The aim of the current thesis was to examine the etiology of individual differences in alcohol use in adolescents and young adults. In this chapter we discuss the main findings presented in this thesis. A summary of the main findings is presented on page 137. We first evaluate the findings on prevalence and development of alcohol consumption in adolescents and young adults. Next, we discuss the role of parents, siblings and friends in alcohol use and the relative contribution of genes and environment. Finally some suggestions for future research are given.

ASPECTS OF ALCOHOL CONSUMPTION IN ADOLESCENTS AND YOUNG ADULTS

Alcohol consumption in adolescents and young adults develops across several stages of use. Most adolescents enter the initiation stage and the subsequent regular drinking stage, but not all young people enter the more advanced stage of problem drinking. The current thesis confirms the presence of these stages in a sample of adolescents and young adults. It reveals that the majority of Dutch adolescents initiated alcohol use before the age of 16. Questionnaires filled out between 1993 and 2000 show that 68%-88% of the 12-15-year-old males and 60%-85% of the 12-15-year-old females indicated that they ever drank alcohol (Chapter 2). Thirty percent of these 12-15-year-old participants reported that they initiated before the age of 13 (Chapter 5). Time trends revealed that 12-15-year olds drank more frequently and consumed more drinks a week in 2000 than in 1993 (Chapter 2). Several factors such as lack of restrictive policy on underage drinking, lack of reinforcement of laws, and allowance of alcohol advertisements in the Netherlands might account for this increase in juvenile drinking. The increase in alcohol use in this age group could also be related to the introduction of so-called alcopops and bottled mixed drinks during the 1990s. These drinks have a sweat taste that conceals the taste of alcohol, and are therefore easy to drink. Other European studies already indicated that the introduction of alcopops accounts for an increase in drinking among 13-16-year olds (Roberts et al., 1999; Romanus, 2000). Dutch research shows that alcopops and bottled mixed are among the most popular alcoholic beverages among students in secondary education (De Zwart et al., 2000; Ter Bogt et al., 2002).

At the age of 12-15-years, regular drinking (16%-29% in males and 11%-24% in females) and problem drinking (4% in males and 2% in females) were not very prevalent, but this thesis shows that regular drinking and problem drinking become more widespread in late ado-
Adolescence and young adulthood. About 70% to almost 90% of the 16-20-year-old and 21-25-year-old males and between 52% and 71% of the 16-20-year-old and 21-25-year-old females were regular drinkers (Chapter 4). Problem drinking was less prevalent. About 16%-33% of the 16-20-year-old and 21-25-year-old males and 5%-10% of the 16-20-year-old and 21-25-year-old females were problem drinkers (Chapter 8). Although problem drinking was less prevalent than regular drinking, both percentages are rather high, particularly in males. These figures on late adolescent and young adult male alcohol use are in line with other studies showing that regular drinking and problem drinking are particularly high in this group (Karam et al., 2007; Van Dijck & Knibbe, 2005).

Prevalence rates for lifetime alcohol use, frequency of drinking, quantity of drinking, lifetime drunkenness, frequency of drunkenness and problem drinking increased with age from age 12 until the age of 25, after which these rates decreased (except for lifetime alcohol use) (Chapter 2). This decrease of alcohol use after the age of 25 might be explained by a change in social role as in general the majority of the people over 25 start working, acquire a partner or become a parent, which has been shown to be associated with a decrease in drinking (Hajema & Knibbe, 1998).

In addition to the age effects on alcohol use, our study confirmed other studies on sex differences in alcohol use by showing that, except in the youngest age group (12-15) and on lifetime alcohol use, males exceed females on all aspects of drinking (e.g., De Zwart et al., 2000; Sutherland & Shepherd, 2001; Van Laar et al., 2002; Young et al., 2002). Sex differences in alcohol consumption might be partly caused by physiological differences in sensitivity to alcohol, as females are in general more sensitive to alcohol than males and, therefore, females need to drink less to obtain the same physical effects from alcohol as males (Ely et al., 1999; Frezza et al., 1990; Wilsnack et al., 2000). Nonetheless, physiological differences in sensitivity to alcohol do not explain sex differences in drunkenness. Sex differences in alcohol use might also be explained by socio-cultural factors. In western cultures a greater tolerance exists towards male drinking than towards female drinking. Drinking is often seen as a demonstration of masculinity, while drinking generally does not fit with expectations of females’ public behavior and feminine roles (e.g., Wilsnack et al., 2000).
**SUMMARY OF RESULTS**

Drinking of fathers and mothers is cross-sectionally related to regular drinking; Fathers’ drinking consistently predicts problem drinking in their offspring.

