

**Adverse adult consequences of different alcohol use patterns in adolescence:
An integrative analysis of data to age 30 years from four Australasian cohorts**

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None

ABSTRACT

Background and Aims: Studies have linked adolescent alcohol use with adverse consequences in adulthood; yet it is unclear how strong the associations are and to what extent they may be due to confounding. Our aim was to estimate the strength of association between different patterns of adolescent drinking and longer-term psychosocial harms taking into account individual, family, and peer factors.

Design: Participant-level data were integrated from four long running longitudinal studies: Australian Temperament Project; Christchurch Health and Development Study; Mater Hospital and University of Queensland Study of Pregnancy; Victorian Adolescent Health Cohort Study.

Setting: Australia and New Zealand.

Participants: Participants were assessed on multiple occasions between ages 13 and 30 years (from 1991-2012). Number of participants varied (up to N=9453) by analysis.

Measurements: Three patterns of alcohol use (frequent, heavy episodic, and problem drinking) were assessed prior to age 17. Thirty outcomes were assessed to age 30 spanning substance use and related problems, antisocial behavior, sexual risk-taking, accidents, socioeconomic functioning, mental health, and partner relationships.

Findings: After covariate adjustment, weekly drinking prior to age 17 was associated with a two to three-fold increase in the odds of binge drinking (OR: 2.14; 95%CI: 1.57-2.90), drink driving (OR: 2.78; 95%CI: 1.84-4.19), alcohol-related problems (OR: 3.04; 95%CI: 1.90-4.84), and alcohol dependence (OR: 3.30; 95%CI: 1.69-6.47) in adulthood. Frequency of drinking accounted for a greater proportion of the rate of most adverse outcomes than the other measures of alcohol use. Associations between frequent, heavy episodic, and problem drinking in adolescence and most non-alcohol outcomes were largely explained by shared risk factors for adolescent alcohol use and poor psychosocial functioning.

Conclusions: Frequency of adolescent drinking predicts substance use problems in adulthood as much as, and possibly more than, heavy episodic and problem drinking independent of individual, family and peer predictors of those outcomes.

Key words: Adolescence, alcohol use, binge drinking, alcohol-related problems, adult psychosocial outcomes, longitudinal studies, integrative analysis

INTRODUCTION

Alcohol use is common among young people in middle- and high-income countries [1]. Among 15-19 year olds, 34% are current drinkers and 12% report recent heavy episodic (binge) use [2]. While adolescent alcohol use has been declining in some countries, prevalence remains high in eastern Europe, Australasia, western Europe, and North America [3] despite major investment in prevention and policy initiatives [4].

Adolescent alcohol use has been linked to physiological and behavioral harms [5-7]. It can affect early brain development [8] and increases the risk of alcohol use disorders and disease in later life [9]. Heavier alcohol use may adversely affect mental health, [10] and increase the risks for other substance use [11], risky sexual behavior [12], gambling [13], violence [14], and persistent delinquent behavior [15] (Appendix 1). Despite these putative harms, recent systematic reviews of the longer-term consequences of adolescent drinking have concluded that evidence is sparse and of poor quality [6, 7]. Limitations of extant studies include insufficient statistical power to examine less common outcomes of adolescent drinking patterns; poor control for confounding; and evaluations of associations limited to single cohorts or social contexts. Hence it is unclear how strong the associations are and which adolescent drinking patterns should be the focus of prevention.

We addressed these issues by integrating data from four longitudinal studies in Australia and New Zealand [16-19]. We integrated participant-level data rather than using meta-analyses to combine study-level estimates. This increased sample size and statistical precision to investigate lower prevalence patterns of alcohol use, such as heavy episodic use at a young age. It also enabled a wide range of potential confounding factors to be included, and augmented our ability to generalize findings to the region and other high-income countries better than any individual study [20, 21].

Our aim was to estimate the longer-term psychosocial consequences of three different patterns of alcohol use in adolescence, namely: frequent, heavy episodic, and problem drinking.

Specifically, we aimed to develop consistent measures of adolescent drinking and each outcome across the cohorts; estimate the association between the pattern of alcohol use before age 17 and each outcome in adulthood using the combined data; and adjust these associations for potential confounding factors that spanned individual, family, and peer characteristics and behavior.

METHODS

Design and participants

Integrative analyses were developed across [22]:

The Australian Temperament Project (ATP) [16]: a longitudinal study that commenced in 1983 as a sample of 2443 infants (aged 4-8 months) and their parents in Victoria, Australia. The ATP has been assessed on 16 occasions in childhood through to adulthood (age 32);

The Christchurch Health and Development Study (CHDS) [17]: a longitudinal birth cohort of 1265 children born in the Christchurch, New Zealand, urban region in 1977. The cohort has been assessed on 24 occasions from birth to age 40;

The Mater Hospital and University of Queensland Study of Pregnancy (MUSP) [18]: a 1981 birth cohort assessed on 10 occasions to age 33, in Queensland, Australia. Assessments on children were conducted on five occasions from age 6 months to age 30.

The Victorian Adolescent Health Cohort Study (VAHCS) [19]: a 1992 longitudinal study of a representative sample of 1943 mid-secondary school adolescents in Victoria, Australia. Participants were assessed at least once during recruitment in Year 9 or Year 10, and on four other occasions during adolescence with four follow-ups to age 35.

Additional information about the cohorts is in Appendix 2. Analyses were based on assessments between ages 13 and 30. The number of participants in the analyses varied (from 807 to 9453) as not all cohorts assessed all measures.

Measures and outcomes

A description of measures used to assess alcohol use and outcomes and the derivation of variables is summarised below, with additional information in Appendix 3. We assessed three different patterns of alcohol use that corresponded to specific adolescent drinking contexts investigated in previous studies [7, 23] for which data were available (assessed 1991-1998) across the cohorts (frequent, heavy episodic, and problem drinking):

Frequency of alcohol use in adolescence: The ATP assessed lifetime use and number of drinking days in the past month at ages 13 and 15. The CHDS assessed past 12 months frequency of use at ages 15 and 16. The MUSP assessed frequency of use at age 14. The VAHCS assessed current drinking status and number of drinking days in the past week using a 7-day drinking diary at six assessments between ages 15-17.5. Using these data, a measure of the maximum frequency of alcohol use prior to age 17 was created for each study (0=never, 1=less than weekly, 2=weekly or more often).

Number of standard drinks consumed per drinking occasion in adolescence: The CHDS assessed the amount of alcohol consumed (in millilitres) per occasion at ages 14, 15 and 16. The MUSP assessed the number of glasses of alcohol consumed per occasion at age 14. The VAHCS assessed the average number of standard drink units consumed per drinking day in the past week at six assessments between ages 15-17.5. Using these data, the distribution of maximum number of standard drinks consumed per drinking occasion prior to age 17 was classified for each study (0= \leq 2 standard drinks; 1=3-4 standard drinks; 2=5-6 standard drinks; 3=7+ standard drinks).

Number of alcohol related problems in adolescence: The ATP assessed the lifetime frequency of five drinking-related problems at age 15. The CHDS assessed the number of alcohol abuse/dependence symptoms in the past 12 months at ages 15 and 16 using the Rutgers Alcohol Problems Index [24]. The VAHCS assessed the frequency of 13 drinking-related

problems in the past six months at six assessments between ages 15-17.5. Using these data, the distribution of maximum number of alcohol-related problems prior to age 17 was classified for each study (0=no problems, 1=1-2 problems, 2=3-4 problems, 3=5+ problems).

Measures of 30 psychosocial outcomes were assessed between ages 21-30 (1998 to 2012) and spanned the following domains and ages (Appendix 3):

1. *Alcohol use and related problems*: Frequency of use and bingeing, number of drinks per drinking occasion, and number of alcohol-related problems, each at age 21; drink-driving at age 21 and by age 30; alcohol dependence by age 24 and by age 30;
2. *Other substance use*: Tobacco use, cannabis use, and other illicit drug use, each at age 21; cannabis dependence by age 30;
3. *Antisocial behavior*: Antisocial behavior at age 21; police contact by age 21;
4. *Sexual risk-taking and early parenthood*: Multiple sexual partners, and unprotected sex, both at age 21; pregnancy, and parenthood, both by age 21;
5. *Accidents*: Vehicle accidents by age 24;
6. *Socioeconomic functioning*: High-school non-completion, and university degree non-attainment, both by age 30; lower income, and welfare dependence, both at age 30;
7. *Mental health*: Substantial symptoms of depression at age 21; suicide attempt by age 25; major depression, and anxiety disorder, both by age 30;
8. *Partner relationships*: Quality of partner relationship at age 21 and 30; and, victim of intimate partner physical abuse at age 25.

We selected a wide range of potential confounding factors correlated with alcohol use and psychosocial outcomes [7, 25] spanning individual background and functioning and parental and peer factors (Appendix 4). Factors assessed antecedent to alcohol use were included where available.

Statistical analysis

We examined the bivariate associations between each adolescent alcohol exposure and the psychosocial outcomes in each cohort in the combined dataset. A generalized linear

regression model framework was used. Logistic regression models were fitted for dichotomous outcomes, negative binomial regression models were used for count data, and linear regression was used for continuous outcomes. Study-specific random intercepts were included to allow for random sources of heterogeneity between cohorts that were not otherwise reflected in the model (Appendix 5).

The bivariate associations were adjusted for confounding using a generalized propensity score approach [20,21]. Propensity scores were estimated from a multinomial logistic regression in which each adolescent alcohol exposure was regressed on the available confounding factors in each study (Appendix 5). Adjusted effect size estimates (odds ratios (OR) for dichotomous outcomes, incidence rate ratios (IRR) for count data) and 95% confidence intervals were obtained. A Bonferroni adjusted p value ($p < 0.002$) was used to minimize false positive findings, computed for a nominal p value of 0.05 and the average correlation between all outcomes (Appendix 5).

The models assumed that the alcohol exposures had a linear effect on each outcome and that the effect of the alcohol exposures across cohorts was reflected in a common slope parameter. To test these assumptions a series of Wald χ^2 tests were done (Appendix 5).

Finally, the regression models were re-analysed by weighting [26] data by the inverse probability of retention to assess the effects of bias from sample attrition and missing data (Appendix 6). STATA SE (version 14) was used.

RESULTS

Table 1 shows the prevalence of each alcohol exposure before age 17 in each cohort in the combined dataset. There were some between-cohort variations in the prevalence of each alcohol exposure, as expected in cohorts that used somewhat different assessment tools at slightly different ages. In the VAHCS, alcohol exposures in adolescence were assessed at a slightly older age than in the other cohorts and the prevalence of frequent/heavy drinkers

was accordingly higher. Conversely, in the MUSP, alcohol exposures were assessed at a slightly younger age than in the other cohorts and the prevalence of frequent/heavy drinkers lower. The associations between each outcome/exposure combination in each cohort are reported in Appendix 7. Tests of non-linearity indicated that the linear model provided an adequate representation of the data (Appendix 8). Results of Wald χ^2 tests of between-study heterogeneity in the effect of the adolescent alcohol exposures were non-significant (Appendix 8) suggesting that the associations were similar across studies for all exposure/outcome combinations.

[Table 1 about here]

The following results report analyses from data combined across the cohorts. Table 2 presents the rate or mean of each outcome according to levels of exposure across the three alcohol use measures.

[Table 2 about here]

In unadjusted analyses, almost all outcomes were significantly associated with at least one adolescent alcohol exposure (Bonferroni corrected $p < 0.002$; Appendix 9). After adjustment for potential confounding factors, 10 outcomes were significantly associated with at least one adolescent alcohol exposure using a Bonferroni corrected p value (Table 3).

[Table 3 about here]

Table 4 shows the covariate adjusted estimates of effect size (OR, 95%CI) for levels of each adolescent alcohol exposure for each outcome in combined data for associations that were statistically significant (Bonferroni corrected p value). There was a dose-response relationship between increasing exposure to alcohol before age 17 and increasing rates of alcohol use and alcohol-related problems, other substance use, and antisocial behavior, in adulthood.

[Table 4 about here]

Strong associations remained after adjustment for confounders between exposure to alcohol before age 17 and frequent/heavier alcohol use and alcohol-related problems in adulthood (Table 4). Adolescents who drank at least weekly before age 17 had three times the odds of a higher number of alcohol-related problems (age 21: OR 3.04; 95%CI 1.90-4.84), drink-driving (age 21: OR 2.78; 95%CI 1.84-4.19) and alcohol dependence (age 30: OR 3.30; 95%CI 1.69-6.47) in adulthood than those who did not drink before age 17 (Table 4).

The associations for all three adolescent alcohol exposures were generally consistent across all alcohol outcomes and ages (21, 24, 30 years) with the exceptions of drink-driving (only associated at age 21 with frequency of drinking) and alcohol dependence (only associated at age 24 with number of alcohol-related problems and at age 30 with frequency of drinking).

Associations were also observed between exposure to alcohol before age 17 and other substance use in adulthood (Table 4). After adjustment, adolescents who were frequent drinkers (weekly+) had 1.6 times the odds of being a tobacco smoker at age 21 (OR 1.60; 95%CI 1.21-2.10) than never drinkers. Heavy drinking adolescents (7+ drinks per session) had about double the odds of other illicit drug use (age 21: OR 1.81; 95%CI 1.32-2.48) than adolescents who drank ≤ 2 drinks per session.

The association between number of alcohol-related problems before age 17 and antisocial behavior at age 21 (OR 3.92; 95%CI 1.97-7.84) was also significant (Table 4).

Table 5 shows the adjusted attributable risk (AR) for each alcohol exposure estimated from the regression models in combined data. It estimates the proportion of the outcome attributable to each alcohol exposure assuming (a) exposure can be limited to the lowest category and (b) exposure to the highest category can be prevented and individuals in the highest category instead had been in the penultimate category (Table 5). For most outcomes the AR estimates for frequency of drinking were greater than those for the other alcohol exposures.

[Table 5 about here]

After adjustment, associations between adolescent alcohol exposures and outcomes related to sexual risk-taking and early parenthood, accidents, socioeconomic functioning, mental health, and partner relationships were no longer significant (Bonferroni corrected p value). Results using an alternate adjustment method were consistent with those reported in the main analysis (Appendix 10).

Analyses using data weighting to assess the impact of missing data produced findings entirely consistent with those of full data (Appendix 6).

DISCUSSION

Study findings extend previous research on the link between adolescent drinking and adverse outcomes in adulthood by integrating data from four studies and controlling for a broader range of covariates than possible in traditional meta-analyses. Adolescent alcohol use assessed in three different ways predicted most adverse outcomes investigated to age 30, however many of the associations were explained by other covariates. Frequency of drinking accounted for a greater proportion of the rate of most adverse outcomes than the other measures of alcohol use.

The findings provide robust evidence that early patterns of drinking are not time-limited to adolescence and extend into adulthood. Heavy alcohol consumption in adolescence was a particularly strong predictor of problem adult drinking, consistent with a large evidence base [12, 27, 28]. Associations between adolescent alcohol use and other substance use were consistent with research that has found adolescent drinking has a small independent effect on later drug use [29] and that people who initiate regular use of one substance at a young age are much more likely to use other substances [30]. Alcohol-related problems in adolescence were found to be a strong predictor of subsequent antisocial behavior, consistent with previous research [15].

Several aspects of the findings support a causal relation between adolescent drinking and substance use and alcohol problems into adulthood. First, there were strong bivariate associations between all three alcohol exposures and these outcomes. Second, there was a dose-response relationship in each in which increasing exposure to alcohol in adolescence was associated with increasing rates of these outcomes in adulthood. Third, the associations were robust to control for a wide range of potential confounding factors assessed before and during adolescence. Support for a more direct linkage between early drinking and adverse consequences comes from evidence of an inverse relationship between minimum legal drinking age and alcohol use [31], binge drinking [32], traffic accidents [31, 33], and other harms [34].

There are several plausible explanations for the associations identified. Adolescence may be a vulnerable developmental period for the neurocognitive effects of alcohol use because alcohol-related brain changes may lead to habituation and disrupted developmental trajectories [8]. Alternatively, early drinking may be associated with childhood adversity which in turn predicts later problems [7, 8]. In the association between adolescent drinking and antisocial behaviour, it is plausible that such behaviour may have preceded alcohol use [35], however, the analyses included a range of externalizing behaviors as covariate factors assessed prior to or early in adolescence.

By contrast, the association between adolescent drinking and other psychosocial outcomes (sexual risk-taking, early parenthood, accidents, socioeconomic function, mental health problems, and relationship issues) were explained by shared risk factors for adolescent alcohol use and poorer psychosocial functioning. This finding supports the conclusions of previous reviews that the contribution of heavy drinking to these outcomes may be due to uncontrolled confounding [7]. It suggests that early individual and contextual influences account for a large part of the risk for these adverse outcomes. Study findings strengthen support for heavier drinking being only one of a number of components in the causal pathway to non-alcohol adverse outcomes. It is plausible, however, that the effects on psychosocial outcomes are weaker because they are indirect, and therefore they may be more likely to occur in high risk groups [7].

