Childhood Risk Factors for Heavy Episodic Alcohol Use and Alcohol Problems in Late Adolescence: A Marginal Structural Model Analysis

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ABSTRACT. Objective: This study seeks to clarify the nature of the association between five well-studied late childhood predictors and alcohol-related behaviors in adolescence. **Method:** We examined, in 7,168 subjects from the Avon Longitudinal Study of Parents and Children (ALSPAC), using linear probability and marginal structural models, the association between parental alcohol problems, peer group deviance, antisocial behavior, and low parental monitoring, and sensation seeking assessed at multiple times from ages 12.5 to 18 years and heavy episodic drinking and alcohol problems at ages 16.5, 17.5, and 20 years. **Results:** Based on the pattern of the attenuation in the association with heavy episodic drinking and alcohol problems from the linear probability to marginal structural models, our five factors were divisible into three groups. For parental alcohol problems, no substantial attenuation was

seen. For peer group deviance and antisocial behavior, the associations in the marginal structural models were modestly attenuated (10%–20%). By contrast, for low parental monitoring and sensation seeking, moderate attenuations of 41% and 35%, respectively, were observed. **Conclusions:** Our results are consistent with the hypothesis that all or nearly all of the association between parental alcohol problems and heavy episodic drinking and alcohol problems in mid to late adolescence is causal. For peer group deviance and antisocial behavior, the large majority of the associations appear to be causal, but confounding influences are also present. However, for low parental monitoring and sensation seeking, our findings suggest that a substantial proportion of the observed association with alcohol outcomes reflects confounding rather than causal influences. (*J. Stud. Alcohol Drugs*, 79, 370–379, 2018)

INDIVIDUAL DIFFERENCES IN LEVELS of alcohol use and alcohol problems arise out of a complex developmental process influenced by a range of biological and environmental factors (Kendler et al., 2011b; Sher et al., 2005; Vaillant, 1983). Many individual putative risk factors have been associated with alcohol-related behaviors from both cross-sectional and longitudinal observational studies. However, these risk factors are frequently intercorrelated, often substantially so. Without randomized controlled experiments, it is challenging to clarify, from observational data, the degree to which these risk factors are causally related to increased alcohol use and problems. However, it is such insights that are needed to inform education, prevention,

and early intervention programs. Two broad classes of approaches can be taken to problems of causal inference in nonexperimental data: natural experiments and specialized statistical methods (Rutter, 2007). In this report, we apply one such statistical method.

Marginal structural models (MSMs; Robins et al., 2000) provide a method to estimate the average causal effect of an exposure on an outcome using observational data in the presence of confounding. This method is particularly useful in cases where exposure and confounding may be time dependent, and confounders are influenced by exposure status. Central to this method is the assignment of a weight to each subject equal to the inverse probability of receiving

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their exposure conditional on the covariates and confounders. These weights provide a counterfactual estimation of the average causal effect—that is, the difference in means if all of a sample versus none of the sample received an exposure.

In this report, we examine five well-studied risk factors for alcohol-related outcomes in offspring generation from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort (Boyd et al., 2013; Golding et al., 2001; Ness, 2004; Pembrey, 2004): parental alcohol problems (Cotton, 1979), antisocial behavior (Fergusson et al., 2007; Heron et al., 2013), peer-group deviance (Dishion & Loeber, 1985; Li et al., 2002), parental monitoring (Webb et al., 2002), and sensation-seeking (Sher et al., 1999; Zuckerman, 1972; Zuckerman & Neeb, 1979) assessed in the offspring at 12.5 to 18 years of age. These risk factors were selected on the basis of a prior large structural equation model analysis (Edwards et al., 2016) because, amongst a broad range of putative predictors of alcohol-related behaviors in late adolescence/early adulthood, they were the ones that demonstrated both strong associations with our alcohol outcomes and with each other, suggesting their value both as potential causal influences and confounders. Using MSMs that contain both standard covariates and all the other risk factors measured before or concurrent with the exposure variable as potential confounders, we predicted, from these five exposures taken from each occasion of measurement, the outcomes of heavy episodic use and alcohol problems as assessed at 16.5, 17.5, and 20 years of age. All risk factors had two or more longitudinal measures (except parental alcohol problems). We compared the results from these MSMs with those obtained by standard linear probability regression so as to gain insight into the degree to which the association between these putative risk factors and our alcohol-related outcomes may be causal. If the attenuation were modest, we would interpret this as supportive of the hypothesis that the association between the risk factor and outcome is largely causal. If the attenuation were stronger, it would be consistent with the hypothesis that the risk factor–outcome association is substantially influenced by noncausal factors, that is, confounders.

