-0.01 (-.04, .01)	-0.12 (-.18, -.05)
		Number of cigarette smoking friends Adjusted[1]	-0.05 (-.11, .01)	0.001 (-.02, .02)	-0.06 (-.12, -.04)
		Number of cannabis using friends Unadjusted	-0.08 (-.14, -.02)	-0.03 (-.06, -.007)	-0.12 (-.18, -.05)
		Number of cannabis using friends Adjusted[1]	-0.06 (-.12, -.03)	-0.008 (-.02, .002)	-0.06 (-.12, -.02)
		Friends' delinquency Unadjusted	-0.10 (-.16, -.03)	-0.02 (-.03, -.006)	-0.12 (-.18, -.05)
		Friends' delinquency Adjusted[1]	-0.05 (-.11,.005)	-0.01 (-.02, .003)	-0.06 (-.12, -.04)

Table 31 continued

Predictor	Outcome	Mediator	Estimates Direct effect c' (95% CI)	Estimates Indirect effect ab (95% CI)	Estimates Total effect c (95% CI)
Pubertal timing	Cannabis	Number of alcohol drinking friends Unadjusted	-0.04 (-.07, .004)	-0.01 (-.02, .0003)	-0.05 (-.09, -.01)
		Number of alcohol drinking friends Adjusted[1]	-0.02 (-.06, .02)	-0.006 (-.01, .002)	-0.03 (-.06, .01)
		Number of cigarette smoking friends Unadjusted	-0.04 (-.08,-.001)	-0.007 (-.02, .007)	-0.05 (-.09, -.01)
		Number of cigarette smoking friends Adjusted[1]	-0.02 (-.06, .01)	-0.002 (-.01, .007)	-0.03 (-.06, .01)
		Number of cannabis using friends Unadjusted	-0.02 (-.06, .01)	-0.02 (-.04, -.005)	-0.05 (-.09, -.01)
		Number of cannabis using friends Adjusted[1]	-0.01 (-.05, .02)	-0.01 (-.03, .01)	-0.03 (-.06, .01)
		Friends' delinquency Unadjusted	-0.03 (-.07, -.01)	-0.01 (-.02, -.004)	-0.05 (-.09, -.01)
		Friends' delinquency Adjusted[1]	-0.02 (-.06, .02)	-0.007 (-.01, .002)	-0.03 (-.06, .01)

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer deviance at age 10 years (having alcohol, cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

Several mediation effects were found in the models unadjusted for confounders: Late pubertal maturation was associated with having fewer cannabis using friends at age 15 years (B= -.05; 95% CI: -0.09, -0.01) and having more cannabis using friends at age 15 years was associated with increased cannabis use at age 16 years (B= 0.45; 95% CI: 0.42, 0.49) with 45% of the effect of pubertal timing on cannabis use at age 16 years being indirectly explained by the number of cannabis using friends at age 15 years.

Partial mediation, where the effect of the predictor on the outcome remains after including the mediator in the model while finding that the predictor affects the mediator and the mediator affects the outcome (MacKinnon, 2008), was also identified. Late pubertal timing was associated with having fewer alcohol drinking friends at age 15 years (B= -0.04; 95% CI: -0.07, -0.001) and having more alcohol drinking friends at age 15 years was associated with increased cigarette use at age 16 years (B= 0.53; 95% CI: 0.45, 0.61) with 18% of the effect of pubertal timing on cigarette use at age 16 years being indirectly explained by the number of alcohol drinking friends at age 15 years. Late pubertal maturation was associated with having fewer cannabis using friends at age 15 years (B= -0.05; 95% CI: -0.10, -0.01) and having more cannabis using friends at age 15 years was associated with increased cigarette use at age 16 years (B= 0.66; 95% CI: 0.60, 0.73) with 28% of the effect of pubertal timing on cigarette use at age 16 years being indirectly explained by the number of cannabis using friends at age 15 years. Late pubertal timing was associated with lower chances of having delinquent friends at age 15 years (B= -0.03; 95% CI: -0.06, -0.01) and having delinquent friends at age 15 years was associated with increased cigarette use at age 16 (B= 0.60; 95% CI: 0.50, 0.70) with 15% of the effect of pubertal timing on cigarette use at age 16 years being indirectly explained by having delinquent friends at age 15 years. Late pubertal timing was associated with a lower chance of having delinquent friends at age 15 years (B= -0.03; 95% CI: -0.06, -0.01) and having delinquent friends at age 15 years was associated with increased cannabis use at age 16 years (B= 0.36; 95% CI: 0.30, 0.41) with 22% of the effect of pubertal timing on cannabis use at age 16 years being indirectly explained by having delinquent friends at age 15 years.

"Indirect-only mediation", where there is no evidence for the predictor affecting the outcome while there is evidence for the predictor affecting the mediator and the mediator affecting the outcome (Hayes, 2009; Zhao et al., 2010), was identified. Late pubertal timing was associated with having fewer cannabis using friends at age 15 years (B= -0.05; 95% CI: -0.10, -0.003) and having more cannabis using friends at age 15 years was associated with increased alcohol use at age 16 years (B= 0.32; 95% CI: 0.28, 0.37); see Figure 16. Also, late pubertal timing was associated with a lower chance of having delinquent friends at age 15 years (B= -0.03; 95% CI: -0.06, -0.003) and having delinquent friends at age 15 years was associated with increased levels of alcohol use at age 16 years (B= 0.35; 95% CI: 0.28, 0.42); see Figure 17. After adjusting for confounders the only mediation effects remaining were the "indirect-only mediation" effects

To test the fourth hypothesis, ordered logistic regression models and the post-estimation command *testparm* were used to test whether the effect of peer deviance at age 15 years on substance use at age 16 years differed for early, on-time and late maturing girls in imputed data. The unadjusted moderation analysis in the imputed data is shown in Table 32.

Table 32 Imputed moderation by pubertal timing of the relationship between peer deviance and substance use.

<table>
<tr><th>Predictor</th><th>Outcome</th><th>Moderator</th><th>Wald $\chi^2(2)$</th><th>p</th></tr>
<tr><td>Number of alcohol drinking friends</td><td>Alcohol</td><td>Pubertal timing</td><td>7.51</td><td>.02</td></tr>
<tr><td colspan="5">Separate group analysis of the effect of the number of alcohol drinking friends on alcohol use: Early maturing girls (OR=2.11; 95% CI: 1.38, 3.22) on-time maturing girls (OR=3.91; 95% CI: 2.91, 5.26) and late maturing girls (OR=5.07; 95% CI: 2.73, 9.41)</td></tr>
<tr><td>Number of cigarette smoking friends</td><td rowspan="3">Alcohol</td><td rowspan="3">Pubertal timing</td><td>1.60</td><td>.45</td></tr>
<tr><td>Number of cannabis using friends</td><td>0.44</td><td>.80</td></tr>
<tr><td>Friends' delinquency</td><td>1.83</td><td>.40</td></tr>
<tr><td>Number of alcohol drinking friends</td><td>Cigarettes</td><td>Pubertal timing</td><td>1.63</td><td>.44</td></tr>
</table>

Table 32 continued

Predictor	**Outcome**	**Moderator**	**Wald $\chi^2(2)$**	***p***
Number of cigarette smoking friends	Cigarettes	Pubertal timing	0.56	.76
Number of cannabis using friends			0.01	.99
Friends' delinquency			0.80	.67
Number of alcohol drinking friends	Cannabis	Pubertal timing	2.05	.36
Number of cigarette smoking friends			1.62	.45
Number of cannabis using friends			0.58	.75
Friends' delinquency			2.22	.33

Pubertal timing moderated the effect of the number of alcohol drinking friends at age 15 years on alcohol use at age 16 years. However, taking a closer look at the separate groups showed that the number of alcohol drinking friends at age 15 years predicted alcohol use at age 16 years in early, on-time and late maturing girls; with the effect being weaker in early maturing girls (OR=2.11; 95% CI: 1.38, 3.22) than in on-time (OR=3.91; 95% CI: 2.91, 5.26) and late maturing girls (OR=5.07; 95% CI: 2.73, 9.41); see Figure 18. No other moderation effects were found.

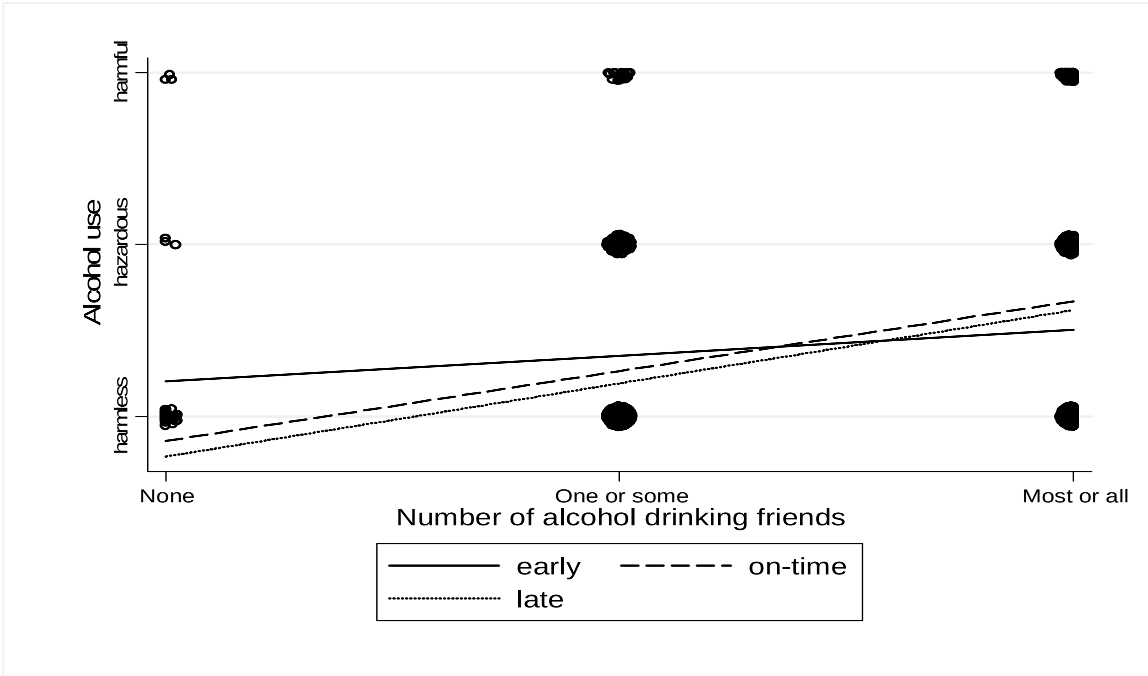


Figure 18. Pubertal timing moderating the effect of the number of alcohol drinking friends on alcohol use

The results of the imputed moderation analysis adjusted for confounders are shown in Table 33.

Table 33 Imputed moderation by pubertal timing of the relationship between peer deviance and substance use adjusted for confounders [1]

<table>
<tr><th>Predictor</th><th>Outcome</th><th>Moderator</th><th>Wald $\chi^2(2)$</th><th>p</th></tr>
<tr><td>Number of alcohol drinking friends</td><td>Alcohol</td><td>Pubertal timing</td><td>7.10</td><td>.03</td></tr>
<tr><td colspan="5">Separate group analysis of the effect of the number of alcohol drinking friends on alcohol use: Early maturing girls (OR=1.82, 95% CI: 1.17, 2.83), on-time maturing girls (OR=3.45, 95% CI: 2.54, 4.70), late maturing girls (OR=4.24, 95% CI: 2.18, 8.23)</td></tr>
<tr><td>Number of cigarette smoking friends</td><td rowspan="3">Alcohol</td><td rowspan="3">Pubertal timing</td><td>1.45</td><td>.48</td></tr>
<tr><td>Number of cannabis using friends</td><td>0.33</td><td>.85</td></tr>
<tr><td>Friends’ delinquency</td><td>2.08</td><td>.35</td></tr>
</table>

Table 33 continued

Predictor	Outcome	Moderator	Wald $\chi^2(2)$	*p*
Number of alcohol drinking friends	Cigarettes	Pubertal timing	1.60	.45
Number of cigarette smoking friends			0.12	.94
Number of cannabis using friends			0.32	.85
Friends' delinquency			0.56	.76
Number of alcohol drinking friends	Cannabis	Pubertal timing	1.46	.48
Number of cigarette smoking friends			1.12	.57
Number of cannabis using friends			0.54	.76
Friends' delinquency			1.90	.39

[1] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and father figure alcohol, cigarette and cannabis use), substance use at age 14 years (alcohol, cigarette and cannabis use), peer behaviour at age 10 years (having alcohol and cigarette using friends, having delinquent friends) and parent-daughter relationship quality at age 15 years (level of communication, conflict and parental monitoring)

Once again the only moderation effect was that pubertal timing moderated the effect of the number of alcohol drinking friends at age 15 years on alcohol use at age 16 years. However, after inspecting the imputed separate groups it was found that the number of alcohol drinking friends at age 15 years predicted alcohol use at age 16 years for early, on-time and late maturing girls with the effect being weaker in early maturing girls (OR=1.82, 95% CI: 1.17, 2.83) than on-time maturing girls (OR=3.45, 95% CI: 2.54, 4.70) and late maturing girls (OR=4.24, 95% CI: 2.18, 8.23).

To summarise the main findings: (1) Late maturing girls had fewer alcohol drinking friends at age 15 years than early maturing girls and this effect remained consistent after adjusting for confounders; (2) Late maturing girls had fewer cannabis using friends at age 15 years than early and on-time maturing girls and these effects remained consistent after adjusting for confounders; (3) Late maturing girls had a lower chance of having delinquent friends at age 15 years than early maturing girls and this effect remained consistent after adjusting for confounders; (4) Higher numbers of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends at age 15 years were associated with increased alcohol, cigarette and cannabis use at age 16 years and these effects remained consistent after adjusting for confounders; (5) The number of cannabis using peers at age 15 years completely mediated the effect of pubertal timing on cannabis use at age 16 years but this effect disappeared after adjusting for confounders; (6) The number of alcohol drinking friends at age 15 years partially mediated the effect of pubertal timing on cigarette use at age 16 years. The number of cannabis using friends at age 15 years partially mediated the effect of pubertal timing on cigarette use at age 16 years and having delinquent friends at age 15 years partially mediated the effect of pubertal timing on cigarette and cannabis use at age 16 years. These effects disappeared after adjusting for confounders; (7) "Indirect-only mediation" was found whereby the number of cannabis using friends at age 15 years mediated the effect of pubertal timing on alcohol use at age 16 years and having delinquent friends at age 15 years mediated the effect of pubertal timing on alcohol use at age 16 years; these effects remained consistent after adjusting for confounders; (8) Pubertal timing moderated the relationship between the number of alcohol drinking friends at age 15 years and alcohol use at age 16 years and this effect remained consistent after adjusting for confounders.

9.7 Comparison of complete case and imputed results

This section is aimed to provide a better overview of the results of the complete case analysis and the imputed analysis with the help of some figures (significant effects are represented by hollow data points).

Figures 19-22 show the effects of pubertal timing on peer deviance.

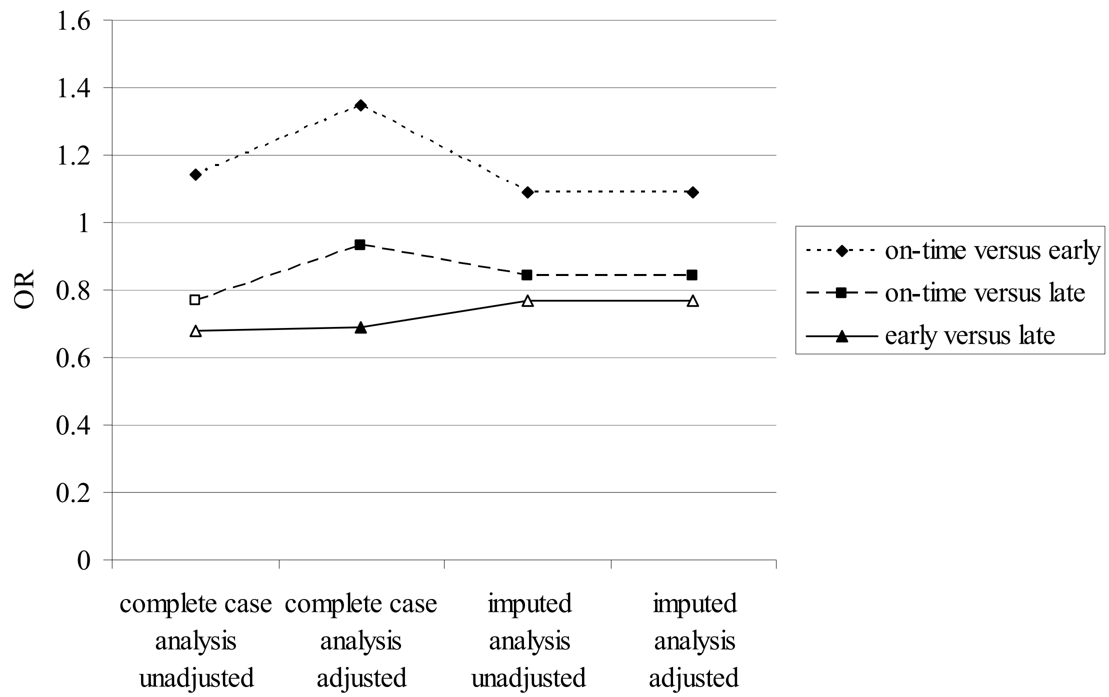


Figure 19. The effects of pubertal timing on the number of alcohol drinking peers

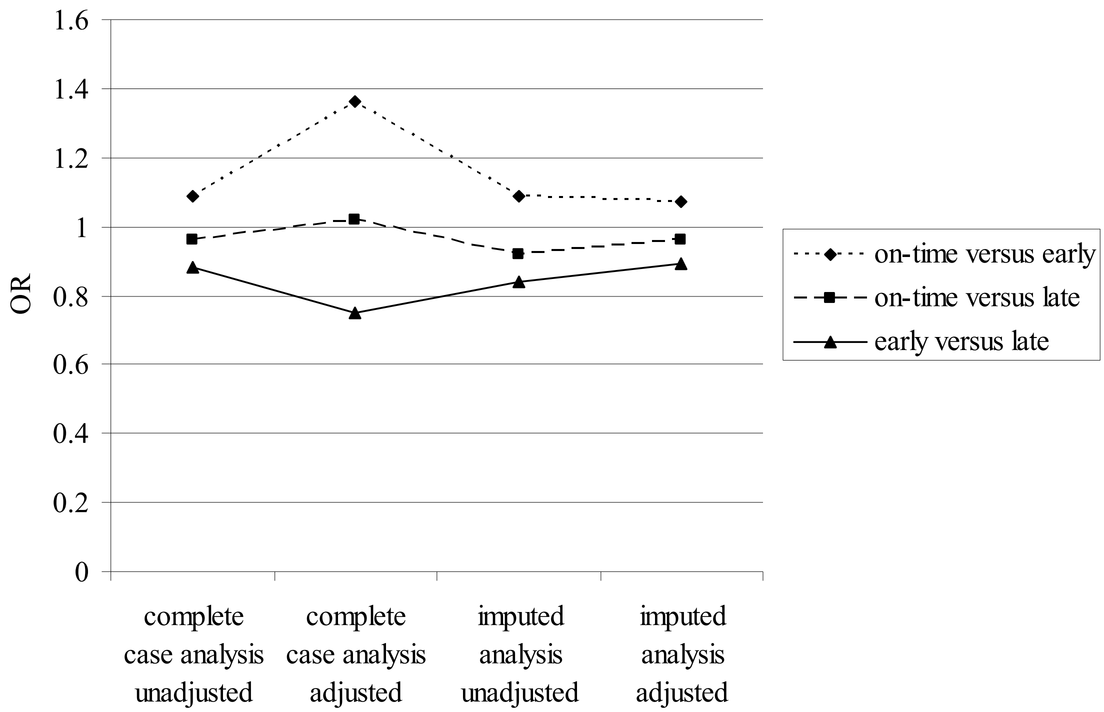


Figure 20. The effects of pubertal timing on the number of cigarette smoking peers

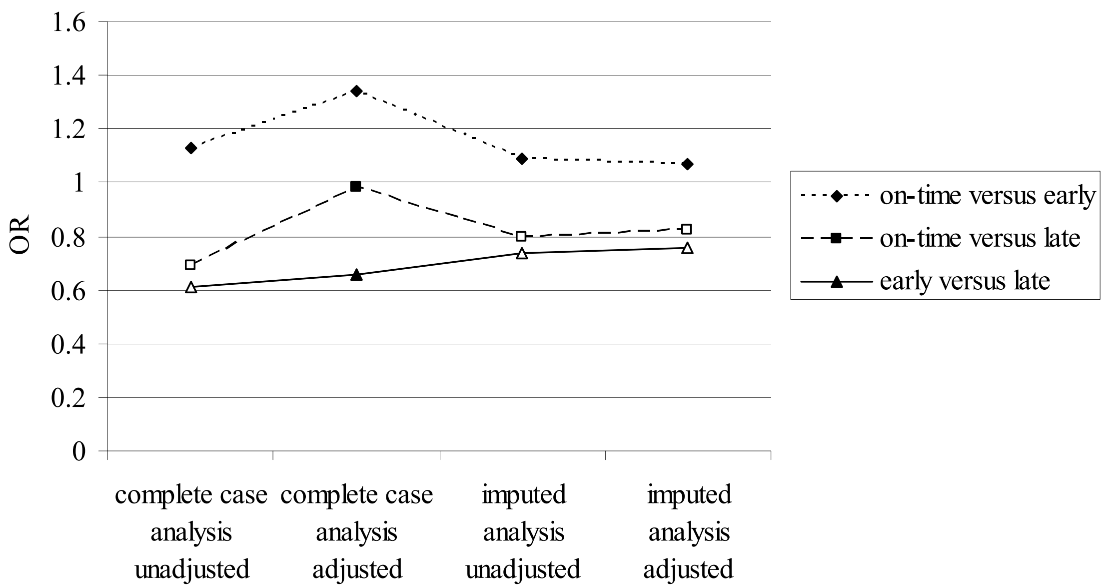


Figure 21. The effects of pubertal timing on the number of cannabis using peers

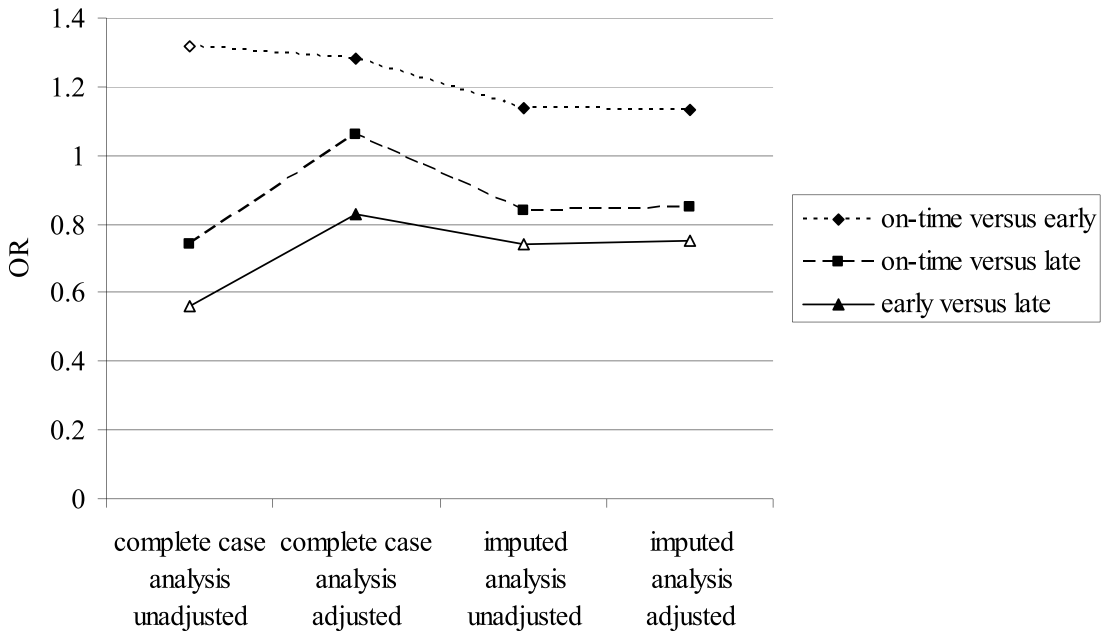


Figure 22. The effects of pubertal timing on having delinquent peers

Figures 23-25 show the effects of peer deviance on substance use (all of these effects were significant).

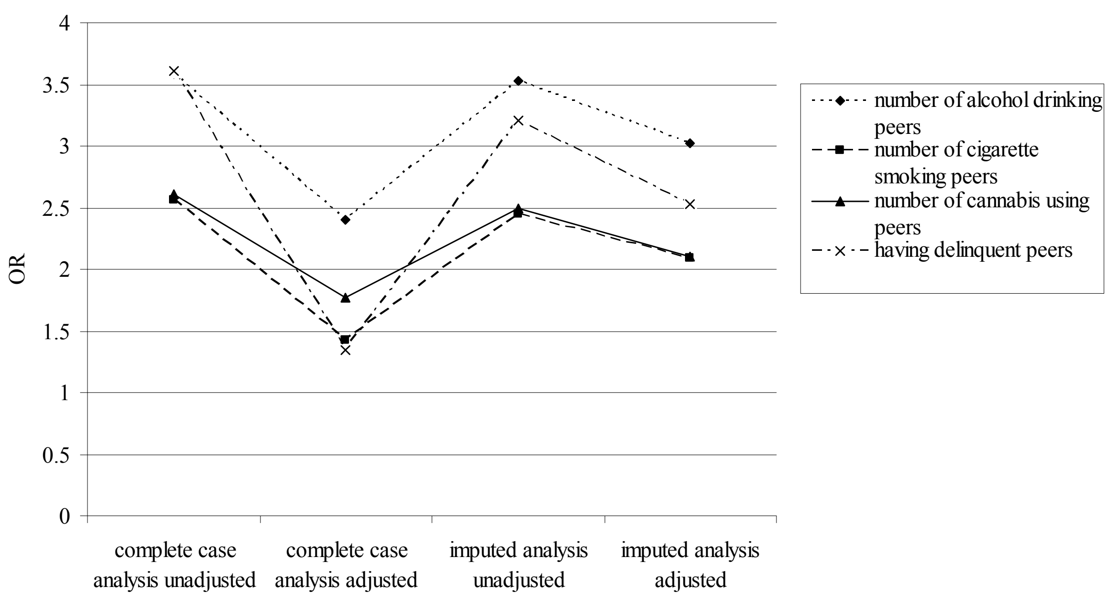


Figure 23. The effects of peer deviance on alcohol use

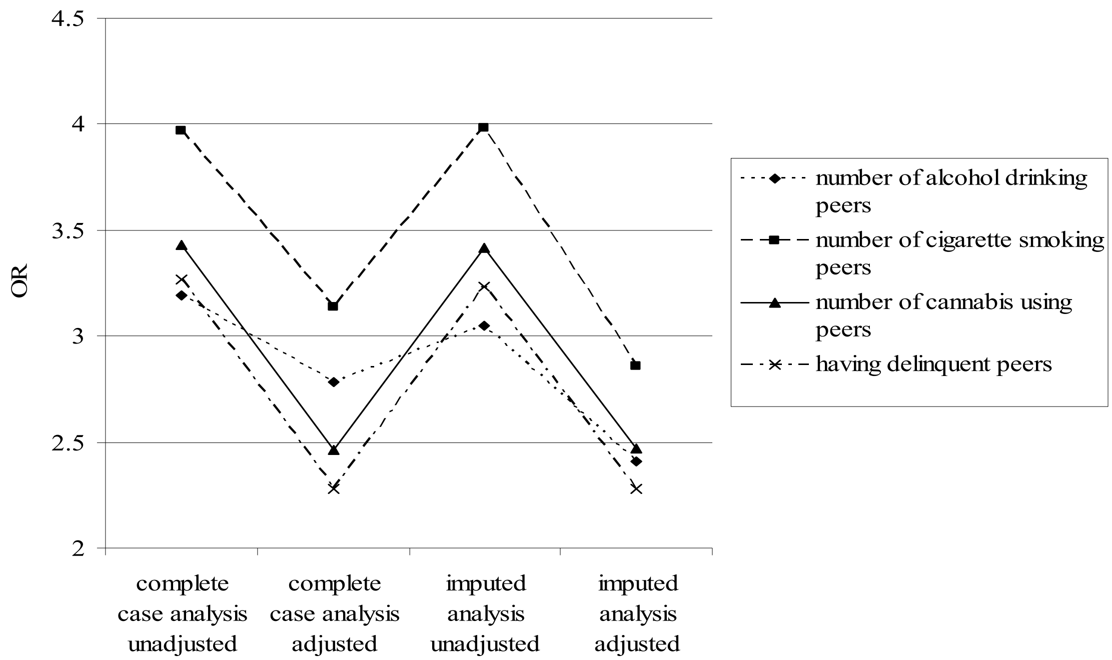


Figure 24. The effects of peer deviance on cigarette use

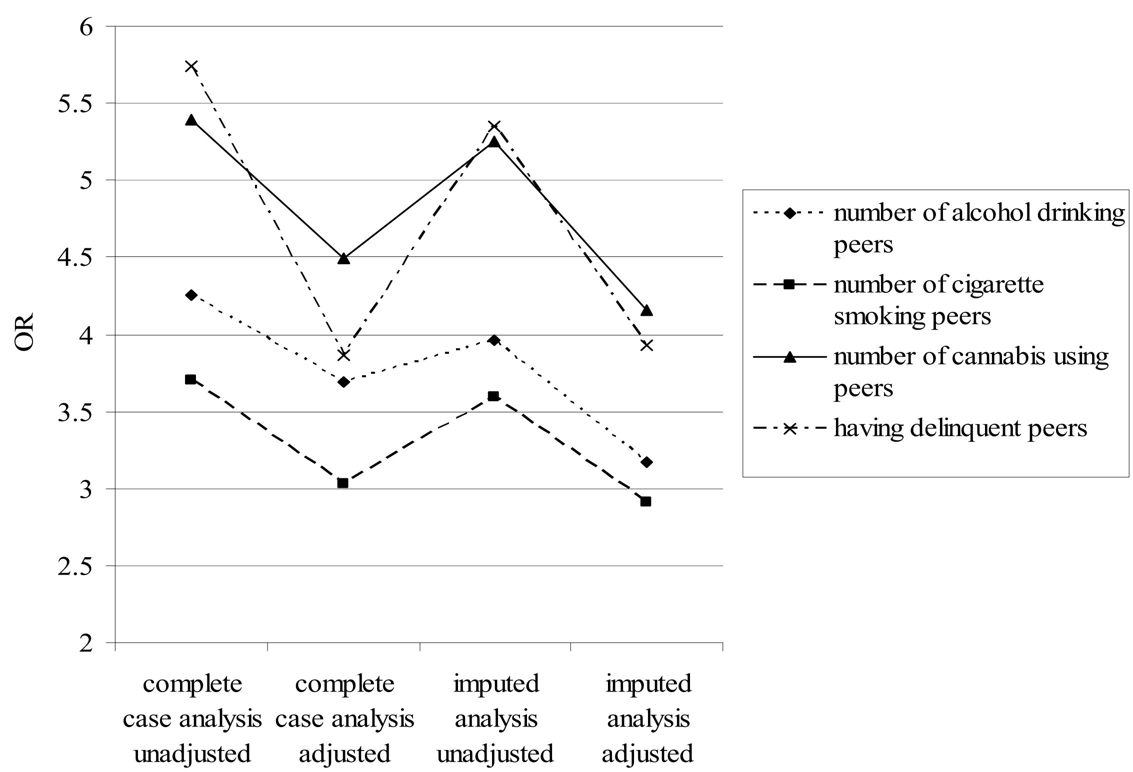


Figure 25. The effects of peer deviance on cannabis use

9.8 Discussion

Few studies have tested the hypothesis that pubertal timing combines with peer deviance to influence adjustment in adolescence. The present study used a large population-based sample to investigate the possible impact of pubertal timing on the longitudinal link between peer deviance and girls' substance use.