Study findings have a number of implications for prevention. While the three alcohol exposures were related to outcomes in a broadly similar way, the findings highlight the potential value of frequency of alcohol use as an indicator of future drinking problems. Frequency of adolescent drinking predicted substance use problems in adulthood as much as, and possibly more than, heavy episodic and problem drinking independent of individual, family and peer predictors of those outcomes. Although large proportions of adolescents are exposed to this risk, current public health measures tend to focus on the amount (quantity) consumed. There are fewer messages recommending less frequent use of alcohol. We found that assuming it were possible to eliminate all alcohol use prior to age 17 then substance use and alcohol problems in adulthood would be expected to reduce by 11-35%. Stopping drinking entirely before age 17 is reasonable given these adolescents are not yet at legal purchase age, however it seems unrealistic in the context of our alcohol culture. Using less stringent criteria, if it were possible prevent weekly drinking or heavy bingeing prior to age 17 then the expected reduction in harmful drinking patterns in adulthood would be smaller (5-11%). This suggests that if a goal is to prevent harmful drinking patterns in adulthood then interventions targeting higher risk drinking behaviors in adolescence may have limited long-term effects. This is consistent with findings from other research on the topic [36] and supports a population level approach to preventing alcohol harm.

This study had several limitations. First, weekly alcohol use in adolescence is socially normative in Australasia and may not encapsulate 'high risk' alcohol use. However, results from analyses of the other measures of adolescent alcohol exposure were generally consistent with analyses of frequency of alcohol use. Second, there were some between-study variations in the frequency of both adolescent alcohol use/problems and psychosocial outcomes. These differences could have implications for both the precision and validity of effect size estimates for the associations in the integrated data. However, Wald tests in adjusted models provided no evidence of between study heterogeneity in effect sizes, suggesting that the findings were robust to differences in measurement between studies. The number of participants varied by analysis and the ability to detect a specific effect if one was present would have been greatest in analyses which included data from all four

cohorts. Third, measures were self-report and so may be subject to social desirability response bias which may vary with age [37]. Such bias could lead to over-reporting or under-reporting of alcohol use. In face-to-face settings (as is generally the case for the cohorts in this study) adolescents might be more likely than adults to underreport risk behaviours [37]; however, under-reporting is more likely to attenuate rather than inflate observed associations. Fourth, although we controlled for many potential confounding factors, the possibility that the associations might show the effects of uncontrolled confounding cannot be completely ruled out [7]. Residual confounding could attenuate the associations. Fifth, similarities in the cultural/social context and epidemiology of alcohol use between Australia, New Zealand, and other high-income countries suggests these findings may be most applicable to other high-income countries. It is less certain how generalizable these findings are to countries where the epidemiology and socio-economic contexts of alcohol use are not as well understood.

Adolescence is a key developmental period during which patterns of alcohol use can become established and is an opportune period to prevent problem drinking patterns from occurring. There is growing concern about the adverse impacts of alcohol use on young people and debate about the most effective ways to reduce these harms [4]. Population-level public health interventions such as alcohol taxation and increasing the minimum legal drinking age appear to be effective strategies in reducing risky drinking [4]. While there is strong evidence that increasing the legal drinking age will reduce alcohol-related harms in young people [32, 34, 38], the approach is contentious and has little community and political support [39]. Approaches such as the legislative control of the secondary supply of alcohol [40] (which prohibits anyone other than a legal guardian allowing their child to drink in private settings) have been implemented and require evaluation. Parents also have an important role in the prevention of harms as they are a major supplier of alcohol to adolescents [41]; and parental supply does not reduce risky drinking [41]. Discouraging or delaying frequent or heavy alcohol use in adolescence is likely to have substantial benefits in adulthood in preventing the entrenchment of harmful drinking behaviors which adversely affect health and wellbeing.

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Table 1: Prevalence of exposure to alcohol prior to age 17 years, by cohort and in combined data

Exposure to alcohol prior to age 17 years											
Cohort	Maximum frequency of alcohol use			Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems			
	Never	<Weekly	Weekly+	≤2	3-4	5-6	7+	0	1-2	3-4	5+
ATP	24.7 (342/1383)	51.8 (716/1383)	23.5 (325/1383)	n/a	n/a	n/a	n/a	79.9 (1042/1304)	16.8 (219/1304)	2.9 (38/1304)	0.4 (5/1304)
CHDS	10.6 (104/977)	72.5 (708/977)	16.9 (165/977)	58.4 (580/994)	13.0 (129/994)	12.8 (127/994)	15.9 (158/994)	81.7 (798/977)	10.9 (106/977)	4.6 (45/977)	2.9 (28/977)
MUSP	65.8 (3395/5157)	33.0 (1702/5157)	1.2 (60/5157)	92.9 (4787/5153)	3.2 (167/5153)	1.9 (100/5153)	1.9 (99/5153)	n/a	n/a	n/a	n/a
VAHCS	25.7 (498/1936)	25.0 (484/1936)	49.3 (954/1936)	62.6 (1212/1936)	7.3 (142/1936)	5.5 (107/1936)	24.5 (475/1936)	50.3 (957/1902)	27.3 (520/1902)	14.8 (281/1902)	7.6 (144/1902)
Combined	45.9 (4339/9453)	38.2 (3610/9453)	15.9 (1504/9453)	81.4 (6579/8083)	5.42 (438/8083)	4.1 (334/8083)	9.1 (732/8083)	66.9 (2797/4183)	20.2 (845/4183)	8.7 (364/4183)	4.2 (177/4183)

Data are % (n/N); ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy; n/a = not assessed.

Table 2: Rate or mean of adult outcomes according to exposure to alcohol prior to age 17 years, in combined data

		Exposure to alcohol prior to age 17 years										
Adult outcome		Maximum frequency of alcohol use			Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems			
		Never	<Weekly	Weekly+	≤2	3-4	5-6	7+	0	1-2	3-4	5+
Continuity of substance use and related problems												
Weekly or more frequent alcohol use		30.1 (942/3043)	48.5 (1359/2801)	70.1 (867/1237)	36.5 (1762/4832)	54.6 (201/368)	58.3 (165/283)	69.4 (405/584)	50.0 (1162/2326)	67.7 (482/712)	69.7 (216/310)	75.0 (108/144)
Weekly or more frequent binge drinking		15.3 (427/2790)	25.8 (584/2266)	45.2 (453/1002)	19.3 (933/4829)	36.7 (135/368)	39.9 (113/283)	48.8 (285/584)	27.2 (427/1541)	41.4 (227/549)	46.4 (129/278)	55.4 (77/139)
Number of standard drinks consumed per drinking occasion ^b ; (mean (SD, N))	At age 21	3.0 (6.1, 487)	6.1 (6.8, 1074)	7.6 (7.8, 958)	4.8 (6.6, 1533)	7.0 (7.2, 248)	7.8 (7.0, 219)	8.9 (8.1, 527)	5.3 (6.8, 1537)	6.6 (7.3, 548)	7.8 (7.6, 276)	9.9 (9.2, 137)
Higher number of alcohol-related problems		6.5 (194/3003)	10.6 (295/2795)	15.4 (190/1235)	7.7 (370/4784)	12.2 (45/368)	14.2 (40/282)	20.1 (117/583)	5.9 (138/2325)	13.9 (99/175)	19.0 (59/311)	27.1 (39/144)
	At age 21 ^a	18.7 (492/2627)	23.6 (562/2382)	28.7 (121/422)	22.3 (854/3837)	29.6 (71/240)	29.4 (55/187)	34.3 (68/198)	13.1 (198/1510)	24.2 (61/252)	29.7 (22/74)	43.8 (14/32)
Drink-driving	By age 30 ^b	1.8 (8/434)	7.4 (77/1042)	12.0 (103/860)	5.1 (72/1416)	7.8 (18/231)	12.4 (25/202)	14.7 (73/496)	5.6 (82/1457)	9.1 (44/485)	12.4 (32/258)	23.0 (28/122)
	By age 24 ^c	7.1 (144/2031)	10.8 (198/1830)	20.2 (182/902)	8.6 (317/3682)	15.1 (48/318)	15.7 (38/242)	23.2 (122/527)	8.5 (121/1431)	16.9 (85/504)	23.5 (62/264)	33.1 (40/121)
Alcohol dependence	By age 30 ^d	7.0 (118/1686)	13.2 (201/1529)	28.1 (52/185)	8.8 (251/2842)	14.8 (31/209)	19.1 (32/168)	31.2 (60/189)	- ^f	- ^f	- ^f	- ^f
Current tobacco use		27.8 (846/3039)	42.2 (1182/2799)	51.5 (629/1222)	32.7 (1577/4818)	48.4 (177/366)	57.5 (162/282)	59.5 (343/577)	30.0 (692/2306)	49.3 (348/706)	56.7 (174/307)	72.7 (101/139)
Daily cannabis use	At age 21	3.3 (98/3019)	5.6 (156/2786)	9.8 (120/1220)	4.5 (218/4815)	7.4 (27/367)	10.3 (29/281)	14.4 (84/583)	2.7 (61/2290)	8.6 (60/702)	12.3 (38/308)	16.0 (23/144)
Recent other illicit drug use		11.8 (356/3029)	18.8 (527/2800)	22.7 (279/1230)	14.3 (688/4819)	24.4 (90/369)	27.2 (77/283)	32.7 (191/584)	10.1 (235/2324)	20.0 (141/704)	30.2 (93/308)	37.8 (54/143)
Cannabis dependence	By age 30 ^c	8.2 (166/2027)	12.3 (232/1894)	24.2 (205/847)	9.5 (353/3699)	15.7 (49/313)	19.0 (47/247)	30.0 (155/517)	9.5 (129/1365)	18.4 (86/467)	29.8 (76/255)	35.3 (41/116)
Antisocial behaviour												
Antisocial behaviour ^a	At age 21	34.6 (911/2634)	34.2 (823/2408)	40.5 (176/435)	34.9 (1330/3816)	29.7 (71/239)	33.0 (62/188)	36.6 (72/197)	22.2 (347/1563)	34.2 (91/266)	50.7 (38/75)	43.8 (14/32)
Police contact ^d	By age 21	19.6 (467/2382)	35.8 (675/1887)	60.1 (122/203)	24.8 (949/3833)	40.1 (99/247)	50.8 (96/189)	58.4 (122/209)	- ^f	-	-	-
Sexual risk-taking and early parenthood												
Multiple sexual partners ^c	At age 21	5.1 (139/2746)	7.1 (160/2260)	6.4 (64/995)	5.5 (261/4774)	8.2 (30/368)	6.4 (18/282)	9.3 (54/583)	4.1 (62/1525)	5.9 (32/545)	7.6 (21/278)	8.6 (12/139)
Unprotected sex ^b		36.1 (105/291)	34.2 (336/979)	57.0 (489/858)	39.0 (466/1194)	37.6 (88/234)	43.9 (90/205)	57.3 (288/503)	33.5 (415/1240)	56.2 (271/482)	60.7 (153/252)	62.7 (84/134)
Pregnancy ^c	By age 21	15.2 (387/2547)	22.9 (417/1821)	18.0 (90/500)	16.8 (694/4141)	24.4 (66/271)	31.0 (57/184)	28.4 (78/275)	13.4 (111/827)	15.4 (46/299)	17.9 (26/145)	23.0 (17/74)

Exposure to alcohol prior to age 17 years

Adult outcome	Maximum frequency of alcohol use			Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems				
	Never	<Weekly	Weekly+	≤2	3-4	5-6	7+	0	1-2	3-4	5+	
Parenthood	6.8 (206/3039)	7.4 (210/2830)	5.7 (71/1243)	7.2 (349/4844)	9.3 (35/376)	10.9 (31/285)	9.6 (57/594)	3.6 (85/2347)	4.6 (33/720)	6.4 (20/311)	7.6 (11/144)	
Accidents												
Vehicle accident	By age 24 ^a	41.8 (1082/2588)	49.2 (1129/2295)	57.7 (220/381)	43.3 (1652/3813)	44.7 (105/235)	51.1 (93/182)	51.5 (104/202)	52.3 (724/1385)	63.9 (147/230)	51.5 (34/66)	71.9 (23/32)
Socioeconomic functioning												
High school non-completion	By age 30	10.7 (225/2098)	24.7 (565/2290)	24.8 (317/1280)	17.2 (615/3583)	30.3 (101/333)	40.2 (106/264)	36.5 (225/616)	24.8 (582/2344)	24.5 (185/754)	29.9 (98/328)	36.7 (59/161)
University degree non-attainment	By age 30	61.2 (1175/1921)	62.8 (1330/2117)	59.4 (632/1064)	62.5 (2001/3202)	67.6 (196/290)	71.0 (164/231)	70.0 (354/508)	54.9 (1145/2087)	58.3 (366/628)	66.0 (184/279)	73.2 (90/123)
Lower income	At age 30	11.1 (216/1951)	11.3 (240/2129)	10.2 (107/1046)	11.0 (354/3226)	10.4 (30/288)	12.2 (28/230)	10.6 (53/502)	10.3 (211/2054)	10.0 (61/613)	11.2 (31/276)	12.4 (15/121)
Welfare dependence	At age 30	12.2 (233/1914)	9.7 (205/2105)	7.5 (81/1076)	12.2 (386/3167)	10.3 (30/291)	12.1 (28/232)	8.5 (43/509)	6.4 (134/2107)	8.1 (51/633)	7.9 (22/279)	10.5 (13/124)
Mental health												
Substantial depression symptoms	At age 21	21.5 (642/2989)	25.9 (723/2790)	30.0 (370/1234)	22.1 (1052/4766)	26.1 (95/364)	28.3 (80/283)	30.3 (177/584)	29.0 (674/2323)	28.2 (201/713)	36.8 (114/310)	37.5 (54/144)
Suicide attempt	By age 25 ^b	1.1 (5/460)	4.4 (48/1089)	2.1 (19/919)	2.3 (34/1494)	3.3 (8/243)	4.6 (10/216)	4.0 (21/524)	2.9 (44/1523)	2.5 (13/528)	2.9 (8/278)	5.6 (7/126)
Major depression	By age 30 ^c	22.2 (445/2004)	31.7 (590/1859)	25.5 (220/863)	24.7 (902/3659)	33.9 (107/316)	37.0 (90/243)	30.6 (158/516)	33.1 (469/1419)	27.9 (133/477)	31.2 (79/253)	36.2 (43/117)
Anxiety disorder	By age 30 ^c	41.2 (830/1982)	41.4 (768/1854)	23.2 (198/855)	39.9 (1449/3633)	37.9 (118/311)	35.4 (86/243)	28.3 (145/512)	28.3 (401/1419)	23.6 (113/478)	24.3 (61/251)	32.8 (39/119)
Partner relationships												
Quality of partner relationship; ^g mean (SD, N)	At age 21 ^a	101.5 (9.4, 2113)	102.2 (10.7, 1769)	100.4 (11.5, 257)	102.5 (9.6, 3133)	103.4 (10.3, 178)	104.3 (10.9, 142)	104.3 (11.6, 131)	99.0 (10.4, 827)	99.0 (11.2, 161)	99.5 (9.7, 51)	103.0 (11.4, 21)
	At age 30 ^a	100.1 (10.2, 1226)	98.1 (10.3, 1434)	95.2 (10.6, 310)	100.6 (10.1, 1902)	98.3 (10.7, 158)	97.1 (11.2, 138)	97.2 (9.8, 150)	95.8 (10.0, 1133)	95.3 (10.0, 202)	96.8 (8.2, 55)	93.5 (10.8, 28)
Victim of intimate partner physical abuse	At age 25 ^d	9.0 (122/1354)	10.0 (120/1199)	13.1 (20/153)	9.3 (209/2251)	6.6 (11/168)	16.4 (24/146)	12.8 (19/148)	- ^f	-	-	-

Data are % (n/N) except for continuous/scale variables where mean (SD, N) reported; SD=Standard deviation. ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS. ; ^fOnly CHDS contributed data; ^gScored such that a higher score indicated a poorer quality relationship.

