Published in final edited form as:
Alcohol Clin Exp Res. 2014 August ; 38(8): 2314–2321. doi:10.1111/acer.12491.

Adolescent Alcohol Abuse and Adverse Adult Outcomes: Evaluating Confounds with Drinking-Discordant Twins

Richard J. Rose, Ph.D.[1,2], **Torsten Winter, Ph.D.**[2], **Richard J. Viken, Ph.D.**[1], and **Jaakko Kaprio, M.D., Ph.D.**[2,3,4]

[1]Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana, USA
[2]Department of Public Health, University of Helsinki, Helsinki, Finland [3]Department of Mental Health and Substance Abuse Services, National Institute for Health and Welfare, Helsinki
[4]Institute for Molecular Medicine FIMM, University of Helsinki, Finland

Abstract

Background—Adolescent alcohol abuse is associated with adverse outcomes in early adulthood, but differences in familial status and structure and household and community environments correlate with both adolescent drinking and adverse adult outcomes and may explain their association. We studied drinking-discordant twin pairs to evaluate such confounds to ask: Will between-family associations replicate in within-family comparisons?

Methods—With longitudinal data from > 3,000 Finnish twins, we associated drinking problems at age 18½ with 13 outcomes assessed at age 25; included were sustained substance abuse, poor health, physical symptoms, early coital debut, multiple sexual partners, life dissatisfaction, truncated education, and financial problems. We assessed associations among twins as individuals with linear regression adjusted for correlated observations; within-family analyses of discordant twin pairs followed, comparing paired means for adult outcomes among co-twins discordant for adolescent problem drinking. Defining discordance by extreme scores on self-reported problem drinking at age 18½ permitted parallel analyses of twins as individuals and discordant twin pairs. Alternate definitions of pair-wise discordance and difference score correlations across the entire twin sample yielded supplementary analyses.

Results—All individual associations were highly significant for all definitions of discordance we employed. Depending on definitions of discordance, 11 to 13 comparisons of all drinking-discordant twin pairs and 3 to 6 comparisons of discordant monozygotic twin pairs replicated between-family associations. For most outcomes, effect size attenuated from individual level analysis to that within discordant MZ twin pairs providing evidence of partial confounding in associations reported in earlier research. The exception was the General Health Questionnaire; at age 25, GHQ-12 had equivalent associations with age 18½ RAPI across all comparisons.

Corresponding Author: Richard J. Rose, Department of Psychological and Brain Sciences, 1101 East 10th Street, Indiana University, Bloomington, Indiana 47405-1301 812-855-8770; fax: 812-855-4691; rose@indiana.edu.

Conclusions—Our analyses control for shared family background, and, partly or fully, for shared genes, to yield within-family replications and more compelling evidence than previously available that adolescent alcohol abuse disrupts transitions into early adulthood.

Keywords

Discordant Twin comparisons; Alcohol Exposure; Adverse Outcomes

More than a quarter-century ago, Kandel et al. (1986) evaluated social/behavioral consequences of adolescent substance use in a 9-year follow-up of adolescents initially studied at ages 15–16. Twenty adult outcomes, including sustained substance use, transitions into work and family roles, educational attainment, and physical health were assessed. Adverse effects of adolescent drug use were found on all 20 measured outcomes.

Subsequent research confirms robust associations of adolescent alcohol abuse with diverse negative outcomes: continuity of problem drinking into early adulthood (Englund et al., 2008; McCarty et al., 2004), enhanced risk of adult alcohol dependency (Bonomo et al., 2001; 2004; Chassin et al., 2002), earlier age at first coitus and multiple sexual partners (Fergusson and Lynskey, 1986; Guo et al., 2002; Wells et al., 2004), truncated education (Delucchi et al., 2007; Hill et al., 2000; Tucker et al., 2003), unemployment (Ellickson et al., 2003), homelessness, psychiatric morbidity, and downward social mobility (Viner and Taylor, 2007).

Yet a central uncertainty remains. Are associations of adolescent alcohol abuse with adverse adult outcomes explained by differences in familial background and shared genetic influences?

Adolescent problem drinking might associate with adverse adult outcomes solely because of between family confounds. Parental drinking, parenting practices, familial socioeconomic status and structure, school and neighborhood characteristics are associated with both drinking patterns in adolescence and behavioral outcomes in early adulthood that are self-recognized as adverse (e.g., truncated education, constrained financial circumstances) or outcomes research links to negative consequences (e.g., early coitus, multiple sexual partners). Similarly, the association between adolescent problem drinking and adverse adult outcomes could be due to their shared genetic influences.