Drinking of siblings other than the co-twin hardly contributes to regular drinking and problem drinking.

Drinking of the co-twin is a strong risk factor for regular drinking, in particular cross-sectionally and over a short period of time; Drinking of the co-twin does not predict problem drinking.

Drinking of friends is cross-sectionally strongly associated with regular drinking; Drinking of friends is a risk for regular drinking and problem drinking over a period of two years but not over a period of seven years.

Friends’ drinking is cross-sectionally and over a short period in time more relevant than parental drinking, while over a longer period of time parents remain important and friends’ drinking is no longer relevant.

Genes are most important in explaining the variation of initiation of alcohol use in early adolescents (12-15-years old) (83% in males and 70% in females).

Common environment explains most of the variation of frequency of drinking in early adolescents (12-15-years old) (82% in both males and females).

Both genes and friends’ drinking explain the variation in frequency of drinking and regular drinking in adolescents and young adults (16-25 years).

Similarity in drinking between friends of twins moderated the estimates of heritability and common environment.

<table>
<thead>
<tr>
<th>Chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>3, 4, 6, 8</td>
</tr>
<tr>
<td>3, 4</td>
</tr>
<tr>
<td>3, 4</td>
</tr>
<tr>
<td>3, 4, 6</td>
</tr>
<tr>
<td>3, 4</td>
</tr>
<tr>
<td>3, 4, 6</td>
</tr>
<tr>
<td>3, 4, 6</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>7</td>
</tr>
</tbody>
</table>
THE ROLE OF FAMILY AND FRIENDS

In the current thesis genetic and environmental contributions to different stages of alcohol use in adolescents and young adults were examined. We will first discuss the role of alcohol use of family and friends from the viewpoint of social interaction and environmental mediation. Family members, unlike friends, share both genes and environment and thus there is no simple interpretation for an association between for example parental drinking and drinking behavior in their offspring. In the next sections we get back to genetic influences on alcohol use in adolescents and young adults, when analyzing the data from monozygotic (MZ) and dizygotic (DZ) twins.

PARENTAL ALCOHOL USE

Cross-sectional examination of associations between drinking of fathers and mothers and drinking in their offspring showed relative small associations for regular drinking (Chapter 3 and 4). This is in line with other studies on the role of parental alcohol use in young people’s drinking (e.g., Duncan et al., 1996; Li et al., 2002; Wood et al., 2004). These associations were persistent over two years and for mothers even over seven years of time (Chapter 4). Moreover, associations with problem drinking of adolescents and young adults were examined in a longitudinal design. In line with Ellickson et al. (2001) and Walden et al. (2007), results showed that fathers’ drinking was consistently related to problem drinking in their offspring (Chapter 8). Relatively frequent drinking of fathers at baseline predicted problem drinking in their children after two and even after seven years. This thesis indicates that drinking of both fathers and mothers contributes to alcohol use in their offspring, and it appears that mother’s drinking plays a larger role in regular drinking and that father’s drinking plays a larger role in problem drinking. However, it should be noted that both parents might be equally relevant to their offspring’s alcohol use, but due to the relatively strong similarities in parental drinking, this might not become visible in multivariate analyses. This is supported by the fact that our cross-sectional univariate analyses on regular drinking did not indicate significant differences between relative risks regarding drinking of fathers and drinking of mothers.

Chapters 3, 4 and 8 did not reveal sex differences in the associations between alcohol use of fathers and mothers and regular drinking and problem drinking in their offspring. We did not found
support for the assumption that alcohol use of the same-sex parent has a larger impact (Harburg et al., 1982; Newcomb et al., 1983). Fathers’ and mothers’ drinking has the same role in male and female regular drinking and problem drinking, as was also shown in other studies (Björkqvist et al., 2004; Seljamo et al., 2006).