Method

Sample

ALSPAC is an ongoing population-based study investigating a range of environmental and other influences on the health and development of children (Boyd et al., 2013; Golding et al., 2001; Ness, 2004; Pembrey, 2004). All pregnant women residing in the Avon district in England with an expected delivery date between April 1, 1991, and December 31, 1992, were invited to participate. The achieved sample was 14,541 pregnant women (80% of those eligible) with 13,988 live infants at age 12 months. ALSPAC parents and

children have been followed up regularly since recruitment, with data obtained through questionnaires completed by mothers, children, and teachers, and through clinical assessments. Full details of all measures, procedures, sample characteristics and response rates are available at: www.alspac.bris.ac.uk. Please note that the study website contains details of all the data that are available through a fully searchable data dictionary: www.bris.ac.uk/alspac/researchers/data-access/datadictionary. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committee.

Sample selection

Individuals chosen for inclusion in the sample were required to have at least one usable measurement of the four risk factors based on self-report (peer group deviance, antisocial behavior, lack of parental monitoring, and sensation seeking), all of which were in the interval from 12 years 6 months to 13 years 6 months. Among individuals meeting this criterion, we created a binary variable indicating whether all parental variables were missing or not, in case nonparticipation by parents had a predictive role. As outlined in Supplemental Table A, the variable that most strongly predicted attrition before early adolescence was parental socioeconomic status. (Supplemental material appears as an online-only addendum to the article on the journal's website.) However, it was previously demonstrated using inverse probability weighting that such attrition had little effect on the association among the variables used in this study (Edwards et al., 2016). All individuals meeting the criterion for inclusion were subjected to multiple imputation using IVEware. This software uses a chained equation approach as described by Raghunathan et al. (2001). Variables used in the imputation model included all outcomes, risk factors, and covariates from the analyses along with earlier measures of lack of parental monitoring and conduct disorder that were not used in the analyses. Five imputed data sets were created.

Variables

Parental socioeconomic status was assessed as a composite of parental education (maximum of maternal and paternal education rated a “less than O level, O level, A level, and university degree”), parental occupational status (maximum for either parent; Kendler et al., 2014), and parental income (mean of 5 ordinal levels assessed at four ages [2 years 9 months, 3 years 11 months, 7 years 1 month, 8 years 1 month]; Melotti et al., 2013). Each variable was standardized and the mean taken. If any were missing, we used the mean of those remaining.

Parental alcohol problems were based on factor-derived scores from the parental alcohol use and alcohol-related

problems as assessed by self and spouse report from before pregnancy (retrospectively) through age 12 of the offspring. (For further details, see Kendler et al., 2013, Table 1.) The sum scores for maternal and paternal problems were standardized and the mean taken (if both available). Otherwise, the score for the available parent was used.

Sensation seeking (Arnett, 1994) was assessed at age 13 years 6 months and again at 18 years.

Peer group deviance was assessed as a sum score of antisocial behaviors engaged in by members of the subjects' peer group at 12 years 6 months and at 17 years 6 months (Edwards et al., 2015).