Are apparent effects of alcohol exposure in late adolescence due to uncontrolled confounding (McCambridge et al., 2011)? Sibling comparisons (Susser et al. 2010) are useful in detecting familial confounding, and within-family analyses of exposure-discordant twin pairs are especially informative (McGue et al., 2010). Our earlier reports evaluating associations of pubertal timing with substance use (Dick et al., 2000), of personal, peer, and family factors with illicit drug use (Korhonen et al., 2008), and of adolescent physical inactivity with adult smoking (Kujala et al., 2007) illustrate. Discordant twin comparisons offer a practical, powerful analytic strategy for evaluating confounds in observational research. In idealized experiments, individuals serve as their own controls; we observe their outcomes when exposed, and at the same time, when not. That study is impossible, but exposure-discordant monozygotic (MZ) twin pairs approximate it. If there is a causal

connection between adolescent alcohol exposure and adverse outcomes, the association between drinking and outcomes *within* families will approach that observed *between* families. Outcome differences between exposure-discordant co-twins will be as great as those for unrelated singletons who similarly differ in exposure. Conversely, if between-family associations of problem drinking with adverse outcomes are entirely due to confounds shared by twin siblings (e.g., household and neighborhood environments), co-twin differences in drinking exposure will not associate with co-twin differences in adverse outcomes. Partial confounding, perhaps the more likely scenario, will attenuate effect size from individual level analyses to comparisons of all discordant same-sex twins, with further attenuation evident in comparisons limited to discordant MZ twins.

We associated adolescent drinking problems with early adult outcomes in a large population-based sample of twin individuals and then identified drinking-discordant twin pairs within the sample and used matched-pair comparisons of their mean differences in measured outcomes. Our analyses evaluate the impact of potential confounds from childhood family history and familial-genetic background in associations of adolescent drinking with adverse outcomes in early adulthood.

Strong inferences drawn from our co-twin control analyses assume that outcome differences observed in drinking-discordant twins are due to differences in their exposure to alcohol. But what led to discordant drinking patterns among adolescent MZ co-twins? To assess stability of within-pair differences in alcohol exposure, we compared frequency of drinking and frequency of intoxicating reported at age 16 among MZ twin pairs discordant for problem drinking reported at age 18½. And following suggestions of Stanek, et al (2011), we compared MZ co-twins from drinking-discordant pairs for three prospective predictors of drinking from personality assessments made when these twins were ages 16 and 17, some 18 to 30 months prior to their self-reported drinking-related problems at age 18½.

MATERIALS AND METHODS

Sample

We analyzed data obtained from questionnaires administered in the *Finn Twin 16–25* study (Rose et al., 1999; Kaprio et al., 2002). The study began in 1991, when Finnish twin pairs born 1975-79, with both members alive and resident in Finland, were sequentially enrolled over five years time, within 60 days of their 16th birthdays. The five birth cohorts contained 3,065 twin pairs eligible for study, and both co-twins in 2,733 pairs (89%) completed baseline questionnaires. Follow-up questionnaires were sent to all respondent twins at ages 17, 18½, and 23–27 (average age 25 and hereafter described as such) with participation rates >83% across occasions. At age 18½, twins completed a 22-item version of the Rutgers Alcohol Problem Index (RAPI; White and Labouvie, 1989), reporting drinking-related problems they experienced during the preceding 18 months. RAPI effectively screens adolescent problem drinking in different cultures (Koposov et al., 2002; Pedersen and Skrondal, 1998; Viken et al., 2007), and with a subset (N = 597) of twins studied here, we found RAPI scores at 18½ predictive of interview diagnoses of alcohol dependency/abuse at age 25 (Dick et al., 2011). In analyses we now report, we used age 18½ RAPI scores to identify individual twins with drinking-related problems in late adolescence. We then

selected a set of questionnaire items included in the fourth-wave assessment at age 25 as outcome measures.

Zygosity was determined from validated items in baseline questionnaires separately sent to twins and their parents. DNA was obtained to confirm zygosity in >750 same-sex adolescent Finnish twin pairs enrolled in laboratory protocols, and results confirmed questionnaire-assigned zygosity in 95%.

Study protocols were approved by Indiana University's IRB and the Ethics Committee of the University of Helsinki. Written permission to contact twins at age 16 was provided by their parents; that triggered mailing individual questionnaires to twins, whose participation was voluntary at each assessment wave.

Measures and Procedures

We identified twins with drinking-related problems in late adolescence by determining, as closely as distributions allowed, the upper quintile (Q5) in gender-specific RAPI scores. Males had slightly higher RAPI scores at age 18½, and we used a cutting score one item greater for males (a score >13 from the 22 items) than for females to approximate equivalent Q5 cut-offs. We then contrasted outcomes in two groups of individual twins in the entire sample, comparing those with a RAPI score in Q5 with all others. Contrasts of individual twins, and subsequent contrasts of co-twins, discordant for Q5 RAPI membership are traditional contrasts of cases vs. controls, but the twin structure of our data permits us to confirm between-family comparisons in within-family contrasts of discordant co-twins.

However, the Q5 versus Q1–4 definition of discordance ignores its magnitude; it may contrast individual twins, and identify as discordant pairs, twins with but a single point difference in adolescent RAPI scores, if those scores fall immediately adjacent to the Q5 cut. To assess the sensitivity of our findings to different definitions of discordance, we conducted several supplemental analyses. In the first, we deleted twins whose scores fell within the 70^{th}–80^{th} percentiles of their RAPI-distributions and effectively contrasted the upper 20% with the lower 70%, rather than the initial 20/80 split. Samples are smaller, but minimal intra-pair discordance is greater. In a second supplementary analysis, applicable only to twin pairs, we used a measure of absolute intra-pair differences for the RAPI measure of adolescent problem drinking to identify discordant pairs, and ignored the magnitude of drinking-related problems reported by either twin. We identified an absolute difference in RAPI scores for all twin pairs that best approximated the sample size obtained from the Q5 *vs*. Q1–4 split; that difference was 9 or more scored items on the 22-item RAPI scale we used. In a third supplementary analysis, we studied intra-pair differences in RAPI scores as a continuous risk factor and correlated signed differences in RAPI scores with signed differences in each outcome for our entire sample of twins with no exclusions, and then, separately, for the subset of MZ twin pairs.