Late maturing girls had fewer alcohol drinking and delinquent friends at age 15 years than early maturing girls and late maturing girls had fewer cannabis using friends at age 15 years than early and on-time maturing girls. These findings supported the existing literature, especially the *maturation disparity hypothesis* (Moffitt, 1993) proposing that early maturing girls engage in more risky behaviours due to their mature physical appearance compared to same-aged peers. Furthermore, Marklein and colleagues (2009) reported that early maturing girls had more substance using friends than on-time and late maturing girls and therefore tended to engage in more risky behaviours. My findings partly support this as I found that late maturing girls had fewer alcohol drinking friends and a lower chance of having delinquent friends than early maturing girls and fewer cannabis using friends than early and on-time maturing girls at age 15 years. However, I did not find any difference between early and on-time maturing girls' peers. This suggests that by age 15 years, on-time maturing girls may have caught-up with early maturing girls in relation to selecting and affiliating with deviant peers. Such catch-up effects had also been discussed by Marklein and colleagues (2009) who suggested that risk associated with early pubertal timing diminishes over the course of adolescence. This might have two reasons: first that the dys-synchrony between early maturing girls' advanced physical appearance and limited emotional and cognitive resources is resolved as the girls cognitive and social skills are developed by late adolescence. Secondly, by late adolescence substance use becomes more age normative and less deviant.

Having more alcohol drinking, cigarette smoking, cannabis using and delinquent friends at age 15 years were each linked to higher levels of alcohol, cigarette and cannabis use at age 16 years. This supports the literature and especially the *social learning theory*, which proposes that individuals learn to take substances in groups. During adolescence special research attention is given to the peer group, especially to peers' substance use, due to the importance adolescents place on peers while they gain autonomy from the parents (Bahr et al., 2005).

9.8.1 Interplay of peer deviance and pubertal timing on substance use. I examined whether specific aspects of peer deviance (number of alcohol drinking, cigarette smoking and cannabis using friends and having delinquent friends at age 15 years) combine with pubertal timing to increase risk of substance use in girls, while adjusting for potential confounding factors.

9.8.1.1 Mediation analysis. Several mediation effects were found in the unadjusted analyses but after adjusting for confounders only two effects of "indirect-only mediation" were found. Although pubertal timing was not associated with substance use at age 16 years, early pubertal timing was associated with having more cannabis using friends and having delinquent friends at age 15 years, which were associated with increased levels of alcohol use at age 16 years. According to Hayes (2009) and Zhao and colleagues (2010) mediation effects can still be present even though no direct effect is found. Therefore, the results provide evidence for a longitudinal effect of pubertal timing on alcohol use at age 16 years via cannabis using and delinquent peers at age 15 years.

The lack of evidence for a direct effect of pubertal timing on substance use supports previous research in which substance use was also assessed in late adolescence (e.g., Al-Sahab et al., 2012; Copeland et al., 2010; Kaltiala-Heino et al., 2011; Marklein et al., 2009). This, as already mentioned above, might be explained by the theory that early pubertal timing being a risk factor diminishes by late adolescence as on-time and late maturing girls catch-up with regards to substance use and early maturing girls gain cognitive resources, which allow them to exhibit more control over their own behaviour.

9.8.1.2 Moderation analysis. Pubertal timing moderated the effect of the number of alcohol drinking friends (age 15 years) on alcohol use at age 16 years, with the effect being weaker for early than on-time and late maturing girls, even though evidence for the effect still was found across all three pubertal timing groups. A moderation effect was also found by Biehl and colleagues (2007); however they reported that having more alcohol drinking friends predicted increased alcohol use in late adolescence for early maturing girls only. This contrasts with the findings of this study, where having more alcohol drinking friends was associated with increased alcohol use in late adolescence for all girls, with the effect being stronger for on-time and late maturing girls than for early maturing girls. However, as this was the only moderation effect detected, it should be interpreted with care.

9.8.1.3 Interpretation of the findings. Within this chapter I looked at the combined effects of peer deviance at age 15 years and pubertal timing on substance use at age 16 years. It was found that although early pubertal timing was not directly linked to increased alcohol use at age 16 years, early maturing girls had more cannabis using friends and were more likely to have delinquent friends at age 15 years, which in turn were associated with higher levels of alcohol use at age 16 years. These findings suggest that by late adolescence alcohol and cigarette use are more age normative and therefore more acceptable among adolescents, which might explain why the number of alcohol drinking and cigarette smoking peers does not affect the relationship between pubertal timing and substance use. However, cannabis use and engaging in delinquent behaviour are illegal in the UK and therefore represent an increased level of deviance. Early maturing girls in this study still show the tendency to affiliate with deviant peers (i.e., cannabis using friends and delinquent friends) in late adolescence. This raises the question whether early pubertal timing is a lasting risk factor with regards to choosing deviant individuals as peers; or whether early maturing girls are still associating with the same deviant peers they associated with in early adolescence. However, as this data does not provide information on how long early maturing girls have been affiliating with these peers, further research is warranted to answer this question.

In relation to main effects it was found that late maturing girls had fewer alcohol drinking friends than early maturing girls, fewer cannabis using friends than early and on-time maturing girls and fewer delinquent friends than early maturing girls. As no differences were found between early and on-time maturing girls, these findings suggest that late pubertal maturation functions as a protective factor with regards to affiliating with deviant peers. This might be explained with the advanced level of emotional and cognitive resources late maturing girls have when they enter puberty. These resources of social and cognitive skills might enable the late adolescent girls to control the reward-sensitive system in the brain, which is activated by the hormonal changes caused by the emergence of puberty (Steinberg, 2010). Therefore, these findings support to some degree Moffitt's *maturation disparity hypothesis*. If the dys-synchrony between physical maturation and emotional and cognitive resources in early maturing girls is responsible for early maturing girls affiliating with deviant peers, late pubertal maturation indeed should be a protective factor against affiliating with deviant peers. This is due to the fact that no such dys-synchrony is present in late maturing girls as by the time their body shows signs of physical maturation they already posses social and cognitive skills.

CHAPTER 10: GENERAL DISCUSSION

10.1 Pubertal timing, parent-daughter relationship quality, peer deviance and substance use

This thesis presented findings relating to the interplay of pubertal timing and psycho-social factors (parent-daughter relationship quality and peer deviance) assessed at age 15 years on substance use (alcohol, cigarette and cannabis use) assessed at age 16 years.

No differences between the pubertal timing groups in substance use at age 16 years were found in the complete case analyses, after adjusting for confounders. However, in the imputed data it was found that late maturing girls drank less alcohol at age 16 years than on-time maturing girls and in addition they also used less cannabis at age 16 years than on-time maturing girls after adjusting for confounders. These findings failed to support the hypothesis that early pubertal timing is associated with increased levels of substance use at age 16 years. However, it is in line with recent research which has also reported the absence of this link in late adolescence (age 15-18 years; Al-Sahab et al., 2012; Kaltiala-Heino et al., 2011; Marklein et al., 2009), which had been found in early/ mid-adolescence (age 9-15 years; Berg-Kelly & Kullander, 1999; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006).

Taken together, these findings are indicative of a catch-up effect, such that by late adolescence, on-time maturing girls have caught-up with early maturing girls in relation to alcohol, cigarette and cannabis use and late maturing girls have caught-up with early maturing girls in relation to cigarette use. Such an effect has also been discussed by Marklein and colleagues in 2009, who reported that the effect of early pubertal timing on increased levels of substance use may dissipate by late adolescence when substance use becomes more normative and less deviant. Early maturing girls may also serve as models in relation to substance use for on-time and late maturing peers and thus act as a risk factor for initiation of substance use by their same age peers. However, it needs to be borne in mind that this does not mean that by late adolescence early maturing girls are no longer at increased risk compared to on-time and late maturing girls. Even though early pubertal timing is no longer linked to increased substance use in late adolescence, early maturing girls are still at risk of having a higher chance of becoming substance dependent. The definition of substance dependence states that one regularly uses a substance over a longer period of time (Triwest, 2013). Early maturing girls initiate substance use at an earlier age than on-time and late maturing girls (Dick et al., 2000; Lanza & Collins, 2002; Westling et al., 2008), therefore they use substances for a longer period of time than on-time and late maturing girls, which places early maturing girls at increased risk of substance dependence. Additionally, early substance initiation is linked to negative health outcomes (i.e., lung and liver damage) also due to a more prolonged duration of substance use (ASH, 2013; NTA, 2013). Based on this it is important to follow-up early maturing girls' substance use (i.e., their regularity of drinking alcohol) into adulthood.

Although relationships were found between parent-daughter relationship quality or peer deviance and substance use at age 16 years, the effects of peer deviance on substance use at age 16 years showed larger effect size than those of parent-daughter relationship quality on substance use at age 16 years. This finding supports research by Bahr and colleagues (2005) who stated that there is an increasing drive towards autonomy from parents during adolescence and that peer behaviour may have a larger effect on adolescents' substance use in late adolescence (Kandel, 1980; Kandel & Andrews, 1987). More generally, this finding supports Erikson's *theory of identity development*, which proposes that adolescents need role models to develop their own sense of identity. Although parents can provide role models, the adolescent may reject them in certain social contexts. This renders peers the main source of identity formation in the adolescent's life, emphasising the importance of the peer group during adolescence (Erikson, 1950 cited by King, 2004).

I did not find any evidence for the combined effects of pubertal timing and parent-daughter relationship quality at age 15 years on substance use at age 16 years. However, negative parent-daughter relationship quality (low levels of parent-daughter communication, high levels of parent-daughter conflict and low levels of parental monitoring) at age 15 years was linked to increased substance use (alcohol, cigarette and cannabis) at age 16 years.

Peer deviance at age 15 years was also linked to increased substance use at age 16 years. Evidence for combined effects of pubertal timing and peer deviance at age 15 years on substance use at age 16 years were found. That is, evidence was found of peer deviance mediating the effect of pubertal timing on substance use at age 16 years. However, after adjusting for *a priori* selected confounders only the following "indirect-only mediation" effects remained: Early pubertal timing was linked to having more cannabis using friends at age 15 years, which was linked to increased alcohol use at age

16 years; and early pubertal timing was also linked to having delinquent friends at age 15 years, which was linked to increased alcohol use at age 16 years. Additionally, a single moderation effect was found: pubertal timing moderated the effect of the number of alcohol drinking peers at age 15 years on alcohol use at age 16 years. However, inspecting the separate pubertal timing groups showed that the link between the number of alcohol drinking friends at age 15 years and increased alcohol use at age 16 years was present for all three pubertal timing groups.

10.2 Strengths and limitations

A major strength of this thesis is the stringent approach to statistical analysis, whereby I controlled for a range of hypothesised confounders (financial difficulties, level of parental education, mothers and father figures' substance use, and adolescents' substance use at age 14 years, parent-daughter relationship quality at age 9 and 15 years and peer deviance at age 10 and 15 years). A second strength is a robust assessment of pubertal timing, which was derived from nine distinct measures of age at menarche assessed on a yearly basis from age 8 to 17 years using a combination of mother-reports, mother/girl-reports and girl self-reports. Girls who had not experienced menarche by age 13 years (assessed at age 13 years) were automatically coded as "late maturers". This allowed for pubertal timing to be assessed prior to the psycho-social factors at age 15 years and substance use at age 16 years, which represents a major advantage to establishing the temporal relationships for the mediation analysis I undertook. Additionally, this meant that the eight girls who had not yet experienced menarche by age 17 years were also included in the study sample as they were automatically coded as "late maturers”. The availability of measures of age at menarche after age 14 years allowed including cases where age at menarche was missing at earlier assessments.

A third and considerable strength is the focus on substance use in late adolescence (age 16 years) rather than studying a wide age range of participants, as had been done by earlier studies. The majority of studies have focussed on pubertal timing and girls’ substance use in early/mid-adolescence (age 9-15 years) and these have all reported that early pubertal timing was associated with increased risk of substance use (Alsaker, 1996; Berg-Kelly & Kullander, 1999; Dawes et al. 2000; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006; Patton & Viner, 2007; Waylen & Wolke, 2004). None of the studies looking at the interplay of pubertal timing, psycho-social factors and adolescent substance use has focussed exclusively on substance use in late adolescence. Negriff and Trickett (2012) focussed on early adolescence and Lynne-Landsman and colleagues (2010) on mid-adolescence. The studies by Shelton and van den Bree (2010), Marklein and colleagues (2009) and Biehl and colleagues (2007) all included participants with a relatively wide age range (11 to 17 years). Due to the participants’ large age range participants in these samples range from early to late adolescence. Such a large age gap does not allow establishing the developmental process girls go through from early to late adolescence. Therefore, more insight into developmental processes is provided by analysing samples with a smaller age gap (i.e., preferably within one of the three specific phases of adolescence), as it was done in my two studies. Additionally, with the exception of the study by Biehl and colleagues (2007), these studies conducted analyses on considerable smaller samples compared to this relatively large sample of 2858 girls.

Very few studies have investigated the relationship between pubertal timing and girls' substance use in late adolescence (e.g., Al-Sahab et al., 2012; Bratberg et al., 2007; Copeland et al., 2010; Kaltiala-Heino et al., 2011). By late adolescence, those at risk of misuse will generally have passed through the experimental phase into habitual patterns of use (McCarty et al., 2004; Viner & Taylor, 2005). Indeed, substance use in late adolescence is a reliable predictor of substance use in adulthood (Englund et al., 2012), which indicates that individuals with heavy substance use in late adolescence represent a reliable target group for intervention (McCarty et al., 2004; Viner & Taylor, 2005). Additionally, because the school leaving age in the UK is currently 16 years, there is still the potential for school-based prevention programs, aimed at all adolescents at this age. After age 16 years, a proportion of young people will leave formal education and will be more difficult and expensive to reach with health promotion and prevention programs.

Although there was only a one year lag between assessment of predictor and outcome variables, which may be argued to be too short a time span to provide results of temporal relationships, previous research has shown that adolescents' levels of substance use are still changing from age 15 to 16 years in this data set (Heron et al., 2012). Additionally, it has been reported that psycho-social factors (i.e., parental monitoring) affect substance use patterns one year later in late adolescence (Siebenbrunner et al., 2006).

Using a longitudinal data set as ALSPAC has some disadvantages, including the relatively high attrition of participating families over time, which is a common problem among large-scale longitudinal cohort studies (McVie, 2003). This loss of information was addressed by conducting multiple imputation. With regards to representativeness, ALSPAC participants completing questionnaires at age 16 years were found to score higher on a test of School Performance based on National Pupil Database (NPD) ‘Key Stage 4’ (KS4) compared to non-ALSPAC pupils and ALSPAC drop-outs. ALSPAC children completing a questionnaire at age 16 years were more likely to be female and less likely to be eligible for free school meals than ALSPAC drop-outs (Boyd et al., 2012). The effect of gender-driven sample bias was partly mitigated by a focus on females but bias may have been introduced because of the attrition of data from socioeconomically disadvantaged families. This might explain the lack of findings regarding the combined effects of parent-daughter relationship quality and pubertal timing on adolescent substance use, as lower quality of family functioning is found in families with low socioeconomic status compared to families with no socioeconomic problems (Conger et al., 2010). Including information from earlier data assessments in the imputation model addresses the issue of this bias; however as only complete case outcome measures were included in the analyses, the bias, due to higher drop-out rates of participants from low socioeconomic background, still needs to be kept in mind. High rates of substance use in adolescence are reported to be linked to low socioeconomic status (Sutherland, 2012), therefore, due to the data attrition from participants from low socioeconomic background, the ALSPAC data set might be biased as adolescents with high levels of substance use might be underrepresented.

Another limitation is that the constructs of primary interest were not assessed using the same measures at each data collection point, which is often difficult to achieve due to age restrictions on questionnaires. The predictor variables in this study were based on the level of parent-daughter communication, conflict, the level of parental monitoring, the number of alcohol drinking, cigarette smoking and cannabis using friends as well as having delinquent friends at age 15 years. These measures were not available at an earlier age. I elected to use a measure of family functioning at age 9 years (how much time spent with mother and father figure doing positive things) as well as binary measures of the number of alcohol drinking and cigarette smoking friends and having delinquent friends at age 10 to act as proximal indices. More specifically, adjusting for these earlier measures did not allow for complete assurance that the findings were not caused by earlier effects of the predictors on the outcome measures. However, as the confounders were still fairly similar to the predictor measures at age 15 years, I am reasonably confident that these analyses controlled for early parent-daughter relationship quality factors and early peer deviance factors.

The parent-daughter relationship quality factors were based on adolescent-reports and some may argue that this leads to bias of single source data collection (Holmbeck et al., 2002), due to the lack of possibility to compare the answers given by the girls with answers given by another source (e.g., parents). However, it has been stated that adolescent-report of the parent-adolescent relationship does offer benefits over alternative approaches (McGue et al., 2005). For example, the effect of parent-adolescent relationship quality on adolescent behaviour is mediated by adolescents' perceptions of this relationship (Neiderhiser et al., 1998) and furthermore there is also substantial support for adolescent-report that the parent-adolescent relationship is reliable and predictive (Metzler at al., 1998). More specifically, it has been reported that when looking at the effect of parent-adolescent relationship quality on adolescent behaviour it is best to use adolescent-reports (Hartos & Power, 2000).

Finally, the variable of peer delinquency was a binary variable created from seventeen yes/no-items assessing peer delinquency (for detailed information see section 6.2.2.2). This means that individuals, who answered a single item of the seventeen items with “yes”, were coded as engaging in delinquent behaviour. This procedure was very strict, as adolescents answering only one item with “yes” were placed in the same category as individuals answering more items with “yes”. However, as no information on a better categorisation could be found, I did not feel comfortable choosing which and how many items of the seventeen should be answered with “yes” to qualify for being in the delinquent group. Therefore only those individuals, who answered all of the seventeen items with “no”, were categorised as not engaging in delinquent behaviour.

10.3 Implications

The findings suggest that by late adolescence on-time and late maturing girls may have caught-up with early maturing girls in levels of cigarette use and that on-time maturing girls have also caught-up with early maturing girls in levels of alcohol and cannabis use. However, early maturing girls remain at risk of substance dependence and impacts on physiological development associated with earlier substance initiation (Spear, 2002), due to a prolonged period of substance use compared to on-time and late maturing girls. This means that although substance use levels are almost even for the three pubertal timing groups by late adolescence, early maturing girls remain at increased risk of organ damage caused by a longer period of substance use exposure and substance use (Spear, 2002). Although I did not find any evidence for combined effects of parent-daughter relationship quality and pubertal timing on substance use in late adolescence, and only a few with regards to peer deviance, this topic is an important one as substance use patterns in late adolescence have health consequences extending into adulthood (McCambridge et al., 2011; McCarty et al., 2004; Newcomb & Bentler, 1987; Viner & Taylor, 2005; Wells et al., 2004) as well as consequences regarding education, work, romantic relationships, and global adaptation in adulthood (Englund et al., 2012).

Lack of finding evidence for the link between early pubertal timing and higher levels of substance involvement extending into late adolescence may have implications for developing practice and policy aimed at prevention (McCarty et al., 2004; Viner & Taylor, 2005). Previous research studies have reported that there is a link between early pubertal timing and increased levels of substance use in early and mid-adolescence (Berg-Kelly & Kullander, 1999; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006; Pickhardt, 2009). Furthermore, it was reported that the effect of early pubertal timing on increased levels of substance use was stronger for adolescents living in moderate and high risk families (based on household stability, household conflict and household resources; Lynne-Landsman et al., 2010) as well as combined effects of early pubertal timing and peer deviance on increased adolescent substance use (Negriff & Trickett, 2012). However, these studies analysed samples of adolescents in early and mid-adolescence. Not finding evidence for the link between early pubertal timing and higher levels of substance involvement extending into late adolescence as well as not finding evidence for combined effects of parent-adolescent relationship quality (and only some evidence for combined effects of peer deviance) on adolescent substance use in late adolescence may have implications for developing practice and policy aimed at prevention (McCarty et al., 2004; Viner & Taylor, 2005). More specifically, such findings call for development specific targeted prevention programmes. According to these findings and the existing literature, early pubertal timing appears to be an individual risk factor which can combine with psycho-social factors to increase risk for substance use especially in early and mid-adolescence (when early maturing girls are in the middle of their pubertal transition). Once early maturing girls have passed through puberty the increased risk seems to diminish. Therefore prevention programmes need to be development- and target-specific, a point I will get back to shortly.

Several prevention programmes have been introduced over the last years aiming at reducing adolescent substance use, whereby one needs to differentiate between universal and selective prevention programmes. Universal programmes address a whole population (for example, all children in a school of a certain age), whereas selective programmes address a subset of this population, who might be at high risk of engaging in increased levels of adolescent substance use (McGrath et al., 2006). In 2002 Foxcroft and colleagues published their systematic review on prevention programmes for adolescent alcohol use. They reported that one prevention programme was especially promising with regards to its long-term effectiveness: the Strengthening Families Programme 10-14 (SFP 10-14; Foxcroft et al., 2002). The SFP 10-14 was developed by Spoth and colleagues in the United States in the late 1990s (Spoth et al., 2001 a); in recent years it has been adapted to be used in the UK, too (Allen et al., 2012). The SFP 10-14 (UK) consists of seven weekly intervention sessions. During each session parents and children between age 10 and 14 years are instructed separately for one hour, which is then followed by an hour of combined intervention. During the separate hours parents are instructed on parenting skills while children are instructed on adolescent specific skills (for example to resist peer pressure); the combined hour is designed to practice the skills acquired during the first hour (for example parent-child communication) and to recognise and value family strengths (Allen et al., 2012). As all children between age 10 and 14 years (with no regard to their status of pubertal development) are able to participate, this programme is a universal prevention programme. As mentioned earlier, the status of pubertal development plays a key role with regards to risk behaviour; therefore the SFP 10-14 (UK) might be even more effective, if it was development specific, which would make it a selective prevention programme. More specifically, prevention programmes (as for example the SFP 10-14 (UK)) aimed at early maturing girls and their parents need to address the issue of parent-daughter relationship quality and affiliating with deviant peers as soon as girls enter puberty, perhaps when they make the transition from primary to secondary school at age 10-11 years, as this is the period when early maturing girls are at the beginning of puberty. Although on-time and late pubertal maturation were not specifically linked to increased adolescent substance use, experimenting with substances is still regarded as a culturally normative part of growing up and which might lead to increased levels of substance use. Therefore, it is also wise to additionally aim prevention programmes at on-time and late maturing girls and their parents. However, as already mentioned, these prevention programmes should be development specific. More specifically, the prevention programmes for on-time maturing girls should be administered right when the on-time maturing girls enter puberty whereas the prevention programmes for late maturing girls need to be administered when late maturing girls enter puberty. This means that the prevention message is more salient if it is delivered when the adolescent is most at risk.

10.4 Future research

This thesis focussed on the combined effects of pubertal timing and psycho-social factors on substance use in late adolescence. I controlled for levels of parental substance use, which might be seen as an indicator of genetic predisposition regarding substance abuse (Kilpatrick et al., 2000; Li et al., 2002). However, the link between high levels of parental substance use and high levels of adolescent substance use might be explained by a genetic predisposition or by social processes whereby adolescents imitate their parents' substance use behaviour, or both. Therefore, to completely understand adolescent substance use future research should include environmental factors (as focussed on in this thesis) and genetic factors (i.e., polymorphism of the serotonin transporter gene (5-HTTLPR), which have been linked to increased risk behaviour in adolescence and adulthood; Brody et al., 2009; Kuhnen et al., 2013).

Furthermore, future longitudinal studies should focus their data collection on assessing items of interest with the exact same questions at each data collection time point. This provides the best possibility to estimate trajectories over time (i.e., how does early maturing girls' substance use develop over the course of adolescence compared to on-time and late maturing girls). Additionally, it is important to continue data collection into adulthood. This allows the researcher to test whether increased adolescent substance use is linked to negative health outcomes in adulthood as well as to look at whether early substance initiation (linked to early pubertal timing) is associated with a higher chance of becoming substance dependent in adulthood. Such a finding would then provide evidence for early pubertal timing being a long lasting risk factor.

In summary, this thesis found no evidence for early pubertal girls engaging in increased levels of alcohol, cigarette and cannabis use in late adolescence compared to on-time and late maturing girls. Furthermore, no evidence for combined effects of parent-daughter relationship quality and pubertal timing on substance use was found. However, with regards to peer deviance, it was found that pubertal timing moderated the effect of the number of alcohol drinking friends (at age 15 years) on alcohol use (at age 16 years) with the effect being stronger for on-time and late maturing girls compared to early maturing girls. Furthermore, trends for mediation were found. Early pubertal timing was linked to having more cannabis using and delinquent friends at age 15 years, which were linked to increased alcohol use at age 16 years. These findings point to the need for development- and target-specific prevention programmes.

REFERENCES

Action on smoking and health (ASH). Fact sheets. Smoking statistics: illness and death (2013). Retrieved June 31st, 2013, from http://ash.org.uk/files/documents/ASH_107.pdf.

Akobeng, A.K. (2005). Understanding systematic reviews and meta-analysis. *Archives of Disease in Childhood, 90*, 845-848.

Albert, D. & Steinberg, L. (2011). *Peer Influences on Adolescent Risk Behavior*. In Bardo, M.T., Fishbein, D.H., & Milich, R. (Eds.), *Inhibitory Control and Drug Abuse Prevention: From Research to Translation* (pp. 211-226). New York: Springer.

Ali, M., Amialchuk, A., & Dwyer, D. (2011). The social contagion effect of marijuana use among adolescents. *Public Library of Science, 6*(1), e16183.

Allen, D., Coombes, L., & Foxcroft, D.R. (2012). *Preventing Alcohol and Drug Misuse in Young People: Adaptation and Testing of the Strengthening Families Programme 10-14 (SFP10-14) for use in the United Kingdom*. AERC – Alcohol Education and Research Council.

Al-Sahab, B., Ardern, C., Hamadeh, M., & Tamim, H. (2012). Age at menarche and current substance use among Canadian adolescent girls: results of a cross-sectional study. *BioMedCentral Public Health, 12*, 195-203.

*Alsaker, F. D. (1995). Is puberty a critical period for socialization? *Journal of Adolescence, 18*, 427-444.

*Alsaker, F. D. (1996). Annotation: The impact of puberty. *Journal of Child Psychology and Psychiatry, 37*, 249-258.

ALSPAC. (2012). Retrieved July 9th, 2013, from http://www.bristol.ac.uk/alspac/researchers/resources-available/cohort/represent/.

American Academy of Child and Adolescent Psychiatry (AACAP). Facts for Families. (2011). Retrieved on December 18th, 2012, from http://www.aacap.org/cs/root/facts_for_families/facts_for_families.

American Academy of Child and Adolescent Psychiatry (AACAP). Conduct problems. (2012). Retrieved on August 2nd, 2013, from http://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/Facts_for_Families_Pages/Conduct_Disorder_33.aspx.

American Academy of Child and Adolescent Psychiatry (AACAP). Marijuana and teens. (2012).Retrieved on July 31st, 2013, from http://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/Facts_for_Families_Pages/Marijuana_and_Teens_106.aspx.

Amos, A., Greaves, L., Nichter, M., & Bloch, M. (2012). Women and tobacco: a call for including gender in tobacco control research, policy and practice. *Tobacco Control, 21*, 236-243.

Ananth, C.V. & Kleinbaum, D.G. (1997). Regression models for ordinal responses: A review of methods and applications. *International Journal of Epidemiology, 26*(6), 1323-1333.

* ° Arim R., Tramonte L., Shapka J., Dahinten V., & Willms J. (2011). The family antecedents and the subsequent outcomes of early puberty. *Journal of Youth Adolescence, 40*, 1423–35.

*Ary, D.V., Duncan, T.E., Duncan, S.C., & Hops, H. (1999). Adolescent problem behaviour: the influence of parents and peers. *Behaviour Research and Therapy, 37*, 217-230.

Australian Drug Foundation (ADF). Alcohol – teenagers. (2013). Retrieved on July 31st, 2013, from http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Alcohol_and_teenagers.

Babor, T., Higgins-Biddle, J., Saunders, J., & Monteiro, M. (2001). AUDIT – the alcohol use disorders identification test. *World Health Organization, Department of Mental Health and Substance Dependence.* Retrieved on August, 21st, 2013, from http://whqlibdoc.who.int/hq/2001/who_msd_msb_01.6a.pdf.

Bahr, S., Hoffmann, J., & Yang, X. (2005). Parental and peer influences on the risk of adolescent drug use. *The Journal of Primary Prevention*, *26*(6), 529-551.