Table 3: Adjusted associations (B, SE) between exposure to alcohol prior to age 17 years and adult outcomes in combined data

Adult outcome	Exposure to alcohol prior to age 17 years												
	Maximum frequency of alcohol use				Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems				
	B	SE	P	N	B	SE	P	N	B	SE	P	N	
<i>Continuity of substance use and related problems</i>													
Weekly or more frequent alcohol use	0.48	0.06	<0.001*	3881	0.20	0.04	<0.001*	3294	0.29	0.07	<0.001*	2693	
Weekly or more frequent binge drinking	0.38	0.08	<0.001*	3271	0.19	0.04	<0.001*	3292	0.23	0.07	0.001*	2094	
Number of standard drinks consumed per drinking occasion ^b	At age 21	0.29	0.05	<0.001*	2096	0.12	0.03	<0.001*	2116	0.19	0.04	<0.001*	2088
Higher number of alcohol-related problems		0.56	0.12	<0.001*	3879	0.32	0.07	<0.001*	3292	0.51	0.10	<0.001*	2694
Drink-driving	At age 21 ^a	0.51	0.11	<0.001*	2605	0.10	0.08	0.213	2026	0.37	0.13	0.003*	1424
	By age 30 ^b	0.31	0.18	0.088	2005	0.12	0.08	0.120	2025	0.27	0.12	0.018*	1998
Alcohol dependence	By age 24 ^c	0.28	0.12	0.015*	2937	0.16	0.06	0.007*	2958	0.29	0.09	0.001*	2082
	By age 30 ^d	0.60	0.17	<0.001*	1643	0.24	0.09	0.008*	1644	- ^f	-	-	-
Current tobacco use		0.23	0.07	0.001*	3856	0.13	0.05	0.003*	3270	0.20	0.07	0.006*	2665
Daily cannabis use	At age 21	0.12	0.16	0.458	3851	0.09	0.08	0.237	3285	0.18	0.11	0.124	2663
Recent other illicit drug use		0.19	0.10	0.043*	3870	0.20	0.05	<0.001*	3294	0.20	0.08	0.013*	2683
Cannabis dependence	By age 30 ^c	0.20	0.13	0.125	2777	0.16	0.06	0.011*	2797	0.05	0.10	0.586	1964
<i>Antisocial behaviour</i>													
Antisocial behaviour ^a	At age 21	0.23	0.09	0.012*	2637	0.15	0.09	0.077	2020	0.46	0.12	<0.001*	1462
Police contact ^d	By age 21	0.22	0.11	0.047*	2038	-0.02	0.07	0.820	2039	- ^f	-	-	-
<i>Sexual risk-taking and early parenthood</i>													
Multiple sexual partners ^c	At age 21	0.13	0.16	0.417	3257	0.14	0.09	0.128	3278	0.06	0.14	0.664	2083
Unprotected sex ^b		0.18	0.09	0.052	1802	0.07	0.05	0.120	1815	0.12	0.08	0.119	1794

Exposure to alcohol prior to age 17 years													
Adult outcome		Maximum frequency of alcohol use				Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems			
		B	SE	P	N	B	SE	P	N	B	SE	P	N
Pregnancy ^c	By age 21	0.28	0.13	0.029*	2324	0.03	0.08	0.743	2334	-0.08	0.13	0.573	1153
Parenthood		0.26	0.15	0.094	3898	-0.002	0.09	0.978	3311	0.19	0.14	0.184	2708
Accidents													
Vehicle accident	By age 24 ^a	0.11	0.08	0.182	2625	-0.02	0.07	0.710	2003	0.27	0.11	0.017*	1445
Socioeconomic functioning													
High school non-completion	By age 30	0.10	0.10	0.309	3384	0.03	0.05	0.542	2863	0.16	0.09	0.064	2721
University degree non-attainment		0.00	0.07	0.988	3140	0.08	0.47	0.084	2615	0.02	0.07	0.834	2497
Lower income	At age 30	0.01	0.11	0.945	3124	0.00	0.07	0.999	2591	0.02	0.11	0.849	2461
Welfare dependence		0.04	0.13	0.758	3134	-0.06	0.08	0.469	2591	-0.13	0.13	0.307	2517
Mental health													
Substantial depression symptoms	At age 21	-0.12	0.07	0.081	3864	-0.06	0.05	0.192	3281	0.06	0.07	0.406	2689
Suicide attempt	By age 25 ^b	-0.26	0.28	0.349	2189	-0.09	0.13	0.472	2213	-0.10	0.20	0.623	2181
Major depression	By age 30 ^c	-0.11	0.09	0.198	2761	-0.03	0.05	0.604	2779	0.21	0.09	0.017*	1978
Anxiety disorder		-0.10	0.08	0.290	2756	-0.07	0.05	0.154	2776	-0.04	0.09	0.664	1979
Partner relationships													
Quality of partner relationship ^g	At age 21 ^a	1.16	0.47	0.013*	1832	-0.28	0.40	0.482	1491	0.08	0.64	0.895	807
	At age 30 ^a	-0.24	0.51	0.642	1651	0.27	0.38	0.469	1243	0.79	0.58	0.169	1147
Victim of intimate partner physical abuse	At age 25 ^d	0.00	0.21	0.987	1334	-0.11	0.14	0.410	1335	- ^f	-	-	-

Footnote for Table 3:

^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fOnly CHDS contributed data; ^gScored such that a higher score indicated a poorer quality relationship. Note: * $p < 0.05$; Bold=Bonferroni adjusted $p < 0.002$; Adjusted using a multiple propensity score approach, with propensity scores computed for each individual based on the available likely predictors of adolescent alcohol use and combined across studies (further information about the specific predictors included from each study can be found in the Appendix and is summarized here. ATP: school problems, 14-15 years; conduct disorder 13-16 years; attentional problems, 13-16 years; tobacco use, 13-16 years; cannabis use, 13-16 years; other illicit drug use before 17 years; depression, 13-16 years; sexual abuse, before 16 years; sex; ethnicity; parental socio-economic status; parental alcohol and tobacco use; parental education; parental divorce; antisocial peer activities, 13-16 years. CHDS: Grade point average, 11-13 years; conduct problems, 7-9 and 14-16 years; attentional problems, 7-9 and 14-16 years; tobacco use, 10-15 years; cannabis use, 15 years; other illicit drug use before 17 years; anxiety disorder, 14-16 years; major depression, 14-16 years; sexual abuse before 16 years; sex; ethnicity; socio-economic status at birth; family living standards, 1-10 years; parental history of criminal offending, parental tobacco use; parental history of alcohol problems; parental illicit drug use; parental history of mental health problems; parental education level at birth, parental separation, 0-10 years; deviant peer affiliations, 15 years. MUSP: conduct problems, 14 years; attentional problems, 14 years; school performance, 14 years; tobacco use, 14 years; cannabis use, 14 years; other illicit drug use, 14 years; symptoms of depression/anxiety, 14 years; sexual abuse before 16 years; sex; family income, 14 years; maternal tobacco/alcohol use, 14 years; maternal anxiety/depression, 14 years; maternal education level at birth of child; parental divorce, 14 years; maternal/paternal ethnicity; deviant behavior happening at school, 14 years. VAHCS: antisocial behaviour before 17 years; tobacco use before 17 years; cannabis use before 17 years; other illicit drug use before 17 years; symptoms of depression/anxiety before 17 years; sexual abuse before 16 years; sex; ethnicity; parental tobacco use; parental alcohol use; parental education; parental divorce/separation; peer alcohol, tobacco and illicit drug use, before 17 years).

Table 4: Summary of significant adjusted associations (OR, 95%CI) between exposure to alcohol prior to age 17 years and adult outcomes in combined data

Adult outcome		Exposure to alcohol prior to age 17 years										
		Maximum frequency of alcohol use			Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems			
		Never	<Weekly	Weekly+	≤2	3-4	5-6	7+	0	1-2	3-4	5+
<i>Continuity of substance use and related problems</i>												
Weekly or more frequent alcohol use		1	1.61 (1.42-1.83)	2.61 (2.03-3.34)	1	1.22 (1.12-1.33)	1.48 (1.25-1.76)	1.81 (1.40-2.34)	1	1.34 (1.17-1.53)	1.80 (1.36-2.35)	2.39 (1.49-3.60)
Weekly or more frequent binge drinking		1	1.46 (1.25-1.70)	2.14 (1.57-2.90)	1	1.21 (1.11-1.32)	1.47 (1.24-1.74)	1.78 (1.37-2.30)	1	1.26 (1.10-1.47)	1.56 (1.20-2.09)	2.00 (1.32-3.02)
Number of standard drinks consumed per drinking occasion ^{b, e}	At age 21	1	1.33 (1.21-1.47)	1.79 (1.47-2.17)	1	1.13 (1.07-1.19)	1.27 (1.15-1.41)	1.44 (1.23-1.67)	1	1.20 (1.11-1.31)	1.45 (1.22-1.72)	1.75 (1.36-2.25)
Number of alcohol-related problems		1	1.74 (1.38-2.10)	3.04 (1.90-4.84)	1	1.37 (1.20-1.56)	1.88 (1.45-2.45)	2.59 (1.75-3.83)	1	1.66 (1.38-2.00)	2.75 (1.89-3.98)	4.55 (2.60-7.95)
Drink-driving	At age 21 ^a	1	1.67 (1.36-2.05)	2.78 (1.84-4.19)	ns	ns	ns	ns	ns	ns	ns	ns
	By age 24 ^c	ns	ns	ns	ns	ns	ns	ns	1	1.34 (1.12-1.60)	1.8 (1.25-2.55)	2.39 (1.40-4.08)
Alcohol dependence	By age 30 ^d	1	1.18 (1.30-2.54)	3.30 (1.69-6.47)	ns	ns	ns	ns	^f	-	-	-
Current tobacco use	At age 21	1	1.26 (1.10-1.45)	1.60 (1.21-2.10)	ns	ns	ns	ns	ns	ns	ns	ns
Recent other illicit drug use	At age 21	ns	ns	ns	1	1.22 (1.10-1.35)	1.48 (1.20-1.83)	1.81 (1.32-2.48)	ns	ns	ns	ns
<i>Antisocial behaviour</i>												
Antisocial behaviour ^a	At age 21	ns	ns	ns	ns	ns	ns	ns	1	1.58 (1.25-1.99)	2.49 (1.57-3.95)	3.92 (1.97-7.84)

Only Bonferroni adjusted significant associations shown; ns=not statistically significant; adjusted using a multiple propensity score approach, with propensity scores computed for each individual based on the available likely predictors of adolescent alcohol use and combined across studies (see Table 3 footnote for information about the specific predictors included). ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eIncidence Rate Ratio; ^fOnly CHDS contributed data.

Table 5: Adjusted estimates of attributable risk (AR) for measures of exposure to alcohol prior to age 17 years on adult outcomes assuming (a) exposure can be limited to the lowest category^a and (b) exposure to the highest category can be prevented^b

Adult outcome	Exposure to alcohol prior to age 17 years					
	Max. frequency of alcohol use %		Max. no. of standard drinks consumed per drinking occasion %		Max. no. of alcohol-related problems %	
	a	b	a	b	a	b
Weekly or more frequent alcohol use at age 21	19.7	4.9	5.6	1.2	6.6	0.5
Weekly or more frequent binge drinking at age 21	22.3	6.8	8.9	2.1	10.4	1.1
Number of alcohol-related problems at age 21	34.8	10.6	16.4	4.7	29.4	3.8
Drink-driving at age 21	21.2	3.1	ns	ns	ns	ns
Alcohol dependence by age 24	ns	ns	ns	ns	20.7	2.7
Alcohol dependence by age 30	31.0	5.4	ns	ns	- ^c	- ^c
Current tobacco use at age 21	10.9	2.9	ns	ns	ns	ns
Recent other illicit drug use at age 21	ns	ns	9.8	2.4	ns	ns
Antisocial behaviour at age 21	ns	ns	ns	ns	10.5	0.6

^aLowest category of exposure for: (1) max frequency of alcohol use is: no alcohol use; (2) max number of standard drinks consumed per drinking occasion is: 0-2 drinks; and, (3) max number of alcohol-related problems is: no problems. ^bHighest exposure category for: (1) max frequency of alcohol use is: weekly+ alcohol use; (2) max number of standard drinks consumed per drinking occasion is: 7+ drinks; and, (3) max number of alcohol-related problems is: 5+ problems; we assumed exposure to the highest category can be prevented and individuals in the highest category instead had been in the penultimate category (i.e., for max frequency of alcohol use we assumed weekly+ drinkers had been <weekly drinkers; for max number of standard drinks consumed per drinking occasion we assumed heavy bingers (7+ drinks per occasion) had been moderate bingers (5-6 drinks per occasion); and for max number of alcohol-related problems we assumed highly problematic drinkers (5+ problems) had been moderately problematic drinkers (3-4 problems)). ^cOnly CHDS contributed data; Note: Only Bonferroni adjusted significant associations between alcohol exposure and categorical outcomes shown; ns=not statistically significant; adjusted using a multiple propensity score approach, with propensity scores computed for each individual based on the available likely predictors of adolescent alcohol use and combined across studies (see Table 3 footnote for information about the specific predictors included).

Appendix for

“Adverse adult consequences of different alcohol use patterns in adolescence: An integrative analysis of data to age 30 years from four Australasian cohorts”

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Appendix 1: Literature review and search strategy

A 2016 systematic review [1] identified adverse effects of alcohol use on young people across a range of social, physical and mental health outcomes while noting that the strength of evidence for causality was weak. We updated this review (April 2015-May 2017 including non-English language publications), but restricted the search to Medline, Web of Science and PubMed. We used the same search strategy (Substance, alcohol-related terms only: Age, adolescent-related terms: Design, epidemiological and risk factor terms: Publication, systematic reviews) (see below). There were 192 non-duplicate references with 10 considered for full-text review. Additional domains identified were persistent delinquent behaviour [2] and gambling [3]. Furthermore, prior findings were extended to low- and middle-income countries on alcohol as a risk factor for; cardiovascular disease [4], suicide ideation [5] and domestic violence [6] (alcohol use by partner).

Literature search strategy (Medline example):

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R) Search Strategy:

1 (alcohol or "alcohol drinking" or alcoholic or "alcoholic beverages" or alcopop* or beer or ethanol or liquor or spirits or wine).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (415349)

2 (adolescence or Adolescent or Adolescent Behavior or Adolescent Development or Adolescent Health Services or Adolescent Medicine or Adolescent Psychiatry or Adolescent Hospitalized or Adolescent, Institutionalized or high school student* or juvenile or "Pregnancy in Adolescence" or "adolescent psychology" or "secondary school student*" or teenager* or teen* or "young people" or youth).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1951595)

3 (age factor* or analysis of variance or associated or association* or characteristic* or correlate* or culture or determinant* or Epidemiologic Factor* or Epidemiologic Measurement* or Epidemiologic Method* or Family or latent class or pattern or peer group or precipitating factor* or process* or protective factor* or psychosocial or Residence Characteristic* or risk factor* or variable* or vulnerability or vulnerable).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (9241185)

4 (Cochrane Review* or meta-analys* or systematic review*).m_titl. (116524)

5 limit 4 to yr="2015 -Current" (46463)

6 1 and 2 and 3 and 5 (88)

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Appendix 2: Description of cohort studies

Additional information about the four longitudinal cohorts involved in this study is provided below and summarised in Table S2.1. All forms of data integration involve consideration of sources of between study heterogeneity. This is particularly important in integrated data analysis where failure to control for measurable sources of heterogeneity may threaten the internal validity of the analysis [1]. Common sources of heterogeneity include heterogeneity due to sampling, timing of historical events and study design characteristics. The present study has a number of advantages that reduce the effect of heterogeneity. Specifically, the cohorts: (1) are population based samples; (2) were born about the same historical time and are culturally similar; (3) adopted broadly similar data collection strategies; (4) have obtained broadly consistent measures of the primary outcomes and exposures.

Australian Temperament Project (ATP) [2] is a longitudinal study of social and emotional development that commenced in 1983 as a sample of 2443 infants (aged 4-8 months) and their parents in Victoria, Australia. The original cohort was sampled (based on an Australian Bureau of Statistics recommended sampling procedure) to represent the population. The ATP has been assessed on a total of 16 occasions in childhood through to adulthood (age 32 years);

Christchurch Health and Development Study (CHDS) [3] is a longitudinal study of a birth cohort of 1265 children born in the Christchurch, New Zealand, urban region in 1977. The cohort is a total population sample of all women giving birth in Christchurch maternity hospitals in a given period. The cohort has now been assessed on a total of 24 occasions from birth to age 40 years;

Mater Hospital and University of Queensland Study of Pregnancy (MUSP) [4] is a 1981 birth cohort now focused on health, developmental, behavioural and social outcomes for three generations of participants. The initial sample included all public patients seeking obstetric care from the hospital and was revised to all women presenting every second week for a period [5]. While the sample underestimates some population characteristics, particularly those associated with economic advantage, results obtained subsequently have been found to reflect associations existing in the broader community [4]. The cohort has been assessed on 10 occasions up to age 33 years, with assessments on children recruited in 1981 at 6 months, 5 years, 14 years, 21 years and 30 years old.

Victorian Adolescent Health Cohort Study (VAHCS) [6]: VAHCS is a 1992 longitudinal study of a representative sample of 1943 mid-secondary school adolescents in Victoria, Australia. The schools were diverse with respect to most outcomes and there was little within-school clustering; movement between schools further reduced clustering effects [7]. Participants were assessed at least once during the recruitment phase in Year 9 or Year 10, and on four other occasions during adolescence with a further three follow-ups in young adulthood to approximately age 30 years.

Table S2.1: Summary of study characteristics

	ATP	CHDS	MUSP	VAHCS
Region	Australia	New Zealand	Australia	Australia
Sampling frame	Victoria	Christchurch urban region	Queensland	Victoria
Number invited	3000 ^b	1310	8556	2032
Number who entered the study	2443	1265	8458	1943
Response proportion	81% ^b	97%	99%	96%
Year of recruitment	1983	1977	1981-1983	1992
Age at recruitment	4-8 months	Birth	Early pregnancy	14 years
Number of waves (assessments)	16	24	10	10
Year of last wave	2014	2017	2015-2018	2012-2014
Age at last wave	32 years	40 years	33 years	35 years
Contactable (retained) sample ^a	1701 (70%) ^c	1026 (81%) ^d	2900 (40%) ^e	1637 (84%) ^f
Annual attrition rate ^g	1.1%	0.5%	2.0%	1.1%

ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy

^aExcludes deceased participants and those who have permanently withdrawn; ^bApproximate figure; ^cBased on assessment at age 28 years (2010); ^dBased on assessment at age 35 years (2012); ^eBased on assessment at age 30 years (2011-2014); ^fBased on assessment at age 29 years; ^gAnnual attrition rate = ((baseline sample – retained sample)/baseline sample) / (year of last wave – year of recruitment)) x 100 (where a wave took more than a year to complete the first year of data collection was used to calculate the attrition rate).

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Appendix 3: Description of measures and derivation of variables

Cohorts varied in measures used to assess alcohol exposures and outcomes, assessment period, and timing of assessment. However, sufficient commonalities existed to enable integration of data and development of measures that were consistent across cohorts.