**ALCOHOL USE OF SIBLINGS**

We found small or non-significant associations between drinking of siblings other than the co-twin and regular drinking and problem drinking of adolescents and young adults in both cross-sectional and longitudinal analyses (Chapter 3, 4 and 8). In contrast, drinking of the MZ and DZ co-twin was a strong risk factor for adolescent and young adult regular drinking, in particular cross-sectionally and over a short period of time (Chapter 3 and 4), but drinking of the MZ and DZ co-twin was not related to problem drinking over time (Chapter 8). Conclusions on the relative importance of twin siblings versus non-twin siblings in alcohol use of adolescents and young adults can only be drawn from relative risk analyses in Chapter 3. This chapter shows that, in particular in 12-15-year olds, regular drinking of MZ co-twins posed the highest risk for regular drinking, followed by same sex DZ co-twins, opposite sex DZ co-twins and non-twin siblings. One of the most important explanations for differences in the impact of MZ co-twins and DZ- co-twins and non-twin siblings are genetic differences. MZ twin siblings are likely to be more similar in alcohol use than non-twin siblings because they share all of their genes, while DZ twin siblings and non-twin siblings share about half of their genes. Twin siblings are also likely to be more similar in alcohol use than non-twin siblings as twins are of the same age. In adolescents and young adults variations in alcohol use are strongly age dependent and twin siblings may therefore be more similar in alcohol use. In addition, MZ and DZ twin siblings could be more important role models for each other than non-twin siblings and thus more strongly affect each other’s behavior. The Social Learning Theory (Bandura, 1977) indicates that modeling of behavior is likely to occur if a person is similar to the role model, for example in age or sex. However, such social interaction models in twins lead to strong predictions of differences in variances (for continuous traits; Boomsma, 2005) or differences in prevalence (for categorical traits; Carey, 1992). We did not obtain evidence that such mechanisms play an important role. Finally, siblings who are close in age (or of the same age in case of twins) are likely to spent time together at home or outside home throughout adolescence. This might result in more shared experiences within the family environment, at school and with friends Boyle et al. (2001), and might lead to similarities in drinking.
FRIENDS’ ALCOHOL USE

Not only alcohol use of parents and siblings might play a role in the development of alcohol use in adolescents and young adults, but also factors outside the family might be relevant. During adolescence young people try to develop an identity independent from their families and spent an increasing time with their friends. Friends might be important role models for alcohol use, because adolescents tend to conform to peer norms during this period.

Cross-sectional analyses in our studies showed that friends’ drinking was strongly associated with adolescent and young adult regular drinking (Chapter 3, 4 and 6). In line with other studies on predictors of adolescents’ regular drinking over a short period of time (Andrews et al., 2002; Ary et al., 1993; Beal et al., 2001; Bot et al., 2005a, Engels et al., 1999; Graham et al. 1991; Reifman et al., 1998; Urberg et al., 1997; Webster et al., 1994; Windle, 2000; Wood et al., 2001), we found that friends’ drinking was a risk for adolescent and young adult regular drinking prospectively, over a period of two years (Chapter 4 and 6). Problem drinking was only examined longitudinally, and these analyses showed, in line with longitudinal analyses on adolescent heavy alcohol use (Griffin et al., 2000; Guilamo-Ramos et al., 2004; Ouellette et al., 1999; Reifman et al., 1998; Tucker et al., 2003) and problem drinking (Ellickson et al., 2001; Windle, 2000) that friends’ drinking was a risk for adolescent and young adult problem drinking over a period of two years. Over a period of seven years, drinking of friends at baseline was no longer a risk factor for regular drinking and problem drinking in young people. It is striking that cross-sectionally and over a short period in time drinking of friends is more relevant to adolescent and young adult drinking than drinking of parents, while over a longer period of time parents remain important and friends’ drinking is no longer relevant (Chapter 4 and 8).

Cross-sectionally and over a short period of time friends might function as role models for young people’s drinking and in that way they actually have an impact on alcohol consumption. However, it should be noted that similarity between friends’ drinking and young people’s alcohol consumption not only results from influence of friends but might also stem from peer selection. Peer selection is the process in which friendships are formed on the basis of common behavior, such as, for example, alcohol use. Several studies argue that the influence of friends in the development of alcohol use in young people might be less significant than is often assumed, because friendships could be formed on basis of common alcohol use (peer selection) (Andrews et al., 2002; Bauman & Ennett, 1996; Engels et al., 1997; Fisher & Bauman, 1988; Sieving et al., 2000). Jaccard et
al. (2005) showed that peer influence was limited if peer selection effects were controlled for. According to the authors, peer influences are often overestimated and are probably not more important than parental influences.

Moreover, not all adolescents are affected in similar ways by alcohol use of their friends, and some adolescents might be more susceptible to peer influence than others. Adolescents who indicate to have a high quality friendship (Jaccard et al., 2005) and adolescents who indicate to have few conflicts in their friendships (Urberg et al., 2003) are more likely to be susceptible to peer influence. Moreover, several personality characteristics have been found to be related to susceptibility to peer influence (Engels et al., 2005; Vitaro et al., 2000). In Chapter 6 of this thesis we examined whether relationship quality with the best friend and individual’s personality characteristics, such as extraversion and agreeableness, moderated the association between alcohol use of best friend’s and alcohol use of adolescents. These findings did not reveal differences in susceptibility to peer influence according to relationship characteristics and individual’s personality. They also illustrate the robustness of lack of strong longitudinal effects of friends’ drinking on adolescent alcohol use, as we did not find significant effects of friends’ drinking in subgroups which might be more susceptible to peer influence.
GENETIC AND ENVIRONMENTAL INFLUENCES ON ALCOHOL USE