Bandura, A. (1971). *Social learning theory*. New York City: General Learning Press.

Barnes, G., Hoffman, J., Welte, J., Farrell, M., & Dintcheff, B. (2006). Effects of parental monitoring and peer deviance on substance use and delinquency. *Journal of Marriage and Family, 68*(4), 1084-1104.

Battaglia, E. (2009). *Parental attitudes and teen substance use.* Retrieved on July 31st, 2013, from http://www.drugalcoholaddictionrecovery.com/parental-attitudes-and-teen-substance-use/.

Bava, S. & Tapert, S. F. (2010). Adolescent brain development and the risk for alcohol and other drug problems. *Neuropsychological Review, 20*, 398-413.

*Becklake, M.R., Ghezzo, H., & Ernst, P. (2005). Childhood predictors of smoking in adolescence: a follow-up study of Montreal schoolchildren. *Canadian Medical Association Journal, 173*, 377-379.

*Belsky J., Steinberg L. D., Houts R. M., Friedman S. L., Dehart G., & Cauffman E. (2007). Family rearing antecedents of pubertal timing. *Child Development, 78*, 1302–21.

*Belsky J., Steinberg L., Houts R. M., & Halpern-Felsher B. L., National Institute of Child Health and Human Development (NICHD). (2010). The development of reproductive strategy in females: early maternal harshness –> earlier menarche –> increased sexual risk taking. *Developmental Psychology, 46*, 120–8.

Bender, R. (2000). Calculating Ordinal Regression Models in SAS and S-Plus. *Biometrical Journal, 42*(6), 677-699.

*Berg-Kelly, K. & Kullander, K. (1999). Gender differences in early adolescence in factors related to outcome of healthy behaviors two years later. *Acta Paediatrica, 88*, 1125-30.

Biehl, M.C., Natsuaki, M.N., & Ge, X. (2007). The influence of pubertal timing on alcohol use and heavy drinking trajectories. *Journal of Youth and Adolescence, 36*, 153-167.

Blakemore, S.J., Burnett, S., & Dahl, R.E. (2010). The role of puberty in the developing adolescent brain. *Human Brain Mapping, 31*(6), 926-933.

Blakemore, S.J. (2008). The social brain in adolescence. *Nature Reviews Neuroscience, 9* (4), 267-277.

Boyd, A., Golding, J., Macleod, J., Lawlor, D.A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2012). Cohort profile: the 'children of the 90s'-the index offspring of the Avon longitudinal study of parents and children. *International Journal of Epidemiology*, 1-17.

Branstetter, S., Low, S., & Furman, W. (2011). The influence of parents and friends on adolescent substance use: a multidimensional approach. *Journal of Substance Use, 16*(2), 150-160.

*Bratberg, G. H., Nilsen, T. I. L., Holmen, T. L., & Vatten, L. J. (2007). Perceived pubertal timing, pubertal status and the prevalence of alcohol drinking and cigarette smoking in early and late adolescence: a population based study of 8950 Norwegian boys and girls. *Acta Pædiatrica, 96*, 292-295.

Brienza, R.S. & Stein, M.D. (2002). Alcohol use disorders in primary care**:** do gender-specific differences exist? *Journal of General Internal Medicine, 17*(5), 387-397

British Medical Association (BMA) Board of Science and Education. Adolescent Health. (2003). Retrieved on August 21st, 2013, from http://image.guardian.co.uk/sys-files/Society/documents/2003/12/08/BMA_AdolescentHealth.pdf.

Brody, G.H., Beach, S.R.H., Philibert, R.A., Chen, Y., Lei, M. McBride Murry, V., & Brown, A.C. (2009). Parenting moderates a genetic vulnerability factor in longitudinal increases in youths' substance use. *Journal of Consulting and Clinical Psychology, 77*(1), 1-11.

Brody G. H. & Ge X. (2001). Linking parenting processes and self regulation to psychological functioning and alcohol use during early adolescence. *Journal of Family and Psychology, 15*, 82–94.

*Brody G. H., Ge X., Katz J., & Arias I. (2000). A longitudinal analysis of internalization of parental alcohol-use norms and adolescent alcohol use. *Applied Developmental Science, 4*, 71–9.

Brown, S.A. & Tapert, S.F. (2004). Adolescence and the trajectory of alcohol use: basic to clinical studies. *Annals of the New York Academy of Sciences, 1021*, 234-244.

*Buck Louis, G.M., Gray, L.E., Marcus, M., Ojeda, S.R., Pescovitz, O.H., Witchel, S. F., Sippell, W., Abbott, D.H., Soto, A., Tyl, R.W., Bourguignon, J., Skakkebaek, N.E., Swan, S.H., Golub, M.S., Wabitsch, M., Toppari, J., & Euling, S.Y. (2008). Environmental factors and puberty timing: expert panel research needs. *Pediatrics, 121*, s192-s207.

Caldwell, B. & Bradley, R. (1984). *HOME Observation for Measurement of the Environment.,* Little Rock (AK), University of Arkansas.

Cannabis Youth Treatment Series (CYS). A 5-volume series on promising new brief therapies for teens who use marijuana. (2001). Retrieved on July 31st, 2013, from http://www.uclaisap.org/dmhcod/assets/Transition%20Age%20Youth/Resources/Adolescent%20Brief%20Treatment%20Manual%20Order%20Form.pdf.

Carlin, J.B., Galati, J.C., & Royston, P. (2008). A new framework for managing and analyzing multiply imputed data in stata. *The Stata Journal, 8*(1), 49-67.

* ° Celio, M., Karnik, N. S., & Steiner, H. (2006). Early maturation as a risk factor for aggression and delinquency in adolescent girls: a review. *International Journal of Clinical Practice, 60*, 1254-62.

Centre for Longitudinal Studies. Welcome to the Longitudinal Study of Young People in England. (2014). Retrieved on March 6th, 2014, from http://www.cls.ioe.ac.uk/page.aspx?&sitesectionid=1246&sitesectiontitle=Welcome+to+the+Longitudinal+Study+of+Young+People+in+England+

Chambers, R.A., Taylor, J.R., & Potenza, M.N. (2003). Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. *American Journal of Psychiatry, 160*(6), 1041-1052.

Chein, J., Albert, D., O'Brien, L., Uckert, K., & Steinberg, L. (2011). Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. *Developmental Science, 14*(2), F1-F10.

Cicchetti, D. (1984). The Emergence of Developmental Psychopathology. *Journal of Child Development, 55*, 1-7.

Cole, D.A. & Maxwell, S.E. (2003). Testing mediational models with longitudinal data: questions and tips in the use of structural equation modeling. *Journal of Abnormal Psychology, 112*(4), 558-577.

Conger, R.D., Conger, K.J., & Martin, M.J. (2010). Socioeconomic status, family processes, and individual development. *Journal of Marriage and Family, 72*(3), 685-704.

*Copeland, W., Shanahan, L., Miller, S., Costello, E.J., Angold, A., & Maughan, B. (2010). Outcomes of early pubertal timing in young women: a prospective population-based study, *American Journal of Psychiatry, 167*, 1218-1225.

* ° Costello E. J., Sung M., Worthman C., & Angold A. (2007). Pubertal maturation and the development of alcohol use and abuse. *Drug and Alcohol Dependence, 88*, S50–S59.

Cruz, J., Emery, R., & Turkheimer, E. (2012). Peer network drinking predicts increased alcohol use from adolescence to early adulthood after controlling for genetic and shared environmental selection. *Developmental Psychology, 48*(5), 1390-1402.

*Dawes, M. A., Antelman, S. M., Vanyokov, M. M., Giancola, P., Tarter, R. E., Susman, E. J., Mezzich, A., & Clark, D. B. (2000). Developmental sources of variation in liability to adolescent substance use disorders. *Drug and Alcohol Dependence, 61*, 3-14.

*Dick, D. M., Rose, R. J., Pulkkinen, L., & Kaprio, J. (2001). Measuring puberty and understanding its impact: a longitudinal study of adolescent twins. *Journal of Youth and Adolescence, 30*, 385-399.

* ° Dick, D.M., Rose, R.J., Viken, R.J., & Kaprio, J. (2000). Pubertal timing and substance use: associations between and within families across late adolescence. *DevelopmentalPsychology, 36*, 180–189.

* ° Dishion, T. J., Nelson, S. E., & Bullock, B. M. (2004). Premature adolescent autonomy: parent disengagement and deviant peer process in the amplification of problem behaviour. *Journal of Adolescence, 27*, 515-530.

*Donovan, J. E. (2004). Adolescent alcohol initiation: a review of psychosocial risk factors. *Journal of Adolescent Health, 35*, 529.e7-529.e7.

*Dorn, L.D., Susman, E.J., & Ponirakis, A. (2003). Pubertal timing and adolescent adjustment and behaviour: conclusions vary by rater. *Journal of Youth and Adolescence, 32*, 157-167.

*Downing, J. & Bellis, M. A. (2009). Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. *BioMedCentral Public Health, 9*, 446.

Ellickson, S., Tucker, J., Klein, D., & McGuigan, K. (2001). Prospective risk factors for alcohol misuse in late adolescence. *Journal of Studies on Alcohol, 62*(6), 773-782.

Ellis, B.J. (2004). Timing of pubertal maturation in girls: an integrated life history approach. *Psychological Bulletin, 130*(6), 920-958.

*Ellis B. J. & Essex M. J. (2007). Family environments, adrenarche, and sexual maturation: a longitudinal test of a life history model. *Child Development, 78*, 1799–817.

Engels, J.M. & Diehr, P. (2004). Imputation of missing longitudinal data: a comparison of methods. *Journal of Clinical Epidemiology, 56*(10), 968-976.

Englund, M.M., Siebenbrunner, J., Oliva, E.M., Egeland, B., Chung, C.T, & Long, J.D. (2012). The developmental significance of late adolescent substance use for early adult functioning. *Journal of Developmental Psychology, 49*(8), 1554-1564.

*Enoch, M. A. (2011). The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology, 214*(1), 17-31.

ESYTC. (2011). Retrieved on December 23rd, 2011, from http://www.law.ed.ac.uk/cls/esytc/

Ewing, J.A. (1984). Detecting alcoholism: the CAGE questionnaire. *Journal of the American Medical Association 252*(14), 1905-1907.

Fowler, T., Lifford, K., Shelton, K., Rice, F., Thapar, A., Neale, M.C., McBride, A., & van den Bree, M. (2007). Exploring the relationship between genetic and environmental influences on initiation and progression of substance use. *Addiction, 101*, 413-422.

Foxcroft, D.R., Ireland, D., Lister-Sharp, D.J., Lowe, G., & Breen, R. (2002). Longer-term primary prevention for alcohol misuse in young people: a systematic review. *Addiction, 98*, 397-411.

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Smith, G., Henderson, J., Macleod, J., Molloy, L., Ness, A., Ring, S., Nelson, S., & Lawlor, D. (2012). Cohort profile: the Avon longitudinal study of parents and children: ALSPAC mother cohort. *International Journal of Epidemiology, 42*(1), 97-110.

*Galambos N. L. & Almeida D. M. (1992). Does parent–adolescent conflict increase in early adolescence. *Journal of Marriage and Family, 54*, 737–47.

*Gaudineau A., Ehlinger V., Vayssiere C., Jouret B., Arnaud C., & Godeau E. (2010). Factors associated with early menarche: results from the french health behaviour in school-aged children (HBSC) study. *BMC Public Health, 10*, 175.

Ge, X. J., Best, K. M., Conger, R. D., & Simons, R. L. (1996). Parenting behaviors and the occurrence and co-occurrence of adolescent depressive symptoms and conduct problems. *Developmental Psychology, 32*(4), 717-731.

*Ge, X. J., Brody, G. H., Conger, R. D., Simons, R. L., & Murry, V. M. (2002). Contextual amplification of pubertal transition effects on deviant peer affiliation and externalizing behavior among African American children. *Developmental Psychology, 38*, 42-54.

*Ge, X., Jin, R., Natsuaki, M. N., Gibbons, F. X., Brody, G. H., Cutrona, C. E., & Simons, R. L. (2006). Pubertal maturation and early substance use risks among african american children. *Psychology of Addictive Behaviors, 20*, 404-414.

*Ge, X., Natsuaki, M. N., Neiderhiser, J. M., & Reiss, D. (2007). Genetic and environmental influences on pubertal timing: results from two national sibling studies. *Journal of Research on Adolescence, 17*, 767-788.

Ge, X. & Natsuaki, M. N. (2009). In search of explanations of early pubertal timing effects on developmental psychopathology. *Current Directions in Psychological Science, 18*, 327–331.

Geuzaine, C. Debry, M., & Liesens, V. (2000). Separation from parents in late adolescence: the same for boys and girls? *Journal of Youth and Adolescence, 29*(1), 79-91.

Glaser, B., Shelton, K., & van den Bree, M. (2010). The moderating role of close friends in the relationship between conduct problems and adolescent substance use. *Journal of Adolescent Health, 47*(1), 35-42.

Gowen, L.K., Feldman, S.S., Diaz, R., & Yisrael, D.S. (2004). A comparison of the sexual behaviors and attitudes of adolescent girls with older vs. similar-aged boyfriends. *Journal of Youth and Adolescence, 33*(2), 167-175.

*Graber J. A., Seeley J. R., Brooks-Gunn J., & Lewinsohn P. M. (2004). Is pubertal timing associated with psychopathology in young adulthood? *Journal of the American Academy of Child and Adolescent Psychiatry, 43*, 718–26.

Graham, J.W. (2009). Missing data analysis: making it work in the real world. *Annual review of Psychology, 60*, 549-576.

Hansen, K. (2012). *Millennium Cohort Study: A guide to the datasets*. London: Centre for Longitudinal Studies.

Hanson, M. & Chen, E. (2007). Socioeconomic status and substance use behaviors in adolescents. *Journal of Health Psychology, 12*, 32-35.

Hartos, J.L. & Power, T.G. (2000). Association between mother and adolescent reports for assessing relations between parent–adolescent communication and adolescent adjustment. *Journal of Youth and Adolescence, 29*(4), 441-450.

Hayes, A.F. (2009). Beyond Baron and Kenny: statistical mediation analysis in the new millennium. *Communication Monographs, 76*(4), 408-420.

*Henricson C. & Roker D. (2000). Support for the parents of adolescents: a review. *Journal of Adolescence, 23*, 763–83.

Heron, J., Hickman, M., Macleod, J., & Munafo, M.R. (2011). Characterizing patterns of smoking initiation in adolescence: comparison of methods for dealing with missing data. *Nicotine & Tobacco Research, 13*(12), 1266-1275.

Heron, J., Macleod, J., Munafo, M.R., Melotti, R., Lewis, G., Tilling, K., & Hickman, M. (2012). Patterns of alcohol use in early adolescence predict problem use at age 16. *Alcohol and Alcoholism, 47*(2), 169-177.

Hibell, B., Guttormsson, U., Ahlstroem, S., Balakireva, O., Bjarnason, T., Kokkevi, A., & Kraus, L. (2007) *The 2007 ESPAD Report. Substance Use Among Students in 35 European Countries.* Retrieved on August 21st, 2013, from http://www.emcdda.europa.eu/attachements.cfm/att_77168_EN_ESPAD_summary_EN.pdf.

Hibell, B., Guttormsson, U., Ahlstroem, S., Balakireva, O., Bjarnason, T., Kokkevi, A., & Kraus, L. (2011). *The 2011 ESPAD Report. Substance Use Among Students in 36 European Countries.* Retrieved on August 21st, 2013, from http://www.espad.org/en/References--Literature/The-2011-ESPAD-Report---Substa/.

Holmbeck, G., Li, S., Schurman, J., Friedman, D., & Coakley, R. (2002). Collecting and managing multisource and multimethod data in studies of pediatric populations. *Journal of Pediatric Psychology, 27*, 5-18.

°Hummel, A., Shelton, K. H., Heron, J., Moore, L., & van den Bree, M. B. M. (2013). A systematic review of the relationships between family functioning, pubertal timing and substance use in adolescence. *Addiction, 108*(3), 487-496.

Jain, R. & Balhara, Y.P.S. (2010). Impact of alcohol and substance abuse on adolescent brain: a preclinical perspective. *Indian Journal of Physiological Pharmacology, 54*, 213-234.

*Jean R., Wilkinson A., Spitz M., Prokhorov A., Bondy M., & Forman M. (2011). Psychosocial risk and correlates of early menarche in Mexican-American girls. *American Journal of Epidemiology, 173*, 1203–10.

Jessor, R. (1991). Risk behaviour in adolescence: a psychosocial framework for understanding and action. *Journal of Adolescent Health, 12*, 597-605.

Joinson, C., Heron, J., Lewis, G., Croudace, T., & Araya, R. (2011). Timing of menarche and depressive symptoms in adolescent girls from a UK cohort. *The British Journal of Psychiatry, 198*, 17-23.

*Kaltiala-Heino, R., Koivisto, A., Marttunen, M., & Fröjd, S. (2011). Pubertal timing and substance use in middle adolescence: a 2-year follow-up study. *Journal of Youth and Adolescence, 40*, 1288-1301.

Kandel, D. (1980). Drug and drinking behavior among youth. *Annual Review of Sociology, 6*, 235-85.

Kandel, D. & Andrews, K. (1987). Process of adolescent socialization by parents and peers. *International Journal of Addictions, 22*, 319-342.

Karpinski, J.P., Timpe, E.M., & Lubsch, L. (2010). Smoking cessation treatment for adolescents. *Journal of Pediatric Pharmacology and Therapeutics, 15*(4), 249-263.

°Kelly A.B., Chan G.C.K., Toumbourou J.W., O'Flaherty M., Homel R., Patton G.C., & Williams J. (2012). Very young adolescents and alcohol: Evidence of a unique susceptibility to peer alcohol use. *Addictive Behaviors, 37*(4), 414-419.

Kilpatrick, D.G., Acierno, R., Saunders, B., Resnick, H.S., Best, C.L., & Schnurr, P.P. (2000). Risk factors for adolescent substance abuse and dependence: data from a national sample. *Journal of Consulting and Clinical Psychology, 68*(1), 19-30.

Kindlundh A., Hagekull B., Isacson D., & Nyberg F. (2001). Adolescent use of anabolic–androgenic steroids and relations to self reports of social, personality and health aspects. *European Journal of Public Health, 11*, 322–328.

King, R.M. (2004). *Adolescence. Overview, Historical Background and Theoretical Perspectives*. Retrieved on December 18th, 2012, from http://www.psyking.net/id183.htm.

Kirkwood, B.R. & Sterne, J.A.C. (2007). *Essential Medical Statistics*. Oxford: Blackwell Publishing Ltd.

Kliegman, R.M., Behrman, R.E., Jenson, H.B., & Stanton, B.F. (2007) *Nelson Textbook of Pediatrics.* Philadelphia: Saunders Elsevier.

Kokkevi, A., Richardson, C., Florescu, S., Kuzman, M., & Stergar, E. (2007). Psychosocial correlates of substance use in adolescence: a cross-national study in six European countries. *Drug and Alcohol Dependence, 86*(1), 67-74.

Korhonen, T., Huizink, A., Dick, D., Pulkkinen, L., Rose, R., & Kaprio, J. (2008). Role of individual, peer and family factors in the use of cannabis and other illicit drugs: a longitudinal analysis among Finnish adolescent twins. *Drug and Alcohol Dependence, 97*(1), 33-43.

Kring, A., Davison, G., Neale, J., & Johnson, S. (2007). *Abnormal Psychology*. New York: John Wiley & Sons.

Kuhn, D. (1999). A developmental model of critical thinking. *Educational Researcher, 28*(2), 16-25.

Kuhnen, C.M., Samanez-Larkin G.R., & Knutson B. (2013) Serotonergic genotypes, neuroticism, and financial choices. *PLoS ONE, 8*(1), e54632.

Lager, A., Berlin, M., Heimerson, I., & Danielsson, M. (2012). Young people's health. Health in Sweden: the national public health report 2012. Chapter 3. *Scandinavian Journal of Publich Health, 40*(9), 42-71.

Lansford, J., Dodge, K., Pettit, G., & Bates, J. (2010). Does physical abuse in early childhood predict substance use in adolescence and early adulthood? *Child Maltreatment*, *15*(2), 190-194.

*Lanza S. T. & Collins L. M. (2002). Pubertal timing and the onset of substance use in females during early adolescence. *Prevention and Science, 3*, 69–82.

Leather, N.C. (2009). Risk-taking behaviour in adolescence: a literature review. *Journal of Child Health Care, 13*, 295-304.

Lempers, J.D., Clark-Lempers, D., & Simons, R.L. (1989). Economic hardship, parenting, and distress in adolescence. *Child Development, 60*(1), 25-39.

Levin, K.A. & Currie, C. (2011). Family structure, mother-child communication, father-child communication, and adolescent life satisfaction. *Health Education, 110*(3), 152-168.

Lewis D. C., Cates-Wessel K. L., Mooney M., Sporcic L., Spalding K., & Feraco A. (2002). *Adolescent Substance Abuse: A Public Health Priority*. Providence: Center for Alcohol and Addiction Studies.

Li, C., Pentz, M.A., & Chou, C.P. (2002). Parental substance use as a modifier of adolescent substance use risk. *Addiction, 97*(12), 1537-1550.

Little, R.J.A. & Rubin, D.B. (2002). *Statistical Analysis with Missing Data*. 2nd ed. New York: Wiley.

Liu, X. & Koirala, H. (2013). Fitting proportional odds models to educational data with complex sampling designs in ordinal logistic regression. *Journal of Modern Applied Statistical Methods, 12*(1), 235-248.

*Lynne-Landsman, S. D., Graber, J. A., & Andrews, J. A. (2010). Do trajectories of household risk in childhood moderate pubertal timing effects on substance initiation in middle school? *Developmental Psychology, 46,* 853-68.

MacArthur, G.J., Smith, M.C., Melotti, R., Heron, J., Macleod, J., Hickman, M., Kipping, R.R., Campbell, R., & Lewis, G. (2012). Patterns of alcohol use and multiple risk behaviour by gender during early and late adolescence: the ALSPAC cohort. *Journal of Public Health, 34*(1), i20-i30.

MacKinnon, D.P. (2008). *Introduction to Statistical Mediation Analysis*. New York: Lawrence Erlbaum Associates Taylor & Francis Group.

MacKinnon, D.P. (2011). Integrating mediators and moderators in research design. *Research on Social Work Practice, 21*(6), 675-681.

McGrath, Y., Sumnall, H., McVeigh, J., & Bellis, M. (2006). *Drug use prevention among young people: a review of reviews.* National Institute for Health and Clinical Excellence.

Maddock, C. & Babbs, M. (2006). Interventions for cannabis misuse. *Advances in Psychiatric Treatment, 12*, 432–439.

Maine Center for Disease Control and Prevention (2013). *Health Effects of Tobacco.* Retrieved on July 31st, 2013, from http://www.tobaccofreemaine.org/channels/parents/learn_more_about_health_effects.php.

Marklein, E., Negriff, S., & Dorn, L. (2009) Pubertal timing, friend smoking, and substance use in adolescent girls. *Prevention Science, 10*, 141-150.

°Marschall-Levesque S., Castellanos-Ryan N., Vitaro F., & Seguin J.R. (2014) Moderators of the association between peer and target adolescent substance use. *Addictive Behaviors, 39*(1), 48-70.

Marshall, W. A. & Tanner, J. M. (1969) Variations in pattern of pubertal changes in girls. *Archives of Disease in Childhood, 44,* 291-303.

Marshall, W. A. & Tanner, J. M. (1970) Variations in the pattern of pubertal changes in boys. *Archieves of Disease in Childhood, 45,* 13-23.

*Martin C.A., Kelly T.H., Rayens M.K., Brogli B.R., Brenzel A., & Smith W.J. (2002). Sensation seeking, puberty, and nicotine, alcohol, and marijuana use in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*, 1495–502.

McCambridge, J., McAlaney, J., & Rowe, R. (2011). Adult consequences of late adolescent alcohol consumption: a systematic review of cohort studies. *Public Library on Science 8*(2), 1-13.

McCarty, C.A., Ebel, B.E., Garrison, M.M., DiGiuseppe, D.L., Christakis, D.A., & Rivara, F.P. (2004). Continuity of binge and harmful drinking from late adolescence to early adulthood. *Pediatrics, 114*(3), 714-719.

McCusker, M.T., Basquille, J., Khwaja, M., Murray-Lyon, I.M., & Catalan, J. (2002). Hazardous and harmful drinking: a comparison of the AUDIT and CAGE screening questionnaires. *Quarterly Journal of Medicine Association of Physicians of Great Britain and Ireland, 95*, 591-595.

McGue, M., Elkins, I., Walden B., & Iacona, W. (2005). Perceptions of the parent–adolescent relationship: a longitudinal investigation. *Developmental Psychology*, *41*(6), 971-984.

McVie, S. (2003). *Technical report: sweeps 3 & 4*. Edinburgh: Centre for Law and Society, University of Edinburgh.

McVie, S, & Holmes, L. (2005). *The Edinburgh Study of Youth Transitions and Crime, No 9: Family Functioning and Substance Use at Ages 12 to 17.* Edinburgh: Centre for Law and Society, University of Edinburgh.

Medeiros, R. (2012) Pred_eq: program to create and test imputation models (equations) for ice. UCLA: academic technology services, Statistical Consulting Group. Retrieved on August 21st, 2013, from www.ats.ucla.edu/stat/stata/ado/alaysis.

Metzler, C. W., Biglan, A., Ary, D. V., & Li, F. (1998). The stability and validity of early adolescents' reports of parenting constructs. *Journal of Family Psychology, 12,* 600–619.

*Meyers, J.L. & Dick, D.M. (2010). Genetic and environmental risk factors for adolescent-onset substance use disorders. *Child & Adolescent Psychiatric Clinics of North America, 19*, 465-477.

*Michaud, P.A., Suris, J.C., & Deppen, A. (2006). Gender-related psychological and behavioural correlates of pubertal timing in a national sample of Swiss adolescents. *Molecular and Cellular Endocrinology*, 172-8.

Moffitt, T.E. (1993). Life-course-persistent and adolescence-limited antisocial behavior: a developmental taxonomy. *Psychological Review, 100*, 674-701.

Moher H., Liberati A., Tetzlaff J., & Altman D.G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med, 6*, e1000097

*Molina B. S. G. & Chassin L. (1996). The parent–adolescent relationship at puberty: hispanic ethnicity and parent alcoholism as moderators *Developmental Psychology, 32*, 675–86.

Monahan, K.C., Steinberg, L., & Cauffman, E. (2009). Affiliation with antisocial peers, susceptibility to peer influence, and antisocial behavior during the transition to adulthood. *Developmental Psychology, 45*(6), 1520-1530.

Morris, D.H., Jones, M.E., Schoemaker, M.J., Ashworth, A., & Swerdlow, A.J. (2010). Determinants of age at menarche in the UK: analyses from the Breakthrough Generations Study. *British Journal of Cancer, 103*, 1760-1764.

*Moss, H.B., Lynch, K.G., Hardie, T.L., & Baron, D.A. (2002). Family functioning and peer affiliation in children of fathers with antisocial personality disorder and substance dependence: associations with problem behaviors. *American Journal of Psychiatry, 159*, 607-614.

Mrug, S., Elliott, M., Gilliland, J., Grunbaum, J.A., Tortolero, S.R., Cuccaro, P., & Schuster, M. (2008). Positive parenting and early puberty in girls – protective effects against aggressive behavior. *Archives of Pediatrics & Adolescent Medicine, 162*(8), 781-786.

National Center for Health Statistics. Health, United States, 2010: With Special Feature on Death and Dying. (2011). Hyattsville, MD.

National Health Service (NHS). The risks of drinking too much. (2012). Retrieved on July 31st, 2013, from http://www.nhs.uk/Livewell/alcohol/Pages/Effectsofalcohol.aspx.

National Health Service (NHS). What are the risks of smoking? (2012). Retrieved on July 31st, 2013, from http://www.nhs.uk/chq/Pages/2344.aspx?CategoryID=53.

National Health Service (NHS). Puberty. (2010). retrieved on April 25th, 2011, from www.nhs.uk/Conditions/Puberty/Pages/Introduction.aspx.

National Institute on Drug Abuse (NIH). Drug Facts: Marijuana. (2012). Retrieved on July 31st, 2013, from http://www.drugabuse.gov/publications/drugfacts/marijuana

National Institute for Health and Clinical Excellence (NICE). (2010). *School-based interventions to prevent the uptake of smoking among children and young people*. London: Authors.

National Treatment Agency for Substance Misuse (NTA). (2013). *Alcohol Treatment in England 2011-12*. London: The National treatment Agency for Substance Misuse.

Negriff, S. & Trickett, P. (2012). Peer substance use as a mediator between early pubertal timing and adolescent substance use: longitudinal associations and moderating effect of maltreatment. *Drug and Alcohol Dependency, 126* (1-2), 95-101.

Neiderhiser, J. M., Pike, A., Hetherington, E. M., & Reiss, D. (1998). Adolescent perceptions as mediators of parenting: genetic and environmental contributions. *Developmental Psychology, 34,* 1459–1469.

Newcomb, M.C. & Bentler, P.M. (1987). The impact of late adolescent substance use on young adult health status and utilization of health services: A structural- equation model over four years. *Social Science & Medicine, 24*(1), 71-82.

Newcomb, M.C. & Bentler, P.M. (1988). *Consequences of Adolescent Drug Use*. Newbury Park, CA: Sage Publications.

NICE. Alcohol-use disorders: preventing harmful drinking. (2010). Retrieved on June 27th, 2013, from http://www.alcoholpolicy.net/2010/06/nice-alcohol-prevention-guidance-released.html.

NICE. Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities. (2008). Retrieved on June 27th, 2013, from http://guidance.nice.org.uk/PH10.

*Obeidallah, D.A., Brennan, R.T., Brooks-Gunn, J., Kindlon, D., & Earls, F. (2000). Socioeconomic status, race, and girls' pubertal maturation: results from the project on human development in Chicago neighborhoods. *Journal of Research on Adolescence, 10*, 443-464.

Office of Adolescent Health (OAH). Preventing and Reducing Teen Tobacco Use. (2013). Retrieved on July 31st, 2013, from http://www.hhs.gov/ash/oah/adolescent-health-topics/substance-abuse/tobacco/index.html.

Ordered Logistic Regression. UCLA: Academic Technology Services, Statistical Consulting Group. (2012). Retrieved on June 20th, 2012, from http://www.ats.ucla.edu/stat/stata/dae/ologit.htm.