Antisocial behavior was assessed as a sum score of antisocial behaviors engaged in by the subject at ages 13 years 11 months, 15 years 6 months, and age 18 years (Edwards et al., 2016). Since the measure at 13 years 11 months concerned behavior in the past 12 months, we treated it as concurrent with the measures at 13 years 6 months. The specific items assessed in these three measures of antisocial behavior are seen in Supplemental Table C.

Lack of parental monitoring was assessed by self-report items reflecting the extent of parental knowledge of the subjects' activities and peers at ages 13 years 6 months and 15 years 6 months (Stattin & Kerr, 2000).

Outcome variables for the models were derived from the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993) administered at ages 16 years 6 months, 17 years 6 months, and 20 years. *Heavy episodic use* was defined as having six or more drinks on one occasion at least monthly at age 16 years 6 months and at least weekly at age 17 years 6 months and 20 years. Alcohol problems were based on Items 4–8 of the AUDIT and were defined as responding positively to at least one of these items at a frequency of monthly or more.

Variables used in creating the inverse probability weights for our marginal structural models were converted to three level ordinal variables to avoid potential problems in MSMs when using continuous or quasi-continuous measures and to base multiple imputation on a similar measurement scale for all variables. These scores were created by dividing the scores approximately into quartiles. The lowest quartile was scored 0. The second and third quartiles were scored 1, and the fourth quartile was scored 2. Certain variables had a substantial number of subjects with scores of 0 (peer group deviance and antisocial behavior). Those with 0 were scored 0. The rest were divided approximately into thirds. The upper third of the remainder was scored 2, whereas the bottom two thirds of this portion were scored 1. These ordinal scores were close to linear in describing the association with outcomes and with other risk factors. As a result, models for estimating effects (either unweighted or using inverse probability weighting) were done as linear probability models (LPMs) as described below rather than as models with multiplicative effects.

Assumptions of marginal structural models

Given that MSMs are likely new to many readers, we provide a brief background, specifically about their assumptions.

Exchangeability or no unmeasured confounding. Although this is unobtainable in an absolute sense, the validity of our estimates will depend on whether we have accounted for a substantial portion of the confounding.

Positivity. The covariates for each individual allow for a nonzero probability of receiving an exposure. Using categorical measures can be helpful toward preserving positivity.

No misspecification of the model for assigning weights. The models for assigning weights should be free of excessively narrow parametric assumptions that may bias estimates.

Creating stabilized inverse probability weights. The intent of inverse probability (IP) weighting is to eliminate confounding by creating a pseudo-population in which each subject has the same probability of receiving each level of exposure and all backdoor paths from exposure to outcome via confounders are eliminated.

The use of stabilized inverse probability weights (where the unconditional probability of exposure is divided by the estimated probability of exposure given the covariates) creates a pseudo-population the same size as the original sample with mean weights of 1. Thus, measured outcomes that are more likely based on covariates are weighted less than 1, whereas outcomes estimated to be less likely receive weights greater than 1. IP weights and stabilized IP weights give the same results, but in certain circumstances, stabilized IP weights will produce narrower confidence intervals.

Useful references for working with marginal structural models and much more include Hernán and Robins (2017; currently accessible in draft form at <https://www.hsph.harvard.edu/miguel-hernan/causal-inference-book>), VanderWeele (2015), and Thoemmes and Ong (2016).

To carry out MSMs, we need stabilized weights for each subject on the exposure variable of interest (A_i) based on potential confounders at the time of measurement and necessary covariates (L_i). Weights (Supplemental Table B) were estimated using generalized logits (SAS Proc Logistic, SAS Institute Inc., Cary, NC) to estimate the probability of an individual receiving their exposure based on these confounders and covariates $\Pr[A_i|L_i]$. The logistic regression treated all the potential confounders and exposures as nominal categorical variables. This enables the avoidance of linearity or proportional odds in the regressions used to estimate weights. Stabilized weights are created by dividing the unconditional probability of exposure by the probability of the observed exposure given the covariates (stabilized inverse probability weights = $\Pr[A_i]/\Pr[A_i|L_i]$). The distribution of weights was examined to ensure that mean weights were 1.0 and the distribution of weights did not contain extreme

