PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	
AUTHORS	

This paper was submitted to the BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently reviewed by one of the same reviewers but for BMJ Open.

REVIEWS AT THE BMJ

REVIEWER	Dr Elizabeth Orton Lecturer and Specialty Registrar in Public Health University of Nottingham, UK I have no competing financial or other interests with this research.
REVIEW RETURNED	16/10/2011

GENERAL COMMENTS	Comparing media and family predictors of alcohol use: A cohort study of US adolescents Originality: This study investigates factors that may influence the onset of alcohol use in young people and occurrence of binge drinking using a cohort of US adolescents aged 10-14 years. Predictor variables included movie alcohol exposure, ownership of alcohol branded materials and family factors. Overall the paper is well written though it lacks detail with regards to the statistical analysis. This is not the first study to look at these influences on alcohol consumption in adolescence although it does uniquely bring them together in the same study: The authors identify some previous studies and in addition Gordon et al 2010 used a cohort study to assess the impact of different types of alcohol marketing on drinking initiation and consumption frequency1; Ferguson and Meehan 2011 used a cohort design to assess the impact of peers on alcohol use, adjusting for media influences2 and Fisher et al, showed that possession of alcohol-branded promotional items is associated with increased likelihood of alcohol initiation. In addition several studies have attempted to identify other influences on alcohol uptake and use in adolescence3-5. However the literature on this topic is not extensive and the current study does distinguish factors that affect alcohol use onset and more hazardous patterns of drinking which adds to the research literature. Importance of the work: alcohol misuse in young people is of concern globally and it is important to understand how this can be

	influenced. Age of onset is thought to influence the likelihood of misuse in later life and risky patterns of drinking, such as binge drinking, put young people at risk of short term adverse events such as assault or accidents as well as potential long term effects. The results of the study would be of interest to policy makers, informing potential restrictions on how alcohol use is portrayed the movie industry/advertising. It is also of interest in terms of potential public health interventions, suggesting that parent factors have less of an influence on binge drinking than media/promotional influences. Methods: 1) Research question: The research question is clearly defined i.e. to estimate the association between a range of media and family factors and alcohol use initiation and progression onto binge drinking in adolescents and a cohort study design is appropriate for this. 2) Participants: the authors describe well the process of recruitment. No exclusion criteria appear to have been applied, except for age and consent being obtained which are both appropriate. However there may be some selection biases associated with the sampling method i.e. participants needed to have a landline telephone, which may have selected out poorer households. 3) Outcome measures: The main outcome measures of time to onset of alcohol use and binge drinking are clear but the STROBE questionnaire did not appear to have been submitted, although correspondence said it had. Ascertaining alcohol use is notoriously difficult because of recall and social desirability biases (people don't necessarily want to admit to their use) so non face-to-face interviews using keypad pressing to answer sensitive questions is a reasonable method to use, although still subject to some of these biases. The authors sought parental consent prior to adolescent consent and in doing so, enrolled 6522 individuals out of a possible 9849. The authors estimated their response rate to be 32% (including non-contactable households in the denominator), which is quite low but to be reasonably representative of the US population with some differences in ethnicity. The comparable US statistics show that the sample is slightly over representative of the higher household incomes and this is important for the study's generalisability given the telephone-based method of data collection and the potential for not recruiting people who move home frequently or do not possess a telephone landline. Other studies have shown conflicting results regarding the importance of socioeconomic status and binge drinking in particular, so this is a limitation of the study. 4) Exposure: Movie alcohol exposure was assessed using a previously validated method. However the nature of the classification does not appear to evaluate the nature of the exposure, whether 'positive' or 'negative' in terms of how alcohol use is depicted. Alcohol branded merchandise was not ascertained at baseline which is unfortunate. A range of other predictor variables were ascertained relating to the individual adolescent's and then family predictors included variables shown in other studies to be important in alcohol use initiation including availability of alcohol in the home, alcohol use and parenting authority. 5) Sample size: The sample size calculation refers to moving smoking and never smokers (p8) which is clearly a careless 'cut and