ADOLESCENT ALCOHOL USE

Maximum frequency of alcohol use prior to age 17 years

All studies included self-reported measures of lifetime alcohol use and frequency of alcohol use in adolescence. For ATP, data were collected on lifetime use (3+ drinks in lifetime; yes/no) and number of drinking days in the past month when participants were aged 13 and 15 years in 1996 and 1998, respectively. The CHDS assessed the frequency of use in the past 12 months when participants were aged 15 and 16 years in 1992 and 1993, respectively (response categories were: never, very occasionally, less than once a month, at least once a month, at least once a week, almost every day). The MUSP assessed the frequency of alcohol use at participant age 14 years in 1995-1997. Possible response categories were: daily, a few times a week, a few times a month, a few times a year, rarely, never. The VAHCS assessed: current drinking status (non-drinker, light, moderate, heavy); and, number of drinking days in the past week using a 7-day retrospective drinking diary (administered after answering other questions about frequency of alcohol consumption). Both items were assessed at each of six biannual assessment waves between 1992-1995 when participants were aged 15-17.5 years. Using these data, a three-level measure of the maximum frequency of alcohol use prior to age 17 was created for each study (0=never, 1=less than weekly, 2=weekly or more often).

Maximum number of standard drinks consumed per drinking occasion prior to age 17 years

Three studies included self-reported measures of the amount of alcohol consumed per drinking occasion in adolescence. The CHDS assessed the amount of alcohol consumed (in millilitres of pure alcohol) on a typical drinking occasion at ages 14, 15, and 16 years (in 1991, 1992 and 1993, respectively). The total millilitres of alcohol consumed on a typical drinking occasion was divided by 12.7 millilitres (the amount of alcohol in one standard drink unit) to give the number of standard drink units consumed. The MUSP (in 1995-1997) assessed the number of glasses of alcohol usually consumed on a drinking occasion at age 14 years. Possible response categories were: never drink, less than 1 glass, 1-2 glasses, 3-4 glasses, 5-6 glasses, 7 or more glasses. Equivalence between one glass of alcohol and one standard drink unit (e.g., 10 grams of alcohol) was assumed. The VAHCS, using a 7-day retrospective drinking diary, assessed the average number of standard drink units (10 grams of alcohol) consumed per drinking day in the past week at each of six biannual assessment waves between 1992-1995 when participants were aged 15-17.5 years. Using these data, the distribution of maximum number of standard drinks consumed per drinking occasion prior to age 17 was classified into four levels for each study (0= \leq 2 standard drinks; 1=3-4 standard drinks; 2=5-6 standard drinks; 3=7+ standard drinks).

Maximum number of alcohol-related problems prior to age 17 years

Three studies assessed a range of self-reported alcohol-related problems in adolescence. Typically, the items that were assessed spanned the domains of difficulties at school, problems with family, injuries and accidents, violence, and regretted sex. The ATP (in 1998) asked about the frequency of five drinking-related problems over the lifetime at age 15 years. The CHDS assessed the number of alcohol abuse/dependence symptoms at age 15 and 16 years (in 1992 and 1993, respectively) using the Rutgers Alcohol Problems Index [1] (23 items). The assessment period was the past 12 months. The VAHCS assessed the frequency of 13 drinking-related problems in the past six months at each of six biannual assessment waves between 1992-1995 when participants were aged 15-17.5 years. For all three studies, non-drinkers were classified as having zero alcohol-related problems. Using these data, the distribution of maximum number of alcohol-related problems prior to age 17 years was classified into four levels for each study (0=no problems, 1=1-2 problems, 2=3-4 problems, 5+ problems).

ADULT OUTCOMES

Weekly or more frequent alcohol use at age 21 years

All studies included measures of frequency of alcohol use during late adolescence and early adulthood. In ATP when participants were aged 19-20 years (in 2002) data were collected on past month alcohol use (yes/no) and the number of days drank alcohol in the past month. In CHDS when participants were aged 21 years (in 1998) data were collected on the frequency of alcohol use in the past year (never, very occasionally, less than once a month, at least once a month, at least once a week, almost every day). The MUSP assessed the frequency of alcohol use (assessment period not specified) when participants were aged 21 years (in 2001-04) using the categories: never, daily, a few times a week, a few times a month, a few times a year, and rarely. In VAHCS, when participants were aged 21 years (in 1998), data were collected on the number of drinking days in the past

week using a 7-day retrospective drinking diary. Using these data, a dichotomous measure of weekly or more frequent alcohol use at age 21 years was created for each study (0=no, 1=yes).

Weekly or more frequent binge drinking at age 21 years

Three studies included measures from which the frequency of heavy episodic (binge) drinking in young adulthood was derived. In CHDS when participants were aged 21 years (in 1998) data were collected on frequency of alcohol use in the past year (never, very occasionally, less than once a month, at least once a month, at least once a week, almost every day) and the quantity of alcohol consumed (in millilitres of pure alcohol) on a usual occasion of drinking. The quantity of alcohol consumed (in millilitres of pure alcohol) was divided by 12.7 (the amount of alcohol in one standard drink) to determine the number of standard drinks consumed on a usual occasion of drinking. The MUSP assessed the frequency of alcohol use (assessment period not specified) when participants were aged 21 years (in 2001-04) using the categories: never, daily, a few times a week, a few times a month, a few times a year, and rarely. The amount of alcohol usually consumed at those times was assessed (less than one glass, one or two glasses, three or four glasses, five or six glasses, seven or more glasses). The VAHCS assessed whether participants had ever had more than four drinks of alcohol within a couple of hours on more than one occasion in the past two weeks (yes/no) when participants were aged 21 years (in 1998). For all three studies, five or more drinks was the cut-point for binge alcohol use. The ATP did not assess binge drinking. Using these data, a dichotomous measure of weekly or more frequent binge drinking at age 21 years was created (0=no, 1=yes).

Number of standard drinks consumed per drinking occasion at age 21 years

Two studies collected data on the number of standard drinks consumed on drinking days in young adulthood. The CHDS assessed the number of standard drink units consumed on the last occasion of drinking (a proxy for regular use) when participants were aged 21 years (in 1998). The VAHCS used a 7-day retrospective drinking diary to assess the average number of standard drink units consumed per drinking day when participants were aged 21 years (in 1998). Using these data, a measure (based on count data) of the number of standard drinks consumed on a typical drinking occasion at age 21 years was created (number of standard drinks).

Higher number of alcohol-related problems at age 21 years

All four studies assessed a range of alcohol-related problems in adolescence and young adulthood which spanned trouble with school/work, violent behaviour, family conflict, regretted sex, binge use, tolerance, and withdrawal. In ATP, CHDS, and VAHCS the period of assessment was the past 12 months, and in MUSP it was the past four weeks. The ATP assessed the frequency of 10 alcohol-related problems (never, once/twice, more often) when participants were aged 19-20 years (in 2002). The MUSP assessed the extent of eight alcohol-related problems at age 21 years (in 2001-2004) using five categories (never, not at all, mildly, moderately, severely). The CHDS (in 1998) and VAHCS (in 1998) assessed the presence of 11 potential symptoms of alcohol abuse/dependence (DSM-IV) at participant age 21 years. Those who had never consumed alcohol were coded as having no alcohol-related problems. Using these data, a 90th percentile cut-point was identified above which lay the 10% of individuals with the highest number of alcohol-related problems. Then, a dichotomous measure of the number of alcohol-related problems at age 21 years was created (0=individuals below the 90th percentile, 1=individuals above the 90th percentile).

Drink-driving at age 21 years

Three studies assessed drink-driving in adolescence and young adulthood. The ATP at age 19-20 years (in 2002) assessed the number of times an individual drove a car or motorbike when probably affected by alcohol (number of trips). The CHDS at age 21 years (in 1998) asked the number times an individual drove a vehicle while drunk or over the limit (never, 1-2 times, 3-5 times, 6-10 times, 11-20 times, 21+ times). The MUSP at age 21 years (in 2001-2004) asked how often an individual had driven even though they may have been over the legal blood-alcohol limit (never, hardly ever, occasionally, quite often, frequently, nearly all the time). The assessment period was the past 10 trips for the ATP, the past year for the CHDS, and was unspecified in the MUSP. Using these data, a dichotomous measure of drink-driving at age 21 years was created (0=no, 1=yes).

Drink-driving by age 30 years

Two studies assessed drink-driving into adulthood. The CHDS at yearly intervals from age 16 years (1993) to age 30 years (in 2007) assessed how many times in the past 12 months individuals had been stopped or arrested for driving while over the legal alcohol limit (never, 1-2 times, 3-5 times, 6-10 times, 11-20 times, 21+ times). The VAHCS asked individuals at age 29 years (in 2008) if they have ever been caught for driving with a blood alcohol reading over the legal limit (yes, no). Using these data, a dichotomous measure of drink-driving by age 30 years was created (0=no, 1=yes).

Alcohol dependence by age 24 years

Three studies included CIDI/DSM measures of alcohol dependence in young adulthood. Past 12 months alcohol dependence was assessed in CHDS yearly between 18-24 years (from 1995-2007), in MUSP at age 21 years (in 2001-2004), and in VAHCS at age 21 years (in 1998) and 24 years (in 2003). Using these data, a dichotomous measure of alcohol dependence by age 24 years was created (0=no, 1=yes).

Alcohol dependence by age 30 years

Two studies included CIDI/DSM measures of alcohol dependence in adulthood. In CHDS, past 12 months alcohol dependence was assessed yearly between ages 18-30 years (from 1995-2007). In MUSP, lifetime alcohol dependence was assessed at age 30 years (in 2009-2012). Using these data, a dichotomous measure of alcohol dependence by age 30 years was created (0=no, 1=yes).

Current tobacco use at age 21 years

All four studies asked about tobacco use in adolescence and young adulthood. The assessment period was the past month in ATP and CHDS, the past week in VAHCS, and 'now' in MUSP. The ATP at age 19-20 years (in 2002) asked on how many days in the past month had individuals smoked cigarettes (number of days). The CHDS at age 21 years (in 1998) asked how many cigarettes had individuals smoked per day in the past month (none, less than one, one to four, five to nine, 10-20, 21+). The MUSP at age 21 years (in 2001-2004) asked people to describe their current smoking status (never smoked, used to smoke, smoke occasionally, smoke regularly). The VAHCS at age 21 years (in 1998) asked if individuals had smoked in the last seven days (yes, no). Using these data, a dichotomous measure of current tobacco use at age 21 years was created (0=no, 1=yes).

Daily cannabis use at age 21 years

All four studies included a measure of frequency of cannabis use in young adulthood. The period of assessment varied depending on study. The ATP at age 19-20 years (in 2002) asked participants how many days in the past month (30 days) they had used cannabis. The CHDS at age 21 years (in 1998) asked participants how often at the present time they use cannabis (nearly every day, at least once a week, at least once a month, less than once a month, only used once or twice, not used cannabis since age 18 years). The MUSP at age 21 years (in 2001-2004) asked participants how often in the last month they had used cannabis (never, every day, every few days, once or so, not in the last month). The VAHCS at age 21 years (in 1998) asked participants if they had ever used cannabis, and in the past 12 months when they were using cannabis most frequently how often they had used it (almost every day, 3-4 days a week, 1-2 days a week, 1-3 days a month, less than once a month). Using these data, a dichotomous measure of daily cannabis use at age 21 years was created (0=no, 1=yes).

Recent other illicit drug use at age 21 years

All four studies obtained data on the past year use of other illicit drugs (i.e., other than cannabis) from the following categories: inhalants, hallucinogens, ecstasy, amphetamines, methamphetamines, heroin, cocaine, and non-medical use of prescription drugs. These data were collected in ATP in 2002 when participants were aged 19-20 years; and in CHDS (in 1998), MUSP (in 2001-2004), and VAHCS (in 1998) when participants were aged 21 years. Using these data, a dichotomous measure of recent other illicit drug use at age 21 years was created (0=no, 1=yes).

Cannabis dependence by age 30 years

Three studies assessed cannabis dependence using the Composite International Diagnostic Interview (CIDI). The measure was administered in the CHDS to lifetime cannabis users on four occasions between 1995-2007 when participants were aged 18, 21, 25, and 30 years; in the MUSP to lifetime cannabis users in 2001-2004 and 2011-2012 when participants were aged 21 and 30 years respectively; and in the VAHCS to weekly cannabis users on three occasions between 1998-2008 when participants were aged 21, 24, and 29 years. The period of assessment was the past 12 months in CHDS and VAHCS, and lifetime in the MUSP. Using these data, a dichotomous measure of cannabis dependence by age 30 years was created (0=no, 1=yes).

Antisocial behaviour at age 21 years

Three studies assessed a range of antisocial behaviours in young adulthood (e.g., getting into fights, physically attacking people, threatening to hurt people, destroying things which belong to others, lying or cheating, stealing, and getting into trouble with the law). The number of behaviours assessed varied by study. The ATP used the Self-Report Delinquency Scale (20 items), the CHDS used the Self-Report Delinquency Inventory (31 items), and the MUSP used the Young Adult Self Report (21 items). These data were collected in ATP in 2002 when participants were aged 19-20 years; and in CHDS (in 1998) and MUSP (in 2001-2004) when participants were aged 21 years. The assessment period was the past year in the ATP and CHDS, and the past six months in the MUSP. Relatively common and alcohol-related antisocial behaviours (e.g., dangerous driving, being drunk in a public place) were excluded in order for the definition to capture property-related offences and

violence/aggression generally *not* associated with alcohol use. Using these data, a dichotomous measure of antisocial behaviour at age 21 years was created (0=no, 1=yes).

Police contact by age 21 years

Two studies assessed contact with the police in young adulthood. The MUSP (in 2001-2004) asked participants aged 21 years if they had ever been given a warning by the police, not including traffic offences (yes, no). The CHDS (in 1998) asked participants aged 21 years how many times since they were 18 years old had they been stopped or interviewed by the police for suspected or actual offending. Using these data, a dichotomous measure of police contact by age 21 years was created (0=no, 1=yes).

Multiple sexual partners at age 21 years

Three studies assessed number of sexual partners in the past year at age 21 years. The CHDS (in 1998) obtained count data on the number of sexual partners. The MUSP (in 2001-2004) and VAHCS (in 1998) used a categorical measure to assess number of sexual partners (MUSP categories: 0, 1, 2, 3, 4, 5+; VAHCS categories: 0, 1, 2-5, 6+). In CHDS and VAHCS individuals who reported six or more sexual partners in the past year, and in MUSP individuals who reported five or more sexual partners in the past year, were categorised as having multiple sexual partners. Using these data, a dichotomous measure of multiple sexual partners at age 21 years was created (0=no, 1=yes).

Unprotected sex at age 21 years

Two studies asked about the frequency of unprotected (condomless) sexual intercourse at age 21 years. The CHDS (in 1998) asked participants how often in the past year when they had sex had they used the following methods of contraception: condom only, pill only, condom and pill, other methods. Response categories were: none, some, half, most, all. The VAHCS (in 1998) asked participants how often in the past 12 months had they or their sexual partner worn a condom while having sex. Response categories were: always, most of the time, sometimes, rarely, never (use no contraception), never (use other contraceptive methods). Using these data, a dichotomous measure of any unprotected sex at age 21 years was created (0=no, 1=yes).

Pregnancy by age 21 years

Three studies asked female participants about any pregnancies by age 21 years. The CHDS (in 1995) at participant age 18 years asked about pregnancy at age 16-17 and 17-18 years, and (in 1998) at participant age 21 years asked about pregnancy in the last three years. The MUSP (in 2001-2004) asked participants at age 21 years how many times had they been pregnant, miscarried, or had a termination. The VAHCS (in 1998) at participant age 21 years asked if they had ever had a miscarriage, stillbirth, or termination (responses from this item were combined with the number of own children participants reported at age 21 years to provide a measure of ever pregnant). Males were coded as missing. Using these data, a dichotomous measure of pregnancy by age 21 years was created (0=no, 1=yes).

Parenthood by age 21 years

All four studies assessed parenthood by young adulthood. The ATP (in 2002) asked participants aged 19-20 years if they were the parent of a child. The CHDS (in 1995) at participant age 18 years asked about becoming a parent since age 16 years, and (in 1998) at participant age 21 years asked about becoming a parent since age 18 years. The MUSP (in 2001-2004) and the VAHCS (in 1998) at participant age 21 years asked individuals how many biological children they have (either in their care or not in their care) and if they had any children of their own, respectively. Using these data, a dichotomous measure of parenthood by age 21 years was created (0=no, 1=yes).

Vehicle accident by age 24 years

Three studies assessed vehicle accidents (in which participants were a driver) in adolescence and young adulthood. The ATP in 2002 at participant age 19-20 years and in 2006 at participant age 23-24 years assessed the number of crashes/accidents since starting to drive where they were the driver. The CHDS in 1998 at participant age 21 years asked about the number of collisions while driving a vehicle since age 18 years; and in 2002 at participant age 25 years asked about the number of collisions while driving a vehicle between age 21-24 years. The MUSP in 2001-2004 at participant age 21 years assessed the lifetime number of traffic accidents whilst driving a vehicle. Using these data, a dichotomous measure of any vehicle accident by age 24 years was created (0=no, 1=yes).

High school non-completion by age 30 years

All four studies obtained data on the completion of high-school. These data were gathered in ATP in 2011 when participants were aged 28 years, in CHDS (in 1995, 1998) and MUSP (in 2011-2012) when participants were aged 30 years, and in VAHCS in 2003 when participants were aged 24 years. Using these data, a dichotomous measure of high-school non-completion by age 30 years was created (0=no, 1=yes).