Variation in alcohol use in adolescents and young adults can be explained by both genetic and environmental factors. In this thesis (Chapter 5 and 7) we used the genetically informative twin design to examine the relative contribution of genes and environment to individual differences alcohol use in adolescents and young adults. Twin studies have shown that estimates of genetic and environmental influences strongly depend upon age and upon the phenotype that is analyzed. Different indicators of alcohol use may lead to different conclusions regarding heritability. It is important, when analyzing drinking behavior, to take into account the developmental stage of young people (e.g., Hopfer et al., 2003; Viken et al., 1999). In the current thesis, the etiology of variation in initiation of alcohol use and frequency of drinking in early adolescents (12-15-years old) and regular drinking in middle and late adolescents and young adults (16-25-years old) was examined in two separate studies.

GENES AND ENVIRONMENT IN EARLY ADOLESCENTS

This thesis shows that genetic factors were most important in explaining the variance of early initiation of alcohol use in early adolescents (12-15-years old), as they explained 83% of the variance in males and 70% of the variance in females. A much smaller part of the variance in early initiation of alcohol use in this group was explained by common environmental factors (2% in males and 19% in females) (Chapter 5). Previous studies showed that initiation of alcohol use was moderately heritable and largely explained by common environmental influences (Fowler et al., 2007a; Koopmans & Boomsma, 1996; Maes et al., 1999; Pagan et al., 2006; Rhee et al., 2003; Rose et al., 2001; Viken et al., 1999). Differences in findings between previous studies and our findings are likely to be explained by differences in phenotype and differences in age between samples. Most other studies mainly examined older adolescents or adolescent samples that were less homogeneous in age (i.e. samples with an age range of 11-19-years). In this thesis we focused on early adolescence as this is the period in which alcohol initiation usually takes place. In contrast to previous study we focused on early adolescent initiation. We made a distinction between adolescents who never initiated, adolescents who
initiated at age 13 or after and adolescents who initiated before the age of 13. Early adolescent initiation has been shown to be related to negative consequences in later life, such as heavy alcohol use, problem drinking and alcohol dependence (Grant et al., 2001; Hawkins et al., 1997; Kuntsche et al., 2008; Pitkänen et al., 2005). Unlike other studies our assessment of initiation of alcohol use perhaps discriminated between more problematic (and genetically induced) early adolescent initiation and later adolescent initiation or abstinence until the age of at least 16.

In addition, common environmental factors explained most of the variance of frequency of drinking in 12-15-year olds (82% of the variance in both males and females), while genetic factors were not involved in the explanation of the variance of frequency of drinking (Chapter 5). Common environmental factors are those influences from the environment that twins who grow up in the same family have in common and that differ between families. These influences tend to make twins from the same family similar to each other, regardless of zygosity. In early adolescence, twins have the tendency to spend a lot of time together and therefore they have shared experiences at home and outside home such as at school and with friends. Variation between families of early adolescents might be caused by parental attitudes and norms towards alcohol use and some parents might set more strict rules towards their children’s alcohol use than others (Van Der Vorst et al., 2008b). Also availability of alcohol and access to alcohol might differ between early adolescents of different families.

We were the first to test whether and to what degree the same factors were related to individual differences in initiation of alcohol use and frequency of drinking in a young group of adolescents that were relatively homogeneous in age. We found that genetic and unique environmental factors were specific for variation in initiation and frequency of drinking, thus variation in initiation and frequency of drinking were explained by different genetic and unique environmental factors. In females, common environmental factors were also specific for variation in initiation of use and frequency of drinking, while in males mostly the same common environmental factors explained the variances in initiation of alcohol use and frequency of drinking (Chapter 5).

These findings indicate that different prevention strategies need to be designed for adolescents who have not yet started to use alcohol and who already have initiated alcohol use, as different factors explained initiation of alcohol use and frequency of drinking. This thesis shows that there is a genetic predisposition for starting
to use alcohol at an early age. Consequently prevention of alcohol initiation should ideally include identification of genetically predisposed adolescents. However, identification and screening based on a person’s genetic makeup is yet technically not well developed and it is still not widely accepted by society. It certainly is possible to pay attention to offspring of parents who misuse alcohol, as these children probably have a hereditary higher risk for early alcohol initiation. Alternatively, the roles of parents in preventing adolescents to start drinking alcohol or to start drinking frequently could be stressed. Most Dutch adolescents start drinking alcohol at home in the presence of their parents (Engels, 1998). Van Der Vorst et al. (2008b) indicated that parents can control alcohol use of their children effectively. Prevention programs may be used, as indicated by Van Der Vorst and colleagues (2008b), to enhance parents’ awareness of their powers to postpone the age of alcohol initiation of their children and to encourage parents to provide and maintain strict rules about their adolescent’s drinking.