	paste' mistake?? The authors need to show what figures they used to calculate the sample size fully and explain why they used these. What was the estimated prevalence of alcohol use at baseline and what did they use as an estimate of movie exposure? Why did they use movie exposure and not ownership of branded materials or parental factors which may be less common? Also, why did they select onset of drinking rather than onset of binge drinking – presumably the latter was less frequent (particularly because the sample size is further reduced as it is for ever drinkers) which raises concerns about whether the study is adequately powered to detect factors associated with progression to binge drinking. 6) Statistical analysis: Based on my understanding of survival analysis there are several limitations here. Survival models were used in the analysis with no reference to which specific method they used (Cox?), whether proportional hazards assumptions held true or which statistical software was used. There is no discussion of how hazard ratios have been adjusted ie. what the modeling strategy was and what covariates were considered for inclusion and why. There is no discussion about collinearity of variables or potential interactions (age is the obvious one). It would be helpful to have indicated how the attributable risk fraction calculations on adjusted data were undertaken. Results: Participants were followed up over three 8 month periods, with approximately 30% attrition by the final phase compared to those eligible, but this still falls within the sample size calculation for onset of drinking. The authors acknowledge that the characteristics of those who dropped out were disproportionately from non-white, poorer groups. The multiple imputation method used to address missing data assumed it was missing at random which clearly it wasn't. Tables 3 and 4 show adjusted hazard ratios for 20 different variables for the onset of consumption (table 3) and onset of binge drinking (table 4). My concern is that the study may not have been adequately powered to detect factors associated with progression to binge drinking (see above). Inclusion of sample numbers rather than just percentages in table 2 would be useful. From a public health perspective it is useful to see the attributable risk fractions presented though how these were done on adjusted data was not clear as previously mentioned. Notwithstanding some of the concerns over whether the study is adequately powered to detect factors associated with progression to binge drinking, there are interesting associations between for example peer alcohol use, parental alcohol use, parenting skills and alcohol availability and the onset of alcohol use, which are, aside from movie exposure, important risk factors. Discussion and references: The authors acknowledge that unmeasured confounding is a limitation of the study (as with other observational studies) and recognise that they were not able to disentangle television and movie alcohol exposure. The conclusions were reasonable given the data presented, although again this depends upon whether the sample was adequately powered to detect all associations with progression to binge drinking.

	References: were comprehensive but the majority were from several years ago, with little recent literature cited. The STROBE questionnaire did not appear to have been submitted, although correspondence suggested it had. Abstract: The abstract was an accurate reflection of the paper and key messages were appropriately presented. Ethics: There is no mention of the ethical approval in the manuscript. Recommendation on paper As the paper currently stands I think there is insufficient statistical detail to assess the results in an informed manner. My concerns are that there is no clarity on the multivariate modelling, whether the survival analysis is appropriate and whether the study is powered to detect factors associated with progression to binge drinking. If not, then the differences in associations found between onset of consumption and progression to binge drinking are potentially erroneous. I would welcome further expert statistical review of the methods. References 1. Gordon R, MacKintosh AM, Moodie C. The impact of alcohol marketing on youth drinking behaviour: a two-stage cohort study. Alcohol Alcohol;45(5):470-80. 2. Ferguson CJ, Meehan DC. With friends like these...: peer delinquency influences across age cohorts on smoking, alcohol and illegal substance use. Eur Psychiatry;26(1):6-12. 3. Melotti R, Heron J, Hickman M, Macleod J, Araya R, Lewis G. Adolescent alcohol and tobacco use and early socioeconomic position: the ALSPAC birth cohort. Pediatrics;127(4):e948-55. 4. Noal RB, Menezes AM, Araujo CL, Hallal PC. Experimental use of alcohol in early adolescence: the 11-year follow-up of the 1993 Pelotas (Brazil) birth cohort study. Cad Saude Publica;26(10):1937-44. 5. Duncan SC, Duncan TE, Strycker LA. Alcohol use from ages 9 to 16: A cohort-sequential latent growth model. Drug Alcohol Depend 2006;81(1):71-81.