TABLE 1. Polychoric correlations among the risk factors^a

Variable	Age	PAP	PGD- 12	ASB- 13.5	LPM- 13.5	SS- 13.5	ASB- 15.5	LPM- 15.5	PGD- 17.5	SS- 18	ASB- 18
Parental alcohol problems (PAP)	<12	—									
Peer group deviance (PGD)	12.5	.10	—								
Antisocial behavior (ASB)	13.5	.10	.41	—							
Low parental monitoring (LPM)	13.5	.07	.33	.41	—						
Sensation seeking (SS)	13.5	.12	.34	.35	.36	—					
Antisocial behavior (ASB)	15.5	.08	.39	.56	.36	.36	—				
Low parental monitoring (LPM)	15.5	.06	.18	.23	.34	.20	.25	—			
Peer group deviance (PGD)	17.5	.12	.34	.38	.28	.29	.48	.22	—		
Sensation seeking (SS)	18	.13	.19	.20	.15	.58	.21	.12	.24	—	
Antisocial behavior (ASB)	18	.12	.37	.43	.28	.38	.50	.22	.51	.31	—

Notes: All *p* values < .0001 except between LPM and PAP, where *p* < .001. ^aAll correlations are positive.

values either high or low indicating that positivity was maintained (Cole & Hernán, 2008). Because each individual was represented by five imputations, we averaged the estimated weights. More extreme weights created by unlikely combinations of imputed variables will receive some smoothing in this approach whereas weights based on actual measurements will be unaffected. This approach is similar to that of Mitra and Reiter (Mitra & Reiter, 2016) for propensity scores in multiple imputation where it was found that the averaging approach had a greater potential for bias reduction as opposed to using each imputation independently.

The MSM models were done as LPMs using a quasi-likelihood approach with an identity link function and a binomial error distribution constrained to keep the estimated probability of a positive outcome between .01 and .99. Each subject in each regression model was weighted by their appropriate stabilized inverse probability weight and robust standard errors were used. In multivariate models, weights were calculated for the variable at each time point of measurement and the model weight for each individual was the product of the weights for individual time points.

The general approach for the MSMs used here for predicting the total counterfactual effect from exposure to a risk factor on an outcome was to include appropriate measurements of the exposure made before or concurrent with the outcome. The inverse probability weight for an exposure was estimated using generalized logit regression including covariates and other potential confounders that were before or concurrent with the exposure whose weight was being calculated. If an exposure was measured at multiple time points before or concurrent with an outcome, stabilized inverse probability weights were calculated at each time

point and the overall stabilized weight was the product of the individual weights (Robins et al., 2000). Because the sample involved data produced by multiple imputation, results were combined as described by Rubin (1987) to obtain the final results for each analysis.

Offspring sex was used as a covariate for models using parental alcohol problems as an exposure as offspring sex was deemed inappropriate as a weighting factor. For all other exposures, weights were created using standard covariates and the appropriate measures of other risk factors as described above, but the MSMs for counterfactual effects were performed with no covariates. Likewise, unweighted LPMs were carried out without covariates as there is no multivariate regression equivalent to longitudinal MSMs with time-varying risks and confounders.

The major focus of our analyses is the degree of attenuation of the associations between the risk factors and alcohol outcomes in our LPM and MSM analyses. For ease of interpretation, we used a crude but informative figure that is the mean reduction in the beta coefficients from the LPMs to the MSMs for each risk factor across ages given that both the LPM and MSM coefficients were statistically significant. In calculating this, we excluded aberrant results (marked by an asterisk in Tables 4 and 5) that would unduly influence our calculations.