Using several definitions of exposure-discordant twin pairs, and correlating differences across all twins without exclusions, these supplementary analyses tested the robustness of within-family associations of adolescent problem drinking with adverse outcomes.

Thirteen measures of social/behavioral outcomes were selected from the age 25 questionnaire. The first assessed continuity of drinking-related problems with the Malmö-modified Michigan Alcohol Screening Test (Mm-MAST). Created as a 9-item, dichotomously scored screen for application to binge-drinking Nordic cultures (Kristenson and Trell, 1982; Seppa et al., 1990), our adaptation of the Mm-MAST added two items ("After you have taken a drink, do you find it hard to stop?" and "Have you ever felt that anyone close to you thinks you should drink less?") to enhance coverage of DSM diagnostic criteria for alcohol dependency.

To this measure of adult problem drinking, we added 12 other outcomes from four domains, assessing each with 3 items. The three measures of current substance use at age 25 were: (i) frequency of drinking to intoxication, and (ii) frequency of high density drinking on a single occasion (consuming >5 bottles of beer, or one bottle of wine or half a bottle of spirits), both offering 9 response alternatives from "never" to "daily", and (iii) quantity of cigarette smoking, with 7 alternative responses, from having never smoked to currently smoking 20 or more cigarettes daily.

Subjective poor health and physical symptoms were assessed with three outcomes: (i) the 12-item General Health Questionnaire or GHQ-12 (Goldberg, 1972; Goldberg et al., 1997; (ii) subjective evaluation of present health with 5 alternative responses from "very good" to "very poor"; and (iii), a 6-symptom checklist (headaches, abdominal pain, low back pain, pain in upper back or neck, tension/nervousness, sleeping difficulties) with a 4-point frequency alternative for each symptom, yielding a response range of 6–24.

Three questionnaire items evaluated social and sexual relationships: the twins' reported age (in years) at first coitus; multi partner cohabitation, ("partners with whom you lived for some time", with 4 numerical response alternatives), and number of sexual partners, with 5 response alternatives.

Three final outcomes assessed transitions into adulthood: four items measuring life satisfaction as "interesting", "happy", "easy", and "lonely" yielded scores from 4 to 16; level of education with 5 response alternatives from completing only the compulsory nine years of school to earning a university/technical school degree; and self-reporting one's "present" financial situation, with 5 alternative responses from "very good" to "very bad".

For some twins, several 'outcomes' temporally preceded the 'predictor' at age 18½; e.g., twins who terminated their formal education at their first opportunity (after completing grade 9 in Finland) did so at age 16, and coital debut for many twins preceded age 18½. Other outcomes, including smoking and drinking patterns, GHQ-12, Mm-MAST, life satisfaction, physical symptoms, and financial circumstances were reported within a concurrent, or recent, time frame at age 25.

Response alternatives for all outcomes were uniformly ordered so that higher scores reflected more adverse outcomes; we then compared mean values of each outcome variable for the high and low RAPI members of each discordant pair using simple t-tests. To maximize samples for analyses, we first conducted these comparisons for our full sample of

all same-sex twin pairs including those of uncertain zygosity, and then, for comparison, for the subset of RAPI-discordant MZ twin pairs.

Finally, we asked whether MZ co-twins from pairs discordant for problem drinking at age 18½ differed for prospectively assessed personality risk factors. We had two prospective predictors obtained from the baseline questionnaire administered at age 16 and a third from the 2nd-wave at age 17. The first is the 12-item MMPI scale of Religious Fundamentalism (REL; Wiggins, 1966). More religious adolescents are more likely abstinent, and among all twin pairs in this sample, those concordant for high REL scores at age 16 were less likely discordant for concurrent alcohol use (Winter, Karvonen, Rose, 2013). A second relevant MMPI scale assessed at age 16 is the 50-item Pd or Scale 4 (Dahlstrom et al, 1972). Earlier analyses of data from this sample (Viken, Kaprio & Rose, 2007) found lagged correlations between Pd scores at 16 and RAPI scores at 18½ of ~ 0.35. Accordingly, we asked whether MZ co-twins from pairs discordant for Q5 RAPI scores in late adolescence were discordant as well for their REL and Pd scores assessed 30 months earlier. A 24-item abbreviated version of the Sensation Seeking Scale (SSS; Zuckerman, 1979) was included in the questionnaire administered at age 17; because SSS and its subscales are predictive of drinking behaviors (Hittner & Swickert, 2006), we tested whether RAPI-discordant MZ twins were discordant for SSS measured 18 months earlier.