University degree non-attainment by age 30 years

All four studies obtained data on university degree attainment. These data were gathered in ATP in 2011 when participants were aged 28 years, in CHDS (in 2002, 2007) and MUSP (in 2011-2012) when participants were aged 30 years, and in VAHCS in 2008 when participants were aged 29 years. Using these data, a dichotomous measure of university degree non-attainment by age 30 years was created (0=no, 1=yes).

The education systems in Australia and New Zealand that applied during the course of these studies were very similar. In both countries school enrolment was compulsory from age six, with 12 years of education required thereafter to complete high school. In both countries school was compulsory to age 16 and enrolment in university was subject to attaining satisfactory grades in high school.

Lower income at age 30 years

All four studies assessed weekly income (from all sources) in adulthood. The ATP in 2011, when participants were aged 28 years, collected data on net (after tax) weekly income. The CHDS (in 2007), MUSP (in 2011-2012), and VAHCS (in 2008), when participants were aged 29-30 years, collected data on gross (before tax) weekly income. Using these data, a 90th percentile cut-point was identified above which lay the 10% of individuals with the lowest weekly income (regardless of currency type (Australian/New Zealand dollar) and net/gross assessment). Then, a dichotomous measure of lower income at age 30 years was created (0=individuals below the 90th percentile (higher income), 1=individuals above the 90th percentile (lower income)).

Welfare dependence at age 30 years

All four studies assessed participants' main source of income in adulthood including multiple categories of Government support. These data were gathered in ATP in 2011 when participants were aged 28 years, in CHDS (in 2007) and MUSP (in 2011-2012) when participants were aged 30 years, and in VAHCS in 2008 when participants were aged 29 years. Individuals who reported that their main source of income was Government support, excluding Government support for full-time study or apprenticeships, were categorized as welfare dependent. Using these data, a dichotomous measure of welfare dependence at age 30 years was created (0=no, 1=yes).

Substantial depression symptom at age 21 years

The four studies assessed symptoms of depression in young adulthood using different measures of depression. The ATP used the depression sub-scale from the short form Depression Anxiety Stress Scale (DASS), administered in 2002 when participants were aged 19-20 years. The CHDS assessed depression using the CIDI in 1998 when participants were aged 21 years. The MUSP assessed depression in 2001-2004 when participants were aged 21 years using the Centre for Epidemiological Studies Depression Scale (CES-D). In the VAHCS the assessment of depression was based on the Clinical Interview Schedule (CIS-R) which was administered in 1998 at age 21 years. The period of assessment in VAHCS and MUSP was the past week, in the ATP it was the past month, and in the CHDS it was the past year. A symptom of depression reported as occurring most or all of the time in the assessment period was regarded as a substantial episode. Using these data, a dichotomous measure of a substantial depression symptom at age 21 years was created (0=no, 1=yes).

Suicide attempt by age 25 years

Two studies assessed suicidality. The CHDS assessed the number of suicide attempts in the past year on three occasions between 1995-2002 when participants were aged 18, 21, and 25 years. Retrospective questioning assessed the number of attempts in the past year at age 17 and the intervening ages between 18-21 years and 21-25 years. The VAHCS used the Beck Self-harm Inventory at four biannual assessment waves between 1993-1995 when participants were aged, on average, 16-17 years (wave 3-6). Further assessments were conducted in 1998 and 2003 when participants were aged, on average, 21 and 24 years respectively (waves 7-8). The reporting period was the past year for waves 3-4 and past six months for waves 5-8. Three items were used to distinguish participants who reported self-harm with a serious intention to end life (e.g., suicide attempt) from other participants (who reported other self-harm or no self-harm): (1) have you deliberately hurt yourself or done something that might have killed you? (yes/no); (2) did you think you would die? (unlikely/maybe/probably); and, (3) were you seriously trying to end your life? (not trying/seriously trying/don't know). Participants were categorized as having attempted suicide if they answered 'yes' to item one and 'probably' to item two or 'seriously trying' to item three. The remainder with valid responses were categorized as not having attempted suicide. Using these data, a dichotomous measure of any suicide attempt by age 25 years was created (0=no, 1=yes).

Major depression by age 30 years

Three studies assessed depressive disorder. The CHDS assessed major depression using the CIDI on four occasions between 1995-2007 when participants were aged 18, 21, 25, and 30 years. The MUSP assessed major depression using the CIDI in 2011-2012 at participant age 30 years. In the VAHCS the assessment of major

depression was based on the Clinical Interview Schedule (CIS-R) administered in 1998 when participants were aged 21 years and the CIDI in 2008 when participants were aged 29 years. The assessment period in the VAHCS was the past week at age 21 years and the past year at age 28 years, in the CHDS it was the past year, and in the MUSP it was lifetime. For the VAHCS, responses to CIS-R items were aligned with ICD-10 criteria for MDD. Using these data, a dichotomous measure of major depression by age 30 years was created (0=no, 1=yes).

Any anxiety disorder by age 30 years

Three studies assessed anxiety disorder. The CHDS assessed anxiety using the CIDI on four occasions between 1995-2007 when participants were aged 18, 21, 25, and 30 years. The MUSP assessed anxiety using the CIDI in 2011-2012 at participant age 30 years. In the VAHCS the assessment of anxiety was based on the Clinical Interview Schedule (CIS-R) administered in 1998 when participants were aged 21 years and the CIDI in 2008 when participants were aged 29 years. The assessment period in the VAHCS was the past week at age 21 years and the past year at age 29 years, in the CHDS it was the past year, and in the MUSP it was lifetime. For the VAHCS, responses to CIS-R items were aligned with ICD-10 criteria for anxiety disorder. Using these data, a dichotomous measure of anxiety disorder by age 30 years was created (0=no, 1=yes).

Quality of partner relationship at age 21 years

Three studies collected data on the quality of romantic partner relationship in young adulthood. The ATP (in 2002) at participant age 19-20 years and the CHDS (in 1998) at participant age 21 years assessed the quality of partner relationship using a scale derived by Braiker and Kelly (1979) [2]. The measure defines separate domains of positive and negative partner relationships and was only asked for people who had been in a relationship in the past 12 months. We computed a single score of overall quality by reverse scoring the negative items and summing across the negative and positive scales. The MUSP (in 2001-2004) at participant age 21 years used the short form of the Spanier Dyadic Adjustment Scale [3] which provides a continuous measure of relationship quality. For the three cohorts, higher scores indicated poorer quality of relationship. Scores were standardised to a common mean (100) and standard deviation (10) and then adjusted to have common median (100). Using these data, a continuous scale of quality of partner relationship at age 21 years was created.

Quality of partner relationship at age 30 years

The three studies described above also collected data on the quality of romantic partner relationship in adulthood. The ATP (in 2011) assessed quality of partner relationship at participant age 28 years, and the CHDS (in 2007) and the MUSP (in 2011-2012) assessed this at participant age 30 years. The scales used and the coding method have been described above. Using these data, a continuous scale of quality of partner relationship at age 30 years was created.

Victim of intimate partner physical abuse at age 25 years

Two studies assessed whether individuals had been the victim of physical abuse in young adulthood. Only items which described a physical (non-sexual) consequence of action were included in the definition (e.g., physically twisted your arm or hair, pushed or shoved you, slapped you). The assessment period was the past year in both cohorts. The CHDS (in 2002) at participant age 25 years asked individuals the frequency with which they had experienced any physical abuse from their partner (12 physical abuse items). The MUSP (in 2001-2004) at participant age 21 years asked about the frequency of 10 physical abuse items. Individuals who were not in a partnership were coded as missing. Using these data, a dichotomous measure of intimate partner physical abuse at age 25 was created (0=no, 1=yes).

References

1. White HR., Labouvie EW. Towards the assessment of adolescent problem drinking. *J Stud Alcohol* 1989; **50**; 30-37.
2. Braiker H., & Kelley HH., 1979. Conflict in the development of close relationships. In R. L. Burgess & T. L. Huston (Eds.), *Social exchange in developing relationships*. New York: Academic.
3. Spanier G.B. Measuring dyadic adjustment: New scales for assessing the quality of marriage and similar dyads. *J Marriage Fam* 1979; **38**; 15-28.

Appendix 4: Potential confounding factors included in analysis

Potential confounding factors were selected based on previous research suggesting that they might be correlated with both alcohol use and psychosocial outcomes [1,2]. A wide range of potential confounding factors were selected from similar domains across the four cohorts and spanned individual, family and peer characteristics and behaviours. Factors assessed antecedent to alcohol use were included where available. The potential confounding factors, and corresponding assessment age, included in the analysis are shown in Table S4.1.

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Table S4.1: Potential confounding factors and assessment age by cohort

	ATP	CHDS	MUSP	VAHCS
Participant level				
Cognition and behaviour	School problems (excluding social); parental report, age 14-15	Grade point average across three years; teacher report, age 11-13	Current school performance; parental report, age 14	
	Conduct disorder; ¹ parental report, age 13-16	Conduct problems, age 7-9 and age 14-16	Conduct problems (CBCL externalising), age 14	Antisocial behaviour; self-report, W1-W2 (aged <17)
	Attentional problems; ¹ parental report, age 13-16	Attentional problems, age 7-9 and age 14-16	Attentional problems (CBCL attention problems), age 14	
Substance use	Smoked 3+ cigarettes in life; self-report, age 13-16	Any tobacco use; parental report age 10, and self-report age 15	Tobacco use in past 6 months, age 14	Ever used tobacco; self-report, W2 (aged <17)
	Ever used cannabis; self-report, age 13-16	Ever used cannabis; self-report, age 15	Ever used cannabis, self-report, age 14	Ever used cannabis; self-report, at W1-W6 (aged <17)
	Other illicit drug use before age 17, self-report	Other illicit drug use before age 17, self-report	Other illicit drug use (heroin, cocaine, inhalants, speed/ecstasy); self-report, age 14	Other illicit drug use; self-report, W1-W6 (aged <17)
Mental health	Maximum mean depression score; ² self-report, age 13-16	Major depression; ^{3,4} self-report, age 14-16	Depression/anxiety (CBCL), age 14	Symptoms of depression and anxiety; ⁵ self-report, W2 (aged <17)
		Anxiety disorder; self-report, age 14-16		
Sexual abuse	Sexual abuse (intra-familial or extra-familial) before age 16 (assessed age 23-24)	Sexual abuse severity before age 16 years (assessed ages 18, 21)	Sexual abuse before age 16 (assessed age 21)	Sexual abuse (with or without contact) before age 16 (assessed W8 and W9)
Demographics	Sex	Sex	Sex	Sex
	Ethnicity (Caucasian/non-Caucasian), based on parental ethnicity	Ethnicity (Caucasian/non-Caucasian), based on parental ethnicity		Ethnicity (Caucasian/non-Caucasian)

	ATP	CHDS	MUSP	VAHCS
Parent level				
Adjustment		Parental history of criminal offending, at child age 15		
Substance use	Mother's tobacco use, at child age 13-14 (augmented with age 18)	Mother's tobacco use; parental report, at child age 10	Mother's tobacco use, parental report, child age 14	Parental tobacco use, W1, W5 and W6 (and augmented with parental-reports and participant reports in young adulthood)
	Father's tobacco use, at child age 13-14 (augmented with age 18)	Father's tobacco use; parental report, at child age 10		
	Mother's drinking, at child age 13-14 (augmented with age 18)	Parental history of alcohol problems, at child age 15	Mother's drinking, parental report, child age 14	Parental drinking, W1, W5 and W6 (aged <17)
	Father's drinking, at child age 13-14 (augmented with age 18)			
Mental health		Parental illicit drug use; parental report, at child age 11		
		Parental history of problems with depression/anxiety/ suicidal behaviour, at child age 15	Maternal anxiety, parental report, at child age 14	
Demographics			Maternal depression, parental report, at child age 14	
	Socio-economic status; parental report, at birth of child	Socio-economic status at birth	Family income, parental survey, at child age 14	
		Family living standards; based on an average of interviewer ratings taken at annual intervals from age 1-10		
	Highest maternal education, at birth of child	Mother's education level at birth of child	Mother's education level at birth of child	Maximum parental education, participant reports in adolescence (augmented with reports in young adulthood)
	Highest paternal education, at birth of child	Father's education level at birth of child		

	ATP	CHDS	MUSP	VAHCS
	Parental divorce, at child age 13-16	Number of parental separations, age 0-10	Parental divorce, at child age 14	Parental divorce/separation by W6
			Mother's ethnicity (Caucasian/non-Caucasian)	
			Father's ethnicity (Caucasian/non-Caucasian)	
Peer level				
Deviant peer affiliations and activities	Antisocial peer activities. ATP derived scale assessing antisocial activities and substance use of up to 3 best friends; age 13-16	Deviant peer affiliations (peer drug use, peer offending, antisocial behaviour); age 15	Extent of deviant behaviours (drug use, violence, aggression, theft) happening at school ⁶ ; age 14	Peers ever used alcohol, tobacco, and illicit drugs (assessed separately), W2 aged <17

ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy; W1=Wave 1, assessed mean age 14.9 years; W2=Wave 2, assessed mean age 15.5 years; W5=Wave 5, assessed mean age 16.8 years; W6=Wave 6, assessed mean age 17.4 years

¹Quay HC., Peterson DR., 1987. Manual for the Revised Behaviour Problem Checklist (RBPQ). Odessa, FL: PAR Inc.

²Angold A., Costello EJ., Messer EC. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. Int J Meth Psych Res 1995: 5; 237-249.

³Costello A., Edelbrock C., Kalas R., Kessler M., Klaric SA., 1982. Interview Schedule for Children (DISC). Bethesda, MD: National Institute of Mental Health.

⁴American Psychiatric Association, 1987. Diagnostic Interview Schedule for Mental Disorders, third edition, revised. Washington: American Psychiatric Association.

⁵Lewis G., Pelosi AJ., Glover E., Wilkinson G., Stansfeld SA., Williams P., et al. The development of a computerised assessment for minor psychiatric disorder. Psychol Med 1988: 18; 737-745.

Appendix 5: Statistical procedure

The first analysis examined the bivariate associations between each of the three adolescent alcohol exposures and the psychosocial outcomes in each cohort and in the combined dataset. We tested statistical significance by fitting a series of generalised linear regression models to the data for each study and to the combined data. Logistic regression models were fitted for dichotomous outcomes; negative binomial regression models were used for the count measure of number of standard drinks; and linear regression was used for the continuous outcome of quality of partner relationships. The models fitted to the combined data were of the general form:

$$F(Y_{ij}) = B0_j + B1 X_{ij}$$

where Y_{ij} was the mean or rate of outcome Y for participant i in study j ; X_{ij} was the corresponding measure of alcohol exposure; and F was the appropriate link function for each outcome (logistic for dichotomous outcomes; log for count data; identity for other continuous outcomes). The effect of alcohol exposure (parameter $B1$) was assumed to be constant across studies. However, the model allowed study specific random intercepts ($B0_j$) to vary to account for random sources of between study heterogeneity that were not otherwise represented in the model. All models were fitted with robust standard errors.

In the second analysis the bivariate associations were adjusted for confounding using a generalised propensity score approach [1,2] in which the fitted regression models for the combined data were extended to incorporate a series of study specific propensity scores of the form:

$$F(Y_{ij}) = B0_j + B1 X_{ij} + \sum B_j P_{ijk}$$

where P_{ijk} was the estimated propensity (probability) that individual i from study j would be assigned to level k of the alcohol exposure (X_{ij}). Propensity scores were estimated from a multinomial logistic regression in which each adolescent alcohol exposure was regressed on the full set of available confounding factors in each study. Adjusted effect size estimates (odds ratios (OR) for dichotomous outcomes, incidence rate ratios (IRR) for the count of number of standard drinks) and associated 95% confidence intervals were obtained from the adjusted models by exponentiating the adjusted parameter $B1$ in the usual manner.

To account for the inflated Type I error rate due to analyses of multiple correlated outcomes a Bonferroni correction was computed based on a nominal p value of 0.05 and an average (Pearsons) correlation between all outcomes of 0.1076 in the combined dataset. To compute the average correlation between outcomes we used the method described in Sankoh et al. (1997) [3] and transformed the correlations into Fishers's z before taking the average and then transformed it back [4]. The Bonferroni adjustment was of the form:

$$a/L^{(1-r)}$$

where a was the nominal significance level, L was the number of tests, and r was the average correlation between the L tests. The Bonferroni adjusted p value was $p < 0.002$.

The above models assumed that the alcohol exposures had a linear effect on each outcome and that the effect of the alcohol exposures across cohorts was reflected in a common slope parameter. To test these assumptions, we first did Wald χ^2 tests to examine the improvement in fit of a categorical representation of each alcohol exposure over and above the linear model. To test the assumption that for each outcome the slope parameters were equal across all studies we extended the models to allow the slope parameter to vary between studies, and used Wald χ^2 to test for between-study heterogeneity in the effect of alcohol exposures on outcomes. A Bonferroni adjusted non-significant Wald test indicated: in the test of linearity, that a linear model provided adequate representation of the data; and, in the test of heterogeneity, an absence of between study heterogeneity in the effect of alcohol exposures on the outcomes. The results of the tests of linearity and heterogeneity are reported in Appendix 8.

Finally, the regression models were re-analysed by weighting [5] data by the inverse probability of retention to assess the effects of bias from sample attrition and missing data in each cohort. Further information about the procedure and results from unweighted/weighted analyses can be found in Appendix 6.