Results

The sample size for all analyses was 7,168 (3,522 males and 3,646 females). For details and predictors of attrition and the proportion of imputed data in each variable, see Supplemental Table A. We first present polychoric correla-

TABLE 2. Polychoric correlations between the risk factor and outcome variables^a

Variable	Age	Heavy episodic use at age			Alcohol problems at age		
		16.5	17.5	20	16.5	17.5	20
Parental alcohol problems (PAP)	<12	.18	.18	.18	.16	.18	.18
Peer group deviance (PGD)	12.5	.23	.21	.08	.22	.22	.17
Antisocial behavior (ASB)	13.5	.27	.23	.13	.25	.18	.17
Low parental monitoring (LPM)	13.5	.26	.23	.09	.22	.23	.17
Sensation seeking (SS)	13.5	.28	.29	.18	.18	.20	.19
Antisocial behavior (ASB)	15.5	.32	.30	.16	.32	.31	.28
Low parental monitoring (LPM)	15.5	.17	.15	.06	.16	.12	.14
Peer group deviance (PGD)	17.5	.41	.41	.25	.34	.41	.34
Sensation seeking (SS)	18	.26	.26	.28	.12	.15	.22
Antisocial behavior (ASB)	18	.36	.36	.23	.29	.36	.31

Notes: All *p* values < .0001 except between LPM and heavy episodic use at age 17.5, where *p* < .001. ^aAll correlations are positive.

tions among our risk factors (Table 1), our risk factors and outcomes (Table 2), and our outcomes (Table 3).

Tables 4 and 5 contain our main findings for the prediction of heavy episodic drinking and alcohol problems at ages 16.5, 17.5, and 20 using both marginal structural and linear probability models by each of our five putative risk factors. All predictor and dependent measures in our analyses are on the same scale so that the beta estimates within and across predictor variables are directly comparable. The frequency of each of these outcomes is presented in Supplemental Table D. We calculate the percent change in the regression coefficients from the linear probability to the marginal structural models. This percentage reflects the degree to which the effect size of the predictor variable declines when controlling for confounding.

We are interested in three features of these results: (a) the relative strength of the prediction of our two alcohol outcomes from our risk factors, (b) the attenuation of the association with time from exposure (as expressed by outcome by age of participants), and (c) most importantly, the reduction in association from the linear probability to the marginal structural models.

Parental alcohol problems were more strongly associated with heavy episodic drinking than alcohol problems and

this effect was strongest at age 17.5 and modestly weaker at ages 16.5 and 20. The average reduction in predictive power when we controlled for confounders in the MSM was less than 1%.

Peer group deviance assessed at age 12.5 was more strongly associated with heavy episodic drinking than alcohol problems at age 16.5 but then predicted alcohol problems at the later ages. Peer deviance assessed at age 17.5 strongly predicted both contemporaneous heavy episodic drinking and alcohol problems with a moderate reduction in predictive effects at age 20. A modest attenuation of predictive power was seen in the MSM versus LPM results, with the mean reduction in the beta coefficient (when outlier results were excluded) equaling 12%.

Antisocial behavior at 13.5 years old was a modest and significant predictor of heavy episodic drinking at ages 16.5 and 17.5 but not age 20 and a significant predictor of alcohol problems only at age 16.5. Antisocial behavior evaluated at age 15.5 was a strong and similar predictor of heavy episodic drinking at ages 15.5 and 17.5 and weakened at age 20. By contrast, this measure predicted alcohol problems most strongly at age 17.5. A modest to moderate attenuation of predictive power was seen in the MSM versus LPM results, with reductions in the beta coefficient averaging 19%.

TABLE 3. Polychoric correlations between the outcome variables^a

Variable	Age	Heavy episodic use at age			Alcohol problems at age		
		16.5	17.5	20	16.5	17.5	20
Heavy episodic use	16.5	—					
	17.5	.59	—				
	20	.34	.33	—			
Alcohol problems	16.5	.67	.46	.23	—		
	17.5	.48	.61	.32	.49	—	
	20	.34	.37	.72	.37	.51	—

Notes: All *p* values < .0001. ^aAll correlations are positive.