RESULTS

Subjects

A total of 4,621 individual twins, 2,057 males and 2,564 females, returned both questionnaires, but missing data for RAPI at age 18½ and/or outcome measures at age 25 reduced study samples, and we limited our analyses to same-sex twin pairs. To enhance power for comparisons of RAPI-discordant twins, we used all available data, including, in individual-level analyses, unpaired twins for whom we lack data from the co-twin and, in discordant twin comparisons, pairs of uncertain zygosity. Our sample included 3,072 individual twins with complete data on RAPI and some or all measured outcomes at age 25. Using cutting scores of > 13 for males and >12 for females on the 22-item RAPI, we identified 538 individual twins as adolescent problem drinkers (approximating Q5 and hereafter so described). For initial discordant pair analyses, we used identical cutting scores and identical contrasts of membership in Q1–4 *vs*. Q5 as for individual-based analyses; in doing so, we identified 269 same-sex twin pairs discordant for RAPI. Included were 146 DZ (plus 11 brother-brother and sister-sister pairs of uncertain zygosity) and 112 MZ pairs. Drinking-discordant twin pairs were disproportionately twin sisters reflecting greater concordance for drinking patterns and drinking problems among twin brothers.

We first identified individual twins whose RAPI score placed them at or above the 80th percentile of gender-specific distributions and compared them to all other twins in the full sample. Table 1 presents results of this comparison of outcomes among individual twins and of twin pairs discordant for Q5 RAPI scores. The first columns of results compare all twins as individuals, with correction for correlated observations within families (*Stata* SE13), showing mean differences between those in the upper 20% and all remaining individuals, its 95% confidence interval or CI, and the one-tailed significance of the corresponding t-test.

All individual-level associations were highly significant, consistent with previous results from between-family study of non-twin subjects. Individuals who report heavy drinking or drinking-related problems in adolescence report more behavioral problems in early adulthood; our results confirm these associations in individual-level analyses of Finnish twins.

The middle set of results in Table 1 document associations for all drinking-discordant same-sex twin pairs. Mean differences significantly differ in patterns consistent with results found for twins as individuals: the co-twin reporting higher-RAPI scores at 18½ reported having experienced the more adverse outcome for 11 of the 13 outcomes we studied. The magnitude of effect is attenuated in most, *albeit not all* within-family comparisons, but eleven of these associations robustly replicate in within-family discordant sibling comparisons.

The far right columns of Table 1 present results for the subset of RAPI-discordant MZ twin pairs within our sample. Controlling for shared genes as well as shared childhood environments further attenuates the magnitude of effect in most associations (with GHQ-12 again the exception), but co-twin differences for three outcomes, continuity of problem drinking, multiple sexual partners, and elevated scores on GHQ-12, remain significant, and several others approach significance.

The results in Table 1 use all discordant pairs identified by the Q5 *vs*. Q1–4 cut. Pairs in which the difference in RAPI scores was but a single point, separating the Q5 cut from Q4 were included. To examine effects of such negligible intra-pair discordance, we re-ran these analyses, using a 20/70 split, limiting the contrast to pairs in which the RAPI score of the lower scoring co-twin was below the 70th percentile. This restriction deleted ~12% of individual twins, ~20% of all same-sex twin pairs, and >25% of discordant MZ pairs, reducing the number of all discordant twin pairs to 195–217 and the subset of discordant MZs pairs to 75–82. Results (Table 1; Supplementary Material), as expected, reveal enhanced individual and intra-pair mean differences. Mean differences were increased in 12/13 outcomes for all discordant twin pairs, but with reduced samples, confidence intervals were enlarged, as well. With the exception of greater life dissatisfaction, all measured outcome associations were significant in contrasts of the full sample of discordant twin pairs and three outcome associations (elevated Mm-MAST scores, multi-partner cohabitation, and multiple sexual partners) reached significance in contrasts of the subset of discordant MZ pairs; association with elevated GHQ scores in this smaller subsample of RAPI-discordant MZ pairs was marginally significant, p =.055.

Either of these approaches to identifying discordant twins ignores pairs with large intra-pair differences in RAPI in which neither member of the pair had a RAPI score above Q5. In an alternate approach, we identified an absolute intra-pair difference in RAPI scores that yielded sample sizes of discordant twins comparable to the samples identified by the 20/80 split. Cutting at a difference >8 on the 22-item RAPI yielded a sample of comparable size, and its overlapping membership with that formed by the 20/80 split correlated but moderately, ~0.65. Table 2 presents these results, first from comparisons of all discordant same-sex twin pairs, collapsed on zygosity. Mean differences for most outcomes exceed

those shown in Table 1, and all 13 associations were highly significant using this categorization of discordance. The higher scoring RAPI twin, in pairs with a RAPI difference >8, reported a significantly more adverse outcome at age 25 for every outcome we assessed. Results for the subset of MZ twins meeting this definition of RAPI-discordance are shown in the second column of Table 2. Again, scores on Mm-MAST and the General Health Questionnaire significantly differ in discordant MZ twin pairs; associations with life (dis)satisfaction and a larger number of sexual partners approach significance, and educational attainment is significantly truncated among the higher RAPI-scoring MZ co-twin with this definition of drinking-discordance. And again, for GHQ-12, there is no attenuation of effect size among discordant MZ pairs from that found for the full sample of all discordant same-sex twin pairs.