References

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Appendix 6: Data weighting procedures to examine possible selection bias from sample attrition and missing data

To examine the possible implications of selection bias arising from sample attrition and missing data in each study, the propensity adjusted regression models were re-analysed using data weighting procedures [1]. This involved a two-stage process. First, estimating a selection bias model predicting inclusion in the analysed sample from variables assessed on everyone at the inception of each study (see Table S6.1). Second, re-running the propensity adjusted regression model for a given outcome/exposure combination weighted by the inverse of the selection bias probability estimate. This process weights individuals who were more likely to be lost from the analysis sample relative to individuals who were more likely to be included in the analysis. Specifically, for each analysis (outcome/exposure combination) the following steps were completed.

In each cohort:

1. A dichotomous (0/1) indicator variable was defined to classify participants according to whether they were included (1) or excluded (0) from the propensity adjusted analysis;
2. A series of variables were identified that were assessed on everyone at the inception of the cohort study;
3. A logistic regression model was fitted to the data to predict the inclusion/exclusion indicator from the available predictors in Step 2;
4. The predicted probability (p_{ij}) of sample inclusion for participant i in study j from the final fitted model was generated in each study. The weight was calculated as the inverse of the predicted probability ($wgt = 1/p_{ij}$);

In the integrated dataset:

5. The propensity adjusted regression model for each outcome/exposure combination was re-run with the data for each individual weighted by w_{ij} using the `pweight` option in Stata;
6. We then compared the estimated effect for the alcohol exposures from the unweighted and weighted analyses.

Table S6.1 shows that the results (B, SE) from the weighted analyses were entirely consistent with those of the unweighted recorded data. This suggests that possible selection bias arising from sample attrition and missing data in each study was unlikely to have influenced the results reported.

References

1. Little R., Rubin D. Statistical analysis with missing data (2nd ed). Wiley, Hoboken, 2002.

Table S6.1: Estimated effect (B, SE) of exposure to alcohol prior to age 17 years on outcomes from unweighted and weighted analyses in combined data after adjustment for confounding

Outcome/Exposure ^g	Unweighted				Weighted ^f			
	B	SE	P	N	B	SE	P	N
<i>Continuity of substance use and related problems</i>								
Weekly or more frequent alcohol use at age 21								
Frequency of alcohol use	0.478	0.063	<0.001*	3881	0.475	0.068	<0.001*	3881
Number of drinks	0.197	0.043	<0.001*	3294	0.200	0.045	<0.001*	3294
Number of alcohol-related problems	0.291	0.069	<0.001*	2693	0.321	0.073	<0.001*	2693
Weekly or more frequent binge drinking at age 21								
Frequency of alcohol use	0.379	0.078	<0.001*	3271	0.353	0.800	<0.001*	3271
Number of drinks	0.192	0.044	<0.001*	3292	0.191	0.045	<0.001*	3292
Number of alcohol-related problems	0.231	0.071	0.001*	2094	0.231	0.071	0.001*	2094
Number of standard drinks consumed per drinking occasion at age 21^b								
Frequency of alcohol use	0.290	0.050	<0.001*	2096	0.297	0.053	<0.001*	2096
Number of drinks	0.121	0.026	<0.001*	2116	0.123	0.023	<0.001*	2116
Number of alcohol-related problems	0.186	0.043	<0.001*	2088	0.187	0.039	<0.001*	2088
Higher number of alcohol-related problems at age 21								
Frequency of alcohol use	0.555	0.119	<0.001*	3879	0.512	0.121	<0.001*	3879
Number of drinks	0.317	0.067	<0.001*	3292	0.338	0.070	<0.001*	3292
Number of alcohol-related problems	0.505	0.094	<0.001*	2694	0.559	0.102	<0.001*	2694
Drink-driving at age 21^a								
Frequency of alcohol use	0.510	0.105	<0.001*	2605	0.475	0.109	<0.001*	2605
Number of drinks	0.102	0.082	0.213	2026	0.110	0.091	0.227	2026
Number of alcohol-related problems	0.373	0.126	0.003*	1424	0.432	0.134	0.001*	1424
Drink-driving by age 30^b								
Frequency of alcohol use	0.315	0.185	0.088	2005	0.304	0.188	0.105	2005
Number of drinks	0.121	0.078	0.120	2025	0.134	0.081	0.099	2025
Number of alcohol-related problems	0.270	0.115	0.018*	1998	0.266	0.126	0.035*	1998
Alcohol dependence by age 24^c								
Frequency of alcohol use	0.282	0.117	0.015*	2937	0.299	0.125	0.017*	2937
Number of drinks	0.161	0.060	0.007*	2958	0.143	0.061	0.019*	2958

Outcome/Exposure ^g	Unweighted				Weighted ^f			
	B	SE	P	N	B	SE	P	N
Number of alcohol-related problems	0.291	0.817	0.001*	2082	0.294	0.092	0.001*	2082
Alcohol dependence by age 30^d								
Frequency of alcohol use	0.598	0.171	<0.001*	1643	0.502	0.173	0.004*	1643
Number of drinks	0.243	0.092	0.008*	1644	0.215	0.095	0.023*	1644
Number of alcohol-related problems ^h	-	-	-	-	-	-	-	-
Current tobacco use at age 21								
Frequency of alcohol use	0.233	0.070	0.001*	3856	0.230	0.074	0.002*	3856
Number of drinks	0.135	0.045	0.003*	3270	0.132	0.047	0.005*	3270
Number of alcohol-related problems	0.196	0.071	0.006*	2665	0.228	0.073	0.002*	2665
Daily cannabis use at age 21								
Frequency of alcohol use	0.122	0.164	0.458	3851	0.114	0.175	0.513	3851
Number of drinks	0.094	0.080	0.237	3285	0.065	0.087	0.452	3285
Number of alcohol-related problems	0.184	0.120	0.124	2663	0.187	0.128	0.143	2663
Recent other illicit drug use at age 21								
Frequency of alcohol use	0.193	0.095	0.043*	3870	0.220	0.098	0.024*	3870
Number of drinks	0.198	0.053	<0.001*	3294	0.200	0.058	0.001*	3294
Number of alcohol-related problems	0.202	0.081	0.013*	2683	0.232	0.084	0.006*	2683
Cannabis dependence by age 30^c								
Frequency of alcohol use	0.201	0.131	0.125	2777	0.212	0.145	0.144	2777
Number of drinks	0.156	0.061	0.011*	2797	0.153	0.065	0.020*	2797
Number of alcohol-related problems	0.052	0.097	0.586	1964	0.050	0.102	0.622	1964
<u>Antisocial behaviour</u>								
Antisocial behaviour at age 21^a								
Frequency of alcohol use	0.228	0.091	0.012*	2637	0.194	0.097	0.044*	2637
Number of drinks	0.153	0.086	0.077	2020	0.112	0.093	0.229	2020
Number of alcohol-related problems	0.456	0.118	<0.001*	1462	0.476	0.122	<0.001*	1462
Police contact by age 21^d								
Frequency of alcohol use	0.219	0.110	0.047*	2038	0.232	0.113	0.042*	2038
Number of drinks	-0.016	0.069	0.820	2039	-0.012	0.073	0.866	2039
Number of alcohol-related problems ^h	-	-	-	-	-	-	-	-
<u>Sexual risk-taking and early parenthood</u>								

Outcome/Exposure ^g	Unweighted				Weighted ^f			
	B	SE	P	N	B	SE	P	N
Multiple sexual partners at age 21^c								
Frequency of alcohol use	0.132	0.163	0.417	3257	0.096	0.163	0.557	3257
Number of drinks	0.137	0.091	0.128	3278	0.142	0.105	0.176	3278
Number of alcohol-related problems	0.060	0.138	0.664	2083	0.065	0.147	0.655	2083
Unprotected sex at age 21^b								
Frequency of alcohol use	0.183	0.094	0.052	1802	0.174	0.094	0.066	1802
Number of drinks	0.075	0.048	0.120	1815	0.073	0.049	0.137	1815
Number of alcohol-related problems	0.118	0.076	0.119	1794	0.112	0.077	0.147	1794
Pregnancy by age 21^c								
Frequency of alcohol use	0.279	0.128	0.029*	2324	0.302	0.134	0.024*	3234
Number of drinks	0.026	0.080	0.743	2334	0.004	0.087	0.965	2334
Number of alcohol-related problems	-0.075	0.133	0.573	1153	-0.068	0.142	0.630	1153
Parenthood by age 21								
Frequency of alcohol use	0.259	0.154	0.094	3898	0.227	0.1713	0.185	3989
Number of drinks	-0.002	0.090	0.978	3311	-0.014	0.096	0.888	3311
Number of alcohol-related problems	0.189	0.142	0.184	2708	0.182	0.152	0.231	2708
<u>Accidents</u>								
Vehicle accident by age 24^a								
Frequency of alcohol use	0.110	0.082	0.182	2625	0.111	0.090	0.219	2625
Number of drinks	-0.025	0.067	0.710	2003	-0.029	0.068	0.675	2003
Number of alcohol-related problems	0.266	0.112	0.017*	1445	0.279	0.124	0.024*	1445
<u>Socioeconomic functioning</u>								
Highschool non-completion by age 30								
Frequency of alcohol use	0.100	0.099	0.309	3384	0.096	0.122	0.431	3384
Number of drinks	0.032	0.053	0.542	2863	0.029	0.057	0.615	2863
Number of alcohol-related problems	0.158	0.085	0.064	2721	0.182	0.099	0.067	2721
University degree non-attainment by age 30								
Frequency of alcohol use	0.001	0.069	0.988	3140	0.019	0.076	0.807	3140
Number of drinks	0.082	0.047	0.084	2615	0.092	0.047	0.051	2615
Number of alcohol-related problems	0.015	0.072	0.834	2497	-0.002	0.075	0.981	2497
Lower income at age 30								

Outcome/Exposure ^g	Unweighted				Weighted ^f			
	B	SE	P	N	B	SE	P	N
Frequency of alcohol use	0.008	0.111	0.945	3124	0.019	0.118	0.874	3124
Number of drinks	0.000	0.074	0.999	2591	0.006	0.070	0.934	2591
Number of alcohol-related problems	0.021	0.111	0.849	2461	-0.015	0.111	0.890	2461
Welfare dependence at age 30								
Frequency of alcohol use	0.039	0.126	0.758	3134	0.164	0.140	0.240	3134
Number of drinks	-0.060	0.082	0.469	2591	-0.082	0.081	0.309	2591
Number of alcohol-related problems	-0.128	0.126	0.307	2517	-0.146	0.127	0.252	2517
<u>Mental Health</u>								
Substantial depression symptoms at age 21								
Frequency of alcohol use	-0.121	0.171	0.081	3864	-0.138	0.073	0.062	3864
Number of drinks	-0.061	0.047	0.192	3281	-0.068	0.045	0.133	3281
Number of alcohol-related problems	0.057	0.069	0.406	2689	0.043	0.073	0.558	2689
Suicide attempt by age 25^b								
Frequency of alcohol use	-0.259	0.277	0.394	2189	-0.276	0.271	0.309	2189
Number of drinks	-0.091	0.126	0.472	2213	-0.098	0.129	0.446	2213
Number of alcohol-related problems	-0.096	0.195	0.623	2181	-0.086	0.209	0.681	2181
Major depression by age 30^c								
Frequency of alcohol use	-0.110	0.0856	0.198	2761	-0.078	0.093	0.404	2761
Number of drinks	-0.027	0.051	0.604	2779	-0.031	0.054	0.569	2779
Number of alcohol-related problems	0.205	0.086	0.017*	1978	0.181	0.088	0.039*	1978
Anxiety disorder by age 30^c								
Frequency of alcohol use	-0.089	0.084	0.290	2756	-0.055	0.090	0.539	2756
Number of drinks	-0.074	0.052	0.154	2776	-0.060	0.055	0.278	2776
Number of alcohol-related problems	-0.038	0.086	0.664	1979	-0.029	0.085	0.988	1979
<u>Partner relationships</u>								
Quality of partner relationship at age 21^{a,1}								
Frequency of alcohol use	1.155	0.465	0.013*	1832	0.830	0.519	0.110	1832
Number of drinks	-0.279	0.397	0.482	1491	-0.359	0.466	0.441	1491
Number of alcohol-related problems	0.084	0.638	0.895	807	0.081	0.596	0.892	807
Quality of partner relationship at age 30^{a,1}								
Frequency of alcohol use	-0.238	0.511	0.642	1651	-0.382	0.627	0.543	1651

Outcome/Exposure ^g	Unweighted				Weighted ^f			
	B	SE	P	N	B	SE	P	N
Number of drinks	0.272	0.375	0.469	1243	0.055	0.422	0.896	1243
Number of alcohol-related problems	0.794	0.577	0.169	1147	0.852	0.658	0.196	1147
Victim of intimate partner physical abuse at age 25^d								
Frequency of alcohol use	0.003	0.214	0.987	1334	-0.001	0.232	0.998	1334
Number of drinks	-0.111	0.135	0.410	1335	-0.087	0.151	0.562	1335
Number of alcohol-related problems ^h	-	-	-	-	-	-	-	-

*p<0.05. Bold=Bonferroni corrected p<0.002; ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fWeighted to the inverse probability of inclusion based on variables assessed on everyone at the inception of each study (for ATP these variables were participant sex, maternal age, maternal socio-economic status, and maternal ethnicity; for CHDS these variables were participant sex, maternal education, maternal socio-economic status, and paternal education; for MUSP these variables were participant sex, maternal education, maternal ethnicity, and paternal ethnicity; and, for VAHCS these variables were participant sex, participant school location, and parental divorce); ^gAll alcohol exposures assessed prior to age 17 years (maximum frequency of alcohol use assessed in ATP, CHDS, MUSP, VAHCS; maximum number of standard drinks consumed per drinking occasion assessed in CHDS, MUSP, VAHCS; maximum number of alcohol-related problems assessed in ATP, CHDS, VAHCS); ^hOnly CHDS contributed data; ⁱScored such that a higher score indicated a poorer quality relationship.

Appendix 7: Unadjusted associations between exposure to alcohol prior to age 17 years and adult outcomes by cohort

Tables S7.1-S7.3 show the unadjusted associations between the exposure to alcohol before age 17 years and adult outcomes in each cohort where data were available. The p value shown is for the association between the exposure to alcohol and each outcome in each cohort. At the individual cohort level, we recorded significant ($p < 0.05$) associations for all outcomes, except:

For maximum frequency of alcohol use prior to age 17 years (Table S7.1): parenthood by age 21 years in ATP; socioeconomic outcomes in ATP; mental health outcomes in ATP, CHDS and VAHCS; and, quality of partner relationship in ATP and CHDS.

For maximum number of standard drinks consumed per drinking occasion prior to age 17 years (Table S7.2): socioeconomic outcomes in MUSP; mental health outcomes in VAHCS; and, quality of partner relationship in CHDS; and,

For maximum number of alcohol-related problems prior to age 17 years (Table S7.3): depression symptoms at age 21 years in ATP and VAHCS; and, quality of partner relationship in ATP and CHDS.