TABLE 4. Beta coefficients [95% confidence interval] predicting heavy episodic drinking at ages 16.5, 17.5, and 20 from five putative risk factors assessed analyzed using marginal structural and linear probability models

Exposure	Age	Model	Heavy episodic drinking age 16.5	Heavy episodic drinking age 17.5	Heavy episodic drinking age 20
Parental alcohol problems	≤12	MSM	.088 [.068, .108]	.091 [.069, .114]	.083 [.059, .106]
		LPM	.088 [.068, .108]	.091 [.068, .114]	.084 [.060, .106]
Peer group deviance	12.5	MSM	.096 [.076, .115]	.036 [.016, .057]	.003 [-.019, .025]
		LPM	.104 [.086, .122]	.047 [.028, .066]	.002 [-.020, .025]
	% change		-7.7	-23.4	+50*
		MSM		.151 [.116, .185]	.089 [.066, .112]
	17.5	LPM		.175 [.145, .204]	.103 [.084, .126]
				-13.7	-13.5
Antisocial behavior	13.5	MSM	.049 [.013, .084]	.038 [.007, .069]	.024 [-.006, .054]
		LPM	.068 [.028, .107]	.054 [.022, .087]	.016 [-.015, .047]
	% change		-27.9	-29.6	+50*
		MSM	.106 [.061, .150]	.103 [.068, .138]	.042 [.007, .077]
	15.5	LPM	.136 [.095, .177]	.130 [.100, .161]	.040 [.008, .071]
			-22.0	-20.8	+5.0
Lack of parental monitoring	18	MSM			.052 [.008, .096]
		LPM			.083 [.032, .134]
	% change				-37.3
		MSM	.068 [.041, .095]	.058 [.026, .090]	.016 [-.025, .056]
	13.5	LPM	.113 [.095, .131]	.100 [.073, .128]	.034 [.003, .065]
			-39.8	-42.0	-52.9
Sensation seeking	15.5	MSM	.038 [.014, .061]	.026 [-.016, .069]	.002 [-.027, .031]
		LPM	.054 [.028, .081]	.047 [.013, .082]	.019 [-.008, .045]
	% change		-29.6	-44.6	-89.5*
		MSM	.092 [.065, .119]	.097 [.068, .126]	.019 [-.029, .067]
	13.5	LPM	.139 [.116, .162]	.147 [.126, .167]	.026 [-.016, .068]
			-33.8	-34.0	-26.9
	18	MSM			.089 [.034, .143]
		LPN			.115 [.059, .172]
	% change				-22.6

Notes: MSM = marginal structural model; LPM = linear probability model. *These values are too extreme and known too imprecisely to be included in the calculation of the mean attenuation of the betas from the LPM to the MSM.

Low parental monitoring assessed at both ages 13.5 and 15.5 was modestly associated with heavy episodic drinking and alcohol problems with effects generally weakening with advancing age. Particularly noteworthy was the substantial attenuation of predictive power seen in the MSM versus LPM results, as the mean reduction in the beta coefficient was 41%.

Finally, sensation seeking measured at 13.5 and 18 years of age predicted heavy episodic drinking more strongly than alcohol problems. The impact of the earlier measurement declined substantially by age 20, especially when compared with the measure obtained at age 18. A modest to moderate attenuation of predictive power was seen in the MSM versus LPM results, with the average reductions in the beta coefficient equally 35%.

Discussion

In this report, we attempted to clarify, through the use of MSMs, the underlying sources of the association between five commonly studied risk factors assessed in early adolescence, and heavy episodic drinking and alcohol problems

assessed at ages 16.5, 17.5, and 20. The results were diverse. Our five risk factors sorted themselves into three broad groups as a function of the attenuation of their association with our alcohol outcomes from our linear probability to marginal structural models.