The manuscript received another review at the BMJ but this reviewer did not give permission for their comments to be published.

VERSION 1 – AUTHOR RESPONSE

Originality: This study investigates factors that may influence the onset of alcohol use in young people and occurrence of binge drinking using a cohort of US adolescents aged 10-14 years. Predictor variables included movie alcohol exposure, ownership of alcohol branded materials and family factors. Overall the paper is well written though it lacks detail with regards to the statistical analysis.

This is not the first study to look at these influences on alcohol consumption in adolescence although it does uniquely bring them together in the same study: The authors identify some previous studies and in addition Gordon et al 2010 used a cohort study to assess the impact of different types of alcohol marketing on drinking initiation and consumption frequency1; Ferguson and Meehan 2011 used a cohort design to assess the impact of peers on alcohol use, adjusting for media influences2 and Fisher et al, showed that possession of alcohol-branded promotional items is associated with increased likelihood of alcohol initiation. In addition several studies have attempted to identify other influences on alcohol uptake and use in adolescence3-5. However the literature on this topic is not extensive and the current study does distinguish factors that affect alcohol use onset and more hazardous patterns of drinking which adds to the research literature.

RESPONSE: We thank the reviewer for pointing out references we missed in our review of the literature. We cited the Gordon article as an example of a study that links alcohol marketing with drinking. We parenthetically note that the Gordon article found an odds ratio of 1.6 for the association between mums drinking and having tried one or more alcoholic drinks, an odds ratio that is similar to ours (1.4) for the association between parent drinking and drinking onset. Since our study was adequately powered to detect that level of association on drinking onset, the odds ratio of 1.4 was statistically significant, whereas the odds ratio of 1.6 in the Gordon study was not. See more on power in our response to queries about power below. We did not mention Ferguson as that study was cross sectional, had what we consider to be inadequate measures of media exposure and no measures of family or peer alcohol use. We did not mention Melotti for similar reasons. The studies by Noal and Duncan are mentioned as prospective studies that link family alcohol with youth alcohol use. Duncan is especially interesting because in that one parent alcohol use was linked with intercept but not slope in a growth model, a finding similar to ours, in which parent alcohol use was linked with initiation but not progression to binge drinking. We point out that similarity in the opening paragraph of the discussion.

Methods:
1) Research question: The research question is clearly defined i.e. to estimate the association between a range of media and family factors and alcohol use initiation and progression onto binge drinking in adolescents and a cohort study design is appropriate for this.

RESPONSE: We agree.

2) Participants: the authors describe well the process of recruitment. No exclusion criteria appear to have been applied, except for age and consent being obtained which are both appropriate. However there may be some selection biases associated with the sampling method i.e. participants needed to have a landline telephone, which may have selected out poorer households.

RESPONSE: The selection process may have selected out some households, but the appendix table suggests that poorer households was not one of the problems. In fact, there were slightly more households in the poorest household income category compared with the US census figures, and we were pleasantly surprised by this fact. Most households have telephone service in the United States. At this time, many poorer households are served by mobile phones, but at the time of this survey, 2003, this was not the case.

3) Outcome measures: The main outcome measures of time to onset of alcohol use and binge drinking are clear but the STROBE questionnaire did not appear to have been submitted, although correspondence said it had.

RESPONSE: We have included our STROBE statement in the revision application.

Ascertaining alcohol use is notoriously difficult because of recall and social desirability biases (people don't necessarily want to admit to their use) so non face-to-face interviews using keypad pressing to answer sensitive questions is a reasonable method to use, although still subject to some of these biases.