Owen Blakemore, J.E., Berenbaum, S.A., & Liben, L.S. (2009). *Gender Development*. Hove: Psychology Press, Taylor & Francis Group.

Oxford Dictionaries. Definition of deviance in English. (2014). Retrieved on March 6th, 2014, from http://www.oxforddictionaries.com/definition/english/deviance

Oxford, M.L., Harachi, T.W., Catalano, R.F., & Abbott, R.D. (2001). Preadolescent predictors of substance initiation: a test of both the direct and mediated effect of family social control factors on deviant peer associations and substance initiation. *The American Journal of Drug and Alcohol Abuse*, *27*(4), 599-616.

Paikoff, R.L. & Brooks-Gunn, J. (1991). Do parent-child relationships change during puberty? *Psychological Bulletin, 110*(1), 47-66.

*Patton, G. C. & Viner, R. (2007). Adolescent health 1 - Pubertal transitions in health. *Lancet (North American Edition), 369*, 1130-1139.

°Patton G.C., McMorris B.J., Toumbourou J.W., Hemphill S.A., Donath S., & Catalano R.F. (2004). Puberty and the onset of substance use and abuse. *Pediatrics, 114*(3), 300-306.

*Pedersen W., Mastekaasa A., & Wichstrom L. (2001). Conduct problems and early cannabis initiation: a longitudinal study of gender differences. *Addiction, 96*, 415–31.

Perez R.G., Ezpeleta L., & Domenech J.M. (2007). Features associated with the non-participation and drop out by socially-at-risk children and adolescents in mental-health epidemiological studies. *Social Psychiatry and Psychiatric Epidemiology, 42,* 251-8.

Peskin, H. (1973). Influence of the developmental schedule of puberty on learning and ego functioning. *Journal of Youth and Adolescence, 2*, 273–290.

Pickhardt, C. (2009). *Surviving (Your Child's) Adolescence*. Retrieved on June 27th, 2012, from http://www.psychologytoday.com/blog/surviving-your-childs-adolescence/200903/late-adolescence-15-18-acting-more-grown.

°Poikolainen, K. (2002). Antecedents of substance use in adolescence. *Current Opinion in Psychiatry, 15*(3), 241-245.

Ponton, L.E. (1997). *Romance of Risk: Why Teenagers Do the Things They Do*. New York: Basic Books.

Radliff, K., Wheaton, J., Robinson, K., & Morris, J. (2012). Illuminating the relationship between bullying and substance use among middle and high school youth. *Addictive Behaviours, 37*(4), 569-572.

Ramchand, R., Griffin, B.A., Suttorp, M., Harris, K.M., & Morral, A. (2011). Using a cross-study design to assess the efficacy of motivational enhancement therapy–cognitive behavioral therapy 5 (MET/CBT5) in treating adolescents with cannabis-related disorders. *Journal of Studies on Alcohol and Drugs, 72*(3), 380-389.

Raphael, D. (2013). Adolescence as a gateway to adult health outcomes. *Maturitas, 75*, 137-141.

Rhodes, T., Lilly, R., Fernandez, C., Giorgino, E., Kemmesis, U., Ossebaard, H., Lalam, N., Faasen, I., & Spannow, K. (2003). Risk factors associated with drug use: the importance of 'risk environment'. *Drugs: education, prevention and policy, 10*(4), 303-329.

Rose, B.M., Holmbeck, G.N., Millstein Coakley, R., & Franks, E.A. (2004). Mediator and moderator effects in developmental and behavioral pediatric research. *Developmental and Behavioral Pediatrics, 25*(1), 58-67.

Rosen, J.B. & Sockrider, M. (2013). *Management of smoking cessation in adolescents***.** Retrieved on July 31st, 2013, from http://www.uptodate.com/contents/management-of- smoking-cessation-in-adolescents.

Royston, P. (2004). Multiple imputation of missing values. *The Stata Journal, 4*(3), 227-241.

Royston, P. (2007). Multiple imputation of missing values: further update of ice, with an emphasis on interval censoring. *The Stata Journal, 7*(4), 445-464.

Royston, P. (2009). Multiple imputation of missing values: further update of ice, with an emphasis on categorical variables. *The Stata Journal, 9*(3), 466-477.

Rubin, D.B. (1976). Inference and missing data. *Biometrika, 63*(3), 581-592.

Rubin, D.B. (1987). *Multiple imputation for non-response in surveys*. New York: Wiley & Sons.

Rucker, D., Preacher, K., Tormala, Z., & Petty, R. (2011). Mediation analysis in social psychology: current practices and new recommendations. *Social and Personality Psychology Compass, 5/6*, 359–371.

Rutter, M. (1999). Psychosocial adversity and child psychopathology. *British Journal of Psychiatry, 174*, 480-493.

Rutter, M. (2005). Environmentally mediated risks for psychopathology: research strategies and findings. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*(1), 3-18.

Rutter, M. & Casear, P. (1991). *Biological risk factors for psychosocial disorders.* Cambridge: Cambridge University Press.

Saraceno, L., Heron,. J., Munafo., M., Craddock., N., & van den Bree., M. (2012). The relationship between childhood depressive symptoms and problem alcohol use in early adolescence: findings from a large longitudinal population-based study. *Addiction, 107* (3), 567-577.

*Saraceno, L., Munafo, M., Heron, J., Craddock, N., & van den Bree, M.B. (2009). Genetic and non-genetic influences on the development of co-occurring alcohol problem use and internalizing symptomatology in adolescence: a review. *Addiction, 104*, 1100-1121.

Schafer, J.L. & Graham, J.W. (2002). Missing data: our view of the state of the art. *Psychological Methods, 7*(2), 147-177.

°Schelleman-Offermans K., Knibbe R.A., & Kuntsche E. (2013). Are the effects of early pubertal timing on the initiation of weekly alcohol use mediated by peers and/or parents? A longitudinal study. *Developmental Psychology, 49*(7), 1277-1285.

Seiffge-Krenke, I. (2010). *Psychoanalytische und tiefenpsychologisch fundierte Therapie mit Jugendlichen*. Stuttgart: Klett-Cotta.

Selzer, M. (1971). The Michigan alcoholism screening test: the quest for a new diagnostic instrument. *American Journal of Psychiatry, 127*, 1653-1658.

*Shelton, K. H., Harold, G. T., Fowler, T. A., Rice, F. J., Neale, M. C., Thapar, A., & van den Bree, M. B. M. (2008). Parent-child relations, conduct problems and cigarette use in adolescence: examining the role of genetic and environmental factors on patterns of behavior. *Journal of Youth and Adolescence, 37*, 1216-1228.

*Shelton, K. H., & van den Bree, M. B. M. (2010). The moderating effects of pubertal timing on the longitudinal associations between parent-child relationship quality and adolescent substance use. *Journal of Research on Adolescence, 20*(4)**,** 1044-1064.

*Short M. B. & Rosenthal S. L. (2008). Psychosocial development and puberty. *Annals of the New York Academy of Sciences, 1135*, 36–42.

Shrive, F.M., Stuart, H., Quan, H., & Ghali, W.A. (2006). Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. *BMC Medical research Methodology, 6*: 57.

Siebenbrunner, J., Englund, M.M., Egeland, B., & Hudson, K. (2006). Developmental antecedents of late adolescence substance use patterns. *Journal of Development and Psychopathology, 18*(2), 551-571.

Simmons, R.G. & Blyth, D. A. (1987). *Moving into adolescenc: the impact of pubertal change and school context*. New York: Aldine De Gruyter.

Skinner, M., Haggerty, K., & Catalano, R. (2009). Parental and peer influences on teen smoking: are white and black families different? *Nicotine and Tobacco Research, 11*(5), 558-563.

Smith, D. (2004). *The Edinburgh Study of Youth Transitions and Crime, No 3: Parenting and Delinquency at Ages 12 to 15*. Edinburgh: Centre for Law and Society, University of Edinburgh.

Spear, L.P. (2002). Alcohol's effect on Adolescents. *Alcohol Research & Health, 26*, 287-291.

Spear, L. (2009). *The behavioral neuroscience of adolescence*. New York: Norton.

Spoth, R.L., Redmond, C., & Shin, C. (2001a). Randomized trial of brief family interventions for general populations adolescent substance use outcomes 4 years following baseline. *Journal of Consulting and Clinical Psychology*, 1-15.

Stata. Stata 12 help for test. (2012). Retrieved on March 12th, 2013, from http://www.stata.com/help.cgi?test.

Stattin H. & Magnusson D. (1990) *Pubertal Maturation in Female Development.* Hillsdale, NJ: Erlbaum.

Steinberg, L. (1987). Impact of puberty on family relations: effects of pubertal status and pubertal timing. *Developmental Psychology, 23*(3), 451-460.

Steinberg, L. (2010). A dual systems model of adolescent risk-taking. *Developmental Psychobiology, 52*, 216-224.

Steinberg, L. & Monahan, K.C. (2007). Age differences in resistance to peer influence. *Developmental Psychology, 43*(6), 1531-1543.

Steinberg, L. & Levine, A. (1997). *You and Your Adolescent: A Parent's Guide for Ages 10-20.* Dunmore: HarperCollins Publishers.

Sterne, J.A.C., White, I.R., Carlin, J.B., Spratt, M., Royston, P., Kenward, M.G., Wood, A.M., & Carpenter, J.R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ, 338*, b2393.

Stice, E., Presnell, K., & Bearman, S. (2001). Relation of early menarche to depression, eating disorders, substance abuse, and comorbid psychopathology among adolescent girls. *Developmental Psychology, 37*, 608–19.

Stuart, E.A., Azur, M., Frangakis, C. & Leaf, P. (2009). Multiple imputation with large data sets: a case study of the children's mental health initiative. *American Journal of Epidemiology, 169*(9), 1133-1139.

Sutherland, A. (2012). Is parental socio-economic status related to the initiation of substance abuse by young people in an English city? An event history analysis. *Social Science & Medicine, 74*(7), 1053-1061.

Tam, C., de Zegher, F., Garnett, S., Baur, L., & Cowell, C. (2006). Opposing influences of prenatal and postnatal growth on the timing of menarche. *Journal of Clinical Endocrinology and Metabolism, 91*, 4369–73.

*Tifflin, P.A., Pearce, M., Kaplan, C., Fundudis, T., & Parker, L. (2007). The impact of socio-economic status and mobility on perceived family functioning. *Journal of Family and Economic Issues, 28*, 653-667.

Tjora, T., Hetland, J., Aarø, L.E., & Øverland, S. (2008). Distal and proximal family predictors of adolescents' smoking initiation and development: a longitudinal latent curve model analysis. *BMC Public Health, 11*(911).

Tomori, M., Zalar, B., & Plesnicar, B.K. (2000). Gender differences in psychosocial risk factors among Slovenian adolescents. *Adolescence, 35*(139), 431-443.

Trim, R.S. & Chassin, L. (2008). Neighborhood socioeconomic status effects on adolescent alcohol outcomes using growth models: exploring the role of parental alcoholism. *Journal of Studies on Alcohol and Drugs, 69*(5), 639-645.

Triwest. Substance abuse versus substance dependence. (2013). Retrieved on September 22nd 2013 from http://www.triwest.com/en/behavioral-health/resource-center/addiction-recovery/substance-abuse/more/

*Turner, C.F., Ku, L., Rogers, S.M., Lindberg, L.D., Pleck, J.H., & Sonnenstein, F.L. (1998). Adolescent sexual behavior, drug use, and violence: increased reporting with computer survey technology. *Science, 280*, 867-873.

United Nations (2003). *World Youth Report 2003, chapter 6: Youth and Drugs*. New York: United Nations Publications.

*Urberg, K.A. & Luo, Q. (2003). A two-stage model of peer influence in adolescent substance use: individual and relationship-specific differences in susceptibility to influence. *Addictive Behaviors, 28*, 1243-1256.

Van Buuren, S., Boshuizen, H.C., & Knook, D.L. (1999). Multiple imputation of missing blood pressure covariates in survival analysis. *Statistics in Medicine, 18*, 681-694.

*van den Bree, M.B. (2005). Combining research approaches to advance our understanding of drug addiction. *Current Psychiatry Reports, 7*(2), 125-132.

*van den Bree, M. B., & Pickworth, W. B. (2005). Risk factors predicting changes in marijuana involvement in teenagers. *Archives of General Psychiatry, 62*(3), 311-319.

*van den Bree, M.B., Whitmer, M D., & Pickworth, W. B. (2004). Predictors of smoking development in a population-based sample of adolescents: a prospective study. *Journal of Adolescent Health, 35*(3), 172-181.

Van der Weele, T.J. (2009). Marginal structural models for the estimation of direct and indirect effects. *Epidemiology, 20*, 18–26.

Vansteelandt, S. (2009). Estimating direct effects in cohort and case-control studies. *Epidemiology, 20*, 851–860.

Viner, R.M., Ozer, E.M., Denny, S., Marmot, M., Resnick, M., Fatusi, A., & Currie, C. (2012). Adolescent Health 2: Adolescence and the social determinants of health. *Lancet, 379*, 1641-1652.

Viner, R.M. & Taylor, B. (2005). Adult outcomes of binge drinking in adolescence: findings from a UK national birth cohort. *Journal of Epidemiology and Community Health, 61*, 902-907.

Volkow, N. (2010). *Drugs, brains and behaviour: The science of addiction*. NIDA National Institute of Drug Abuse. National Institutes of Health US Department of Health and Human Services.

*Wang M., Dishion T., Stormshak E., & Willett J. (2011). Trajectories of family management practices and early adolescent behavioral outcomes. *Developmental Psychology, 47*, 1324–41.

Wasserman, R.M., Holmbeck, G.N., Lennon, J.M., & Almaro, C.M. (2012). A longitudinal assessment of early pubertal timing as a predictor of psychosocial changes in adolescent girls with and without Spina Bifida. *Journal of Pediatric Psychology, 37*(7), 755-768.

* ° Waylen, A. & Wolke, D. (2004). Sex 'n' drugs 'n' rock 'n' roll: the meaning and social consequences of pubertal timing. *European Journal of Endocrinology, 151 Supplement 3*, U151-9.

Weichold K. & Silbereisen R.K. (2006). Cross-cultural research on the development of adolescent substance misuse. *Sucht, 52*, 229–31.

West, P. & Sweeting, H. (2003). Fifteen, female and stressed: changing patterns of psychological distress over time. *Journal of Child Psychology and Psychiatry, 44*(3), 399-411.

* ° Westling, E., Andrews, J., Hampson, S., & Peterson, M. (2008). Pubertal timing and substance use: the effects of gender, parental monitoring and deviant peers. *Journal of Adolescent Health, 42*(6), 555-563.

White, I. R.., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine, 30*(4), 377-399.

°Whitesell, N.R., Asdigian, N.L., Kaufman, C.E., Big Crow, C., Shangreau, C., Keane, E.M., Mousseau, A.C., & Mitchell, C.M. (2013). Trajectories of substance use among young american Indian adolescents: patterns and predictors. *Journal of Youth and Adolescence, 43*(3), 437-453.

Williams, R. (2006). Generalized ordered logit/partial proportional odds models for ordinal dependent variables. The Stata Journal, 6(1), 58-82.

* ° Windle, M., Spear, L.P., Fuligni, A.J., Angold, A., Brown, J.D., & Pine, D. (2008). Transitions into underage and problem drinking: developmental processes and mechanisms between 10 and 15 years of age. *Pediatrics, 121*, s273-s289.

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. *The British Journal of Psychiatry, 195***,** 249-56.

*Wolock, I. & Magura, S. (1996). Parental substance abuse as a predictor of child maltreatment rr-reports. *Child Abuse and Neglect, 20*, 1183-1193.

Wood, M., Read, J., Mitchell, R., & Brand, N. (2004). Do parents still matter? Parent and peer influences on alcohol involvement among recent High School graduates. *Psychology of Addictive Behaviors, 18*(1), 19-30.

World Health Organization (WHO) 10 facts on adolescent health. (2008). Retrieved on April 25th, 2011, from www.who.int/features/factfiles/adolescent_health/en/index.html.

Wright, V. (2011). *Smoking, drinking and drug use among young people in England in 2010*. The Health and Social Care Information Centre, National Centre for Social Research, London.

Young, A.M. & d'Arcy, H. (2005). Older boyfriends of adolescent girls: the cause or a sign of the problem? *Journal of Adolescent Health, 36*(5), 410-419.

Zhao, X., Lynch, J.G., & Chen, Q. (2010). Reconsidering Baron and Kenny: myths and truths about mediation analysis. *Journal of Consumer Research, 37*, 197-206.

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REVIEW

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A systematic review of the relationships between family functioning, pubertal timing and adolescent substance use

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ABSTRACT

Aims Experiences linked to poor family functioning and pubertal timing have each been associated with increased risk of substance misuse in adolescence. However, it remains unclear to what extent family functioning and pubertal timing combine to put adolescents at particular risk. **Method** A systematic review was planned, undertaken and reported according to the 27 items of the PRISMA statement. Databases World of Knowledge, PsycINFO and PubMed were searched. Fifty-eight papers were retained and are discussed in this review after screening titles, abstracts and full papers against pre-established exclusion criteria. **Results** The combination of off-time pubertal timing and poor parent–adolescent relationship quality has been related to higher levels of substance use. However, this is an under-studied area of research and the evidence is less strong for boys than girls. **Conclusions** Adolescents experiencing both poor parent–adolescent relationship quality and off-time pubertal timing may represent a high-risk group that can benefit from approaches aimed at reducing risk of substance misuse.

Keywords Adolescence, alcohol use, cigarette use, family functioning, puberty, smoking, substance use.

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INTRODUCTION

Experimentation with substances usually takes place during adolescence [1,2]. Although the majority of adolescents emerge from this period without any problems, a proportion develops patterns of heavy/problem use associated with future risk of substance use disorder. For example, Lewis and colleagues estimated that more than 20% of 17-year-olds in the United States drink more than 5 units of alcohol in a row regularly and smoke cigarettes daily [3]. Furthermore, adolescent-onset substance abuse has been characterized by rapid development of multiple drug dependencies and disruption in brain functioning affecting memory, learning, motivation, judgement and behaviour control [4,5], while early-onset alcohol initiation (before 13 years), specifically, may increase the risk of alcohol abuse and dependence [4], cigarette and drug use [6]. Alcohol is the most frequently used substance during adolescence in both the United States [1] and the United Kingdom [2]. US statistics indicate that in 2010 14.9% of 13–14-year-olds had used alcohol in the past month; and 6.5% had used cigarettes and marijuana, respectively [1]. UK statistics for 2010 showed that among 11–15-year-olds in England, 13% had drunk alcohol in the last week, 5% were regular smokers and 7% had taken drugs in the last month [7]. The European School Survey Project on Alcohol and other drugs (ESPAD, 2007), collected substance use data from 15–16-year-olds in 35 European countries. They reported that 29% had smoked cigarettes, 61% had drunk alcohol and 18% had been intoxicated during the last month, while 19% had used cannabis during their life-time [8]. Adolescents may have a greater tolerance for substances than adults and therefore be more likely to engage in heavy substance use [9]. The risk of heavy substance use is increased further because adolescents are highly vulnerable to social influences [5] and have a greater reward sensitivity and proclivity to risk-taking (possibly related to changes in the developing brain) [10]. Heavy substance use is associated with an increased risk of delinquency, hazardous driving, risky sexual behaviour, psychiatric problems and school dropout [10]. It is therefore important to understand the factors that put adolescents at increased risk for problem substance use.

The role of family functioning

A number of studies have indicated that children from homes characterized by poor family functioning are at increased risk of early substance use initiation and progression to heavy/problem use [11,12]. Among family-related variables, the parent–child relationship in particular has received research attention, e.g. [13,14], with findings indicating that low levels of positive parent–child communication quality and low levels of parental monitoring are associated with increased adolescent substance use [15,16]. A possible explanation for these findings is that parent–child relationships that are non-supportive or characterized by conflict can undermine adolescents' ability to regulate their behaviour in a goal-orientated way, with low levels of self-regulation associated with greater risk of alcohol use [17]. Adolescents from non-supportive homes may also be more likely to engage with deviant peers to gain social support and a sense of belonging [12]. It has also been suggested that adolescents use substances as a way to cope with family relationships characterized by hostility and low levels of warmth and affection [18].

The role of puberty

Puberty, defined as the developmental period during which the body reaches sexual maturation [19], has also been identified as a risk factor for substance use. Pubertal timing relative to the peer group, and not status *per se*, may particularly convey risk [20,21]. Two categories of off-time pubertal development have been distinguished: early maturers, who show development of breasts/testes at an early age compared to their same-age peers, and late maturers, who show no breasts/testes development when the majority of their same-age peers show these changes. Each of these two groups accounts for approximately 10–15% of adolescents [20].

According to Peskin's early timing hypothesis, early maturers are at increased risk of early substance initiation because they are less well prepared for pubertal change [22]. It has been hypothesized that the higher risk of substance use in early-maturing girls is due to their maturational dys-synchrony, which can result in incongruity in the timing of hormonal, physical, psychological and social processes occurring during puberty [23]. This maturational dys-synchrony can render the early maturer more vulnerable to environmental stressors such as peer pressure. Early-maturing girls show a frequent pattern of socializing with older peers [23]. This might be explained by the maturation disparity hypothesis (see review [24]), which states that girls' changing physical appearance during puberty creates an environment of new social experiences (especially risk-taking behaviours such as delinquency and sexual behaviours) for the girls. Early-maturing girls are at higher risk in the context of these experiences because they have lower levels of emotional and cognitive resources compared to same-aged girls who enter puberty at a later age [25]. This may lead to them engage in behaviours such as experimental substance use that are age-normative for the peer group, but not for them [26]. Marklein and colleagues reported that early-maturing girls had more friends using substances than on-time and late-maturing girls, which is a possible explanation for early-maturing girls' increased substance use [27]. It was reported that early-maturing boys may not be exposed to equivalent risks because their advanced physical development confers higher status in the peer group, due to their high achievements in athletics compared to same-aged peers [28], as well as higher levels of social and emotional functioning [29].

Interplay between family functioning and pubertal timing

A number of studies have identified links between aspects of parenting behaviour, parent–child relationship quality and adolescent substance use [13,15,16]. Similarly, early pubertal timing has been associated with earlier and higher levels of substance use compared to same-age peers [30–32]. According to Ge *et al.*'s contextual amplification theory, social processes (e.g. parenting) interact with pubertal transition to increase the risk of adjustment problems (e.g. externalizing problems, substance use [25]). It has been reported that family functioning and pubertal timing interact to put early-maturing children at increased risk of substance use [25]. Early maturation is argued to curtail the time available to adolescents to acquire and assimilate skills that allow them to adapt successfully to stressful experiences [25]. Consistent with this interpretation, research shows that the parent–child relationship in the families of early-maturing boys and girls is characterized by more conflict and a greater reduction in closeness in the early and middle adolescent years compared to families with later-maturing adolescents [25]. In this context, early pubertal maturation may be seen as a risk factor for premature disengagement from the family, which is intensified by harsh and inconsistent family functioning and decreased by supportive and involved family functioning [25]. This theory provides a framework to understand the interplay between pubertal timing and family functioning in the aetiology of substance use.

A systematic review

In light of the evidence reviewed above, documenting the main effects of family function and pubertal timing, respectively, on adolescent substance use, together with work supporting a contextual amplification of links between pubertal timing and adjustment problems [25], we set out to review systematically the literature on the inter-relations between the psychosocial context of family life, pubertal timing and substance use. This paper fills a gap in the literature, because previous reviews have focused either on the relationship between family functioning and adolescent substance use [6,23,33,34] or on pubertal timing and adolescent substance use [35–38], but not on the possible inter-relationships between all three factors. Thus, it remains unclear to what extent the links between family functioning and adolescent substance use may be explained by pubertal timing and vice versa. Elucidating these issues will have important implications for prevention strategies. Furthermore, with the exception of the reports by Celio *et al*. [35] and Patton & Viner [36], previous reviews have been non-systematic. Our aim was to review systematically the evidence for the following three research questions:

1 Is early pubertal maturation associated with increased substance use for males and females?
2 Is there a stronger relationship between poor family functioning and substance use for early-maturing adolescents compared to late-maturing adolescents?
3 Does family functioning influence pubertal timing and vice versa in the prediction of substance use?

METHOD

A systematic review was designed and reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. The PRISMA statement consists of a 27-item checklist, which gives exact instructions on how to conduct and report the systematic search, and a four-phase flow diagram as a guideline for authors to ensure the highest standards in systematic reviews [39].

Electronic search. Databases World of Knowledge (WoK), PubMed (PM) and PsycINFO (PI) were searched up to April 2012, using the keywords shown in Table 1.

Citation search. Additional papers were identified from citations yielded by the electronic search.

Exclusion criteria. Exclusion criteria were postulated prior to the search. Papers were excluded if titles and/or abstracts indicated that studies focused on animal research, study populations older than 18 years of age, teenage sexuality/pregnancy, clinical populations (e.g. deviant pubertal development due to medical conditions) and/or environmental factors (e.g. deviant pubertal development due to chemical exposure).

Table 1 Specification of search parameters.

Operator	*Definition*
# 1 Keywords[a]	Family OR parent OR sibling[b]
# 2 Keywords[a]	Puberty OR menarche
# 3 Keywords[a]	Substance OR alcohol OR cigarette OR marijuana OR addiction
# 4 Boolean operator	#1 AND #2 AND #3
# 5 Limits language	English language
# 6 Limits kind of studies	Classical article OR comparative study OR evaluation studies OR journal article OR review OR twin study
# 7 Limits subjects of studies	(Male OR female) AND (humans) AND (adolescence[c])
# 8 Boolean operator	#4 AND #5 AND #6 AND #7
# 9 Selection	Removal of duplicates and manual exclusion of articles not meeting inclusion criteria

[a]The search also included additional-related search terms (e.g. parent, parenting, puberty, pubertal, substance, substance use, substance misuse, substance abuse, etc.). [b]Although theories on family functioning and substance use in adolescence are based primarily on parenting behaviour, we included the search terms 'family', 'parent' and 'sibling' to capture as many studies assessing the relationship between family functioning and adolescent substance use as possible. [c]Based on the definition provided by the World Health Organization referring to those aged between 10 and 19 years [40].

Abstract screening. Titles and abstracts were screened by two independent researchers (one of whom was the first author). An overall agreement level of 96% was achieved. In a final meeting, the remaining 4% were discussed and 100% agreement was achieved.

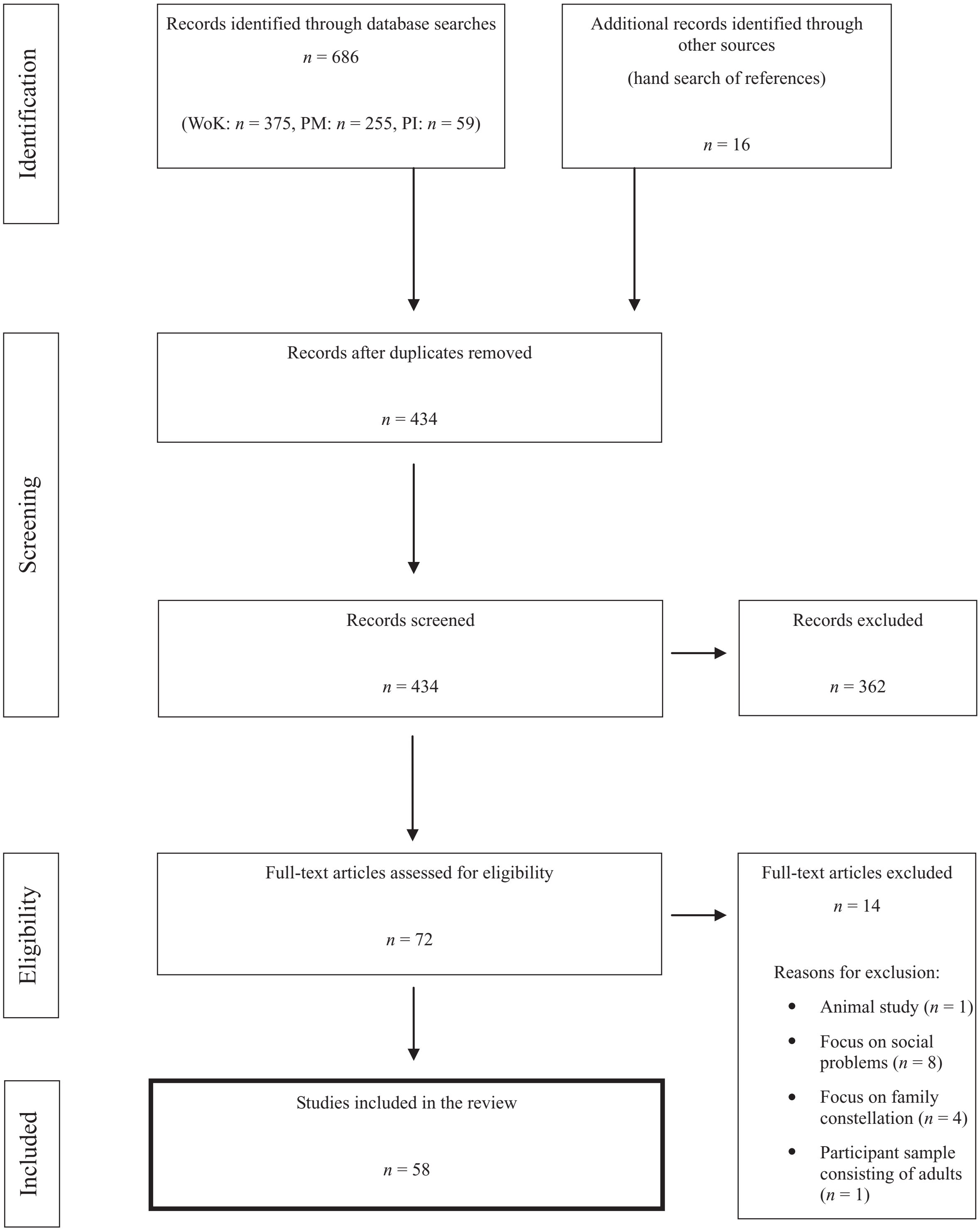
Screening of full papers. Full papers were read in detail by the first author and excluded according to the criteria outlined above (see Fig. 1).

RESULTS

Fifty-eight papers were included in the review (references marked with * in the reference list). These could be organized into four categories, which are discussed below.