Once early adolescents have initiated alcohol use, common environmental effects predominate as influences on variation in frequency of drinking. These common environmental effects might incorporate factors from inside the family, such as drinking of parents and rules and norms of parents about alcohol use. Many Dutch parents allow adolescents to drink alcohol at home (e.g., Van Der Vorst et al., 2005) and about half of the Dutch early adolescents report to drink with their parents (NIGZ, 2006). In addition to intra-familial influences the common environment might include extra-familial influences such as shared peer effects. Adolescent siblings are likely to spent time together outside home, which results in shared experiences with friends (Boyle et al., 2001).

In addition, Chapter 5 implies that for a part the variance of frequency of drinking in males is explained by different common environmental factors than frequency of drinking in females. This sex difference might have its origin in differences in pubertal development in early adolescence as girls mature earlier than boys (Dick et al., 2000). Adolescents tend to form an identity independent from their parents and foster tighter bonds with their peers during adolescence. Girls do this earlier than boys because they mature earlier, which might imply that girls are more influenced by their peers than boys in early adolescence. Studies on this topic showed that early maturing girls are likely to affiliate with older and deviant peers (Caspi et al., 1993). Associations presented in Chapter 3 of this thesis indeed showed a trend being indicative that friends’ drinking was a greater risk factor for drinking in females compared to males (Chapter 3).
GENES AND ENVIRONMENT IN LATE ADOLESCENTS AND YOUNG ADULTS

With regard to alcohol use in adolescents and young adults (16-25 years) this thesis shows that both genes and friends’ drinking are relevant in explaining the variation in frequency of drinking and regular drinking. Our study was the first to examine the moderating effect of similarity in drinking between friends of twin 1 and friends of twin 2 on estimates of heritability and common environment. Findings indicate that genetic factors were more important in the explanation of variation in alcohol use in twins with behaviorally different friends (47%-50% explained variance for frequency of drinking and 33%-36% explained variance for regular drinking in males and females respectively) than in twins with behaviorally similar friends (19%-21% explained variance for frequency of drinking and 14%-15% explained variance for regular drinking in males and females respectively). In contrast, common environmental effects were less important in the explanation of variation in alcohol use in twins with behaviorally different friends (18%-19% explained variance for frequency of drinking and 34%-36% explained variance for regular drinking in males and females respectively) than in twins with behaviorally similar friends (53%-56% explained variance for frequency of drinking and 66%-69% explained variance for regular drinking in males and females respectively) (Chapter 7).

The estimates of explained variance detected in other twin studies were more or less in line with our results for twins with friends with different alcohol use. Other twin studies assessing alcohol use in adolescents aged 16 years and older indicated that genetic factors accounted for about 40% and common environmental factors for about 30% of the variance in frequency of drinking in 16-17-year olds (Pagan et al., 2006; Viken et al., 1999). In young adults aged 25 the variance of frequency of drinking in males was mainly explained by genes (48%) and for 8% by common environment. In females heritability was 19% and common environment explained 31% (Pagan et al., 2006). The genetic components detected in these studies were higher than the genetic component in twins with friends with similar alcohol use. The estimates of the common environmental factors in previous twin studies were lower than the common environmental factors in twins with friends with similar alcohol use in our study.

This thesis seems to provide contrary findings with regard to the importance of friends in young people’s alcohol use. In Chapter 7 the role of friends in alcohol use appeared to be evident, but according to findings described in Chapters 3, 4, 6 and 8 the role of friends’ drinking in young people’s alcohol use is less prominent. We suspect
that differences in findings are caused by differences in cross-sectional or short-term longitudinal investigation versus long-term longitudinal investigation. We think that longitudinal examination of influences of friends over a longer period of time might lead to underestimation of the role of friends in young people’s alcohol use. As friendships change rapidly during adolescence (Ennett & Bauman, 1994), influences of friends on adolescent alcohol use can only be detected in longitudinal designs with short-term follow-up assessments. This reasoning is in line with observational, correlational and experimental studies showing that strong direct imitation effects of peers in drinking contexts such as bars (Bot et al., 2007; Larsen, Engels, Granic & Overbeek, 2008; Quigley & Collins, 1999).