For one risk factor—parental alcohol problems—the magnitude of the association did not appreciably change from our LPM to our MSM. This is not unexpected given the modest correlations seen between parental alcohol problems and the other risk factors. Furthermore, this was the only risk factor that was not assessed by offspring self-report. These results are consistent with, but not proof of, the hypothesis that the majority of the association between parental alcohol problems and our alcohol outcomes was causal. These findings would be congruent with a range of family, twin, and adoption studies showing that both levels of alcohol consumption and various measures of problematic alcohol use are strongly transmitted in families, probably as a result of both genetic and shared environmental factors (Hettema et al., 1999; Kendler et al., 2015; Prescott et al., 1994; Swan et al., 1990; Verhulst et al., 2015).

For two risk factors—peer group deviance and antisocial

TABLE 5. Beta coefficients [95% confidence interval] predicting alcohol problems at ages 16.5, 17.5, and 20 from five putative risk factors assessed analyzed using marginal structural and linear probability models

Exposure	Age	Model	Alcohol problems age 16.5	Alcohol problems age 17.5	Alcohol problems age 20
Parental alcohol problems	≤12	MSM	.056 [.033, .078]	.075 [.047, .104]	.073 [.050, .096]
		LPM	.056 [.033, .078]	.076 [.047, .104]	.074 [.051, .097]
Peer group deviance	12.5	MSM	.073 [.052, .094]	.053 [.034, .073]	.034 [.002, .064]
		LPM	.071 [.049, .093]	.046 [.029, .062]	.031 [.002, .059]
	% change				
			+1.3	+9.6*	
	17.5	MSM		.129 [.102, .155]	.101 [.074, .129]
		LPM		.146 [.142, .172]	.119 [.091, .146]
Antisocial behavior	13.5	MSM	.038 [.016, .060]	.002 [-.024, .029]	.000 [-.028, .028]
		LPM	.046 [.025, .068]	.023 [-.003, .049]	.004 [-.028, .036]
	% change				
			-17.4	-100%*	
	15.5	MSM	.076 [.051, .101]	.103 [.074, .132]	.078 [.038, .118]
		LPM	.094 [.068, .120]	.122 [.090, .155]	.082 [.050, .114]
Lack of parental monitoring	18	MSM	-15.5	-4.9	.081 [.037, .125]
		LPM			.098 [.035, .162]
	% change				
				-17.3	
	13.5	MSM	.034 [-.010, .077]	.058 [.026, .091]	.038 [.010, .066]
		LPM	.063 [.027, .099]	.087 [.047, .126]	.056 [.029, .084]
Sensation seeking	15.5	MSM	.028 [-.009, .064]	.011 [-.012, .034]	.023 [-.003, .049]
		LPM	.040 [.006, .074]	.028 [-.001, .058]	.042 [.020, .064]
	% change				
			-30.0	-45.2	
	13.5	MSM	.036 [-.002, .074]	.048 [.022, .075]	.023 [-.028, .074]
		LPM	.065 [.030, .099]	.084 [.057, .110]	.043 [-.010, .095]
	18	MSM	-42.9	-46.5	.051 [.002, .099]
		LPN			.072 [.010, .134]
	% change			-29.2	

Notes: MSM = marginal structural model; LPM = linear probability model. *These values are aberrant, too extreme, and/or known too imprecisely to be included in the calculation of the mean attenuation of the betas from the LPM to the MSM.

behavior—the magnitude of the association declined modestly from our linear probability to our marginal models, in the range of 10% to 20%. These findings are consistent with the hypothesis that most of the associations observed between these risk factors and heavy episodic use and alcohol problems in adolescence are causal but a small proportion of the association arises from confounders. Prior literature supports the hypothesis that a portion of the peer deviance–alcohol problems association might not be causal. For example, longitudinal studies suggested that prior externalizing behavior in adolescents predicts selection into deviant peer groups (Kandel, 1985). Peer deviance has been shown to be heritable (Kendler et al., 2007), with heritability increasing with age as individuals become more able to form their own social environment. Some have suggested that peer deviancy may be a result of gene–environment correlation (Hill et al., 2008). As predicted by this hypothesis, Harden et al. (2008) have shown that the genetic factors that influence selection of drug-using peers are positively correlated with the genes that predict substance use.