Table S7.1: Unadjusted associations (B, SE) between maximum frequency of alcohol use prior to age 17 years and adult outcomes in each cohort

Adult outcome		Maximum frequency of alcohol use prior to age 17 years															
		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
<i>Continuity of substance use and related problems</i>																	
Weekly or more frequent alcohol use		0.79	0.19	<0.001*	1020	1.01	0.14	<0.001*	932	0.40	0.07	<0.001*	3533	0.76	0.06	<0.001*	1596
Weekly or more frequent binge drinking		n/a	n/a	n/a	n/a	0.94	0.14	<0.001*	932	0.30	0.09	0.001*	3530	0.70	0.07	<0.001*	1596
Number of standard drinks consumed per drinking occasion ^b	At age 21	n/a	n/a	n/a	n/a	0.52	0.06	<0.001*	931	n/a	n/a	n/a	n/a	0.44	0.05	<0.001*	1588
Higher number of alcohol-related problems		0.61	0.15	<0.001*	1022	1.02	0.21	<0.001*	932	0.55	0.11	<0.001*	3483	1.21	0.17	<0.001*	1596
Drink-driving	At age 21 ^a	0.69	0.14	<0.001*	975	1.04	0.17	<0.001*	932	0.60	0.08	<0.001*	3524	n/a	n/a	n/a	n/a
	By age 30 ^b	n/a	n/a	n/a	n/a	1.23	0.22	<0.001*	953	n/a	n/a	n/a	n/a	0.68	0.16	<0.001*	1383
	By age 24 ^c	n/a	n/a	n/a	n/a	1.04	0.23	<0.001*	910	0.63	0.13	<0.001*	2430	0.46	0.09	<0.001*	1423
Alcohol dependence	By age 30 ^d	n/a	n/a	n/a	n/a	1.16	0.18	<0.001*	968	0.66	0.13	<0.001*	2432	n/a	n/a	n/a	n/a
Current tobacco use		0.77	0.10	<0.001*	1023	0.92	0.14	<0.001*	932	0.69	0.07	<0.001*	3541	0.81	0.07	<0.001*	1564
Daily cannabis use	At age 21	0.45	0.37	0.228	985	1.30	0.26	<0.001*	932	0.87	0.14	<0.001*	3523	0.80	0.16	<0.001*	1585
Recent other illicit drug use		0.77	0.15	<0.001*	1010	0.67	0.17	<0.001*	932	0.70	0.08	<0.001*	3521	0.82	0.11	<0.001*	1596
Cannabis dependence	By age 30 ^c	n/a	n/a	n/a	n/a	1.07	0.18	<0.001*	954	0.54	0.12	<0.001*	2553	0.84	0.12	<0.001*	1261
<i>Antisocial behaviour</i>																	
Antisocial behaviour ^a	At age 21	0.39	0.10	<0.001*	1043	0.92	0.18	<0.001*	932	0.40	0.07	<0.001*	3502	n/a	n/a	n/a	n/a
Police contact ^d	By age 21	n/a	n/a	n/a	n/a	0.58	0.13	<0.001*	967	0.47	0.08	<0.001*	3505	n/a	n/a	n/a	n/a
<i>Sexual risk-taking and early parenthood</i>																	
Multiple sexual partners ^c	At age 21	n/a	n/a	n/a	n/a	0.80	0.25	0.001*	932	0.34	0.13	0.008*	3493	0.52	0.18	0.004*	1576
Unprotected sex ^b		n/a	n/a	n/a	n/a	0.57	0.15	<0.001*	932	n/a	n/a	n/a	n/a	0.27	0.08	0.001*	1196
Pregnancy ^c	By age 21	n/a	n/a	n/a	n/a	0.82	0.23	<0.001*	490	0.56	0.08	<0.001*	3513	0.59	0.17	<0.001*	865
Parenthood		0.71	0.42	0.094	1019	0.60	0.20	0.003*	967	0.38	0.11	0.001*	3531	0.61	0.24	0.011*	1595
<i>Accidents</i>																	

Adult outcome		Maximum frequency of alcohol use prior to age 17 years															
		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
Vehicle accidents	By age 24 ^a	0.31	0.10	0.003*	838	0.30	0.13	0.020*	909	0.10	0.07	0.149	3517	n/a	n/a	n/a	n/a
<i>Socioeconomic functioning</i>																	
High school non-completion	By age 30	0.33	0.20	0.087	881	0.75	0.13	<0.001*	967	0.14	0.16	0.360	2017	0.18	0.08	0.018*	1803
University degree non-attainment		0.10	0.10	0.311	881	0.33	0.14	0.019*	908	0.21	0.10	0.040*	1930	0.19	0.07	0.004*	1383
Lower income	At age 30	0.07	0.16	0.641	890	0.01	0.21	0.963	907	0.30	0.13	0.027*	2007	-0.17	0.11	0.122	1322
Welfare dependence		-0.17	0.26	0.508	906	0.16	0.24	0.512	908	0.19	0.13	0.128	1895	-0.10	0.11	0.399	1386
<i>Mental health</i>																	
Substantial depression symptoms	At age 21	-0.08	0.10	0.410	1022	0.05	0.14	0.738	932	0.28	0.08	0.001*	3463	-0.07	0.07	0.309	1596
Suicide attempt	By age 25 ^b	n/a	n/a	n/a	n/a	0.35	0.26	0.171	968	n/a	n/a	n/a	n/a	0.14	0.34	0.672	1500
Major depression	By age 30 ^c	n/a	n/a	n/a	n/a	0.18	0.12	0.156	951	0.18	0.10	0.057	2444	-0.15	0.08	0.078	1331
Anxiety disorder		n/a	n/a	n/a	n/a	0.02	0.13	0.894	951	0.24	0.08	0.004*	2409	-0.02	0.09	0.815	1331
<i>Partner relationships</i>																	
Quality of partner relationship ^f	At age 21 ^a	0.70	0.64	0.281	557	0.86	0.85	0.312	523	2.25	0.35	<0.001*	3059	n/a	n/a	n/a	n/a
	At age 30 ^a	-0.58	0.57	0.311	631	-0.83	0.68	0.225	809	0.29	0.52	0.577	1530	n/a	n/a	n/a	n/a
Victim of intimate partner physical abuse	At age 25 ^d	n/a	n/a	n/a	n/a	0.13	0.24	0.595	763	0.28	0.15	0.063	1943	n/a	n/a	n/a	n/a

*p<0.05. Bold=Bonferroni adjusted p<0.002; ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fScored such that a higher score indicated a poorer quality relationship. Note: ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy; n/a=not assessed; The p value shown is for the association between the exposure to alcohol and each outcome in each cohort.

Table S7.2: Unadjusted associations (B, SE) between maximum number of standard drinks consumed per drinking occasion prior to age 17 years and adult outcomes in each cohort

Adult outcome		Maximum number of standard drinks consumed per drinking occasion prior to age 17 years															
		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
<i>Continuity of substance use and related problems</i>																	
Weekly or more frequent alcohol use		n/a	n/a	n/a	n/a	0.27	0.06	<0.001*	940	0.31	0.07	<0.001*	3531	0.41	0.04	<0.001*	1596
Weekly or more frequent binge drinking		n/a	n/a	n/a	n/a	0.36	0.06	<0.001*	940	0.35	0.08	<0.001*	3528	0.35	0.04	<0.001*	1596
Number of standard drinks consumed per drinking occasion ^b	At age 21	n/a	n/a	n/a	n/a	0.19	0.03	<0.001*	939	n/a	n/a	n/a	n/a	0.24	0.03	<0.001*	1588
Higher number of alcohol-related problems		n/a	n/a	n/a	n/a	0.42	0.09	<0.001*	940	0.40	0.09	<0.001*	3481	0.57	0.07	<0.001*	1596
Drink-driving	At age 21 ^a	n/a	n/a	n/a	n/a	0.28	0.07	<0.001*	940	0.45	0.07	<0.001*	3522	n/a	n/a	n/a	n/a
	By age 30 ^b	n/a	n/a	n/a	n/a	0.43	0.09	<0.001*	962	n/a	n/a	n/a	n/a	0.38	0.07	<0.001*	1383
	By age 24 ^c	n/a	n/a	n/a	n/a	0.52	0.10	<0.001*	917	0.36	0.12	0.002*	2429	0.30	0.05	<0.001*	1423
Alcohol dependence	By age 30 ^d	n/a	n/a	n/a	n/a	0.47	0.07	<0.001*	977	0.59	0.10	<0.001*	2431	n/a	n/a	n/a	n/a
Current tobacco use		n/a	n/a	n/a	n/a	0.52	0.06	<0.001*	940	0.62	0.08	<0.001*	3539	0.44	0.04	<0.001*	1564
Daily cannabis use	At age 21	n/a	n/a	n/a	n/a	0.45	0.11	<0.001*	940	0.53	0.10	<0.001*	3521	0.47	0.07	<0.001*	1585
Recent other illicit drug use		n/a	n/a	n/a	n/a	0.39	0.08	<0.001*	940	0.64	0.07	<0.001*	3519	0.51	0.05	<0.001*	1596
Cannabis dependence	By age 30 ^c	n/a	n/a	n/a	n/a	0.50	0.07	<0.001*	963	0.50	0.10	<0.001*	2552	0.49	0.06	<0.001*	1261
<i>Antisocial behaviour</i>																	
Antisocial behaviour ^a	At age 21	n/a	n/a	n/a	n/a	0.42	0.08	<0.001*	940	0.32	0.07	<0.001*	3500	n/a	n/a	n/a	n/a
Police contact ^d	By age 21	n/a	n/a	n/a	n/a	0.17	0.06	0.002*	975	0.45	0.07	<0.001*	3503	n/a	n/a	n/a	n/a
<i>Sexual risk-taking and early parenthood</i>																	
Multiple sexual partners ^c	At age 21	n/a	n/a	n/a	n/a	0.53	0.10	<0.001*	940	0.14	0.12	0.266	3491	0.26	0.10	0.005*	1576
Unprotected sex ^b		n/a	n/a	n/a	n/a	0.34	0.06	<0.001*	940	n/a	n/a	n/a	n/a	0.12	0.04	0.009*	1196
Pregnancy ^c	By age 21	n/a	n/a	n/a	n/a	0.38	0.09	<0.001*	495	0.44	0.07	<0.001*	3511	0.44	0.09	<0.001*	865
Parenthood		n/a	n/a	n/a	n/a	0.43	0.08	<0.001*	975	0.38	0.09	<0.001*	3529	0.19	0.12	0.106	1595
<i>Accidents</i>																	
Vehicle accidents	By age 24 ^a	n/a	n/a	n/a	n/a	0.04	0.06	0.529	917	0.07	0.07	0.349	3515	n/a	n/a	n/a	n/a

		Maximum number of standard drinks consumed per drinking occasion prior to age 17 years															
Adult outcome		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
<i>Socioeconomic functioning</i>																	
High school non-completion	By age 30	n/a	n/a	n/a	n/a	0.35	0.06	<0.001*	975	0.25	0.15	0.114	2018	0.18	0.05	<0.001*	1803
University degree non-attainment		n/a	n/a	n/a	n/a	0.36	0.07	<0.001*	917	0.20	0.13	0.124	1931	0.18	0.04	<0.001*	1383
Lower income	At age 30	n/a	n/a	n/a	n/a	0.13	0.09	0.139	916	0.03	0.16	0.841	2008	-0.02	0.07	0.741	1322
Welfare dependence		n/a	n/a	n/a	n/a	0.28	0.10	0.005*	917	0.16	0.14	0.244	1896	-0.15	0.08	0.067	1386
<i>Mental health</i>																	
Substantial depression symptoms	At age 21	n/a	n/a	n/a	n/a	0.15	0.07	0.014*	940	0.21	0.08	0.007*	3461	-0.05	0.04	0.296	1596
Suicide attempt	By age 25 ^b	n/a	n/a	n/a	n/a	0.28	0.11	0.009*	977	n/a	n/a	n/a	n/a	0.16	0.20	0.414	1500
Major depression	By age 30 ^c	n/a	n/a	n/a	n/a	0.17	0.06	0.003*	960	0.06	0.10	0.573	2443	-0.03	0.05	0.640	1331
Anxiety disorder		n/a	n/a	n/a	n/a	0.12	0.06	0.036*	960	0.06	0.09	0.498	2408	-0.01	0.05	0.898	1331
<i>Partner relationships</i>																	
Quality of partner relationship ^f	At age 21 ^a	n/a	n/a	n/a	n/a	0.55	0.37	0.143	527	1.17	0.36	0.001*	3057	n/a	n/a	n/a	n/a
	At age 30 ^a	n/a	n/a	n/a	n/a	-0.30	0.30	0.322	817	1.02	0.59	0.090	1531	n/a	n/a	n/a	n/a
Victim of intimate partner physical abuse	At age 25 ^d	n/a	n/a	n/a	n/a	0.17	0.10	0.092	769	0.30	0.14	0.038*	1944	n/a	n/a	n/a	n/a

*p<0.05. Bold=Bonferroni adjusted p<0.002; ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fScored such that a higher score indicated a poorer quality relationship. Note: ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy; n/a=not assessed; The p value shown is for the association between the exposure to alcohol and each outcome in each cohort.

Table S7.3: Unadjusted associations (B, SE) between maximum number of alcohol-related problems prior to age 17 years and adult outcomes in each cohort

Adult outcome		Maximum number of alcohol-related problems prior to age 17 years															
		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
<i>Continuity of substance use and related problems</i>																	
Weekly or more frequent alcohol use		0.62	0.15	<0.001*	985	0.26	0.10	0.008*	932	n/a	n/a	n/a	n/a	0.57	0.61	<0.001*	1575
Weekly or more frequent binge drinking		n/a	n/a	n/a	n/a	0.33	0.10	0.001*	932	n/a	n/a	n/a	n/a	0.50	0.06	<0.001*	1575
Number of standard drinks consumed per drinking occasion ^b	At age 21	n/a	n/a	n/a	n/a	0.22	0.04	<0.001*	931	n/a	n/a	n/a	n/a	0.30	0.05	<0.001*	1567
Higher number of alcohol-related problems		0.98	0.15	<0.001*	987	0.67	0.12	<0.001*	932	n/a	n/a	n/a	n/a	0.73	0.09	<0.001*	1575
Drink-driving	At age 21 ^a	0.90	0.14	<0.001*	936	0.39	0.11	<0.001*	932	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	By age 30 ^b	n/a	n/a	n/a	n/a	0.55	0.12	<0.001*	953	n/a	n/a	n/a	n/a	0.62	0.10	<0.001*	1369
	By age 24 ^c	n/a	n/a	n/a	n/a	0.75	0.12	<0.001*	910	n/a	n/a	n/a	n/a	0.45	0.07	<0.001*	1410
Alcohol dependence	By age 30 ^d	n/a	n/a	n/a	n/a	0.18	0.11	<0.001*	968	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Current tobacco use		0.91	0.13	<0.001*	983	0.58	0.10	<0.001*	932	n/a	n/a	n/a	n/a	0.79	0.06	<0.001*	1543
Daily cannabis use	At age 21	0.89	0.30	0.004*	948	0.72	0.13	<0.001*	932	n/a	n/a	n/a	n/a	0.59	0.09	<0.001*	1564
Recent other illicit drug use		0.89	0.15	<0.001*	972	0.43	0.11	<0.001*	932	n/a	n/a	n/a	n/a	0.73	0.07	<0.001*	1575
Cannabis dependence	By age 30 ^e	n/a	n/a	n/a	n/a	0.69	0.11	<0.001*	954	n/a	n/a	n/a	n/a	0.65	0.08	<0.001*	1249
<i>Antisocial behaviour</i>																	
Antisocial behaviour ^a	At age 21	0.61	0.12	<0.001*	1004	0.58	0.11	<0.001*	932	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Police contact ^d	By age 21	n/a	n/a	n/a	n/a	0.55	0.11	<0.001*	967	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
<i>Sexual risk-taking and early parenthood</i>																	
Multiple sexual partners ^c	At age 21	n/a	n/a	n/a	n/a	0.48	0.14	0.001*	932	n/a	n/a	n/a	n/a	0.36	0.12	0.003*	1555
Unprotected sex ^b		n/a	n/a	n/a	n/a	0.47	0.10	<0.001*	932	n/a	n/a	n/a	n/a	0.22	0.06	0.001*	1176
Pregnancy ^c	By age 21	n/a	n/a	n/a	n/a	0.37	0.14	0.009*	490	n/a	n/a	n/a	n/a	0.51	0.11	<0.001*	855
Parenthood		0.79	0.37	0.031*	981	0.43	0.12	<0.001*	967	n/a	n/a	n/a	n/a	0.44	0.15	0.005*	1574
<i>Accidents</i>																	

Maximum number of alcohol-related problems prior to age 17 years

Adult outcome		Maximum number of alcohol-related problems prior to age 17 years															
		ATP				CHDS				MUSP				VAHCS			
		B	SE	P	N	B	SE	P	N	B	SE	P	N	B	SE	P	N
Vehicle accidents	By age 24 ^a	0.31	0.14	0.031	804	0.20	0.10	0.041	909	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
<i>Socioeconomic functioning</i>																	
High school non-completion	By age 30	0.50	0.21	0.016*	840	0.48	0.11	<0.001*	967	n/a	n/a	n/a	n/a	0.35	0.06	<0.001*	1780
University degree non-attainment		0.30	0.13	0.029*	840	0.34	0.13	0.007*	908	n/a	n/a	n/a	n/a	0.31	0.06	<0.001*	1369
Lower income	At age 30	-0.15	0.23	0.526	846	0.19	0.14	0.177	907	n/a	n/a	n/a	n/a	0.06	0.10	0.528	1311
Welfare dependence		-0.60	0.50	0.222	863	0.36	0.14	0.013*	908	n/a	n/a	n/a	n/a	0.02	0.10	0.880	1372
<i>Mental health</i>																	
Substantial depression symptoms	At age 21	-0.01	0.13	0.912	983	0.47	0.10	<0.001*	932	n/a	n/a	n/a	n/a	0.06	0.06	0.308	1575
Suicide attempt	By age 25 ^b	n/a	n/a	n/a	n/a	0.32	0.16	0.044*	968	n/a	n/a	n/a	n/a	0.80	0.25	0.002*	1487
Major depression	By age 30 ^c	n/a	n/a	n/a	n/a	0.64	0.11	<0.001*	951	n/a	n/a	n/a	n/a	0.07	0.07	0.342	1315
Anxiety disorder		n/a	n/a	n/a	n/a	0.23	0.10	0.017*	951	n/a	n/a	n/a	n/a	0.14	0.07	0.062	1316
<i>Partner relationships</i>																	
Quality of partner relationship ^f	At age 21 ^a	-0.31	0.74	0.678	537	1.05	0.60	0.082	523	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	At age 30 ^a	0.39	0.76	0.606	609	-0.59	0.50	0.237	809	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Victim of intimate partner physical abuse	At age 25 ^d	n/a	n/a	n/a	n/a	0.54	0.13	<0.001*	763	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

*p<0.05. Bold=Bonferroni adjusted p<0.002; ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fScored such that a higher score indicated a poorer quality relationship. Note: ATP=Australian Temperament Project; CHDS=Christchurch Health and Development Study; VAHCS=Victorian Adolescent Health Cohort Study; MUSP=Mater Hospital and University of Queensland Study of Pregnancy; n/a=not assessed; The p value shown is for the association between the exposure to alcohol and each outcome in each cohort.