All correlations of signed intra-pair differences in RAPI with intra-pair differences in outcomes were of modest magnitude, and only one of 13 exceeds 0.2. But in the full sample of twin pairs (N >1,380), all difference correlations were statistically significant, and six outcomes, elevated scores on Mm-MAST and GHQ-12, multiple physical symptoms, life dissatisfaction, multiple sexual partners by age 25 and truncated education, remained significant in difference score analysis of MZ twin pairs (Table 2 of Supplementary Materials).

Our exploratory analyses found no evidence that higher-scoring twins in RAPI-discordant MZ pairs differed from their lower scoring co-twins for three dispositional risk factors for alcohol exposure assessed 18 to 30 months earlier. As expected, mean scores for Pd and SSS were slightly higher, and REL scores slightly lower, among higher-scoring twins, but none of these differences approached statistical significance. We then compared co-twins from RAPI-discordant MZ pairs for the frequency of drinking and frequency of drinking to intoxication they reported at age 16. Both mean differences significantly differed, with the higher-RAPI scoring twins reporting more frequent drinking and more frequent intoxicating than their MZ co-twins (p <.01; paired t-tests). MZ twins discordant for drinking-related problems in late adolescence significantly differed in alcohol exposure at age 16.

DISCUSSION

Our research yielded five results for discussion. First, previous research findings associating problem drinking in late adolescence with adverse outcomes reported in early adulthood were robustly replicated in individual-based analyses of our large population-based sample of Finnish twins. For all 13 measured outcomes at age 25, the more adverse outcome was significantly more likely among individual twins with elevated drinking problems at age 18½ in quantitative comparisons of outcome means of twins as individuals. At the individual level, between-family associations of adverse consequences in early adulthood with problem drinking in late adolescence replicate across cultures and across a range of behavioral outcomes.

Second, we could replicate nearly all between-family associations in within-family comparisons, using the same criterion of discordance with our sample of discordant same-sex twin pairs. Paired comparisons of outcome means in discordant twin siblings replicated

11 of the 13 associations found for twins as individuals when discordance was defined by extreme (80^{th} percentile) RAPI scores, and a 12^{th} comparison was marginally significant. A supplementary analysis that deleted pairs in which the RAPI score of the lower-scoring twin fell within the 70^{th} −80^{th} percentile of the RAPI distribution enhanced most of these mean differences. And in a second supplementary analysis, discordant twin comparisons replicated all 13 outcomes when discordance was defined by a large intra-pair RAPI difference, regardless of score levels. Finally, although very modest in magnitude, correlations of signed differences in RAPI with signed differences in outcomes for the entire same-sex twin sample were significant for all 13 outcomes. These results from different within-family comparisons of discordant twin pairs convincingly rule out between family confounds as the sole source of associations of adolescent problem drinking with adverse outcomes.

Third, for nearly all associations, magnitude of effect was attenuated from individual-level comparisons to those of all discordant twin pairs and was further attenuated in comparisons of discordant MZ pairs. That pattern of attenuation carries a clear implication: while between family confounds do not explain away the associations, they have measureable effects on most associations we studied. To no surprise, household and neighborhood environments influence associations of adolescent alcohol exposure with adverse adult outcomes.

Fourth, and with equal clarity, our results show that confounding is *not* the whole story. We could replicate some associations between problem drinking in adolescence and adverse behavioral outcomes in adulthood in our samples of discordant MZ twin pairs. And importantly, these associations consistently replicated across different definitions of intra-pair discordance. Continuity of problem drinking to age 25 and sexual behavior with multiple sexual partners by age 25 are the most common results reported in earlier longitudinal studies with non-twins; both replicated in our sample of discordant MZ twin pairs. And a third association, not apparent in earlier studies, is the most striking of all: adolescent problem drinking is associated with elevated scores on the General Health Questionnaire at age 25. Within rounding error, that association shows *no* attenuation of effect from individual-level analyses to comparisons of discordant MZ twin pairs. That association replicated, as well, in the correlation of intra-pair differences in RAPI at 18½ with intra-pair differences in GHQ at 25 across all 663 MZ pairs in our sample. These MZ twin comparisons match for childhood environment and control for genetic variation; for GHQ-12, such control does not diminish magnitude of effect associated with within-pair discordance for adolescent problem drinking. While these analyses cannot confirm causality, our results are consistent with an inference that the association of adolescent alcohol exposure with symptoms of psychological distress assessed by the GHQ-12 is causal in nature.

Fifth, our results show that different definitions of intra-pair discordance yielded comparable findings. Our first approach used extreme scores on self-reported drinking problems to define and contrast “cases” with “controls”; a second approach required large intra-pair discordance in those scores without requiring an extreme score in either co-twin. Membership in the two samples so defined was but moderate (see Tables S3 & S4,

Supplementary Materials), so the consistency of results across these two analyses underscores the robust association of within-pair differences in RAPI with adult outcomes. A third approach, using the entire twin sample in difference score analyses, yielded corroborative results – all associations significant for all twins, and for six of 13 outcomes among analyses limited to MZ pairs only.