Pubertal timing and adolescent substance use

The literature we reviewed showed a relationship between pubertal timing and substance use in adolescence, with early maturers being at higher risk of using



Key: WoK = World of Knowledge; PM = PubMed; PI = PsycINFO

Figure 1 A schematic of the selection of research for inclusion. Key: WoK: World of Knowledge; PM: PubMed; PI: PsycINFO

substances than late maturers [31,32]. Most papers on pubertal timing and substance use in adolescence ($n = 19$) assessed effects separately for males and females, so the findings are summarized accordingly.

Pubertal timing and substance use in adolescent girls

All studies reported that early-maturing girls had higher levels of substance use than on-time maturing girls

[23,32,38,41–46]. A number of studies differentiated between substances such as alcohol, tobacco and marijuana and also between direct and indirect effects. Early maturation in girls has been linked to increased alcohol use and abuse [31,36,47–50]. It was found that 40% of early-maturing girls experienced early alcohol initiation (before age 13) [51], thus increasing the risk of later alcohol use disorder [48]. Early maturation in girls has also been linked to increased risk of cigarette smoking [31,36,47,51,52]. Pedersen and colleagues reported that the association between marijuana use and early maturation in girls appeared indirect via links between pubertal timing and conduct problems [53]. Two studies found that late-maturing girls were not at increased risk of substance use compared to on-time and early-maturing girls [36,54].

Pubertal timing and substance use in adolescent boys

Fewer papers examined pubertal timing in boys ($n = 12$), and even fewer compared associations between early and late-maturing boys. All except one paper [47] indicated that early maturation in boys was related to higher levels of substance use [32,42,43,46,50,55], higher levels of alcohol use and abuse [31,47] and increased risk of cigarette use [31]. Arim and colleagues [47], however, reported no significant difference in alcohol and cigarette use between boys who experienced early maturation compared to those who did not.

More papers have studied late maturation among boys ($n = 5$) than among girls ($n = 2$), but the findings are inconsistent. Reviews by Alsaker [20] and Waylen & Wolke [38] reported higher levels of substance use in late-maturing boys compared to on-time maturing boys. In contrast, longitudinal studies by Berg-Kelly & Kullander [54] and Graber *et al*. [55] found lower levels of substance use in late-maturing boys compared to on-time maturing boys. Graber *et al*. [55], however, reported that late-maturing boys were at greater risk of alcohol abuse in young adulthood, suggesting a catch-up effect. Such findings highlight the value of follow-up studies beyond the adolescent years.

Family functioning and substance use in adolescence

The majority of research investigating the relationship between family functioning and substance use has focused on parenting and parent–adolescent relationships ($n = 7$). Studies with adolescent samples have indicated that poor family functioning predicted initiation of experimental smoking in girls, but not boys [56]; that negative parenting (low levels of mother–child warmth and high levels of mother–child hostility) was associated with increased cigarette use [13]; and that boys and girls who undertook more activities with their mothers were more likely to discontinue regular marijuana use [57]. Kaltiala-Heino *et al*. [15] focused on parental monitoring and substance use in adolescents. Their results showed that alcohol, cigarette and marijuana use among boys and girls was associated with lower levels of parental monitoring. This was also reported by Wang and colleagues, who found lower levels of alcohol and cigarette use among boys and girls experiencing higher levels of parental monitoring [58]. Belsky *et al*. examined the link between early rearing experiences and adolescents' risk-taking in an all-girl sample [59]. They reported that high levels of maternal harshness during childhood were related to higher levels of young people's substance use. Brody *et al*. found that fathers engaging in positive problem-solving and effective arguing were more successful in conveying alcohol-related norms to their adolescents [60]. All seven of these studies used a longitudinal research design, with findings suggesting that family-related factors pre-date, and may therefore contribute to, the initiation and progression of adolescent substance use.

A review by Donovan [6] concluded that high levels of parental support were associated with lower levels of alcohol use, while poor-quality parent–adolescent relationship was a risk factor for substance use [16], substance abuse [34] and early-onset substance initiation [33]. The findings support the conclusion that poor-quality parent–adolescent relationships increase the risk of substance use in adolescence.

Pubertal timing and family functioning

We found three studies examining the relation between quality of parenting during childhood and pubertal timing. Belsky *et al*. reported that negative parenting during childhood was associated with earlier maturation in girls. The authors proposed an evolutionary theory of socialization, stating that girls who are reared in more threatening circumstances (i.e. characterized by greater contextual risk and uncertainty) may mature earlier in order to increase the probability of passing on their genes by having offspring [59]. Interestingly, in an earlier longitudinal study, this effect had not been found for boys [61] and it also seemed to be more pronounced for girls who had experienced harsh maternal compared to harsh paternal parenting [59]. This was the first report indicating that the quality of maternal versus paternal parenting could have a differential outcome in terms of pubertal development. Where previous studies had assessed paternal parenting behaviour based on mothers' reports, Belsky *et al*. [61] obtained father self-reports and observed father–child interactions and the rigour of this approach may have contributed to the ability to discriminate between the rearing styles of fathers and mothers.

Conversely, positive parenting during childhood, as characterized by high levels of parental support, has been associated with a lower probability of early maturation in both boys and girls [62]. Findings indicated that for parental supportiveness, in contrast to harsh parenting, the relationship with the father might be related more strongly to pubertal maturation than maternal supportiveness for both girls and boys. The reasons for these parent figure-related differences in parenting style remain unclear.

A cross-sectional study by Ge and colleagues [25] of African American children identified positive parenting as a protective factor in the relationship between early pubertal maturation and affiliation with deviant peers. They reported that early-maturing adolescents affiliated with deviant peers less when they received supportive–involved parenting and more when they received harsh–inconsistent parenting.

We found only two studies examining the relation between pubertal development and subsequent parent–adolescent relationship quality. Both of these focused on puberty, rather than pubertal timing. One longitudinal study compared parent–child relationships prior to puberty and subsequently after the onset of puberty and reported a decrease in conflict about chores, appearance and politeness between adolescent and parent, but an increase in conflict about finances and substance use [63]. A longitudinal study by Molina & Chassin [64] investigated differences between white and Hispanic adolescents in the relationships they had with their parents prior to and during puberty. The results showed that pubertal girls reported an increase in conflict and a decrease in support from their mothers, irrespective of ethnic background. Additionally, white (but not Hispanic) pubertal girls reported a decrease in support from their fathers. White boys reported a decrease and Hispanic boys an increase in parental support with the onset of puberty.

Collectively, findings suggest that parenting behaviour during childhood is associated with pubertal timing, especially in girls. Puberty itself appears to influence the parent–adolescent relationship, with one study suggesting cultural differences. Positive parenting in adolescence also appears to function as a protective factor for deviant–peer affiliation.

Pubertal timing, family functioning and substance use in adolescence

Six studies examined links between pubertal timing, family functioning and substance use. Two reviews and one longitudinal study reported that early-maturing girls experienced higher levels of family conflict and substance use than on-time maturing girls [29,35,37]. None of these reports presented findings indicating whether there was any relationship between family conflict and adolescent substance use or examined the interplay between all three factors. Shelton & van den Bree [18] found that the across-time association between parent–adolescent relationship quality and cigarette use was stronger for late-maturing girls compared to early- and on-time maturing girls. No effects were observed for early- and late-maturing boys in pathways between parent–child relationship quality and substance use. Lynne-Landsman and colleagues [65] conducted a longitudinal study examining substance use of early maturers in relation to their family risk, measured in household resources (parental education and family income), stability of household structure (family structure over time) and household conflict (level of conflict in the household, quality of parent–adolescent relationship and parental substance use) compared to on-time maturers. Early maturers in the moderate and high-risk family groups were found to have higher levels of binge drinking, cigarette and marijuana use. Belsky *et al*. [59] reported direct effects of harsh maternal parenting during childhood on pubertal timing and on substance use in girls; however, no interaction effects were found between the three factors.

DISCUSSION

We set out to review systematically the published evidence of relationships between family functioning, pubertal timing and substance use in adolescence. Our first research question was to evaluate the evidence that early maturers are at higher risk of substance use than late maturers. The literature suggested that early-maturing girls were at higher risk of substance use compared to on-time and late-maturing girls. The literature was less consistent for boys, with some evidence for increased risk of substance use in early-maturing boys but varying findings for late-maturing boys. Our second research question aimed to evaluate the evidence for a stronger relationship between family functioning and substance use for early than late maturers. The literature suggested that this may be the case for girls, but was inconclusive for boys. The reasons for the inconsistency in the boys' findings remain unclear.

Thirdly, we evaluated the evidence that off-time pubertal maturation predates worsening relations with the parents and subsequent substance use and vice versa. Evidence was found that poor-quality parenting during childhood is associated with early pubertal timing for girls but not for boys, while a single study [61] indicated that this effect may be more pronounced in the context of harsh maternal parenting. Furthermore, puberty itself may also impact upon parent–adolescent relationships, with one study suggesting that these effects may vary between cultures. However, we found no studies examining whether off-time pubertal timing preceded worsening of relationships with the parent. We found two longitudinal studies reporting an interaction between pubertal timing and family functioning with regard to substance use [18,65]; however, these findings are mixed, which calls for further longitudinal studies looking at these inter-relationships with regard to their direction over time.

However, our review indicates that harsh–inconsistent parenting during childhood is linked to early pubertal maturation, which itself is linked to increased substance use in adolescence. Additionally, supportive–involved parenting in adolescence serves as a protective factor with regard to the association with deviant peers. This highlights the importance of supportive–involved parenting during childhood and adolescence, which supports the contextual amplification theory stating that the negative effect of early pubertal maturation on substance use may be reduced by a supportive and involved family environment [25].

Limitations

Some limitations of this systematic review are noteworthy. Through systematic search, a total of 58 papers were included in this review. These included reviews ($n = 17$), cross-sectional studies ($n = 8$), longitudinal studies ($n = 30$) and twin studies ($n = 3$). Furthermore, there was considerable variation in measurement approaches, with 65.8% of pubertal timing measures, 96.8% of substance use measures and 38.5% of family functioning measures collected through self-report. The heterogeneity in research designs makes comparisons difficult.

Future directions

Several factors should be kept in mind for future research. Although we included search terms on family, parent and sibling relationships, our results showed that the only research combining family functioning with pubertal timing and substance use focused on parenting behaviour. Thus, there is a paucity of studies into other familial influences on adolescent behaviour, such as sibling behaviour, interparental conflict, marital dissatisfaction, divorce and family structure.

The majority (65.8%) of the studies measured pubertal timing using self-report, 10.5% used parent-report, 15.8% used physical examination and 7.9% used a combination of self-report and parent-report. This might result in differences in the quality of the studies, as physical examination and self-reports are rated as most reliable [66]. Physical examination, however, is impractical and cost-prohibitive, particularly in large studies; self-report measures should therefore be used preferentially [67]. The onset of puberty tends to differ for the sexes, with girls generally entering puberty before boys. Another complicating factor is that pubertal maturation is not marked by a discrete biological event for boys, as is the case for girls [68]. To allow comparisons between the sexes, researchers have assigned girls and boys separately into early, on-time and late maturers relative to their same-gender peers [20,21].

In light of the dearth of studies looking into the inter-relationships between the three factors, future longitudinal research should focus on the extent to which supportive–involved parenting may act as a direct protective factor for early pubertal maturation as well as a direct and indirect (via pubertal timing) protective factor for increased substance use. To reflect these relationships optimally, obtaining high-quality information on relevant potential confounders is important. Research has linked the following factors to increased substance use in adolescence: conduct problems [53], personality traits [14], socio-economic status (SES) [69–72], parental substance use/abuse [73–77] and finally the peer group. The latter represents an important factor which may be particularly salient for adolescents from poor-functioning families [78,79] while, furthermore, Ge and colleagues [25] have reported the link between early pubertal maturation and affiliation with deviant peers which can be attenuated by positive parenting [14].

In conclusion, to obtain a correct picture of the relationship between family functioning and adolescent substance use/misuse it is important to understand the role of pubertal timing. If adolescents who experience both poor-quality relationships with their parents and off-time pubertal development are at particularly increased risk of development of substance use disorders, as suggested by the studies we identified, this group needs to be a focus of prevention/intervention approaches. However, because of the paucity in this area, these conclusions need to be interpreted with caution. More longitudinal studies are needed, which should examine the mutual developmental relationships of family relationship quality and pubertal timing with regard to substance use development over time. In addition, relevant confounders should also be included to elucidate these complex relationships further.

Declarations of interest

None.

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References

**Papers included in the review*

1. National Center for Health Statistics. *Health, United States, 2010: With Special Feature on Death and Dying*. Hyattsville, MD: National Center for Health Statistics; 2011.
2. British Medical Association (BMA) Board of Science and Education. *Adolescent Health*. London: BMA Publishing Unit; 2003.
3. Lewis D. C., Cates-Wessel K. L., Mooney M., Sporcic L., Spalding K., Feraco A. *Adolescent Substance Abuse: A Public Health Priority*. Providence: Center for Alcohol and Addiction Studies; 2002.
4. Spear L. P. Alcohol's effect on adolescents. *Alcohol Res Health* 2002; **26**: 287–91.
5. Volkow N. Drugs, brains and behaviour: the science of addiction. NIDA National Institute of Drug Abuse. National Institutes of Health US Department of Health and Human Services; 2010.
6. *Donovan J. E. Adolescent alcohol initiation: a review of psychosocial risk factors. *J Adolesc Health* 2004; **35**: 529.e7–529.e18.
7. Wright V. Smoking, drinking and drug use among young people in England in 2010. London: The Health and Social Care Information Centre, National Centre for Social Research; 2011.
8. Hibell B., Guttormsson U., Ahlstroem S., Balakireva O., Bjarnason T., Kokkevi A. *et al*. The 2007 ESPAD Report. Substance Use Among Students in 35 European Countries; 2007. Stockholm: The Swedish Council for Information on Alcohol and Other Drugs (CAN).
9. Jain R., Balhara Y. P. S. Impact of alcohol and substance abuse on adolescent brain: a preclinical perspective. *Indian J Physiol Pharmacol* 2010; **54**: 213–34.
10. Bava S., Tapert S. F. Adolescent brain development and the risk for alcohol and other drug problems. *Neuropsychol Rev* 2010; **20**: 398–413.
11. Slomkowski C., Conger K. J., Rende R., Heylen E., Little W. M., Shebloski B. *et al*. Sibling contagion for drinking in adolescence: a micro process framework. *Eur J Dev Sci* 2009; **3**: 161–73.
12. Weichold K., Silbereisen R. K. Cross-cultural research on the development of adolescent substance misuse. *Sucht* 2006; **52**: 229–31.
13. *Shelton K. H., Harold G. T., Fowler T. A., Rice F. J., Neale M. C., Thapar A. *et al*. Parent–child relations, conduct problems and cigarette use in adolescence: examining the role of genetic and environmental factors on patterns of behavior. *J Youth Adolesc* 2008; **37**: 1216–28.
14. *van den Bree M. B. Combining research approaches to advance our understanding of drug addiction. *Curr Psychiatry Rep* 2005; **7**: 125–32.
15. *Kaltiala-Heino R., Koivisto A., Marttunen M., Fröjd S. Pubertal timing and substance use in middle adolescence: a 2-year follow-up study. *J Youth Adolesc* 2011; **40**: 1288–301.
16. *Dishion T. J., Nelson S. E., Bullock B. M. Premature adolescent autonomy: parent disengagement and deviant peer process in the amplification of problem behaviour. *J Adolesc* 2004; **27**: 515–30.
17. Brody G. H., Ge X. Linking parenting processes and self-regulation to psychological functioning and alcohol use during early adolescence. *J Fam Psychol* 2001; **15**: 82–94.
18. *Shelton K. H., van den Bree M. B. M. The moderating effects of pubertal timing on the longitudinal associations between parent–child relationship quality and adolescent substance use. *J Res Adolesc* 2010; **20**: 1044–1064.
19. National Health Service (NHS). *Puberty*. 2010. Available at: http://www.nhs.uk/Conditions/Puberty/Pages/Introduction.aspx (accessed 25 April 2011). Archieved at http://www.webcitation.org/67POHmgM9 on 4 May 2012.
20. *Alsaker F. D. Annotation: the impact of puberty. *J Child Psychol Psychiatry* 1996; **37**: 249–58.
21. *Buck Louis G. M., Gray L. E., Marcus M., Ojeda S. R., Pescovitz O. H., Witchel S. F. *et al*. Environmental factors and puberty timing: expert panel research needs. *Pediatrics* 2008; **121**: s192–207.
22. Peskin H. Influence of the developmental schedule of puberty on learning and ego functioning. *J Youth Adolesc* 1973; **2**: 273–90.
23. *Dawes M. A., Antelman S. M., Vanyokov M. M., Giancola P., Tarter R. E., Susman E. J. *et al*. Developmental sources of variation in liability to adolescent substance use disorders. *Drug Alcohol Depend* 2000; **61**: 3–14.
24. Ge X., Natsuaki M. N. In search of explanations of early pubertal timing effects on developmental psychopathology. *Curr Dir Psychol Sci* 2009; **18**: 327–31.
25. *Ge X. J., Brody G. H., Conger R. D., Simons R. L., Murry V. M. Contextual amplification of pubertal transition effects on deviant peer affiliation and externalizing behavior among African American children. *Dev Psychol* 2002; **38**: 42–54.
26. Stattin H., Magnusson D. *Pubertal Maturation in Female Development*. Hillsdale, NJ: Erlbaum; 1990.
27. Marklein E., Negriff S., Dorn L. Pubertal timing, friend smoking, and substance use in adolescent girls. *Prev Sci* 2009; **10**: 141–50.
28. Kindlundh A., Hagekull B., Isacson D., Nyberg F. Adolescent use of anabolic–androgenic steroids and relations to self-reports of social, personality and health aspects. *Eur J Public Health* 2001; **11**: 322–8.
29. *Westling E., Andrews J. A., Hampson S. E., Peterson M. Pubertal timing and substance use: the effects of gender, parental monitoring and deviant peers. *J Adolesc Health* 2008; **42**: 555–63.
30. Biel M., Natsuaki M., Ge X. The influence of pubertal timing on alcohol use and heavy drinking trajectories. *J Youth Adolesc* 2007; **36**: 153–67.
31. *Bratberg G. H., Nilsen T. I. L., Holmen T. L., Vatten L. J. Perceived pubertal timing, pubertal status and the prevalence of alcohol drinking and cigarette smoking in early and late adolescence: a population based study of 8950 Norwegian boys and girls. *Acta Paediatr* 2007; **96**: 292–5.
32. *Downing J., Bellis M. A. Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. *BMC Public Health* 2009; **9**: 446.
33. *Enoch M. A. The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology (Berl)* 2011; **214**: 17–31.

34. *Henricson C., Roker D. Support for the parents of adolescents: a review. *J Adolesc* 2000; **23**: 763–83.
35. *Celio M., Karnik N. S., Steiner H. Early maturation as a risk factor for aggression and delinquency in adolescent girls: a review. *Int J Clin Pract* 2006; **60**: 1254–62.
36. *Patton G. C., Viner R. Adolescent health 1—pubertal transitions in health. *Lancet* 2007; **369**: 1130–9.
37. *Short M. B., Rosenthal S. L. Psychosocial development and puberty. *Annals of the New York Academy of Sciences* 2008; **1135**: 36–42.
38. *Waylen A., Wolke D. Sex ‘n’ drugs ‘n’ rock ‘n’ roll: the meaning and social consequences of pubertal timing. *Eur J Endocrinol* 2004; **151**: U151–9.
39. Moher H., Liberati A., Tetzlaff J., Altman D. G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.
40. World Health Organization (WHO) 10 facts on adolescent health. 2008. Retrieved on 25.4.11 from www.who.int/features/factfiles/adolescent_health/en/index.html. Archieved at http://www.webcitation.org/6CMypJsYq on 22 November 2012
41. *Copeland W., Shanahan L., Miller S., Costello E. J., Angold A., Maughan B. Outcomes of early pubertal timing in young women: a prospective population-based study. *Am J Psychiatry* 2010; **167**: 1218–25.
42. *Alsaker F. D. Is puberty a critical period for socialization? *J Adolesc* 1995; **18**: 427–44.
43. *Dick D. M., Rose R. J., Pulkkinen L., Kaprio J. Measuring puberty and understanding its impact: a longitudinal study of adolescent twins. *J Youth Adolesc* 2001; **30**: 385–99.
44. *Ge X., Jin R., Natsuaki M. N., Gibbons F. X., Brody G. H., Cutrona C. E. *et al*. Pubertal maturation and early substance use risks among African American children. *Psychol Addict Behav* 2006; **20**: 404–14.
45. *Lanza S. T., Collins L. M. Pubertal timing and the onset of substance use in females during early adolescence. *Prev Sci* 2002; **3**: 69–82.
46. *Michaud P. A., Suris J. C., Deppen A. Gender-related psychological and behavioural correlates of pubertal timing in a national sample of Swiss adolescents. *Mol Cell Endocrinol* 2006; **254-255**: 172–8.
47. *Arim R., Tramonte L., Shapka J., Dahinten V., Willms J. The family antecedents and the subsequent outcomes of early puberty. *J Youth Adolesc* 2011; **40**: 1423–35.
48. *Costello E. J., Sung M., Worthman C., Angold A. Pubertal maturation and the development of alcohol use and abuse. *Drug Alcohol Depend* 2007; **88**: S50–9.
49. *Gaudineau A., Ehlinger V., Vayssiere C., Jouret B., Arnaud C., Godeau E. Factors associated with early menarche: results from the French Health Behaviour in School-aged Children (HBSC) study. *BMC Public Health* 2010; **10**: 175.
50. *Martin C. A., Kelly T. H., Rayens M. K., Brogli B. R., Brenzel A., Smith W. J. *et al*. Sensation seeking, puberty, and nicotine, alcohol, and marijuana use in adolescence. *J Am Acad Child Adolesc Psychiatry* 2002; **41**: 1495–502.
51. *Dick D. M., Rose R. J., Viken R. J., Kaprio J. Pubertal timing and substance use: associations between and within families across late adolescence. *Dev Psychol* 2000; **36**: 180–9.
52. *Jean R., Wilkinson A., Spitz M., Prokhorov A., Bondy M., Forman M. Psychosocial risk and correlates of early menarche in Mexican-American girls. *Am J Epidemiol* 2011; **173**: 1203–10.
53. *Pedersen W., Mastekaasa A., Wichstrom L. Conduct problems and early cannabis initiation: a longitudinal study of gender differences. *Addiction* 2001; **96**: 415–31.
54. *Berg-Kelly K., Kullander K. Gender differences in early adolescence in factors related to outcome of healthy behaviours two years later. *Acta Paediatr* 1999; **88**: 1125–30.
55. *Graber J. A., Seeley J. R., Brooks-Gunn J., Lewinsohn P. M. Is pubertal timing associated with psychopathology in young adulthood? *J Am Acad Child Adolesc Psychiatry* 2004; **43**: 718–26.
56. *van den Bree M. B., Whitmer M. D., Pickworth W. B. Predictors of smoking development in a population-based sample of adolescents: a prospective study. *J Adolesc Health* 2004; **35**: 172–81.
57. *van den Bree M. B., Pickworth W. B. Risk factors predicting changes in marijuana involvement in teenagers. *Arch Gen Psychiatry* 2005; **62**: 311–9.
58. *Wang M., Dishion T., Stormshak E., Willett J. Trajectories of family management practices and early adolescent behavioral outcomes. *Dev Psychol* 2011; **47**: 1324–41.
59. *Belsky J., Steinberg L., Houts R. M., Halpern-Felsher B. L., National Institute of Child Health and Human Development (NICHD). The development of reproductive strategy in females: early maternal harshness –> earlier menarche –> increased sexual risk taking. *Dev Psychol* 2010; **46**: 120–8.
60. *Brody G. H., Ge X., Katz J., Arias I. A longitudinal analysis of internalization of parental alcohol-use norms and adolescent alcohol use. *Appl Dev Sci* 2000; **4**: 71–9.
61. *Belsky J., Steinberg L. D., Houts R. M., Friedman S. L., Dehart G., Cauffman E. *et al*. Family rearing antecedents of pubertal timing. *Child Dev* 2007; **78**: 1302–21.
62. *Ellis B. J., Essex M. J. Family environments, adrenarche, and sexual maturation: a longitudinal test of a life history model. *Child Dev* 2007; **78**: 1799–817.
63. *Galambos N. L., Almeida D. M. Does parent–adolescent conflict increase in early adolescence. *J Marriage Fam* 1992; **54**: 737–47.
64. *Molina B. S. G., Chassin L. The parent–adolescent relationship at puberty: hispanic ethnicity and parent alcoholism as moderators. *Dev Psychol* 1996; **32**: 675–86.
65. *Lynne-Landsman S. D., Graber J. A., Andrews J. A. Do trajectories of household risk in childhood moderate pubertal timing effects on substance initiation in middle school? *Dev Psychol* 2010; **46**: 853–68.
66. *Dorn L. D., Susman E. J., Ponirakis A. Pubertal timing and adolescent adjustment and behavior: conclusions vary by rater. *J Youth Adolesc* 2003; **32**: 157–67.
67. *Turner C. F., Ku L., Rogers S. M., Lindberg L. D., Pleck J. H., Sonenstein F. L. Adolescent sexual behavior, drug use, and violence: increased reporting with computer survey technology. *Science* 1998; **280**: 867–73.
68. *Ge X., Natsuaki M. N., Neiderhiser J. M., Reiss D. Genetic and environmental influences on pubertal timing: results from two national sibling studies. *J Res Adolesc* 2007; **17**: 767–88.
69. *Hanson M., Chen E. Socioeconomic status and substance use behaviors in adolescents. *J Health Psychol* 2007; **12**: 32–5.
70. *Saraceno L., Munafo M., Heron J., Craddock N., van den Bree M. B. Genetic and non-genetic influences on the development of co-occurring alcohol problem use and internalizing symptomatology in adolescence: a review. *Addiction* 2009; **104**: 1100–21.

71. *Tiffin P. A., Pearce M., Kaplan C., Fundudis T., Parker L. The impact of socio-economic status and mobility on perceived family functioning. *J Fam Econ Issues* 2007; **28**: 653–67.
72. *Obeidallah D. A., Brennan R. T., Brooks-Gunn J., Kindlon D., Earls F. Socioeconomic status, race, and girls' pubertal maturation: results from the project on human development in Chicago neighborhoods. *J Res Adolesc* 2000; **10**: 443–64.
73. *Becklake M. R., Ghezzo H., Ernst P. Childhood predictors of smoking in adolescence: a follow-up study of Montreal schoolchildren. *Can Med Assoc J* 2005; **173**: 377–9.
74. *Meyers J. L., Dick D. M. Genetic and environmental risk factors for adolescent-onset substance use disorders. *Child Adolesc Psychiatr Clin N Am* 2010; **19**: 465–77.
75. *Windle M., Spear L. P., Fuligni A. J., Angold A., Brown J. D., Pine D. *et al*. Transitions into underage and problem drinking: developmental processes and mechanisms between 10 and 15 years of age. *Pediatrics* 2008; **121**: S273–89.
76. *Moss H. B., Lynch K. G., Hardie T. L., Baron D. A. Family functioning and peer affiliation in children of fathers with antisocial personality disorder and substance dependence: associations with problem behaviors. *Am J Psychiatry* 2002; **159**: 607–14.
77. *Wolock I., Magura S. Parental substance abuse as a predictor of child maltreatment rr-reports. *Child Abuse Negl* 1996; **20**: 1183–93.
78. *Ary D. V., Duncan T. E., Duncan S. C., Hops H. Adolescent problem behavior: the influence of parents and peers. *Behav Res Ther* 1999; **37**: 217–30.
79. *Urberg K. A., Luo Q. A two-stage model of peer influence in adolescent substance use: individual and relationship-specific differences in susceptibility to influence. *Addict Behav* 2003; **28**: 1243–56.

Pubertal timing and substance use in adolescent girls: Relations with family and peer influences

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Abstract:	Pubertal timing and relationships with parents and peers have been linked to substance use in adolescent girls. Few studies have tested the relationships between these factors in the prediction of substance use. Evaluate 1) main effects and two models examining whether the links 2) between pubertal timing and girl's substance use are indirect via psycho-social factors (mediation); 3) between psycho-social factors and substance use differ across pubertal timing groups (moderation). Data for 2,858 girls from the Avon Longitudinal Study of Parents and Children (ALSPAC) was analyzed. Pubertal timing was assessed yearly between ages 8 and 17, parent-daughter relations and peer deviance at age 15, and alcohol, cigarette and cannabis use at age 16. Late maturing girls had lower levels of cannabis use compared to on-time maturing girls. Late maturing girls had fewer alcohol using, cannabis using and delinquent friends than early maturing girls and fewer cannabis using friends than on-time maturing girls. Late maturing girls' lower levels of substance use were partly explained by having fewer cannabis using and delinquent friends. In late adolescence, the combined effects of peer deviance and pubertal timing are more influential than the combined effects of parenting and pubertal timing, in predicting adolescent substance use. Abstract_1.8.13.doc

Family, peers, pubertal timing and substance use

Background: Pubertal timing and relationships with parents and peers have been linked to substance use in adolescent girls. Few studies have tested the relationships between these factors in the prediction of substance use.

Aim: Evaluate 1) main effects and two models examining whether the links 2) between pubertal timing and girl's substance use are indirect via psycho-social factors (mediation); 3) between psycho-social factors and substance use differ across pubertal timing groups (moderation).

Methods: Data for 2,858 girls from the Avon Longitudinal Study of Parents and Children (ALSPAC) was analyzed. Pubertal timing was assessed yearly between ages 8 and 17, parent-daughter relations and peer deviance at age 15, and alcohol, cigarette and cannabis use at age 16.

Results: Late maturing girls had lower levels of cannabis use compared to on-time maturing girls. Late maturing girls had fewer alcohol using, cannabis using and delinquent friends than early maturing girls and fewer cannabis using friends than on-time maturing girls. Late maturing girls' lower levels of substance use were partly explained by having fewer cannabis using and delinquent friends.

Conclusion: In late adolescence, the combined effects of peer deviance and pubertal timing are more influential than the combined effects of parenting and pubertal timing, in predicting adolescent substance use.

Keywords: parenting, peers, pubertal timing, substance use, ALSPAC.