Appendix 8: Tests of linearity and heterogeneity

The regression models used in the analysis assumed that the alcohol exposures had a linear effect on each outcome and that the effect of the alcohol exposures across cohorts was reflected in a common slope parameter. To test these assumptions, we first did Wald χ^2 tests to examine the improvement in fit of a categorical representation of each alcohol exposure over and above the linear model. Secondly, we extended the models to allow the slope parameter to vary between studies, and used Wald χ^2 to test for between-study heterogeneity in the effect of alcohol exposures on outcomes. A Bonferroni adjusted non-significant Wald test indicated: in the test of linearity, that a linear model provided adequate representation of the data; and, in the test of heterogeneity, an absence of between study heterogeneity in the effect of alcohol exposures on the outcomes.

Table S8.1 summarises the results (p value) of the tests of linearity and heterogeneity in adjusted models between each exposure to alcohol prior to age 17 years and adult outcomes in combined data.

Tests of non-linearity indicated that the linear model provided an adequate representation of the data. Results of Wald χ^2 tests of between-study heterogeneity in the effect of the three adolescent alcohol exposures were non-significant suggesting that the associations were similar across studies for all exposure/outcome combinations.

Table S8.1: Summary results (p value) of the tests of linearity and heterogeneity in adjusted models between each exposure to alcohol prior to age 17 years and adult outcomes in combined data

Adult outcome	Exposure to alcohol prior to age 17 years					
	Maximum frequency of alcohol use		Maximum number of standard drinks consumed per drinking occasion		Maximum number of alcohol-related problems	
	Linearity p value	Heterogeneity p value	Linearity p value	Heterogeneity p value	Linearity p value	Heterogeneity p value
Weekly or more frequent alcohol use at age 21	0.841	0.020*	0.220	0.624	0.207	0.072
Weekly or more frequent binge drinking at age 21	0.822	0.104	0.092	0.221	0.573	0.398
Number of standard drinks consumed per drinking occasion at age 21	0.315	0.221	0.520	0.970	0.944	0.636
Higher number of alcohol-related problems at age 21	0.315	0.120	0.510	0.384	0.3414	0.641
Drink-driving at age 21	0.795	0.513	0.557	0.837	0.849	0.496
Drink-driving by age 30	0.250	0.052	0.878	0.720	0.672	0.419
Alcohol dependence by age 24	0.681	0.257	0.421	0.021*	0.853	.0457*
Alcohol dependence by age 30	0.617	0.385	0.303	0.317	- ^a	- ^a
Current tobacco use at age 21	0.158	0.187	0.737	0.040*	0.338	0.916
Daily cannabis use at age 21	0.976	0.620	0.175	0.159	0.685	0.227
Recent other illicit drug use at age 21	0.020*	0.393	0.234	0.179	0.592	0.090
Cannabis dependence by age 30	0.719	0.799	0.673	0.542	0.719	0.352
Antisocial behaviour at age 21	0.489	0.202	0.836	0.213	0.360	0.685
Police contact by age 21	0.692	0.711	0.924	0.602	- ^a	- ^a
Multiple sexual partners at age 21	0.538	0.4043	0.6891	0.1573	0.7801	0.9603
Unprotected sex at age 21	0.305	0.9457	0.1803	0.7298	0.6155	0.7553
Pregnancy by age 21	0.532	0.2941	0.5990	0.2600	0.7007	0.7298
Parenthood by age 21	0.250	0.8257	0.9314	0.3373	0.9160	0.9544

Adult outcome	Exposure to alcohol prior to age 17 years					
	Maximum frequency of alcohol use		Maximum number of standard drinks consumed per drinking occasion		Maximum number of alcohol-related problems	
	Linearity p value	Heterogeneity p value	Linearity p value	Heterogeneity p value	Linearity p value	Heterogeneity p value
Vehicle accident by age 24	0.917	0.3408	0.4102	0.8021	0.0941	0.8259
Highschool non-completion by age 30	0.570	0.0158*	0.0626	0.9599	0.9326	0.3698
University degree non-attainment by age 30	0.178	0.2526	0.8130	0.5126	0.6559	0.1682
Lower income at age 30	0.616	0.5024	0.4339	0.9374	0.8902	0.3480
Welfare dependence at age 30	0.116	0.2824	0.7899	0.7346	0.4768	0.3192
Substantial depression symptoms at age 21	0.560	0.106	0.177	0.716	0.029*	0.073
Suicide attempt by age 25	0.553	0.325	0.730	0.833	0.142	0.370
Major depression by age 30	0.691	0.2858	0.8890	0.9050	0.8973	0.0118*
Anxiety disorder by age 30	0.462	0.2418	0.5462	0.9788	0.3952	0.2682
Quality of partner relationship at age 21	0.158	0.034*	0.8508	0.8405	0.8163	0.2514
Quality of partner relationship at age 30	0.872	0.9209	0.3623	0.7797	0.0693	0.4188
Victim of intimate partner physical abuse at age 25	0.150	0.2108	0.2550	0.3546	- ^a	- ^a

*p<0.05. Bold=Bonferroni corrected p<0.002; ^aOnly CHDS contributed data.

Appendix 9: Unadjusted associations between exposure to alcohol prior to age 17 years and adult outcomes in combined data

The unadjusted associations between exposure to alcohol prior to age 17 years and adult outcomes in combined data are shown in Table S9.1.

Table S9.1: Unadjusted associations (B, SE) between exposure to alcohol prior to age 17 years and adult outcomes in combined data

Adult outcome	Exposure to alcohol prior to age 17 years												
	Maximum frequency of alcohol use				Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems				
	B	SE	P	N	B	SE	P	N	B	SE	P	N	
<i>Continuity of substance use and related problems</i>													
Weekly or more frequent alcohol use	0.67	0.041	<0.001*	7081	0.35	0.031	<0.001*	6067	0.51	0.049	<0.001*	3492	
Weekly or more frequent binge drinking	0.59	0.050	<0.001*	6058	0.36	0.031	<0.001*	6064	0.45	0.049	<0.001*	2507	
Number of standard drinks consumed per drinking occasion ^b	At age 21	0.45	0.037	<0.001*	2519	0.22	0.021	<0.001*	2527	0.28	0.032	<0.001*	2498
Higher number of alcohol-related problems		0.76	0.070	<0.001*	7033	0.48	0.044	<0.001*	6017	0.76	0.063	<0.001*	3494
Drink-driving	At age 21 ^a	0.68	0.062	<0.001*	5431	0.36	0.050	<0.001*	4462	0.56	0.085	<0.001*	1868
	By age 30 ^b	0.88	0.134	<0.001*	2336	0.40	0.057	<0.001*	2345	0.59	0.077	<0.001*	2322
Alcohol dependence	By age 24 ^c	0.58	0.076	<0.001*	4763	0.36	0.042	<0.001*	4769	0.52	0.063	<0.001*	2320
	By age 30 ^d	0.83	0.105	<0.001*	3400	0.51	0.060	<0.001*	3408	- ^f	-	-	-
Current tobacco use		0.77	0.042	<0.001*	7060	0.49	0.031	<0.001*	6043	0.76	0.050	<0.001*	3458
Daily cannabis use	At age 21	0.87	0.093	<0.001*	7025	0.48	0.052	<0.001*	6046	0.64	0.076	<0.001*	3444
Recent other illicit drug use		0.74	0.056	<0.001*	7059	0.51	0.036	<0.001*	6055	0.67	0.054	<0.001*	3479
Cannabis dependence	By age 30 ^e	0.76	0.077	<0.001*	4768	0.48	0.041	<0.001*	4776	0.66	0.063	<0.001*	2203
<i>Antisocial behaviour</i>													
Antisocial behaviour ^a	At age 21	0.44	0.053	<0.001*	5477	0.37	0.052	<0.001*	4440	0.59	0.081	<0.001*	1936
Police contact ^d	By age 21	0.50	0.067	<0.001*	4472	0.27	0.046	<0.001*	4478	- ^f	-	-	-
<i>Sexual risk-taking and early parenthood</i>													
Multiple sexual partners ^c	At age 21	0.46	0.095	<0.001*	6001	0.31	0.058	<0.001*	6007	0.41	0.932	<0.001*	2487
Unprotected sex ^b		0.33	0.069	<0.001*	2128	0.19	0.037	<0.001*	2136	0.29	0.054	<0.001*	2108
Pregnancy ^c	By age 21	0.59	0.069	<0.001*	4868	0.43	0.048	<0.001*	4871	0.45	0.089	<0.001*	1345
Parenthood		0.46	0.085	<0.001*	7112	0.36	0.054	<0.001*	6099	0.45	0.092	<0.001*	3522

Adult outcome		Exposure to alcohol prior to age 17 years											
		Maximum frequency of alcohol use				Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems			
		B	SE	P	N	B	SE	P	N	B	SE	P	N
<i>Accidents</i>													
Vehicle accident	By age 24 ^a	0.18	0.052	<0.001*	5264	0.05	0.044	0.282	4432	0.24	0.081	0.004*	1713
<i>Socioeconomic functioning</i>													
High school non-completion	By age 30	0.31	0.059	<0.001*	5668	0.24	0.035	<0.001*	4796	0.39	0.052	<0.001*	3587
University degree non-attainment		0.19	0.046	<0.001*	5102	0.23	0.035	<0.001*	4231	0.32	0.050	<0.001*	3117
Lower income	At age 30	0.03	0.072	0.706	5126	0.04	0.053	0.504	4246	0.07	0.075	0.346	3064
Welfare dependence		0.03	0.077	0.716	5095	0.03	0.055	0.590	4199	0.09	0.083	0.300	3143
<i>Mental health</i>													
Substantial depression symptoms	At age 21	0.03	0.43	0.454	7013	0.05	0.033	0.145	5997	0.14	0.047	0.003*	3490
Suicide attempt	By age 25 ^b	0.28	0.209	0.182	2468	0.25	0.094	0.007*	2477	0.45	0.128	<0.001*	2455
Major depression	By age 30 ^c	0.03	0.057	0.589	4726	0.06	0.035	0.074	4734	0.25	0.057	<0.001*	2266
Anxiety disorder		0.10	0.054	0.070	4691	0.054	0.036	0.130	4699	0.17	0.058	0.003*	2267
<i>Partner relationships</i>													
Quality of partner relationship ^g	At age 21 ^a	1.76	0.286	<0.001*	4139	0.87	0.258	0.001*	3584	0.51	0.468	0.279	1060
	At age 30 ^a	-0.27	0.338	0.413	2970	-0.02	0.267	0.926	2384	-0.28	0.418	0.496	1418
Victim of intimate partner physical abuse	At age 25 ^d	0.24	0.127	0.064	2706	0.21	0.082	0.012*	2713	- ^f	-	-	-

*p<0.05. Bold=Bonferroni corrected p<0.002. ^aAssessed in ATP, CHDS, MUSP; ^bAssessed in CHDS, VAHCS; ^cAssessed in CHDS, MUSP, VAHCS; ^dAssessed in CHDS, MUSP; ^eAssessed in ATP, CHDS, VAHCS; ^fOnly CHDS contributed data; ^gScored such that a higher score indicated a poorer quality relationship. Note: The p value shown is for the association between the exposure to alcohol and each outcome in combined data adjusted for study-specific effects.

Appendix 10: Alternate approach to covariate adjustment

To examine the robustness of the conclusions from the adjustment approach used in the main analysis, results were compared with those from an analysis which used an alternate approach (Table S10.1). In this approach, fitted regression models for the combined data were extended to incorporate the complete set of covariates available across all studies (see Appendix 4) and defined such that any covariate not assessed by a given study was set to zero for that study. All adjusted coefficients were within +/- .02 of the original models, with one additional significant association between maximum number of standard drinks consumed per drinking occasion prior to age 17 years and tobacco use at age 21 years.

Table S10.1: Comparison of (a) propensity score^a and (b) covariate^b adjusted associations (B, SE) between exposure to alcohol prior to age 17 years and adult outcomes in combined data

Adult outcome ^c	Exposure to alcohol prior to age 17 years												
	Maximum frequency of alcohol use				Maximum number of standard drinks consumed per drinking occasion				Maximum number of alcohol-related problems				
		B	SE	P	N	B	SE	P	N	B	SE	P	N
Weekly or more frequent alcohol use at age 21	a	0.48	0.06	<0.001	3881	0.20	0.04	<0.001	3294	0.29	0.07	<0.001	2693
	b	0.52	0.06	<0.001	3881	0.20	0.04	<0.001	3274	0.31	0.07	<0.001	2963
Weekly or more frequent binge drinking at age 21	a	0.38	0.08	<0.001	3271	0.19	0.04	<0.001	3292	0.23	0.07	0.001	2094
	b	0.40	0.08	<0.001	3271	0.19	0.04	<0.001	3272	0.24	0.07	0.001	2094
Number of standard drinks consumed per drinking occasion at age 21 ^{d,e}	a	0.29	0.05	<0.001	2096	0.12	0.03	<0.001	2116	0.19	0.04	<0.001	2088
	b	0.26	0.05	<0.001	2096	0.12	0.03	<0.001	2096	0.17	0.04	<0.001	2088
Higher number of alcohol-related problems at age 21	a	0.56	0.12	<0.001	3879	0.32	0.07	<0.001	3292	0.51	0.10	<0.001	2694
	b	0.60	0.12	<0.001	3831	0.35	0.07	<0.001	3224	0.52	0.10	<0.001	2694
Drink-driving at age 21 ^f	a	0.51	0.11	<0.001	2605	0.10	0.08	0.213	2026	0.37	0.13	0.003	1424
	b	0.56	0.11	<0.001	2605	0.12	0.08	0.131	2026	0.30	0.13	0.022	1424
Alcohol dependence by age 24 ^g	a	0.28	0.12	0.015	2937	0.16	0.06	0.007	2958	0.29	0.09	0.001	2082
	b	0.32	0.12	0.006	2937	0.19	0.06	0.002	2938	0.30	0.09	0.001	2082
Alcohol dependence by age 30 ^h	a	0.60	0.17	<0.001	1643	0.24	0.09	0.008	1644	. _i	-	-	-
	b	0.73	0.18	<0.001	1643	0.27	0.09	0.003	1644				
Current tobacco use at age 21	a	0.23	0.07	0.001	3856	0.13	0.05	0.003	3270	0.20	0.07	0.006	2665
	b	0.27	0.07	<0.001	3856	0.15	0.05	0.001	3250	0.18	0.07	0.12	2665
Recent other illicit drug use at age 21	a	0.19	0.10	0.043	3870	0.20	0.05	<0.001	3294	0.20	0.08	0.013	2683
	b	0.21	0.10	0.034	3870	0.19	0.05	0.001	3274	0.17	0.08	0.042	2683
Antisocial behaviour at age 21 ^f	a	0.23	0.09	0.012	2637	0.15	0.09	0.077	2020	0.46	0.12	<0.001	1462
	b	0.27	0.10	0.005	2673	0.17	0.09	0.052	2020	0.42	0.13	0.001	1462

Footnote for Table S10.1:

^aAdjusted using a multiple propensity score approach, with propensity scores computed for each individual based on the available likely predictors of adolescent alcohol use and combined across studies; ^bAdjusted using a covariate approach, where regression models were extended to incorporate the complete set of covariates available across all studies and defined such that any covariate not assessed by a given study was set to zero for that study; ^cOnly outcomes where the propensity score adjusted associations between exposure and outcome were significant at the Bonferroni adjusted level ($p < 0.002$) are shown; ^dAssessed in CHDS, VAHCS; ^eIncidence Rate Ratio; ^fAssessed in ATP, CHDS, MUSP; ^gAssessed in CHDS, MUSP, VAHCS; ^hAssessed in CHDS, MUSP; ⁱOnly CHDS contributed data; Bold=Bonferroni adjusted $p < 0.002$; Note: Further information about the specific predictors/covariates included from each study can be found in the Appendix and is summarized here. ATP: school problems, 14-15 years; conduct disorder 13-16 years; attentional problems, 13-16 years; tobacco use, 13-16 years; cannabis use, 13-16 years; other illicit drug use before 17 years; depression, 13-16 years; sexual abuse, before 16 years; sex; ethnicity; parental socio-economic status; parental alcohol and tobacco use; parental education; parental divorce; antisocial peer activities, 13-16 years. CHDS: Grade point average, 11-13 years; conduct problems, 7-9 and 14-16 years; attentional problems, 7-9 and 14-16 years; tobacco use, 10-15 years; cannabis use, 15 years; other illicit drug use before 17 years; anxiety disorder, 14-16 years; major depression, 14-16 years; sexual abuse before 16 years; sex; ethnicity; socio-economic status at birth; family living standards, 1-10 years; parental history of criminal offending, parental tobacco use; parental history of alcohol problems; parental illicit drug use; parental history of mental health problems; parental education level at birth, parental separation, 0-10 years; deviant peer affiliations, 15 years. MUSP: conduct problems, 14 years; attentional problems, 14 years; school performance, 14 years; tobacco use, 14 years; cannabis use, 14 years; other illicit drug use, 14 years; symptoms of depression/anxiety, 14 years; sexual abuse before 16 years; sex; family income, 14 years; maternal tobacco/alcohol use, 14 years; maternal anxiety/depression, 14 years; maternal education level at birth of child; parental divorce, 14 years; maternal/paternal ethnicity; deviant behavior happening at school, 14 years. VAHCS: antisocial behaviour before 17 years; tobacco use before 17 years; cannabis use before 17 years; other illicit drug use before 17 years; symptoms of depression/anxiety before 17 years; sexual abuse before 16 years; sex; ethnicity; parental tobacco use; parental alcohol use; parental education; parental divorce/separation; peer alcohol, tobacco and illicit drug use, before 17 years).