RESPONSE: We agree with the reviewer that ascertaining alcohol use among adults is notoriously difficult, social desirability and denial being big issues with that demographic. Among adolescents there is less social desirability bias to under-report. In fact, alcohol use can improve social standing among adolescents, and that may be why, in the school setting, adolescents tend to over-report their alcohol use.

The authors sought parental consent prior to adolescent consent and in doing so, enrolled 6522 individuals out of a possible 9849. The authors estimated their response rate to be 32% (including non-contactable households in the denominator), which is quite low but to be reasonably representative of the US population with some differences in ethnicity. The comparable US statistics show that the sample is slightly over representative of the higher household incomes and this is important for the study's generalisability given the telephone-based method of data collection and the potential for not recruiting people who move home frequently or do not possess a telephone landline. Other studies have shown conflicting results regarding the importance of socioeconomic status and binge drinking in particular, so this is a limitation of the study.

RESPONSE: Please review the data on household incomes for the appendix Table. In fact, low income households are slightly over represented and affluent families under represented. We wonder if the reviewer is referring to the fact that adolescents from poorer households were more likely to drop out, an issue that we have discussed in our handling of attrition below.

4) Exposure: Movie alcohol exposure was assessed using a previously validated method. However the nature of the classification does not appear to evaluate the nature of the exposure, whether 'positive' or 'negative' in terms of how alcohol use is depicted.

RESPONSE: It is impossible to ascertain how the adolescent reacted to each scene of alcohol use in a movie using our content coding scheme and our method for ascertaining exposure. This is a limitation of our method; we suggest that assessing response to positive and negative alcohol scenes would be a better topic for an experimental research project. We have more complete data on movie tobacco use and found that it didn't matter whether the character depicting tobacco use was a "good" guy or a "bad" guy, that adolescents responded with increased smoking to each exposure.[1] Based on that study, we would be surprised if ascertainment of character valence would make much of a difference for alcohol.

4 continued) Alcohol branded merchandise was not ascertained at baseline which is unfortunate.

RESPONSE: We would have preferred to have assessed ABM at baseline, but it was assessed at the second wave. Since there was an association between ABM ownership and drinking outcomes, net other exposures, it isn't clear in our mind why this would be a major problem with the study, except that the hazard ratio is averaged over two observation periods rather than three.

4 continued) A range of other predictor variables were ascertained relating to the individual adolescent's and then family predictors included variables shown in other studies to be important in alcohol use initiation including availability of alcohol in the home, alcohol use and parenting authority.

RESPONSE: We agree that the large range of covariates represents a major strength of the study. The association between movie alcohol and alcohol branded merchandise and the outcomes is independent of this large range of covariates.

5) Sample size: The sample size calculation refers to moving smoking and never smokers (p8) which

is clearly a careless 'cut and paste' mistake?? The authors need to show what figures they used to calculate the sample size fully and explain why they used these. What was the estimated prevalence of alcohol use at baseline and what did they use as an estimate of movie exposure? Why did they use movie exposure and not ownership of branded materials or parental factors which may be less common?

RESPONSE: It is unfortunate that the reviewer interpreted this sentence pejoratively, as a careless cut and paste mistake. Please see our response to point 5 for reviewer 1. We make clear in the revision why the study was powered on smoking and not alcohol. The questions that follow on point 5 are hypotheticals, but since we did not do a sample size calculation based on alcohol, they seem less relevant. It is worth mentioning here that adolescents start using alcohol about the same time as they start smoking, and that studies powered to study smoking as an outcome during early adolescence are generally adequately powered to study alcohol. It seems rather extraordinary to be facing criticism that our longitudinal study of over 6,000 adolescents is inadequately powered, but that often happens when studies make a point out of a null finding, as we have in this case for family predictors of alcohol use on binge drinking. If the reviewer wishes to explicate the particular variables that the study may be inadequately powered for, we can then look at the estimate and determine how many individuals would have to be in the study in order to detect an effect. For associations like the availability of alcohol in the home on binge drinking (AHR 1.12) the sample size necessary to detect this effect as significant is likely to be in the tens of thousands and clearly beyond the scope of this or any of the other longitudinal studies of alcohol use during adolescence cited in this article. The pertinent question here is, "Is an AHR of 1.12 important from a clinical or public health standpoint?" We would say no.