Pubertal timing and substance use in adolescent girls: Relations with family and peer influences

Experimentation with substances usually takes place during adolescence (British Medical Association (BMA), 2003; National Center for Health Statistics, 2011). Adolescents have a greater tolerance for substances than adults and this may increase risk of heavy use (Jain & Balhara, 2010). Early-onset alcohol initiation (before 13 years) has been associated with increased risk of development of alcohol abuse and dependence (Spear, 2002); cigarette and drug use (Donovan, 2004). Moreover, adolescent-onset substance abuse is characterized by more rapid development of multiple drug dependencies and more severe psychopathology (Spear, 2002; Volkow, 2010). Heavy substance use is associated with a variety of adverse psycho-social consequences, including delinquency, hazardous driving, risky sexual behavior, psychiatric problems and school drop-out (Bava & Tapert, 2010). Substance use rates and patterns can differ for males and females (Heron et al., 2011; Hibell et al., 2007; MacArthur et al., 2012), findings which have led researchers to call for gender-specific substance research to inform policy and practice (Amos et al., 2012). Additionally, it is important to focus on different substances, i.e. alcohol, cigarettes and cannabis, separately because their use in adolescence has been linked to different behavioral outcomes in adolescence and adulthood (Newcomb & Bentler, 1988). The etiology of alcohol, cigarette and cannabis use is also unlikely to be equivalent (Kring et al., 2007).

Biological and psycho-social processes play a role in the development of substance use/ misuse in adolescence (van den Bree et al., 2004), as adolescents are highly vulnerable to social influences (Volkow, 2010) and have a greater reward sensitivity and proclivity to risk taking than older people (which may be related to changes in the developing brain; Bava & Tapert, 2010). Adolescents who experience multiple risk factors have an increased chance of engaging in substance misuse (van den Bree & Pickworth, 2005), and the importance of understanding the interplay of such factors with regards to substance use in adolescence has been highlighted (Glaser et al., 2010; Rhodes et al., 2003).

Adolescent substance use and pubertal timing

One biological factor that has been related to substance use in young people is pubertal development. Puberty, which marks the beginning of adolescence, is defined by physical changes as well as changes in cognitive ability and social interactions (US Department of Health and Human Services, 2012). Puberty is marked more clearly by a discrete biological event for girls (onset of menarche) and girls also tend to enter puberty earlier compared to boys (Ge et al., 2007). This highlights the importance of focusing on girls and boys separately. Pubertal timing relative to the peer group rather than status *per se*, has been associated with risk of substance misuse (Alsaker, 1996, Buck et al., 2008), with the majority of findings for girls indicating an association between early pubertal timing and increased substance use (Hummel et al., 2013).

Adolescent substance use and psycho-social factors

Considerable research attention has been directed towards links between family functioning and peer behavior as risk factors for adolescent substance use (van den Bree et al., 2004). The rationale for looking at family functioning with regards to pubertal timing and adolescent substance use was highlighted by Ge *et al*.'s *contextual amplification theory*, stating that social processes (e.g., parenting) interact with pubertal transition to increase the risk of adjustment problems (e.g. externalizing problems, substance use; Ge et al., 2002). There is substantial evidence indicating associations between adolescent alcohol, cigarette and drug use and poor family functioning (see reviews by Celio et al., 2006; Donovan, 2004; Enoch, 2011; Hummel et al., 2013), including aspects of parenting behavior specifically (e.g., Dishion et al., 2004; Ge et al., 1996; Kaltiala-Heino et al., 2011; Shelton et al., 2008). The associations between family factors and substance use have been reported to be different between the sexes (Saraceno et al., 2012; van den Bree et al., 2004) and there is evidence for sex differences in parent-child relationships following the onset of puberty (Celio et al., 2006; Dawes et al., 2000). Amongst parent-daughter relationship quality indicators, three domains have been reported to show the strongest associations with risk of substance (mis) use in adolescence: level of parent-daughter communication, level of parent-daughter conflict and parent monitoring (McVie & Holmes, 2005).

The rationale for looking at peer behavior and adolescent substance use was highlighted by the *social learning theory*, stating that individuals learn to take substances in small groups (Bahr et al., 2005). During adolescence, attention is given to peer groups, especially to peers' substance use, due to the importance adolescents place on peers while they gain autonomy from their parents (Bahr et al., 2005).There is substantial evidence indicating associations between adolescent alcohol, cigarette and drug use and affiliation with deviant peer groups (involved in substance misuse and delinquency; e.g. Ali et al., 2011; Branstetter et al., 2011; Cruz et al., 2012; Glaser et al., 2010; Skinner et al., 2009).

Modeling the relationship between pubertal timing, psycho-social factors and substance use over time

The psychosocial development of young people (including their substance use/ misuse) is best understood as the result of the combined effects of individual factors over time (Rutter, 1999, Rutter & Casear, 1991) and would therefore be imperfectly captured by cross-sectional models focusing on main effects only (Cicchetti, 1984; Rutter, 2005; Rutter, 1999). Mediation and moderation models represent informative ways of specifying the unfolding relationships between risk factors and psychosocial traits. Mediation analyses permit tests of whether the direct effect of early pubertal timing on increased adolescent substance use is explained indirectly by relationships with parents and peers; therefore establishing whether prevention programs should address the indirect effect rather than the direct effect. Moderation analyses allow examination of whether the effect of parent and peer relationships on adolescent substance use is different for early, on-time and late maturing girls; therefore identifying the risk group for targeting by a prevention program. Consequently, the findings of such models can contribute to increased understanding and ultimately lead to more efficacious prevention approaches.

Although early pubertal maturation, poor parent-adolescent relationship quality and affiliation with deviant peers have each been identified as individual risk factors for increased substance use in adolescence, to our knowledge only a handful of studies have examined the links between these factors. Negriff and Trickett (2012) reported that the effect of pubertal timing on alcohol and cannabis use at age 13 was mediated by peers' alcohol and cannabis use at age 12. Biehl and colleagues (2007) reported that early maturing girls with more alcohol drinking friends used more alcohol at age range 12-16 than early maturing girls with fewer alcohol drinking friends. Marklein and colleagues (2009), however, found no evidence that peers' cigarette use moderated the relationship between pubertal timing and girls' alcohol, cigarette and cannabis use at age range 11-17 years. This lack of evidence might be due to their small sample size (N=264 girls). Lynne-Landsman and colleagues (2010) looked at moderation and found that early maturing girls in average and high risk families (based on household resources, conflict and stability of household structure) had higher levels of binge drinking, cigarette and cannabis use at age 14 than on-time and late maturing girls. Shelton and van den Bree (2010) finally, reported that pubertal timing moderated the effect of parent-adolescent relationship quality (warmth and closeness) on cigarette use at age range 12-15 years where the effect was stronger for late maturing girls than for early and on-time maturing girls.

Taken together, studies have focused either on the effect of adolescent substance use, pubertal timing and the family environment or on the effect of adolescent substance use, pubertal timing and the peer environment. This complicates interpretation of the relative importance of the family and peer environment, as findings have mostly been based on different samples. Additionally, only one study has examined whether peers mediate the relation between pubertal timing and substance use (Negriff & Trickett, 2012) and no research appears to have tested the mediating role of the family environment. Two studies have focused on the moderating role of peer relations (Biehl et al., 2007; Marklein et al., 2009), which reported inconsistent findings. Finally, of the two studies that have examined the moderating role of pubertal timing on family relationships one focused on alcohol and cannabis and the other on cigarettes (Lynne-Landsman et al., 2010; Shelton & van den Bree, 2010). We aimed to advance the existing literature by conducting a study using a sample larger than all (Lynne-Landsman et al., 2010; Marklein et al., 2009; Negriff et al., 2012; Shelton & van den Bree, 2010), but one (Biehl et al., 2007), previous studies to conduct mediation and moderation analyses of the effects of pubertal timing and the parent-adolescent relationship as well as pubertal timing and the peer environment with regards to adolescent substance use. We adjusted for *a priori* selected confounders (including earlier measures of substance use, parent-child relationship quality and peer behavior, parental substance use and socioeconomic factors), thus limiting the possibility that these earlier influences explained the effects tested.

The present study

This study set out to test specific hypotheses about the relationships between pubertal timing, psycho-social factors and substance use in adolescence by conducting mediation as well as moderation analyses in a large longitudinal birth cohort (Avon Longitudinal Study of Parents and Children).

The specific aims were to examine whether:

1. There is evidence for differences in alcohol, cigarette and cannabis use for girls who experienced early, on-time or late pubertal timing. We hypothesized that early maturing girls would show higher levels of alcohol, cigarette and cannabis use compared to on-time and late maturing girls.

2. Parent-daughter relationship quality and peer behavior mediate the link between pubertal timing and substance use. We hypothesized that the effect of early pubertal timing on increased substance use would be explained indirectly by poor parent-daughter relationship quality and affiliation with deviant peers.

3. Pubertal timing moderates the effect of parent-daughter relationship quality and peer behavior on substance use in late adolescence. We hypothesized that the effect of poor parent-daughter relationship quality and affiliation with deviant peers on increased substance use would be stronger for early compared to on-time and late maturing girls.

Method

Sample

The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing longitudinal cohort study. All pregnant women resident in Avon, UK, with expected dates of delivery between 1st April 1991 and 31st of December 1992 were eligible for participation. 14,541 pregnant women were enrolled in the study of which 14,062 had live births. 13,988 children were alive at one year of age (6,747 females) (ALSPAC, 2011). The sample is representative of the British population as indicated by comparisons with the 1991 census (Boyd et al., 2012). Since 1991/92 the children's health and development has been followed by collecting genetic and environmental information through questionnaires, focus clinics and lab-based assessments on a yearly basis (ALSPAC, 2011). The sample for this study consisted of young girls who were assessed at age 15 (mean age = 15.5, *SD*= 0.3) and 16 (mean age = 16.7, *SD* = 0.2). Questionnaires were sent to 9,994 adolescents with 5,131 questionnaires being completed and returned (3,032 questionnaires were answered by girls). Information was given by the girls on their alcohol use (n=2,599), cigarette use (n=2,851) and cannabis use (n=2,858) at age 16.

Measures

Pubertal timing: Age at menarche. Postal questionnaires were sent to the mothers for completion (age 8-13 years) and information of pubertal timing was derived from the questions: "Has your daughter started menarche? [Yes/No]", if yes: "How old was your daughter when she had her first period?" From age 14 to age 17 questionnaires were sent to the study children for completion. As advocated by Joinson et al. (2011) the first reported age at onset of menarche of each girl was used to avoid recall bias. This information was used to create the variable "age at menarche", which was categorized into three levels: 'early pubertal timing' (before age 12; 23.1% of the sample, 95% CI: 22%, 24%); 'on-time pubertal timing' (between 12 and 13 years; 62.6% of the sample, 95% CI: 61%, 64%) and 'late pubertal timing' (after age 13; 14.3% of the sample, 95% CI: 13%, 15%). A similar categorization has been used in previous studies (Joinson et al., 2011; Stice et al., 2001; Tam et al., 2006). The variable was coded as 1=on-time, 2=early and 3=late for all analyses except mediation analysis where the variable was coded 1=early, 2=on-time and 3=late.

Adolescent substance use. Alcohol, cigarette and cannabis use was assessed through a self-report questionnaire, which was sent in the post when the girls were 16 years old.

Alcohol use. Alcohol involvement was assessed with ten items from the Alcohol Use Disorders Identification Test (AUDIT) questionnaire (Babor et al., 2001). The internal consistency of these ten items was acceptable ($\alpha = 0.78$). These items were scored and added according to the AUDIT scoring system into a single categorical variable with three levels (1 = harmless, 2 = hazardous, 3 = harmful; Babor et al., 2001).

Cigarette and cannabis use. Cigarette and cannabis involvement were each assessed with two self-report items from the Survey of Drug Use, Smoking and Drinking among Schoolchildren in England questionnaire (Wright, 2011): "Young person has ever smoked a cigarette/roll-up"/"Frequency young person smokes cigarettes" and "Young person has ever tried cannabis"/"Frequency young person smokes cannabis". These items were combined into two separate categorical variables with four levels in the cigarette variable (1 = non-smoker, 2 = only ever once or twice, 3 = occasional smoker, 4 = regular smoker) and three levels in the cannabis variable (1 = non-user, 2 = only ever once or twice, 3 = user).

Parent-adolescent relationship quality. These measures were all assessed with the Edinburgh Study of Youth Transitions and Crime questionnaire (ESYTC, 2011; see McVie & Holmes, 2005; Smith, 2004), which was completed by the girls during a walk-in focus clinic at the age of 15 years.

Parent-daughter communication. It was assessed with two items: "Frequency young person tells parents about things that happen at school" and "Frequency young person tells parents about what they do when they are out" with the answers being categorized into three categories (hardly ever/never, sometimes, often). The internal consistency of these items was acceptable (α = 0.75). The items were summed to create a single categorical variable with three levels, where the lowest category 1 ('often communicates') was used as the reference category in the analysis.

Parent-daughter conflict. This was assessed with six items: "Frequency young person argues with parents about tidiness of room", "Frequency young person argues with parents about what they do when they go out", "Frequency young person argues with parents about what time they come home", "Frequency young person argues with parents about who they hang out with", "Frequency young person argues with parents about clothes/appearance" and "Frequency young person argues with parents about other things" with the answers being categorized into four categories (hardly ever/never, < once a week, at least once a week, most days). The internal consistency of these items was good (α = 0.82). The items were summed to create a single categorical variable with four levels, where the lowest category 1 ('hardly ever/never' has conflict) was used as the reference category in the analysis.

Parent-daughter monitoring. This was assessed with four items: "Frequency parents knew where young person was going, when they went out", "Frequency parents knew who young person was going out with, when they went out", "Frequency parents knew what young person was doing, when they went out" and "Frequency parents knew what time young person would be home, when they went out", with the answers being categorized into 4 categories (never, sometimes, usually, always). The internal consistency of these items was good (α = 0.82). The items were summed to create a single categorical variable with three levels, where the lowest category1 ('always' monitored) was used as the reference category in the analysis.

Peer deviance. Information on peer deviance (substance use and delinquency) was obtained with the Edinburgh Study of Youth Transitions and Crime questionnaire (ESYTC, 2011) assessed through girl-report during a walk-in focus clinic at the age of 15 years.

Peer substance use. Peer substance use was queried with the following questions: "Number of friends that drank alcohol during the last year", "Number of friends that smoked cigarettes during the last year" and "Number of friends that took illegal drugs during the last year". These items were categorized into three categories (none, one or some, most) and the lowest category 1 (no friends using this substance) was used as the reference category in the analysis.

Peers' delinquency. This was assessed with seventeen binary items (e.g., "Some friends damaged someone's property on purpose during last year"). The internal consistency of these items was good (α = 0.87). The items were summed to create a single binary variable, which was coded: no=0 and yes=1; whereas the yes=1 categorization was used as soon as the participant had answered any of the seventeen original items with "yes".

Confounders. We adjusted the analyses for several *a priori* selected confounders, which have been previously reported to be relevant to the relationships of interest. These included girls' substance use in early adolescence (Lansford et al., 2010), parental substance use (Bahr et al., 2005), socioeconomic factors (i.e., level of parental education and financial difficulties; Sutherland, 2012), pre-adolescent parent-child relationship quality and pre-adolescent peer behavior (Oxford et al., 2001). Additionally, family as well as peer factors have been identified as predictors of substance use in adolescence (Barnes et al., 2006); we therefore adjusted for peer factors and earlier family factors while looking at family factors as the predictor/mediator and vice versa.

Earlier substance use. Girls' earlier substance was based on the question: "How old were you when you first had a whole drink?", "How old were you when you first smoked a cigarette?" and "How old were you when you first tried cannabis?" The information on earlier alcohol use was assessed via self-report questionnaires in a walk-in focus clinic at age 14, whereas information on earlier cigarette and cannabis use was assessed via postal questionnaires at age 14. The earlier substance use scores were dichotomized and coded as 0 = did not use substance by age 13 and 1 = used substance by age 13.

Socioeconomic factors. Information on the parents' level of education was assessed through parent self-report via postal questionnaire during pregnancy. Information on financial difficulties was assessed through mother-report via postal questionnaire when the child was 11 years old.

Parental substance use. Information on mother's substance use was assessed using father reports about the mother and father's substance use was assessed using mother reports about the father through postal questionnaire when the child was 9 years old.

Earlier parent-child interaction. Mother-child interaction and father-child interaction was created by combining 18 mother-report items of a postal questionnaire regarding time spent with the child e.g. "How often does her mother or other adult female sing to her"; "How often does her father or other adult male take her to the park or playground". The internal consistency of the mother-child interaction items and the father-child interaction items was good (α= .80 & 0.87, respectively). The items were combined to create two distinct continuous variables with a high score reflecting more positive parent-child interaction at age 9 years.

Earlier peer behavior. Earlier peers' alcohol and cigarette use was assessed through girl report via questionnaire at a walk-in focus clinic with the questions "Friends drunk alcohol" and "Friends smoked cigarettes" at age 10 years. The variables were categorized: 0 = no, 1 = yes. Earlier peers' conduct problems were assessed with eight items through girl report via questionnaire at a walk-in focus clinic at age 10 years. The internal consistency of the items were just acceptable ($\alpha = 0.63$); however, as peer delinquency is not common at the age of 10 years we decided to still include all available information in the variable. The items were combined and dichotomized with the categories: 0 = no, 1 = yes.

Statistical analysis

As the three outcome variables (alcohol, cigarette and cannabis) are ordinal, ordered logistic regression analysis was used to analyze the effects of pubertal timing, parent-daughter relationship quality and peer deviance on substance use. The underlying assumption for this analysis is that the relationship between each pair of outcome groups is the same. In Stata 11 this proportional odds assumption is tested using the *omodel* command, which is based on a likelihood-ratio test (Stata 11; Ordered Logistic Regression, 2012). Analyses indicated that the proportional odds assumption was not violated for alcohol ($\chi^2(8) = 2.32$, $p = .97$), cigarette ($\chi^2(16) = 17.47$, $p = .36$), nor cannabis ($\chi^2(8) = 6.21$, $p = .62$) response categories.

Mediation and moderation analysis. To test the second hypothesis that parent-daughter relationship quality and peer deviance mediate the effect of pubertal timing on substance use in late adolescence, mediation analysis (see Figure 1a) was conducted. The indirect impact of the peer deviance and parent-daughter relationship quality on the relationship of pubertal timing on substance use at age 16 was estimated by assessing the indirect effect of pubertal timing on peer deviance and parent-daughter relationship quality at age 15 (i.e., path a) as well as the indirect effect of peer deviance and parent-daughter relationship quality at age 15 on substance use at age 16 (i.e., path b). As advocated by Rucker and colleagues (2011) our mediation analysis moved away from focusing on the total (i.e., path c) and direct effects (i.e., path c') and paid more attention on the indirect effects (i.e., path a and b). However, to calculate the ratio between the indirect effect and total effect (i.e., $B_{indirect}/B_{total}$), which is used to estimate the extent to which the mediator explains the effect of the predictor on the outcome variable, we had to assess the total effect (i.e., path c) and compute the indirect effect, which was done by using the product of coefficient method (i.e., path a*path b).

(Insert Figure 1a here)

To test the third hypothesis that pubertal timing moderates the effect of parent-daughter relationship quality and peer deviance on substance use in late adolescence, analysis (see Figure 1b) was conducted using ordinal regression models and the *testparm* command of Stata 11. This command is based on the Wald test statistic. In these regression models an interaction term of predictor and moderator was included which was then tested for significance in the post-estimation analysis using the *testparm* command.

(Insert Figure 1b here)

Multiple imputation. Over time, the ALSPAC sample has experienced somewhat higher attrition rates among less affluent families, ethnic minorities and male participants, a common finding for long-running longitudinal studies (Boyd et al., 2012; Fraser et al., 2012; Perez et al., 2007). The pattern of missing values is shown in Table 1.

(Insert Table 1 here)

We dealt with the problem of loss of power and biased estimates caused by attrition by conducting imputation analysis, where imputed datasets were created using the *ice* package in Stata 11 (Royston, 2007). It was assumed that data was missing at random (MAR) which allowed us to address this problem by creating eighty imputed datasets using multiple imputation by chained equation (Van Buuren, 1999). As MAR cannot be statistically confirmed (Sterne et al., 2009), the best way to avoid biased imputed data is the inclusion of several auxiliary variables, especially early assessments of measures included in the analyses in the imputation model (Graham, 2009).

Missing values of all variables were imputed with specifications in the imputation command addressing categorical, binary and skewed continuous variables as well as interaction terms and the inclusion of a number of auxiliary variables (Royston, 2009). As the inclusion of imputed outcome data in analyses may lead to biased estimates (White et al., 2011), we decided to use data sets with imputed predictor, moderator and confounding variables and complete case data of outcome variables for our analyses of imputed data. Ordered logistic regression in imputed data was performed on each imputed dataset and the imputation-specific coefficients were combined using Rubin's rules (Rubin, 1987). The significance of each prognostic factor was assessed using the Wald test statistic. Analyses of imputed data and complete case data produced similar results (full results are available from the first author); we therefore present the results of the imputed datasets. As descriptive statistics cannot be conducted for imputed data these values are reported for complete case data only.

Results

Descriptive statistics based on the complete cases (i.e., participants with no missing data on any of the variables in this study) are shown in Table 2. Chi-square tests show differences between the three pubertal timing groups for cigarette and cannabis use, the number of alcohol drinking friends, the number of cannabis using friends and having friends with conduct problems. The mean age at onset of menarche for the girls in the ALSPAC cohort was 12.3 years (*SD* = 1.29, range: 8-17) with eight girls reporting not having started their period by age 17.

(Insert Table 2 here)

Table 3 presents the main effects of pubertal timing on adolescents' alcohol, cigarette and cannabis use.

(Insert Table 3 here).

Late maturing girls used less alcohol than on-time maturing girls (B= -0.28) and the parameter estimate remained consistent after taking the confounding variables into account. Late maturing girls also used fewer cigarettes than early (B= -0.38) and on-time (B= -0.27) maturing girls but after adjusting for confounders the parameter estimate of the late maturing girls compared to the early maturing girls was reduced to B= -0.16 and the parameter estimate of the late maturing girls compared to the on-time maturing girls was reduced to B= -0.12. Late maturing girls were also found to use less cannabis than early (B= -0.39) and on-time maturing girls (B= -0.45), but after adjustment for confounders the parameter estimate of the late maturing girls compared to the early maturing girls was reduced to B= -0.27 and the parameter estimate of the late maturing girls compared to the on-time maturing girls was reduced to B= -0.39. The associations between pubertal timing and the two psycho-social factors (peer deviance and parent-daughter relationship quality) are shown in Table 4.

(Insert Table 4 here).

Late maturing girls had fewer alcohol drinking friends (B= -033) and delinquent friends (B= -0.37) than early maturing girls. They also had fewer cannabis using friends than early (B= -0.37) and on-time (B= -0.34) maturing girls. The parameter estimates were not significantly reduced after adjusting for confounding variables.

Having more friends who drink alcohol, smoke cigarettes, use cannabis and having delinquent friends (at age 15) were associated with higher levels of alcohol, cigarette and cannabis use at age 16 in the unadjusted as well as adjusted models. Lower levels of communication between parents and daughters, higher levels of conflict and lower levels of parental monitoring (age 15) were all associated with increased alcohol, cigarette and cannabis use one year later (age 16) in the unadjusted as well as the adjusted models (see Table 5).

(Insert Table 5 here)

Mediation analysis

We first evaluated the evidence for peer deviance (number of alcohol using friends, number of cigarette smoking friends, number of cannabis using friends, friends' delinquency) as a mediator in (first half of Table 6) the relationship between pubertal timing and adolescent girls' use of alcohol, cigarettes and cannabis respectively. A number of mediated effects were found in the unadjusted analyses. Late pubertal maturation was associated with having fewer cannabis using friends at age 15 (indirect effect, path a, Table 6; for path a also see Figure 1a) (B= -.05; 95% CI: -0.09, -0.01) and having more cannabis using friends at age 15 was associated with increased cannabis use at age 16 (indirect effect, path b, Table 6; for path b also see Figure 1a) (B= 0.45; 95% CI: 0.42, 0.49) with 45% of the effect of pubertal timing on cannabis use at age 16 explained indirectly by the number of cannabis using friends at age 15.

Partial mediation, where the effect of the predictor on the outcome remains present after including the mediator in the model while finding that the predictor affects the mediator and the mediator affects the outcome (MacKinnon, 2008), was also identified. Late pubertal timing was associated with having fewer alcohol drinking friends at age 15 (indirect effect, path a) (B= -0.04; 95% CI: -0.07, -0.001) and having more alcohol drinking friends at age 15 was associated with increased cigarette use at age 16 (indirect effect, path b) (B= 0.53; 95% CI: 0.45, 0.61) with 18% of the effect of pubertal timing on cigarette use at age 16 explained indirectly by the number of alcohol drinking friends at age 15. Late pubertal maturation was associated with having fewer cannabis using friends at age 15 (indirect effect, path a) (B= -0.05; 95% CI: -0.10, -0.01) and having more cannabis using friends at age 15 was associated with increased cigarette use at age 16 (indirect effect, path b) (B= 0.66; 95% CI: 0.60, 0.73) with 28% of the effect of pubertal timing on cigarette use at age 16 explained indirectly by the number of cannabis using friends at age 15. Late pubertal timing was associated with lower chances of having delinquent friends at age 15 (indirect effect, path a) (B= -0.03; 95% CI: -0.06, -0.01) and having delinquent friends at age 15 was associated with increased cigarette use at age 16 (indirect effect, path b) (B= 0.60; 95% CI: 0.50, 0.70) with 15% of the effect of pubertal timing on cigarette use at age 16 explained indirectly by having delinquent friends at age 15. Late pubertal timing was associated with a lower chance of having delinquent friends at age 15 (indirect effect, path a) (B= -0.03; 95% CI: -0.06, -0.01) and having delinquent friends at age 15 was associated with increased cannabis use at age 16 (indirect effect, path b) (B= 0.36; 95% CI: 0.30, 0.41) with 22% of the effect of pubertal timing on cannabis use at age 16 explained indirectly by having delinquent friends at age 15.

"Indirect-only mediation", where there is no evidence for the predictor affecting the outcome while there is evidence for the predictor affecting the mediator and the mediator affecting the outcome (Hayes, 2009; Zhao et al., 2010), was identified. Late pubertal timing was associated with having fewer cannabis using friends at age 15 (indirect effect, path a) (B= -0.05; 95% CI: -0.10, -0.003) and having more cannabis using friends at age 15 was associated with increased alcohol use at age 16 (indirect effect, path b) (B= 0.32; 95% CI: 0.28, 0.37). Also, late pubertal timing was associated with a lower chance of having delinquent friends at age 15 (indirect effect, path a) (B= -0.03; 95% CI: -0.06, -0.003) and having delinquent friends at age 15 was associated with increased levels of alcohol use at age 16 (indirect effect, path b) (B= 0.35; 95% CI: 0.28, 0.42). After adjusting for confounders the only mediation effects remaining were the "indirect-only mediation" effects (see Table 6). No mediation effects were found for parent-daughter relationship quality at age 15 mediating the effect of pubertal timing on substance use at age 16 (second half of Table 6)

(Insert Table 6 here)

Moderation analyses

Pubertal timing moderated the effect of the number of alcohol drinking friends at age 15 on alcohol use at age 16, with the effect being stronger in on-time and late maturing girls than in early maturing girls (see Table 7). However, when looking at the three pubertal timing groups separately, the number of alcohol drinking friends at age 15 still predicted alcohol use at age 16 for early (OR = 1.82, 95% CI: 1.17, 2.83), on-time (OR = 3.45, 95% CI: 2.54, 4.70) and late maturing girls (OR = 4.24, 95% CI: 2.18, 8.23). No evidence for moderation effects was found for parent-daughter relationship quality, i.e., pubertal timing did not appear to combine with aspects of parent-adolescent relationship to increase risk of substance use. These results did not change when the confounders were included in the analyses.

(Insert Table 7 here).

Discussion

Few studies have tested the hypothesis that pubertal timing combines with psycho-social factors, including parent-adolescent relationship quality and peer behavior, to influence adjustment in adolescence. We used a large population based sample to examine whether specific aspects of parent-daughter relationship quality (communication and conflict as well as parental monitoring at age 15) and peer behavior (number of alcohol drinking, cigarette smoking and cannabis using peers and having delinquent peers) might combine with pubertal timing to increase risk of substance use in girls, while adjusting for potentially confounding factors. Longitudinal research assessing multiple risk factors is important if we are to move closer to capturing the complex relationships that unfold during the pubertal transition and which have been theoretically implicated in adolescent psychopathology.

Mediation analysis

We did not find evidence that parent-adolescent relationship quality at 15 mediated the relationship between pubertal timing and substance use at age 16 years. Although pubertal timing didn't predict substance use at age 16, we found that early pubertal timing was associated with having more cannabis using friends and having delinquent friends at age 15, which were associated with increased levels of alcohol use at age 16. According to Hayes (2009) and Zhao et al., (2010) mediation effects can still be found in the absence of direct effects and are termed indirect-only mediation. Our findings provide evidence for an indirect effect of pubertal timing on alcohol use at age 16 via the number of cannabis using peers and having delinquent peers at age 15. The lack of evidence for pubertal timing predicting substance use supports previous research in which substance use was assessed in late adolescence (e.g. Al-Sahab et al., 2012; Copeland et al., 2010; Kaltiala-Heino et al., 2011; Marklein et al., 2009).

We found that compared to the effect sizes for the relationship between peer behavior and later substance use, the effect sizes for the relationship between parent-daughter relationship quality and later substance use were smaller. This supports research by Bahr et al. (2005) who stated that there is an increasing drive towards autonomy from parents during adolescence and that therefore peer behavior may have a larger effect on adolescents' substance use in late adolescence (Kandel, 1980; Kandel & Andrews, 1987).