Finally, MZ co-twins discordant for self-reported drinking problems at age 18½ were not discordant for three risk-relevant, prospectively assessed personality dimensions. The cause of their discordance for drinking problems in late adolescence lies elsewhere. It has roots in whatever caused the differing drinking patterns we documented in their age 16 reports of frequency of drinking and frequency of drinking to intoxication. What explains *those* differences? A likely candidate is non-overlapping peer networks in early adolescence and effects of peer socialization, effects that emerge early and endure throughout late adolescence (Burk et al. 2012).

Important strengths of our study include the large population-based twin sample, with almost exhaustive ascertainment and very high participation, and the matched-pair analysis, nested within a longitudinal design that permits comparisons of adult outcomes among exposure-discordant twin pairs matched for household, school, and neighborhood environments and half or all their genes.

Our study has limitations as well. Although our initial sample of twin pairs was large, co-twin similarities for adolescent alcohol exposure and life course outcomes inevitably constrain the number of informatively discordant twin pairs as traditionally defined; large data sets are required for discordant twin-pair analyses to be fully informative for alcohol exposure (Madsen and Osler, 2009). All our outcome measures were based on self-report, albeit years after the exposure assessment. Many measured outcomes were of limited metric, and some suffered from ceiling effects. The precision with which we measured outcomes varied. Some, including the 12-item GHQ, the 11-item Mm-MAST, the four-item Life Satisfaction scale, and the six-symptom checklist were multi-item assessments, and their distributions permitted quasi-continuous evaluation of the more adverse outcomes. But most outcomes were measured by a single question with limited response options embedded into the 95-item age 25 questionnaire.

Our sample is of Finnish twins who reached adolescence during the early 1990’s, when Finland experienced severe, albeit brief, economic strain following dissolution of the USSR. And the common drinking pattern of Finnish adolescents (Hibell et al., 1997) is high-density weekend drinking, one not observed in all societies. Cohort and cultural effects could contribute to our results.

Finally, our follow-up was but seven years, and there is temporal overlap of ‘outcome’ and ‘predictor’ for some associations we, and others in research literature, have studied. Directionality of causation in such associations is uncertain, but our aim was to evaluate confounding, not causality. Whether associations from adolescent drinking persist into later adulthood and elevate risk for mortality as well as social morbidity must be addressed with longer-term follow-up.

Despite limitations, our results with discordant twin siblings offer new evidence that associations reported in earlier research linking adverse consequences in early adulthood with problem drinking in late adolescence are not wholly due to between-family confounds. And results from comparisons limited to discordant MZ twin pairs suggest that some of these associations may arise from causal effects of adolescent alcohol exposure. Those results are suggestive, but not definitive, encouraging further research with longer follow-up, more precise outcome assessments, and larger samples to enhance power and permit outcome comparisons separated by gender.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We gratefully acknowledge the ongoing participation and continuing interest of Finnish twins born 1975-79 over more than two decades of our longitudinal research studies. Data-collection and manuscript preparation were supported by the National Institute on Alcohol Abuse and Alcoholism (Grants R37 AA-12502 and R01 AA-09203 to RJR) with supplementary funding to JK from the Academy of Finland (grants 118555; 100499; 205585).

REFERENCES

Bonomo Y, Coffey C, Wolfe R, Lynskey M, Bowes G, Patton G. Adverse outcomes of alcohol use in adolescents. Addiction. 2001; 96:1485–1496. [PubMed: 11571067]

Bonomo YA, Bowes G, Coffey C, Carlin JB, Patton GC. Teenage drinking and the onset of alcohol dependence: a cohort study over seven years. Addiction. 2004; 99:1520–1528. [PubMed: 15585043]

Burk WJ, van der Vorst H, Kerr M, Stattin H. Alcohol use and friendship dynamics: Selection and socialization effects in early-, middle- and late-adolescent peer networks. J Stud Alcohol Drugs. 2012; 73:89–98. [PubMed: 22152666]

Chassin L, Pitts SC, Prost J. Binge drinking trajectories from adolescence to emerging adulthood in a high-risk sample: predictors and substance abuse outcomes. J Consult Clin Psychol. 2002; 70:67–78. [PubMed: 11860058]

Dahlstrom, WG.; Welsh, GS.; Dahlstrom, LE. An MMPI Handbook Vol. 1: Clinical Interpretation. Minneapolis: Univ Minnesota Press; 1972.

Delucchi KL, Matzger H, Weisner C. Alcohol in emerging adulthood: 7-year study of problem and dependent drinkers. Addict Behav. 2007; 33:134–142. [PubMed: 17537582]

Dick DM, Johnson JK, Viken RJ, Rose RJ. Testing between-family associations in within-family comparisons. Psychol Science. 2000; 11:409–413.

Dick DM, Aliev F, Viken R, Kaprio J, Rose RJ. Rutgers Alcohol Problem Index Scores at age 18 predict alcohol dependence diagnoses seven years later. Alcohol Clin Exp Res. 2011; 35:1011–1014. [PubMed: 21323682]

Ellickson PL, Tucker JS, Klein DJ. Ten-year prospective study of public health problems associated with early drinking. Pediatrics. 2003; 111:949–955. [PubMed: 12728070]

Englund MM, Egeland D, Oliva EM, Collins WA. Childhood and adolescent predictors of heavy drinking and alcohol use disorders in early adulthood: A longitudinal developmental analysis. Addiction. 2008; 10312(Suppl):3–35.