The relationship between antisocial behaviors and alcohol misuse has been conceptualized as part of the “externalizing

pathway” to alcohol problems (Babor et al., 1992; Cloninger et al., 1996). A component of this association likely arises from a genetic correlation between alcohol misuse and other forms of externalizing behavior (Edwards & Kendler, 2012; Kendler et al., 2011a; Malone et al., 2004).

Last, with two of our risk factors—sensation seeking and low parental monitoring—the magnitude of the association declined substantially (specifically 35% and 41%, respectively) from our LPM to MSM analyses. These results suggest that a considerable proportion of the associations observed between these risk factors and key alcohol outcomes in adolescence result from confounders. The causal effects are likely present but are substantially upwardly biased in standard regression analyses. These results are consistent with other evidence. Previous studies have demonstrated associations between temperament/personality, conduct problems, and alcohol outcomes (Fergusson et al., 2007; Grekin et al., 2006; Kendler et al., 2011b; McGue & Iacono, 2008; Pardini et al., 2007; Whelan et al., 2014) and suggested genetic links between personality and substance use and abuse (Agrawal et al., 2004).

There have also been concerns about the direction of

effects for parental monitoring (Fletcher et al., 1995). Low parental monitoring might arise because children are unresponsive to parental requests for information or are deceptive in the information they provide, or when parents at first try to control an unruly adolescent's behavior and then give up (Crouter & Head, 2002). Apart from the direction of effect of this putative risk factor, the mechanism underlying its association with alcohol or other substance use outcomes is likely complicated. A study of Finnish twins found that parental monitoring had only a modest main effect on adolescent smoking, but that it moderated genetic and environmental influences on smoking (Dick et al., 2007). Fletcher and colleagues (1995) found interactions between parental monitoring and peer behavior in their impact on adolescent substance use.

These results have implications for efforts at prevention of negative alcohol-related outcomes. If our results are correct, efforts to reduce heavy episodic use or alcohol problems in late adolescence by improving parental monitoring in early adolescence will be less effective than expected in the results from standard longitudinal analyses. The causal impact of parental alcohol problems may be difficult to mitigate because of its genetic component. However, risk is also likely to be conferred via environmental exposure to the parent(s), given results from adoption studies that demonstrate an increased risk of alcohol use disorder in the adoptive children of alcoholic parents (Cloninger et al., 1981; Kendler et al., 2015). Thus, through medical, educational, or other social programs that improve parental alcohol outcomes, this risk factor may yet be a target for intervention.

Limitations

These results should be interpreted in the context of four potential limitations. First, these results are specific to the ALSPAC cohort and may or may not extrapolate to other samples. In particular, differences exist in the age at onset of drinking behavior in the United Kingdom and the United States (Hibell et al., 2007; Johnston et al., 2008). Second, we examined five factors as an illustration of how to test for causal associations—rather than a definitive exploration of all potential risk factors measured in childhood and adolescent drinking behaviors. Furthermore, we made no attempt to clarify, at a psychological or biological level, the mediating mechanisms underlying the observed associations that appeared likely to be substantially causal. These are important questions to be addressed in subsequent analyses. Third, the ALSPAC cohort underwent substantial attrition (Boyd et al., 2013; Golding et al., 2001; Ness, 2004; Pembrey, 2004). Multiple imputations provided complete data for variables missing responses due to attrition between the initial waves of data used in this study (12.5 and 13.5 years) and later outcomes. However, there is no way within MSM methodology to account for attrition before measurement

of the initial exposures. In an earlier study (Edwards et al., 2016), we found that attrition before the early teen years was most strongly associated with parental socioeconomic status. There we found that inverse probability weighting for attrition before the exposure period had only a negligible effect on associations in our SEM model.

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