Moderation analysis

We did not find evidence that early maturing girls had more negative parent-daughter relationship quality than on-time and late maturing girls. However, because we did not have data available on parent-child relationship quality at an earlier age of adolescence, we could not examine whether such links were present in early or mid-adolescence. Our results are therefore inconsistent with previous research by Shelton and van den Bree (2010) who reported a moderating effect of pubertal timing on the relationship between parent-adolescent relationship quality and cigarette use in adolescence, with a stronger effect in late-maturing girls than in early and on-time maturing girls. The findings are also inconsistent with the work of Lynne-Landsman and colleagues (2010) who reported higher levels of binge drinking, cigarette and cannabis use in early maturers in average and high-risk family groups compared to on-time maturers. The discrepancy in findings across studies might be due to differences in sample characteristics (sample size, age, nationality), measurement (e.g. pubertal timing, measures of parent-adolescent relationship quality) and differences in adjustment for confounders. Shelton and van den Bree (2010) did not adjust for confounders and Lynne-Landsman and colleagues (2010) adjusted for gender, cohort and ethnicity factors only. Moreover, we used a repeated measures approach to establish pubertal timing and this may offer a more accurate index of assessing pubertal timing than previous studies.

Pubertal timing moderated the relationship between the number of alcohol drinking friends at age 15 and alcohol use at age 16: the effect was weaker for early compared to on-time and late maturing girls. Nevertheless, the effect was found across all three pubertal timing groups. A moderation effect was also reported by Biehl et al., (2007); however, they reported that having fewer alcohol drinking friends predicted increased alcohol use in late adolescence for early maturing girls. This contrasts with our finding that having more alcohol drinking friends was associated with increased alcohol use in late adolescence for all girls, with the effect being stronger for on-time and late maturing girls than for early maturing girls. As this was the only moderation effect we identified, it should be interpreted cautiously.

We found no evidence for links between early pubertal timing and increased substance involvement in late adolescence (age 15-18 years; Pickhardt, 2009). This stands in contrast with studies focusing on girls' substance use in early/mid-adolescence (age 9-15 years; Berg-Kelly & Kullander, 1999; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006; Pickhardt, 2009), but concurs with several (Al-Sahab et al., 2012; Kaltiala-Heino et al., 2011; Marklein et al., 2009), but not all (Bratberg et al., 2007) studies in which girls' substance use was assessed in late adolescence. Our findings, however, differed across the three substances, suggesting that by the time girls reach late adolescence (age 16) there are differences in alcohol, cigarette and cannabis use across the three pubertal timing groups. That said, after adjusting for confounders, the only remaining difference was that late maturing girls used less cannabis than on-time maturing girls. These findings suggest that by the time girls reach late adolescence, on-time maturing girls may have caught up with early maturing girls in their levels of alcohol, cigarette and cannabis use and late maturing girls may have caught up with regards to alcohol and cigarette use, a finding consistent with three earlier studies (Al-Sahab et al., 2012; Kaltiala-Heino et al., 2011; Marklein et al., 2009).

These findings concur with some of the tenets of the *early timing hypothesis* (Peskin, 1973) and the *maturation disparity hypothesis* (see Ge & Natsuaki, 2009). These perspectives propose that early maturing girls are at higher risk of increased substance use because they have fewer cognitive resources to deal with social expectations placed on them commensurate with their mature appearance, compared to girls who mature at a later age (Ge et al., 2002). By the time girls reach late adolescence, their ability to cope with such social expectations may have increased. In addition, adults' expectations may have adjusted to more age appropriate expectations. This, in turn, may attenuate a link between early timing and substance use.

Strengths and limitations

A major strength of this study was the stringent approach to statistical analysis whereby we adjusted for a range of hypothesized confounders (financial difficulties, level of parental education, mothers and fathers' substance use, and adolescents' substance use at age 14, mother-child interaction, father-child interaction at age 9 and peer deviance at age 10). A second strength was a relatively robust measure of pubertal timing, which was derived from ten distinct measures of age at menarche assessed on a yearly basis from age 8 to 17 using a combination of mother-reports, mother/girl-reports and girl self-reports. A third strength was a focus on substance use in late adolescence (all participants were aged 16) rather than studying a wide age range of participants.

Our outcome measures of substance use were assessed at age 16. The majority of studies have focused on pubertal timing and girls' substance use in early/mid-adolescence (age 9-15 years; Pickhardt, 2009) and these all reported that early pubertal timing was associated with increased risk of substance use (Alsaker, 1996; Berg-Kelly & Kullander, 1999; Dawes et al. 2000; Dick et al., 2001; Downing & Bellis, 2009; Ge et al., 2006; Ge et al., 2002; Lanza & Collins, 2002; Marklein et al., 2009; Michaud et al., 2006; Patton & Viner, 2007; Waylen & Wolke, 2004). Additionally, none of the studies looking at the interplay of pubertal timing, psycho-social factors and adolescent substance use focused exclusively on substance use in late adolescence. Negriff and Trickett (2012) focused on early adolescence and Lynne-Landsman and colleagues (2010) focused on mid-adolescence. The studies by Shelton and van den Bree (2010), Marklein et al., (2009) and Biehl et al., (2007) all included participants with a relatively wide age range (11 to 17 years). Additionally, with the exception of the study by Biehl et al., (2007), these studies conducted analyses on considerable smaller samples compared to our relatively large sample of 2858 girls.

Very few studies have investigated the relationship between pubertal timing and girls' substance use in late adolescence (e.g. Al-Sahab et al., 2012; Bratberg et al., 2007; Copeland et al., 2010; Kaltiala-Heino et al., 2011). By late adolescence, those at risk of misuse will generally have passed through the experimental phase into habitual patterns of use (McCarty et al., 2004; Viner & Taylor, 2005). Indeed, substance use in late adolescence is a reliable predictor of substance use in adulthood (Englund et al., 2012) which marks substance use in late adolescence as a target for intervention (McCarty et al., 2004; Viner & Taylor, 2005). Additionally, age 16 provides the last chance to direct intervention programs to all school-children in the UK (school leaving age in the UK is currently 16). After age 16, many young people will leave formal education and are harder and more expensive to reach with health promotion and intervention programs. Although we used a lag of only one year between assessment of predictor and outcome, previous research has shown that adolescents' level of substance use is still changing from age 15 to 16 within this data set (Heron et al., 2012). It has also been reported that psycho-social factors (i.e., parental monitoring) affect substance use patterns one year later in late adolescence (Siebenbrunner et al., 2006).

Using a large longitudinal data set as ALSPAC has some disadvantages, including the relatively high attrition of participating families over time, which is a common problem among large-scale longitudinal cohort studies (McVie, 2003). This loss of information was addressed by conducting the most sophisticated and currently recommended approach (Shrive et al., 2006) of multiple imputation and by comparing the imputed results to complete case analysis. With regards to representativeness, ALSPAC participants completing questionnaires at age 16 were found to score higher on a test of School Performance based on National Pupil Database (NPD) 'Key Stage 4' (KS4) compared to non-ALSPAC pupils and ALSPAC drop-outs. ALSPAC children completing a questionnaire at age 16 were more likely to be female and less likely to be eligible for free school meals than ALSPAC drop-outs (Boyd et al., 2012). However, because we focused exclusively on girls we are less worried about sample bias as the majority of drop-out has been among male participants.

Another limitation is that the constructs of primary interest were not assessed using the same measures at each data collection point. The predictor variables in this study were based on the level of parent-daughter communication, conflict, the level of parental monitoring, the number of alcohol drinking, cigarette smoking and cannabis using friends as well as having delinquent friends at age 15. These measures were not available at an earlier age. We elected to use a measure of family functioning at age 9 (how much time spent with mother and father doing positive things) as well as binary measures of the number of alcohol drinking and cigarette smoking friends and having delinquent friends at age 10 to act as proximal indices.

Our parent-daughter relationship quality factors were based on adolescent-reports and some may argue that this leads to bias (Holmbeck et al., 2002). However, it has been stated that adolescent-report of the parent-adolescent relationship does offer benefits over alternative approaches (McGue et al., 2005). For example, the effect of parent-adolescent relationship quality on adolescent behavior is mediated by adolescent perceptions of this relationship (Neiderhiser et al., 1998) and there is also substantial support that adolescent-report of the parent-adolescent relationship is reliable and predictive (Metzler at al., 1998). Another limitation might be that at age 16, a small group of girls (16) had not yet experienced menarche. However, all girls who had not experienced menarche by age 13 were automatically categorized as late maturers and were included in the study sample; the assessments of menarche after age 13 were therefore used to inform the mean age of age at menarche and to provide information for menarche measures missing at earlier time points of assessment.

More longitudinal research is needed to elucidate the interplay of parent-daughter relationship quality and pubertal timing on substance use and the interplay of peer behavior and pubertal timing on substance use in late adolescence. Therefore, pubertal timing, parent-daughter relationship quality and peer behavior should be combined within one mediation model and one moderation model, as we had planned as a final analytic step. However, this step was dropped because there was insufficient evidence for mediation and moderation in the separate models. Our findings suggest that by late adolescence on-time and late maturing girls have caught up with early maturing girls in relation to alcohol and cigarette use and that on-time maturing girls have caught up in relation to cannabis use. However, early maturing girls remain at risk of substance use disorders and impacts on physiological development associated with earlier substance initiation (Spear, 2002). Although substance use levels adjust to similar levels by late adolescence, early maturing girls remain at increased risk of organ damage caused by a longer period of substance use exposure and substance use.

Although we did not find much evidence for combined effects of peer behavior, parent-daughter relationship quality and pubertal timing with regards to substance use in late adolescence this topic is an important one as substance use patterns in late adolescence have health consequences extending into adulthood (McCambridge et al., 2011; McCarty et al., 2004; Newcomb & Bentler, 1987; Viner & Taylor, 2005; Wells et al., 2004) as well as consequences regarding education, work, romantic relationships, and global adaptation in adulthood (Englund et al., 2012). Resolving whether links between early pubertal timing and higher levels of substance involvement extend into late adolescence may have implications for developing practice and policy aimed at prevention (McCarty et al., 2004; Viner & Taylor, 2005). Future research needs to confirm our findings and continue to examine the combined effects of pubertal timing and psycho-social factors on substance use into adulthood to follow-up on substance use trajectories.

References

Ali, M., Amialchuk, A., & Dwyer, D. (2011). The social contagion effect of marijuana use among adolescents. *Public Library of Science, 6(1)*, e16183

Al-Sahab, B., Ardern, C., Hamadeh, M., & Tamim, H. (2012). Age at menarche and current substance use among Canadian adolescent girls: results of a cross-sectional study. *BioMedCentral Public Health, 12*, 195-203.

Alsaker, F. D. (1996) Annotation: The Impact of Puberty. *Journal of Child Psychology and Psychiatry, 37*, 249-258.

ALSPAC (2011) retrieved from http://www.bristol.ac.uk/alspac/ on 23.12.2011

Amos, A., Greaves, L., Nichter, M., & Bloch, M. (2012). Women and tobacco: a call for including gender in tobacco control research, policy and practice. *Tobacco Control, 21*, 236-243.

Babor, T., Higgins-Biddle, J., Saunders, J., & Monteiro, M. (2001). AUDIT – The Alcohol Use Disorders Identification Test. *World Health Organization, Department of Mental Health and Substance Dependence.*

Bahr, S., Hoffmann, J., & Yang, X. (2005). Parental and Peer Influences on the Risk of Adolescent Drug Use. *The Journal of Primary Prevention*, 26(6), 529-551.

Barnes, G., Hoffman, J., Welte, J., Farrell, M., & Dintcheff, B. (2006). Effects of Parental Monitoring and Peer Deviance on Substance Use and Delinquency. *Journal of Marriage and Family, 68(4)*, 1084-1104.

Bava, S., & Tapert, S. F. (2010) Adolescent Brain Development and the Risk for Alcohol and Other Drug Problems. *Neuropsychological Review, 20*, 398-413.

Berg-Kelly, K. & Kullander, K. (1999) Gender differences in early adolescence in factors related to outcome of healthy behaviors two years later. *Acta Paediatrica, 88*, 1125-30.

Biehl, M.C., Natsuaki, M.N., & Ge, X. (2007). The Influence of Pubertal Timing on Alcohol Use and Heavy Drinking Trajectories. *Journal of Youth and Adolescence, 36*, 153-167.

Boyd, A., Golding, J., Macleod, J., Lawlor, D.A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2012). Cohort Profile: The 'Children of the 90s'- the index offspring of the Avon Longitudinal Study of Parents and Children. *International Journal of Epidemiology*, 1-17.

Branstetter, S., Low, S., & Furman, W. (2011). The Influence of Parents and Friends on Adolescent Substance Use: A Multidimensional Approach. *Journal of Substance Use, 16(2)*, 150-160.

Bratberg, G. H., Nilsen, T. I. L., Holmen, T. L. & Vatten, L. J. (2007) Perceived pubertal timing, pubertal status and the prevalence of alcohol drinking and cigarette smoking in early and late adolescence: a population based study of 8950 Norwegian boys and girls. *Acta Pædiatrica, 96*, 292-295.

British Medical Association (BMA) Board of Science and Education (2003) *Adolescent Health.* London: BMA Publishing Unit.

Buck Louis, G. M., Gray, L. E., Marcus, M., Ojeda, S. R., Pescovitz, O. H., Witchel, S. F., Sippell, W., Abbott, D. H., Soto, A., Tyl, R. W., Bourguignon, J., Skakkebaek, N. E., Swan, S. H., Golub, M. S., Wabitsch, M., Toppari, J. & Euling, S. Y. (2008) Environmental Factors and Puberty Timing: Expert Panel Research Needs. *Pediatrics, 121*, s192-s207.

Celio, M., Karnik, N. S. & Steiner, H. (2006) Early maturation as a risk factor for aggression and delinquency in adolescent girls: A review. *International Journal of Clinical Practice, 60*, 1254-62.

Cicchetti, D. (1984). The Emergence of Developmental Psychopathology, *Journal of child Development, 55*, 1-7.

Copeland, W., Shanahan, L., Miller, S., Costello, E.J., Angold, A., & Maughan, B. (2010) Outcomes of Early Pubertal Timing in Young Women: A Prospective Population-Based Study, *American Journal of Psychiatry, 167*, 1218-1225.

Cruz, J., Emery, R., & Turkheimer, E. (2012). Peer Network Drinking Predicts Increased Alcohol Use From Adolescence to Early Adulthood After Controlling for Genetic and Shared Environmental Selection. *Developmental Psychology, 48(5)*, 1390-1402.

Dawes, M. A., Antelman, S. M., Vanyokov, M. M., Giancola, P., Tarter, R. E., Susman, E. J., Mezzich, A. & Clark, D. B. (2000). Developmental sources of variation in liability to adolescent substance use disorders. *Drug and Alcohol Dependence, 61*, 3-14.

Dick, D. M., Rose, R. J., Pulkkinen, L. & Kaprio, J. (2001). Measuring puberty and understanding its impact: A longitudinal study of adolescent twins. *Journal of Youth and Adolescence, 30*, 385-399.

Dishion, T. J., Nelson, S. E. & Bullock, B. M. (2004) Premature adolescent autonomy: Parent Disengagement and deviant peer process in the amplification of problem behaviour.

Journal of Adolescence, 27, 515-530.

Donovan, J. E. (2004) Adolescent alcohol initiation: A review of psychosocial risk factors. *Journal of Adolescent Health, 35*, 529.e7-529.e7.

Downing, J. & Bellis, M. A. (2009) Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. *BioMedCentral Public Health, 9*, 446.

Englund, M.M., Siebenbrunner, J., Oliva, E.M., Egeland, B., Chung, C.T, & Long, J.D. (2012). The developmental significance of late adolescent substance use for early adult functioning. *Journal of Developmental Psychology*

Enoch, M. A. (2011) The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology, 214(1)*, 17-31.

ESYTC (2011) retrieved from http://www.law.ed.ac.uk/cls/esytc/ on 23.12.2011

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Smith, G., Henderson, J., Macleod, J., Molloy, L., Ness, A., Ring, S., Nelson, S., & Lawlor, D. (2012). Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mother cohort. *International Journal of Epidemiology, 42(1)*, 97-110.

Ge, X., & Natsuaki, M. N. (2009). In search of explanations of early pubertal timing effects on developmental psychopathology. *Current Directions in Psychological Science, 18*, 327–331.

Ge, X., Natsuaki, M. N., Neiderhiser, J. M. & Reiss, D. (2007) Genetic and Environmental Influences on Pubertal Timing: Results From Two National Sibling Studies. *Journal of Research on Adolescence, 17*, 767-788.

Ge, X., Jin, R., Natsuaki, M. N., Gibbons, F. X., Brody, G. H., Cutrona, C. E. & Simons, R. L. (2006) Pubertal Maturation and Early Substance Use Risks Among African American Children. *Psychology of Addictive Behaviors, 20*, 404-414.

Ge, X. J., Brody, G. H., Conger, R. D., Simons, R. L. & Murry, V. M. (2002). Contextual amplification of pubertal transition effects on deviant peer affiliation and externalizing behavior among African American children. *Developmental Psychology, 38*, 42-54.

Ge, X. J., Best, K. M., Conger, R. D., & Simons, R. L. (1996). Parenting behaviors and the occurrence and co-occurrence of adolescent depressive symptoms and conduct problems. *Developmental Psychology, 32(4)*, 717-731.

Glaser, B., Shelton, K., van den Bree, M. (2010). The moderating role of close friends in the relationship between conduct problems and adolescent substance use. *Journal of Adolescent Health, 47(1)*, 35-42.

Graham, J. (2009). Missing Data Analysis: Making It Work in the Real World. *Annual Review of Psychology, 60*, 549-576.

Hayes, A.F. (2009). Beyond Baron and Kenny: Statistical Mediation Analysis in the New Millennium. *Communication Monographs, 76(4)*, 408-420.

Heron, J., Hickman, M., Macleod, J., & Munafo, M.R. (2011). Characterizing Patterns of Smoking Initiation in Adolescence: Comparison of Methods for Dealing With Missing Data. *Nicotine & Tobacco Research, 13(12)*, 1266-1275.

Heron, J., Macleod, J., Munafo, M.R., Melotti, R., Lewis, G., Tilling, K., & Hickman, M. (2012). Patterns of Alcohol Use in Early Adolescence Predict Problem Use at Age

16. *Alcohol and Alcoholism, 47(2)*, 169-177.

Hibell, B., Guttormsson, U., Ahlstroem, S., Balakireva, O., Bjarnason, T., Kokkevi, A., & Kraus, L. *The 2007 ESPAD Report. Substance Use Among Students in 35 European Countries.*

Holmbeck, G., Li, S., Schurman, J., Friedman, D., Coakley, R. (2002). Collecting and managing multisource and multimethod data in studies of pediatric populations. *Journal of Pediatric Psychology, 27*, 5-18.

Hummel, A., Shelton, K. H., Heron, J., Moore, L., & van den Bree, M. B. M. (2013) A systematic review of the relationships between family functioning, pubertal timing and substance use in adolescence. *Addiction, 108(3)*, 487-496.

Jain, R., & Balhara, Y.P.S. (2010) Impact of Alcohol and Substance Abuse on Adolescent Brain: A Preclinical Perspective. *Indian Journal of Physiological Pharmacology, 54*, 213-234.

Joinson, C., Heron, J., Lewis, G., Croudace, T., & Araya, R. (2011). Timing of menarche and depressive symptoms in adolescent girls from a UK cohort. *The British Journal of Psychiatry, 198*, 17-23.

Kaltiala-Heino, R., Koivisto, A., Marttunen, M., & Fröjd, S. (2011). Pubertal Timing and Substance Use in Middle Adolescence: A 2-Year Follow-up Study. *Journal of Youth and Adolescence, 40*, 1288-1301.

Kandel, D. (1980). Drug and drinking behavior among youth. *Annual Review of Sociology, 6*, 235-85.

Kandel, D., & Andrews, K. (1987). Process of adolescent socialization by parents and peers. *International Journal of Addictions, 22*, 319-342.

Kring, A., Davison, G., Neale, J., & Johnson, S. (2007). *Abnormal Psychology*. New York: John Wiley & Sons.

Lansford, J., Dodge, K., Pettit, G., & Bates, J. (2010). Does Physical Abuse in Early Childhood Predict Substance Use in Adolescence and Early Adulthood? *Child Maltreatment*, *15*(2), 190-194.

Lanza, S. T. & Collins, L. M. (2002) Pubertal timing and the onset of substance use in females during early adolescence. *Prevention Science, 3*, 69-82.

Lynne-Landsman, S. D., Graber, J. A. & Andrews, J. A. (2010) Do trajectories of household risk in childhood moderate pubertal timing effects on substance initiation in middle school? *Developmental Psychology, 46***,** 853-68.

MacArthur, G.J., Smith, M.C., Melotti, R., Heron, J., Macleod, J., Hickman, M., Kipping, R.R., Campbell, R., & Lewis, G. (2012). Patterns of alcohol use and multiple risk behaviour by gender during early and late adolescence: the ALSPAC cohort. *Journal of Public Health, 34(1)*, i20-i30.

MacKinnon, D.P. (2008). *Introduction to Statistical Mediation Analysis*. New York: Lawrence Erlbaum Associates Taylor & Francis Group.

Marklein, E., Negriff, S., & Dorn, L. (2009) Pubertal Timing, Friend Smoking, and Substance Use in Adolescent Girls. *Prevention Science, 10*, 141-150.

McCambridge, J., McAlaney, J., & Rowe, R. (2011). Adult Consequences of Late Adolescent Alcohol Consumption: A Systematic Review of Cohort Studies. *Public Library on*

Science 8(2), 1-13.

McCarty, C.A., Ebel, B.E., Garrison, M.M., DiGiuseppe, D.L., Christakis, D.A., & Rivara, F.P. (2004). Continuity of Binge and Harmful Drinking From Late Adolescence to Early Adulthood. *Pediatrics, 114(3)*, 714-719.

McGue, M., Elkins, I., Walden B., & Iacona, W. (2005). Perceptions of the Parent–Adolescent Relationship: A Longitudinal Investigation. *Developmental Psychology*, *41*(6), 971-984.

McVie, S, & Holmes, L. (2005). *The Edinburgh Study of Youth Transitions and Crime, No 9: Family Functioning and Substance Use at Ages 12 to 17.* Edinburgh: Centre for Law and Society, University of Edinburgh.

McVie, S. (2003). *Technical report: sweeps 3 & 4*. Edinburgh: Centre for Law and Society, University of Edinburgh.

Metzler, C. W., Biglan, A., Ary, D. V., & Li, F. (1998). The stability and validity of early adolescents' reports of parenting constructs. *Journal of Family Psychology, 12,* 600–619.

Michaud, P. A., Suris, J. C. & Deppen, A. (2006) Gender-related psychological and behavioural correlates of pubertal timing in a national sample of Swiss adolescents. *Molecular and Cellular Endocrinology*, 172-8.

National Center for Health Statistics (2011). *Health, United States, 2010: With Special Feature on Death and Dying.* Hyattsville, MD.

Neiderhiser, J. M., Pike, A., Hetherington, E. M., & Reiss, D. (1998). Adolescent perceptions as mediators of parenting: Genetic and environmental contributions. *Developmental*

Psychology, 34, 1459–1469.

Negriff, S., & Trickett, P. (2012). Peer substance use as a mediator between early pubertal timing and adolescent substance use: Longitudinal associations and moderating effect of maltreatment. *Drug and Alcohol Dependency, 126 (1-2)*, 95-101.

Newcomb, M. D., & Bentler, P. M. (1988). *Consequences of Adolescent Drug Use*. Newbury Park, CA: Sage Publications.

Ordered Logistic Regression (2012). UCLA: Academic Technology Services, Statistical Consulting Group, retrieved on 20. June 2012 from http://www.ats.ucla.edu/stat/stata/dae/ologit.htm

Oxford, M.L., Harachi, T.W., Catalano, R.F., & Abbott, R.D. (2001). Preadolescent predictors of substance initiation: a test of both the direct and mediated effect of family social control factors on deviant peer associations and substance initiation. *The American Journal of Drug and Alcohol Abuse*, *27*(4), 599-616.

Patton, G. C. & Viner, R. (2007) Adolescent health 1 - Pubertal transitions in health. *Lancet (North American Edition), 369*, 1130-1139.

Perez R.G., Ezpeleta L.,Domenech J.M. (2007). Features associated with the non-participation and drop out by socially-at-risk children and adolescents in mental-health epidemiological studies. *Social Psychiatry and Psychiatric Epidemiology, 42,* 251-8.

Peskin, H. (1973). Influence of the developmental schedule of puberty on learning and ego functioning. *Journal of Youth and Adolescence, 2*, 273–290.

Pickhardt, C. (2009). *Surviving (Your Child's) Adolescence*. Retrieved on 27th of June 2012 from http://www.psychologytoday.com/blog/surviving-your-childs-adolescence/200903/late-adolescence-15-18-acting-more-grown

Rhodes, T., Lilly, R., Fernandez, C., Giorgino, E., Kemmesis, U., Ossebaard, H., Lalam, N., Faasen, I., & Spannow, K. (2003). Risk Factors Associated With Drug Use: the importance of 'risk environment'. *Drugs: education, prevention and policy, 10(4)*, 303-329.

Royston, P. (2009). Multiple imputation of missing values: Further update of ice, with an emphasis on categorical variables. *The Stata Journal, 9(3)*, 466-477.

Royston, P. (2007). Multiple imputation of missing values: further update of ice, with an emphasis on interval censoring. *Stata Journal, 7(4)*, 445-464.

Rubin, D.B. (1987). *Multiple imputation for non-response in surveys*. Wiley.

Rucker, D., Preacher, K., Tormala, Z., & Petty, R. (2011). Mediation Analysis in Social Psychology: Current Practices and New Recommendations. *Social and Personality Psychology Compass, 5/6*, 359–371.

Rutter, M. (2005). Environmentally Mediated Risks for Psychopathology: Research strategies and Findings. *Journal of the American Academy of Child and Adolescent Psychiatry, 44(1)*, 3-18.

Rutter, M. (1999). Psychosocial adversity and child psychopathology. *British journal of Psychiatry, 174*, 480-493.

Rutter, M. & Casear, P. (1991). *Biological risk factors for psychosocial disorders.* Cambridge: Cambridge University Press.

Saraceno, L., Heron,. J., Munafo., M., Craddock., N., & van den Bree., M. (2012). The relationship between childhood depressive symptoms and problem alcohol use in early adolescence: findings from a large longitudinal population-based study. *Addiction, 107 (3)*, 567-577.

Shelton, K. H. & van den Bree, M. B. M. (2010). The Moderating Effects of Pubertal Timing on the Longitudinal Associations between Parent-Child Relationship Quality and Adolescent Substance Use. *Journal of Research on Adolescence, 20(4)***,** 1044-1064.

Shelton, K. H., Harold, G. T., Fowler, T. A., Rice, F. J., Neale, M. C., Thapar, A. & van den Bree, M. B. M. (2008). Parent-Child Relations, Conduct Problems and Cigarette Use in Adolescence: Examining the Role of Genetic and Environmental Factors on Patterns of Behavior. *Journal of Youth and Adolescence, 37*, 1216-1228.

Shrive, F.M., Stuart, H., Quan, H., & Ghali, W.A. (2006). Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. *BMC Medical research Methodology, 6: 57*.

Siebenbrunner, J., Englund, M.M., Egeland, B., & Hudson, K. (2006). Developmental antecedents of late adolescence substance use patterns. *Journal of Development and Psychopathology, 18(2)*, 551-571.

Skinner, M., Haggerty, K., & Catalano, R. (2009). Parental and peer influences on teen smoking: Are White and Black families different? *Nicotine and Tobacco Research, 11(5)*, 558-563.

Smith, D. (2004). *The Edinburgh Study of Youth Transitions and Crime, No 3: Parenting and Delinquency at Ages 12 to 15.* Edinburgh: Centre for Law and Society, University of Edinburgh.

Spear, L.P. (2002). Alcohol's effect on Adolescents. *Alcohol Research & Health, 26*, 287-291.

Sterne, J., White, I., Carlin, J., Spratt, M., Royston, P., Kenward, M., Wood, A., & Carpenter, J. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *British Medical Journal, 3*(38), b2393.

Stice, E., Presnell, K., & Bearman, S. (2001). Relation of early menarche to depression, eating disorders, substance abuse, and comorbid psychopathology among adolescent girls. *Developmental Psychology, 37*, 608–19.

Sutherland, A. (2012). Is parental socio-economic status related to the initiation of substance abuse by young people in an English city? An event history analysis. *Social Science & Medicine, 74*(7), 1053-1061.

Tam, C., de Zegher, F., Garnett, S., Baur, L., & Cowell, C. (2006). Opposing influences of prenatal and postnatal growth on the timing of menarche. *Journal of Clinical Endocrinology and Metabolism, 91*, 4369–73.

US Department of Health and Human Services (2012). Office of Adolescent Health, retrieved on 19. June 2012 from http://www.hhs.gov/ash/oah/resources-and-publications/info/parents/just-facts/puberty.html

Van Buuren, S., Boshuizen, H.C., Knook, D.L. (1999). Multiple imputation of missing blood pressure covariates in survival analysis. *Statistics in Medicine, 18*, 681-694.

van den Bree, M. B., & Pickworth, W. B. (2005). Risk factors predicting changes in marijuana involvement in teenagers. *Archives of General Psychiatry, 62*(3), 311-319.

van den Bree, M. B., Whitmer, M. D., & Pickworth, W. B. (2004). Predictors of smoking development in a population-based sample of adolescents: a prospective study. *Journal of Adolescent Health, 35*(3), 172-181.

Viner, R.M. & Taylor, B. (2005). Adult outcomes of binge drinking in adolescence: findings from a UK national birth cohort. *Journal of Epidemiology and Community Health, 61*, 902-907.

Volkow, N. (2010). *Drugs, brains and behaviour: The science of addiction*. NIDA National Institute of Drug Abuse. National Institutes of Health US Department of Health and Human Services.

Waylen, A. & Wolke, D. (2004) Sex 'n' drugs 'n' rock 'n' roll: the meaning and social consequences of pubertal timing. *European Journal of Endocrinology, 151 Supplement 3*, U151-9.

Wells, J.E., Horwood, L.J., & Fergusson, D.M. (2004). Drinking patterns in mid-adolescence and psychosocial outcomes in late adolescence and early adulthood. *Addiction, 99(12)*, 1529-1541.

White, I. R.., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine, 30(4)*, 377-399.

Wright, V. (2011*). Smoking, drinking and drug use among young people in England in 2010.* The Health and Social Care Information Centre, National Centre for Social Research, London.

Zhao, X., Lynch, J.G., & Chen, Q. (2010). Reconsidering Baron and Kenny: Myths and Truths about Mediation Analysis. *Journal of Consumer Research, 37*, 197-206.