Fergusson D, Lynskey MT. Alcohol misuse and adolescent sexual behaviors and risk taking. Pediatrics. 1986; 98:91–96. [PubMed: 8668418]

Goldberg, DP. The Detection of Psychiatric Illness by Questionnaire. Oxford: Oxford University Press; 1972. Maudsley Monograph No. 21.

Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinell M, Gureje O, Rutter C. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med. 1997; 27:191–197. [PubMed: 9122299]

Guo J, Chung I-J, Hill KG, Hawkins JD, Catalano RF, Abbott RD. Developmental relationships between adolescent substance use and risky sexual behavior in young adulthood. J Adolesc Health. 2002; 31:354–362. [PubMed: 12359381]

Hibell, B.; Andersson, B.; Bjarnason, T.; Kokkevi, A.; Morgan, M.; Narusk, A. Alcohol and other drug use among students in 26 European countries. Stockholm, Sweden: Modin Tryck AB; 1997. The 1995 ESPAD report

Hill KG, While HR, Chung I-J, Hawkins JD, Catalano RF. Early adult outcomes of adolescent binge drinking: person- and variable-centered analyses of binge drinking trajectories. Alcohol Clin Exp Res. 2000; 24:892–901. [PubMed: 10888080]

Hittner JB, Swickert R. Sensation-seeking and alcohol use: A meta-analytic review. Addict Behav. 2006; 8:1383–1401. [PubMed: 16343793]

Kandel DB, Davies M, Karus D, Yamaguchi K. The consequences in young adulthood of adolescent drug involvement. Arch Gen Psychiatry. 1986; 43:746–754. [PubMed: 3729669]

Kaprio J, Pulkkinen L, Rose RJ. Genetic and environmental factors in health-related behaviors: Studies on Finnish twins and twin families. Twin Res. 2002; 5:366–371. [PubMed: 12537860]

Koposov RA, Ruchkin VV, Eisemann M, Sidorov PL. Alcohol use in adolescents from Northern Russia: The role of the social context. Alcohol Alcohol. 2002; 37:297–303. [PubMed: 12003922]

Korhonen T, Huizink AC, Dick DM, Pulkkinen L, Rose RJ, Kaprio J. Role of individual, peer and family factors in the use of cannabis and other illicit drugs: A longitudinal analysis among Finnish adolescent twins. Drug Alcohol Depend. 2008; 97:33–43. [PubMed: 18455885]

Kristenson H, Trell E. Indicators of alcohol consumption: Comparisons between a questionnaire (MmMAST), interviews and serum γ-glutamyl tranferase (GGT) in a health survey of middle-aged males. Br J Addict. 1982; 77:297–304. [PubMed: 6128016]

Kujala U, Rose RJ, Kaprio J. Physical activity in adolescence and smoking in young adulthood: A prospective twin cohort study. Addiction. 2007; 102:1151–1157. [PubMed: 17567404]

Madsen M, Osler M. Commentary: Strengths and limitations of the discordant twin-pair design in social epidemiology. Where do we go from here? Int J Epidem. 2009; 38:1322–1323.

McCambridge J, McAlaney J, Rowe R. Adult consequences of late adolescent alcohol consumption: A systematic review of cohort studies. PLoS Med. 2011; 8:1–13.

McCarty CA, Ebel BE, Garrison MM, DiGiuseppe DL, Christakis DA, Rivara FP. Continuity of binge and harmful drinking from late adolescence to early adulthood. Pediatrics. 2004; 114:714–719. [PubMed: 15342844]

McGue M, Osler M, Christensen K. Causal inference and observational research: The utility of twins. Perspect Psychol Sci. 2010; 5:546–556. [PubMed: 21593989]

Pedersen W, Skrondal A. Alcohol consumption debut: Predictors and consequences. J Stud Alcohol. 1998; 59:32–42. [PubMed: 9498313]

Rose RJ, Kaprio J, Winter T, Koskenvuo M, Viken RJ. Familial and socioregional environmental effects on abstinence from alcohol at age sixteen. J Stud Alcohol Suppl No. 1999; 13:63–74.

Seppä K, Sillanaukee P, Koivula T. The efficiency of a questionnaire in detecting heavy drinkers. Br J Addict. 1990; 85:1639–1645. [PubMed: 2289065]

Stanek KC, Iacono WG, McGue M. Returns to education: What do twin studies control? Twin Res Hum Genet. 2011; 14:509–516. [PubMed: 22506306]

Susser E, Eide MG, Begg M. Invited commentary: The use of sibship studies to detect familial confounding. Int. J. Epidemiol. 2010; 172:537–539.