5 continued) Also, why did they select onset of drinking rather than onset of binge drinking – presumably the latter was less frequent (particularly because the sample size is further reduced as it is for ever drinkers) which raises concerns about whether the study is adequately powered to detect factors associated with progression to binge drinking.

RESPONSE: Although onset of binge drinking is less frequent (see Table 2), it does occur at high enough frequency to detect significant associations for a number of variables, including race, age, movie exposure, ownership of alcohol branded merchandise, sensation seeking, and rebelliousness. Because different predictors may predict different drinking transitions, we prefer the current approach, which is similar to using growth models to predict intercept and slope.

6) Statistical analysis: Based on my understanding of survival analysis there are several limitations here. Survival models were used in the analysis with no reference to which specific method they used (Cox?), whether proportional hazards assumptions held true or which statistical software was used.

We stated in the statistical methods section, "Discrete time hazard survival models were fit to each of the imputed complete datasets following standard procedures for pooling the estimates and obtaining standard errors." The Cox model is a continuous time survival model. Discrete time hazard models are appropriate when data are collected in survey waves, as they are here. We added to the statistical methods section to make it clear that the survival models were fit using the logistic regression routine in the R statistical package. The proportional hazards assumption in this framework implies that the effect of a baseline predictor stays constant throughout the discrete time periods that make up the longitudinal follow up. This amounts to a moderation of a substantive predictor effect by time, which was not of direct theoretical interest for this manuscript. For brevity, we focused this manuscript on the main effects of the predictors.

There is no discussion of how hazard ratios have been adjusted ie. what the modeling strategy was and what covariates were considered for inclusion and why.There is no discussion about collinearity of variables or potential interactions (age is the obvious one). It would be helpful to have indicated how the attributable risk fraction calculations on adjusted data were undertaken.

Response: All variables were entered in the model simultaneously. Covariates were selected to rule out the possibility of a spurious relation for the variables of direct theoretical interest, movie alcohol exposure and owning alcohol branded merchandise. Pathological collinearity of variables was not an issue and moderation due to age, follow up time and other interactions were not the theoretical focus of the manuscript. For brevity, we focused this manuscript on the main effects of the predictors. Unfortunately, the reviewer appears to have overlooked the explanation on page 11, lines 33-54 for the attributable risk calculations. If there are still concerns about the explication of the statistical methods in the manuscript, we would be happy to submit a technical appendix for publication.

Results:
Participants were followed up over three 8 month periods, with approximately 30% attrition by the final phase compared to those eligible, but this still falls within the sample size calculation for onset of drinking. The authors acknowledge that the characteristics of those who dropped out were disproportionately from non-white, poorer groups. The multiple imputation method used to address missing data assumed it was missing at random which clearly it wasn't.

RESPONSE: Unfortunately, the reviewer misunderstands the common terminology in use for missing data methods, a frequent problem because of the confusing terms applied by experts that study attrition methods. Missing at random, the so called MAR assumption, means missing at random conditional on covariates included in the model. Missing completely at random, MCAR, is the term for missingness that is completely unpredictable. Thus, the fact that predictors included in the model are significantly related to the fact of missingness does not invalidate the MAR assumption. The imputation model included all of the predictors in the model and some auxiliary variables not included in the model that were nonetheless predictive of missingness. This helps to make the MAR assumption more plausible and improves the quality of the imputations.[2] It is also commonly and erroneously assumed that the MAR assumption can be tested. Unfortunately, it cannot unless the missing data can somehow be recovered. Nevertheless, MAR based methods are still the current method of choice because they outperform older methods (in terms of power and bias) based on using only subjects with complete data or single imputation. Much as we would like to include this kind of background information in all our manuscripts to help educate reviewers and readers, space limitations preclude it.