Table 1

Pattern of missingness across the main variables of interest in N= 6747 girls

	Missing N (%)	Observed N (%)
Alcohol use	4148 (61.5%)	2599 (38.5%)
Cigarette use	3896 (57.7%)	2851 (42.3%)
Cannabis use	3889 (57.6%)	2858 (42.4%)
Alcohol drinking friends	4067 (60.3%)	2680 (39.7%)
Cigarette smoking friends	4064 (60.2%)	2683 (39.8%)
Cannabis using friends	4069 (60.3%)	2678 (39.7%)
Delinquent friends	4081 (60.5%)	2666 (39.5%)
Communication	4057 (60.1%)	2690 (39.9%)
Conflict	4059 (60.2%)	2688 (39.8%)
Monitoring	4056 (60.1%)	2691 (39.9%)
Pubertal timing	2787 (41.3%)	3960 (58.7%)

Figure 1a: Mediation model

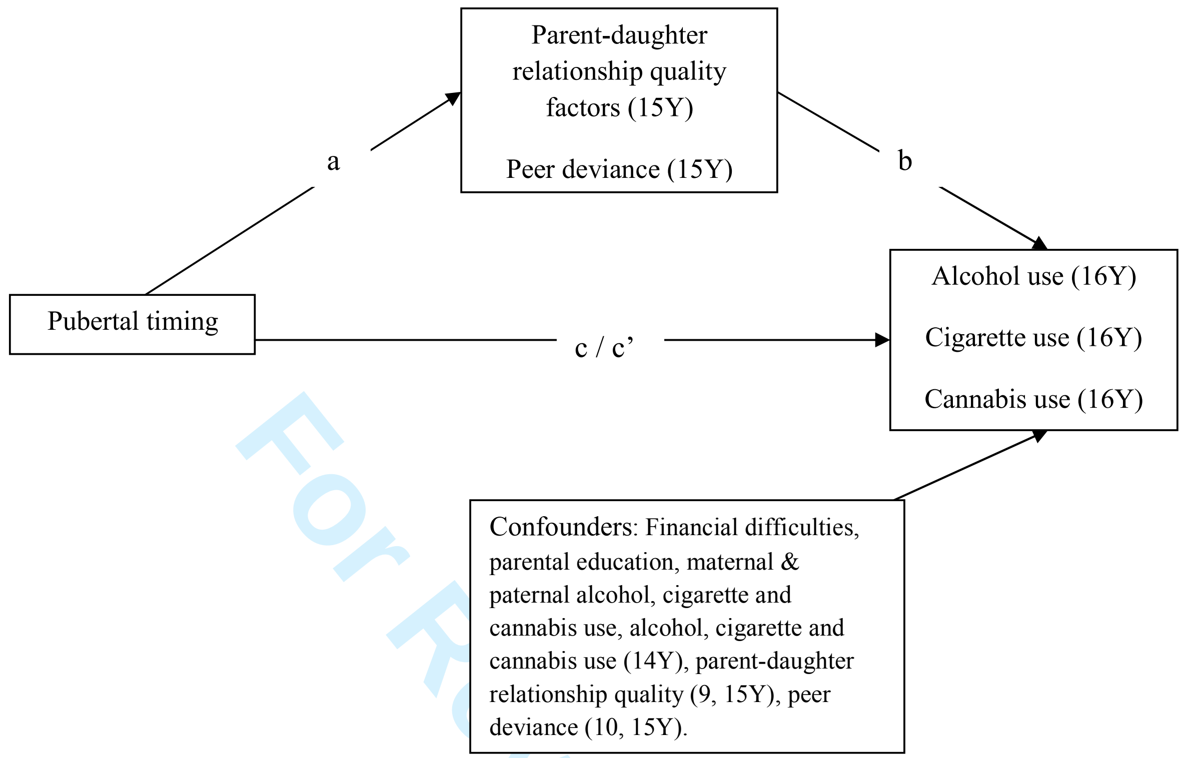

Figure 1b: Moderation model

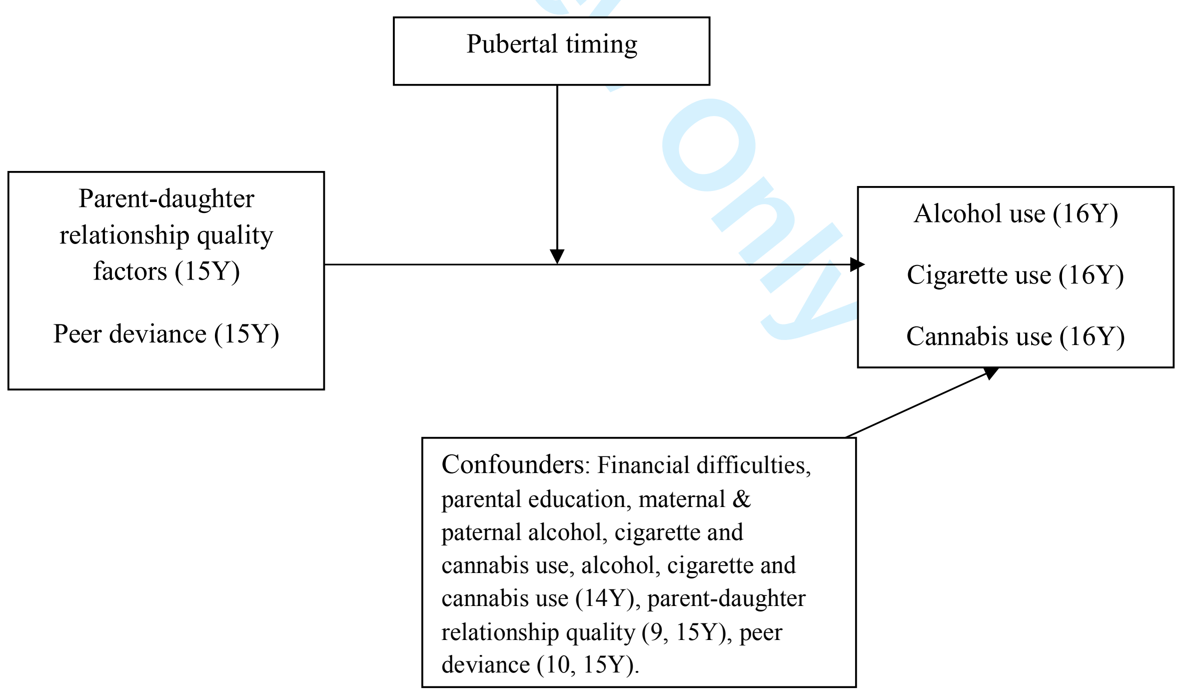

Table 2

Frequencies of substance use and social factors (parent-daughter relationship quality and peer deviance) for the three pubertal timing groups (complete cases)

	N (%)	Early n (%)	On-time n (%)	Late n (%)	χ^2
Alcohol					χ^2=7.1
harmless	1554 (63%)	348 (65%)	955 (61%)	251 (67%)	*p*= .13
hazardous	579 (23%)	124 (23%)	377 (24%)	78 (21%)	
harmful	347 (14%)	67 (12%)	236 (15%)	44 (12%)	
Cigarette					χ^2=16.6
non-smoker	1269 (47%)	268 (45%)	785 (46%)	216 (52%)	*p*= .01
only ever once or twice	811 (30%)	161 (27%)	527 (31%)	123 (30%)	
occasional smoker	236 (9%)	57 (10%)	147 (9%)	32 (8%)	
regular smoker	399 (14%)	107 (18%)	250 (14%)	42 (10%)	
Cannabis					χ^2=14.3
non-user	1926 (71%)	420 (71%)	1185 (69%)	321 (78%)	*p*= .006
only ever once or twice	551 (20%)	115 (19%)	373 (22%)	63 (16%)	
user	245 (9%)	59 (10%)	159 (9%)	27 (7%)	
Communication					χ^2=7.0
often	1145 (44%)	253 (46%)	707 (43%)	185 (45%)	*p*= .14
sometimes	1195 (46%)	235 (43%)	783 (48%)	177 (43%)	
hardly ever / never	264 (10%)	63 (11%)	153 (9%)	48 (12%)	
Conflict					χ^2=12.0
hardly ever / never	347 (13%)	85 (15%)	203 (12%)	59 (14%)	*p*= .06
< once a week	1529 (59%)	312 (57%)	975 (60%)	242 (59%)	
at least once a week	550 (21%)	105 (19%)	366 (22%)	79 (19%)	

	N (%)	Early n (%)	On-time n (%)	Late n (%)	
most days	176 (7%)	49 (9%)	98 (6%)	29 (8%)	
Monitoring					χ^2=4.3
always	1421 (55%)	299 (54%)	882 (54%)	240 (58%)	*p*= .36
usually	1055 (40%)	223 (41%)	674 (41%)	158 (38%)	
sometimes / never	130 (5%)	29 (5%)	87 (5%)	14 (4%)	
Alcohol drinking friends					χ^2(4)=11.6 *p*= .02
none	70 (3%)	18 (3%)	37 (2%)	15 (4%)	
one or some	724 (28%)	132 (24%)	461 (28%)	131 (32%)	
most or all	1803 (69%)	400 (73%)	1142 (70%)	261 (64%)	
Cigarette smoking friends					χ^2(4)=1.3 *p*= .86
none	414 (16%)	84 (15%)	261 (16%)	69 (17%)	
one or some	1488 (57%)	309 (56%)	945 (58%)	234 (57%)	
most or all	698 (27%)	157 (29%)	435 (26%)	106 (26%)	
Cannabis using friends					χ^2(4)=19.9
none	1174 (45%)	227 (41%)	723 (44%)	224 (55%)	*p*= .001
one or some	1150 (44%)	258 (47%)	746 (46%)	146 (36%)	
most or all	271 (11%)	64 (12%)	168 (10%)	39 (9%)	
Friends with conduct problems					χ^2(2)=14.2 *p*= .001
no	597 (23%)	102 (19%)	377 (23%)	118 (29%)	
yes	1986 (77%)	446 (81%)	1251 (77%)	289 (71%)	

Family, peers, pubertal timing and substance use

Table 3

Regression analysis of pubertal timing on substance use[1]

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[2] OR [95% CI.]
Alcohol outcome	*Pubertal timing*		
	On-time versus early	0.86 [0.71, 1.05]	0.85 [0.70, 1.04]
	On-time versus late	0.76 [0.60, 0.96]	0.76 [0.60, 0.96]
	Early versus late	0.88 [0.67, 1.16]	0.89 [0.67, 1.17]
		$\chi^2(2)$= 6.33, p = .04	$\chi^2(2)$ = 6.45, p = .04
Cigarette outcome	*Pubertal timing*		
	On-time versus early	1.12 [0.94, 1.33]	1.05 [0.87, 1.26]
	On-time versus late	0.76 [0.63, 0.94]	0.88 [0.71, 1.09]
	Early versus late	0.68 [0.54, 0.87]	0.84 [0.66, 1.09]
		$\chi^2(2)$ = 10.26, p = .006	$\chi^2(2)$ = 1.84, p = .40
Cannabis outcome	*Pubertal timing*		
	On-time versus early	0.95 [0.77, 1.16]	0.88 [0.71, 1.09]
	On-time versus late	0.64 [0.50, 0.82]	0.68 [0.52, 0.88]
	Early versus late	0.67 [0.51, 0.82]	0.77 [0.57, 1.04]
		$\chi^2(2)$= 12.19, p = .002	$\chi^2(2)$ = 8.95, p = .01

[1] Imputed data (see Methods)

[2] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and paternal use), and substance use at age 14

Table 4

Regression analysis of pubertal timing and social factors (with peer deviance and parent-daughter relationship quality)[1]

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[2] OR [95% CI.]
Number of alcohol drinking friends	*Pubertal timing*		
	On-time versus early	1.09 [0.93, 1.27]	1.09 [0.93, 1.27]
	On-time versus late	0.84 [0.69, 1.01]	0.84 [0.70, 1.01]
	Early versus late	0.77 [0.62, 0.96]	0.77 [0.62, 0.96]
		$\chi^2(2)$= 7.90, p = .02	$\chi^2(2)$ = 7.60, p = .02
Number of cigarette smoking friends	*Pubertal timing*		
	On-time versus early	1.09 [0.94, 1.26]	1.07 [0.93, 1.24]
	On-time versus late	0.92 [0.77, 1.09]	0.96 [0.80, 1.14]
	Early versus late	0.84 [0.68, 1.05]	0.89 [0.72, 1.11]
		$\chi^2(2)$ = 1.20, p = .55	$\chi^2(2)$ = 0.05, p = .97
Number of cannabis using friends	*Pubertal timing*		
	On-time versus early	1.09 [0.94, 1.25]	1.07 [0.93, 1.24]
	On-time versus late	0.80 [0.67, 0.95]	0.82 [0.69, 0.97]
	Early versus late	0.74 [0.60, 0.91]	0.76 [0.62, 0.94]
		$\chi^2(2)$= 15.81, p < .001	$\chi^2(2)$ = 12.89, p = .002

Table 4 continued

		Unadjusted for confounders OR [95% CI.]	Adjusted for confounders[2] OR [95% CI.]
Friends' conduct problems	*Pubertal timing*		
	On-time versus early	1.14 [0.95, 1.36]	1.13 [0.94, 1.35]
	On-time versus late	0.84 [0.68, 1.03]	0.85 [0.69, 1.04]
	Early versus late	0.74 [0.59, 0.93]	0.75 [0.59, 0.95]
		$\chi^2(2)= 14.23$, $p < .001$	$\chi^2(2)= 12.88$, $p = .002$
Parent-daughter communication	*Pubertal timing*		
	On-time versus early	0.97 [0.84, 1.12]	0.97 [0.84, 1.12]
	On-time versus late	1.00 [0.85, 1.18]	1.00 [0.85, 1.18]
	Early versus late	1.03 [0.85, 1.25]	1.03 [0.85, 1.25]
		$\chi^2(2)= 0.26$, $p = .88$	$\chi^2(2)= 0.29$, $p = .86$
Parent-daughter conflict	*Pubertal timing*		
	On-time versus early	0.98 [0.84, 1.14]	0.97 [0.83, 1.13]
	On-time versus late	0.96 [0.80, 1.16]	0.96 [0.80, 1.16]
	Early versus late	0.98 [0.78, 1.24]	0.99 [0.78, 1.26]
		$\chi^2(2)= 1.02$, $p = .60$	$\chi^2(2)= 0.98$, $p = .61$
Parental monitoring	*Pubertal timing*		
	On-time versus early	1.00 [0.86, 1.15]	0.99 [0.86, 1.14]
	On-time versus late	0.91 [0.76, 1.08]	0.91 [0.76, 1.08]
	Early versus late	0.91 [0.75, 1.11]	0.92 [0.75, 1.12]
		$\chi^2(2)= 3.32$, $p = .19$	$\chi^2(2)= 3.35$, $p = .19$

[1] Imputed data (see Methods)

[2] Adjusted for: socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and paternal use), substance use at age 14 and parent-child interaction at age 9

Table 5

Relationships between social factors (parent-daughter relationship quality and peer deviance) (at age 15) and substance use (at age 16) [1]

Substances	Peer deviance	Unadjusted for confounders			Adjusted for confounders[2]		
		$X^2(1)$, *p*	OR	95% CI	$X^2(12)$, *p*	OR	95% CI
Alcohol	Number of alcohol drinking friends	148.62, <.001	3.53	2.79, 4.46	68.67, <.001	3.02	2.37, 3.87
	Number of cigarette smoking friends	144.87, <.001	2.45	2.10, 2.84	65.83, <.001	2.09	1.78, 2.45
	Number of cannabis using friends	168.61, <.001	2.50	2.18, 2.87	70.39, <.001	2.10	1.81, 2.43
	Friends' delinquency	107.40, <.001	3.21	2.51, 4.11	59.53, <.001	2.53	1.96, 3.28
Cigarettes	Number of alcohol drinking friends	185.28, <.001	3.05	2.55, 3.65	245.60, <.001	2.41	1.99, 2.92
	Number of cigarette smoking friends	364.94, <.001	3.98	3.44, 4.61	274.53, <.001	2.86	2.44, 3.34
	Number of cannabis using friends	330.04, <.001	3.42	2.99, 3.91	251.04, <.001	2.47	2.14, 2.85
	Friends' delinquency	134.85, <.001	3.23	2.65, 3.94	203.41, <.001	2.28	1.85, 2.82

Table 5 continued

		Unadjusted for confounders			Adjusted for confounders[2]		
		$X^2(1)$, *p*	OR	95% CI	$X^2(12)$, *p*	OR	95% CI
Cannabis	Number of alcohol drinking friends	167.63, <.001	3.96	3.08, 5.08	215.98, <.001	3.17	2.46, 4.09
	Number of cigarette smoking friends	248.92, <.001	3.59	3.02, 4.28	230.46, <.001	2.91	2.40, 3.52
	Number of cannabis using friends	435.48, <.001	5.25	4.45, 6.21	272.77, <.001	4.16	3.49, 4.98
	Friends' delinquency	155.51, <.001	5.35	3.92, 7.29	182.46, <.001	3.93	2.84, 5.44
Substances	Parent-daughter relationship quality						
Alcohol	Parent-daughter communication	52.08, <.001	1.56	1.36, 1.78	75.63, <.001	1.34	1.17, 1.54
	Parent-daughter conflict	71.89, <.001	1.55	1.38, 1.75	77.22, <.001	1.33	1.18, 1.52
	Parental monitoring	144.06, <.001	2.41	2.06, 2.82	85.87, <.001	1.83	1.55, 2.17
Cigarettes	Parent-daughter communication	95.70, <.001	1.61	1.43, 1.82	299.94, <.001	1.31	1.15, 1.50
	Parent-daughter conflict	137.85, <.001	1.68	1.50, 1.88	286.83, <.001	1.34	1.19, 1.51
	Parental monitoring	200.73, <.001	2.25	1.96, 2.58	296.35, <.001	1.49	1.29, 1.74
Cannabis	Parent-daughter communication	55.73, <.001	1.54	1.34, 1.77	266.21, <.001	1.25	1.07, 1.46
	Parent-daughter conflict	76.91, <.001	1.59	1.41, 1.79	255.85, <.001	1.27	1.11, 1.45
	Parental monitoring	202.21, <.001	2.49	2.14, 2.90	290.24, <.001	1.65	1.39, 1.97

[1] Imputed data (see Methods)

[2] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and paternal alcohol, cigarette and cannabis sue), substance use at age 14 (alcohol, cigarette and cannabis use), peer deviance at age 15 and 10 (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 15 (level of communication, conflict and parental monitoring) and 9 (mother-child interaction and father-child interaction)

Table 6

Mediation by social factors (parent-daughter relationship quality and peer deviance) of the association between pubertal timing and substance use[1] unadjusted and adjusted[2] for confounders

Predictor	Outcome	Mediator	Estimates Total effect c (95% CI)	Estimates Direct effect c' (95% CI)	Estimates Indirect effect a (95% CI)	Estimates Indirect effect b (95% CI)
Peer deviance as mediator						
Pubertal timing	Alcohol	Number of alcohol drinking friends	-0.01 (-0.06, 0.04)	0.003 (-0.04, 0.05)	-0.04 (-0.07,0.001)	0.36 (0.30, 0.42)
			-0.01 (-0.05, 0.04)[2]	0.003 (-0.04, 0.05)[2]	-0.04 (-0.07,0.01)[2]	0.29 (0.23, 0.35)[2]
		Number of cigarette smoking friends	-0.01 (-0.06, 0.04)	-0.004 (-0.05, 0.04)	-0.02 (-0.06, 0.02)	0.30 (0.25, 0.35)
			-0.01 (-0.05, 0.04)[2]	-0.003 (-0.05, 0.04)[2]	-0.02 (-0.06, 0.03)[2]	0.23 (0.18, 0.28)[2]
		Number of cannabis using friends	-0.01 (-0.06, 0.04)	0.01 (-0.04, 0.05)	-0.05 (-0.10, -0.03)	0.32 (0.28, 0.37)
			-0.01 (-0.05, 0.04)[2]	0.004 (-0.04, 0.05)[2]	-0.05 (-0.09,-0.01)[2]	0.25 (0.20, 0.30)[2]
		Friends' delinquency	-0.01 (-0.06, 0.04)	0.001 (-0.05, 0.05)	-0.03 (-0.06, -0.03)	0.35 (0.28, 0.42)
			-0.01 (-0.05, 0.04)[2]	0.001 (-0.05, 0.05)[2]	-0.03 (-0.06,-0.01)[2]	0.25 (0.18, 0.33)[2]
	Cigarettes	Number of alcohol drinking friends	-0.12 (-0.18, -0.05)	-0.10 (-0.16, -0.03)	-0.04 (-0.07, -0.01)	0.53 (0.45, 0.61)
			-0.06 (-0.12,-0.02)[2]	-0.06 (-0.12,-0.03)[2]	0.002 (-0.04, 0.04)[2]	0.45 (0.39, 0.52)[2]
		Number of cigarette smoking friends	-0.12 (-0.18, -0.05)	-0.10 (-0.17, -0.04)	-0.02 (-0.06, 0.02)	0.69 (0.63, 0.75)
			-0.06 (-0.12,-0.04)[2]	-0.05 (-0.11, 0.01)[2]	-0.03 (-0.06, 0.01)[2]	0.32 (0.25, 0.40)[2]

Table 6 continued

Predictor	Outcome	Mediator	Estimates Total effect c (95% CI)	Estimates Direct effect c' (95% CI)	Estimates Indirect effect a (95% CI)	Estimates Indirect effect b (95% CI)
		Number of cannabis using friends	-0.12 (-0.18, -0.05)	-0.08 (-0.14, -0.02)	-0.05 (-0.10, -0.01)	0.66 (0.60, 0.73)
			-0.06 (-0.12,-0.02)[2]	-0.06 (-0.12,-0.03)[2]	0.002 (-0.04, 0.04)[2]	0.45 (0.39, 0.52)[2]
		Friends' delinquency	-0.12 (-0.18, -0.05)	-0.10 (-0.16, -0.03)	-0.03 (-0.06, -0.01)	0.60 (0.50, 0.70)
			-0.06 (-0.12,-0.04)[2]	-0.05 (-0.11, 0.05)[2]	-0.03 (-0.07, 0.02)[2]	0.27 (0.19, 0.35)[2]
	Cannabis	Number of alcohol drinking friends	-0.05 (-0.09, -0.01)	-0.04 (-0.07, 0.04)	-0.04 (-0.07, 0.04)	0.30 (0.25, 0.35)
			-0.03 (-0.06, 0.01)[2]	-0.02 (-0.06, 0.02)[2]	-0.03 (-0.07, 0.01)[2]	0.20 (0.16, 0.25)[2]
		Number of cigarette smoking friends	-0.05 (-0.09, -0.01)	-0.04 (-0.08, -0.01)	-0.02 (-0.06, 0.02)	0.34 (0.29, 0.38)
			-0.03 (-0.06, 0.01)[2]	-0.02 (-0.06, 0.01)[2]	-0.01 (-0.05, 0.03)[2]	0.24 (0.20, 0.29)[2]
		Number of cannabis using friends	-0.05 (-0.09, -0.01)	-0.02 (-0.06, 0.01)	-0.05 (-0.09, -0.01)	0.45 (0.42, 0.49)
			-0.03 (-0.06, 0.01)[2]	-0.01 (-0.05, 0.02)[2]	-0.04 (-0.08, 0.01)[2]	0.35 (0.32,0.39)[2]
		Friends' delinquency	-0.05 (-0.09, -0.01)	-0.03 (-0.07, 0.01)	-0.03 (-0.06, -0.01)	0.36 (0.30, 0.41)
			-0.03 (-0.06, 0.01)[2]	-0.02 (-0.06, 0.02)[2]	-0.03 (-0.06,-0.04)[2]	0.24 (0.18, 0.29)[2]
Parent-daughter relationship quality as mediator						
Pubertal timing	Alcohol	Parent-daughter communication	-0.01 (-0.06, 0.04)	-0.01 (-0.06, 0.04)	0.01 (-0.04, 0.05)	0.16 (0.11, 0.21)
			0.01 (-0.03, 0.06)[2]	0.01 (-0.03, 0.06)[2]	0.01 (-0.04, 0.06)[2]	0.09 (0.05, 0.14)[2]

Table 6 continued

Predictor	Outcome	Mediator	Estimates Total effect c (95% CI)	Estimates Direct effect c' (95% CI)	Estimates Indirect effect a (95% CI)	Estimates Indirect effect b (95% CI)
		Parent-daughter conflict	-0.01 (-0.06, 0.04)	-0.01 (-0.06, 0.03)	0.01 (-0.04, 0.07)	0.16 (0.12, 0.20)
			0.01 (-0.03, 0.06)[2]	0.01 (-0.04, 0.05)[2]	0.03 (-0.03, 0.08)[2]	0.09 (0.05, 0.14)[2]
		Parental monitoring	-0.01 (-0.06, 0.04)	-0.01 (-0.05, 0.04)	-0.01 (-0.06, 0.03)	0.32 (0.26, 0.37)
			0.01 (-0.03, 0.06)[2]	0.01 (-0.03, 0.06)[2]	-0.001 (-0.04, 0.04)[2]	0.21 (0.15, 0.26)[2]
	Cigarettes	Parent-daughter communication	-0.12 (-0.18, -0.05)	-0.12 (-0.18, -0.05)	0.01 (-0.04, 0.05)	0.27 (0.20, 0.33)
			-0.06 (-0.12,-0.04)[2]	-0.05 (-0.11, 0.01)[2]	-0.03 (-0.06, 0.01)[2]	0.33 (0.24, 0.42)[2]
		Parent-daughter conflict	-0.12 (-0.18, -0.05)	-0.12 (-0.18, -0.05)	0.01 (-0.04, 0.06)	0.30 (0.24, 0.36)
			-0.04 (-0.10, 0.01)[2]	-0.05 (-0.10, 0.01)[2]	0.02 (-0.03, 0.06)[2]	0.11 (0.05, 0.17)[2]
		Parental monitoring	-0.12 (-0.18, -0.05)	-0.11 (-0.18, -0.05)	-0.01 (-0.05, 0.03)	0.45 (0.37, 0.53)
			-0.04 (-0.10, 0.01)[2]	-0.04 (-0.10, 0.01)[2]	0.01 (-0.03, 0.04)[2]	0.18 (0.11, 0.24)[2]
	Cannabis	Parent-daughter communication	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.01)	0.01 (-0.04, 0.05)	0.14 (0.09, 0.18)
			-0.01 (-0.05, 0.02)[2]	-0.01 (-0.05, 0.02)[2]	0.02 (-0.03, 0.06)[2]	0.05 (0.02, 0.09)[2]
		Parent-daughter conflict	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.01)	0.005 (-0.05, 0.06)	0.14 (0.10, 0.17)
			-0.01 (-0.05, 0.02)[2]	-0.01 (-0.05, 0.02)[2]	0.02 (-0.03, 0.07)[2]	0.05 (0.02, 0.09)[2]

Table 6 continued

Predictor	Outcome	Mediator	Estimates Total effect c (95% CI)	Estimates Direct effect c' (95% CI)	Estimates Indirect effect a (95% CI)	Estimates Indirect effect b (95% CI)
		Parental monitoring	-0.05 (-0.09, -0.01)	-0.03 (-0.07, 0.01)	-0.01 (-0.05, 0.03)	0.28 (0.24, 0.33)
			-0.01 (-0.05, 0.02)[2]	-0.01 (-0.05, 0.02)[2]	0.004 (-0.04, 0.04)[2]	0.13 (0.09, 0.17)[2]

[1] Imputed data (see Methods)

[2] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and paternal alcohol, cigarette and cannabis sue), substance use at age 14 (alcohol, cigarette and cannabis use), peer deviance at age 15 and 10 (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 15 (level of communication, conflict and parental monitoring) and 9 (mother-child interaction and father-child interaction)

Path a: Indirect effect of pubertal timing on psycho-social factors at age 15

Path b: Indirect effect of psycho-social factor at age 15 on substance use at age 16

Total effect c: Effect of pubertal timing on substance use at age 16

Direct effect c': Effect of pubertal timing on substance use at age 16 while adjusting for psycho-social factor

Table 7

Moderation by pubertal timing of the relationship between substance use and social factors (parent-daughter relationship quality and peer deviance) [1, 2]

Predictor	Outcome	Moderator	Wald F(2, 1000)	p
Peer deviance as predictor				
Number of alcohol drinking friends	Alcohol	Pubertal timing	7.10	.03
Number of cigarette smoking friends			1.45	.48
Number of cannabis using friends			0.33	.85
Friends' delinquency			2.08	.35
Separate group analysis of the effect of the number of alcohol drinking friends on alcohol use: Early maturing girls (OR=1.82, 95% CI: 1.17, 2.83), on-time maturing girls (OR=3.45, 95% CI: 2.54, 4.70), late maturing girls (OR=4.24, 95% CI: 2.18, 8.23)				
Number of alcohol drinking friends	Cigarettes	Pubertal timing	1.60	.45
Number of cigarette smoking friends			0.12	.94
Number of cannabis using friends			0.32	.85

Table 7 continued

Predictor	Outcome	Moderator	Wald F (2, 1000)	p
Friends' delinquency			0.56	.76
Number of alcohol drinking friends	Cannabis	Pubertal timing	1.46	.48
Number of cigarette smoking friends			1.12	.57
Number of cannabis using friends			0.54	.76
Friends' delinquency			1.90	.39
Parent-daughter relationship quality as predictor				
Parent-daughter communication	Alcohol	Pubertal timing	1.18	.55
Parent-daughter conflict			3.87	.14
Parental monitoring			0.86	.65
Parent-daughter communication	Cigarettes	Pubertal timing	0.83	.66
Parent-daughter conflict			2.10	.35
Parental monitoring			0.31	.86
Parent-daughter communication	Cannabis	Pubertal timing	0.11	.95
Parent-daughter conflict			0.34	.84
Parental monitoring			0.13	.94

[1] Imputed data (see Methods)

[2] Adjusted for socioeconomic factors (financial difficulties, parental education), parental substance use (maternal and paternal alcohol, cigarette and cannabis use), substance use at age 14 (alcohol, cigarette and cannabis use), peer deviance at age 15 and 10 (number of alcohol, cigarette and cannabis using friends, having delinquent friends) and parent-daughter relationship quality at age 15 (level of communication, conflict and parental monitoring) and 9 (mother-child interaction and father-child interaction).