Tucker JS, Orlando M, Ellickson PL. Patterns and correlates of binge drinking trajectories from early adolescence to young adulthood. Health Psychol. 2003; 22:79–87. [PubMed: 12558205]

Viken RJ, Kaprio J, Rose RJ. Personality at ages 16 and 17 and drinking problems at ages 18 and 25: genetic analyses of data from Finn Twin16-25. Twin Res Hum Genet. 2007; 10:25–32. [PubMed: 17539362]

Viner RM, Taylor B. Adult outcomes of binge drinking in adolescence: findings from a UK national birth cohort. J Epidemiol Community Health. 2007; 61:902–907. [PubMed: 17873228]

Wells JE, Horwood LJ, Fergusson DM. Drinking patterns in mid-adolescence and psychosocial outcomes in late adolescence and early adulthood. Addiction. 2004; 99:1529–1541. [PubMed: 15585044]

White HR, Labouvie EW. Toward the assessment of binge drinking in adolescence. J Stud Alcohol. 1989; 50:30–37. [PubMed: 2927120]

Wiggins J. Substantive dimensions of self report in the MMPI item pool. Psychol Monogr. 1966; 80(22):1–42. Whole no. 630. [PubMed: 4381983]

Zuckerman, M. Sensation Seeking: Beyond the Optimal level of Arousal. Hillsdale, NJ: Lawrence Erlbaum; 1979.

TABLE 1

Association of adolescent drinking problems, defined as Q5 RAPI score at age 18, with adverse adult outcomes at 25.

	Twins as Individuals[1] N = 2638–3072			All Discordant SS Pairs[2] N = 247–269			Discordant MZ Pairs N=104–112		
Age 25 Adult Outcome[3]	Diff[4]	95% CI	*p*	Diff[4]	95% CI	*p*	Diff[4]	95% CI	*p*
Elevated Mm-MAST Score	1.91	1.71 – 2.11	.000	1.12	.82 – 1.42	.000	.78	.39 – 1.18	.000
Frequent Intoxication	1.04	.77 – 1.32	.000	.42	.14 – .71	.002	.20	−.20 – .60	.162
Frequent High Density Drinking	1.18	.86 – 1.49	.000	.52	.14 – .90	.004	.22	−.46 – .90	.258
Frequent Smoking	1.17	.98 – 1.37	.000	.49	.22 – .76	.000	−.08	−.42 – .25	.302
Elevated GHQ Score	.09	.06 – .12	.000	.09	.04 – .14	.001	.10	.01 – .18	.013
Subjective Poor Health Rating	.26	.18 – .32	.000	.13	.02 – .24	.014	.06	−.09 – .22	.223
Multiple Physical Symptoms	.19	.14 – .25	.000	.07	.00 – .15	.046	.05	−.05 – .16	.162
Earlier Coital Debut	1.10	.90 – 1.30	.000	.22	− .05 – .51	.057	.18	− 23 – .60	.192
Multi-Partner Cohabitation	.23	.16 – .30	.000	.11	.01 – .21	.019	.11	−.02 – .24	.058
Mutiple Sexual Partners	.90	.78 – 1.01	.000	.36	.18 – .54	.000	.22	−.02 – .46	.037
Life (Dis)satisfaction	.82	.54 – 1.10	.000	.51	.02 – 1.00	.021	.49	−.26 – 1.24	.099
Truncated Education	.39	.26 – .52	.000	.16	.01 – .32	.018	.14	−.06 – .34	.086
Financial Difficulties	.21	.12 – .31	.000	.07	−.06 – .22	.152	−.12	−.34 – .09	.122

[1] All individual twins from same-sex pairs, including those unpaired and twins from pairs of uncertain zygosity were included in individual-level analyses.

[2] Eleven same-sex twin pairs whose zygosity awaits confirmation were included in these analyses.

[3] All response categories in the age 25 questionnaire were used to compare outcomes.

[4] Outcome differences were computed as mean measured outcome of higher-scoring RAPI twins minus mean of lower-scoring cotwins.

Table 2

Outcome differences in all same-sex pairs identified as discordant by RAPI score difference >8.

	All Discordant SS Twin Pairs N = 259–290			Discordant MZ Twin Pairs N=104–117		
Age 25 Adult Outcome	Mean Diff	95% CI	*p*	Mean Diff	95% CI	*p*
Elevated Mm-MAST Score	1.16	.86 – 1.46	.000	.68	.28 – 1.06	.000
Frequent Intoxication	.62	.19 – 1.04	.003	.04	−.58 – .66	.454
Frequent High Density Drinking	.68	.26 – 1.10	.001	.03	−.61 – .68	.452
Frequent Smoking	.62	.36 – .88	.000	− .02	−.32 – .27	.432
Elevated GHQ Score	.08	.02 – .13	.004	.08	−.01 – .16	.037
Subjective Poor Health Rating	.16	.05 – .26	.002	.05	−.11 – .21	.260
Multiple Physical Symptoms	.11	.03 – .18	.003	.06	−.04 – .16	.143
Earlier Coital Debut	.41	.12 – .71	.003	.23	−.18 – .64	.131
Multi-Partner Cohabitation	.12	.02 – .22	.011	.06	−.08 – .20	.194
Multiple Sexual Partners	.41	.23 – .58	.000	.18	−.06 – .42	.079
Life (Dis)satisfaction	.48	.02 – .95	.021	.54	−.22 – 1.31	.083
Truncated Education	.23	.08 – .38	.001	.17	−.02 – .36	.045
Financial Difficulties	.18	.05 – .31	.004	.12	−.08 – .31	.116