Tables 3 and 4 show adjusted hazard ratios for 20 different variables for the onset of consumption (table 3) and onset of binge drinking (table 4). My concern is that the study may not have been adequately powered to detect factors associated with progression to binge drinking (see above). Inclusion of sample numbers rather than just percentages in table 2 would be useful.

RESPONSE: See our detailed response to power. Again, it would help if the reviewer would explicate exactly which variables she feels the study was inadequately powered to address and why, based on the proportion affected and the adjusted hazard estimates, she feels that particular variable is important from a population or clinical standpoint.

From a public health perspective it is useful to see the attributable risk fractions presented though how these were done on adjusted data was not clear as previously mentioned.

RESPONSE: See our response above concerning the explanation of attributable risk calculations. We think that Reviewer 2 may have overlooked the explanation on page 11, lines 33-54 for the attributable risk calculations.

Notwithstanding some of the concerns over whether the study is adequately powered to detect factors associated with progression to binge drinking, there are interesting associations between for example peer alcohol use, parental alcohol use, parenting skills and alcohol availability and the onset of alcohol use, which are, aside from movie exposure, important risk factors.

Response: Yes, and these associations suggest that power was adequate to detect effects of public health significance.

Discussion and references:

The authors acknowledge that unmeasured confounding is a limitation of the study (as with other observational studies) and recognise that they were not able to disentangle television and movie alcohol exposure. The conclusions were reasonable given the data presented, although again this depends upon whether the sample was adequately powered to detect all associations with progression to binge drinking.

Response: Powering a study to detect all non-zero associations with an outcome is not even remotely practical. Investigators need to make decisions about how big an effect must be to be important and then power studies accordingly. The reviewer needs to be more specific about what effect size her power concerns pertain to in order for us to answer the concern more specifically.

References: were comprehensive but the majority were from several years ago, with little recent literature cited. The STROBE questionnaire did not appear to have been submitted, although correspondence suggested it had.

Abstract: The abstract was an accurate reflection of the paper and key messages were appropriately presented.

Ethics: There is no mention of the ethical approval in the manuscript.

RESPONSE: In the methods section, we included a sentence at the end of the first paragraph, "All aspects of the survey were approved by the institutional review boards at Dartmouth Medical School and Westat." Is there something additional the reviewer was looking for?

Recommendation on paper

As the paper currently stands I think there is insufficient statistical detail to assess the results in an informed manner. My concerns are that there is no clarity on the multivariate modelling, whether the survival analysis is appropriate and whether the study is powered to detect factors associated with progression to binge drinking. If not, then the differences in associations found between onset of consumption and progression to binge drinking are potentially erroneous. I would welcome further expert statistical review of the methods.

RESPONSE: We hope that our responses to the specific concerns addressed above are satisfactory to assuage concerns about the statistical analysis and power to detect an effect of clinical or public health importance.

REFERENCES

1. Tanski SE, Stoolmiller M, Dal Cin S, Worth K, Gibson J, Sargent JD. Movie character smoking and adolescent smoking: who matters more, good guys or bad guys? *Pediatrics* 2009;124(1):135-43.
2. Graham JW. Missing data analysis: Making it work in the real world. *Annual Review of Psychology* 2009;60:549-76.

VERSION 2 – REVIEW

REVIEWER	Dr Elizabeth Orton Lecturer and Specialty Registrar in Public Health University of Nottingham, UK I have no competing financial or other interests with this research.
REVIEW RETURNED	11/12/2011

THE STUDY	Regarding the referencing, it is fair to say that there is a lack of comparable literature on this topic. I suggested some additional studies for consideration in my previous review and the authors commented on these appropriately.
GENERAL COMMENTS	I have reviewed this paper previously and made many comments. The authors gave a thorough response to these comments and I am satisfied that they have made appropriate clarifications in the revised manuscript.