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Title

Do young people with comorbid mental and alcohol disorders experience worse behavioural problems?

Authors

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Abstract
This article examines whether young individuals in the general population with comorbid alcohol use and mental health disorders experience worse internalising and externalising behaviour problems than those with single disorders. A large cohort of women at the Mater Misericordiae Hospital in Brisbane, Australia, was enrolled during pregnancy in a longitudinal study. Mother/offspring dyads were followed over twenty-one years. At age 21, offspring behaviour problems were examined using the Young Adult Self Report, alcohol and mental health disorders with the Composite International Diagnostic Interview. Associations between comorbidity and behaviour problems were assessed using multinomial logistic regression, accounting for life-course factors. Twelve percent of young adults had alcohol/mental health DSM-IV disorders with significant temporal overlap. A further 16% had alcohol disorders only and 23% mental health disorders only. The comorbid group scored significantly higher on total and externalizing behaviour problems but not internalizing behaviour problems. Stronger associations of aggression/delinquency with comorbidity were not fully accounted for by factors known to influence separate development of mental health and alcohol disorders. Young adults with comorbid alcohol/mental health disorders experience more, and more severe, behavioural problems than those with single disorder types, indicating an increased burden from comorbidity, with implications for treatment and public order.

Keywords
Comorbidity; epidemiology; alcohol-related disorders; behaviour; mental health
1. Introduction
There is increased interest in co-occurring disorders of substance use, mental health and behaviour (Boden et al., 2012; Balan et al., 2013; Heron et al., 2013; Kidorf et al., 2013; Terry-McElrath et al., 2013). Mental health and alcohol use disorders frequently co-occur in clinical settings (Hirschfeld et al., 1989; Swendsen and Merikangas, 2000; Kessler, 2004; Teesson et al., 2009; Alegria et al., 2010).

It is becoming increasingly apparent that in addition to integrated care requirements (Davis et al., 2008; Carroll et al., 2009; Kidorf et al., 2013), patients with comorbid alcohol and mental health disorders (CAMHD) are characterised by more severe clinical outcomes (Hirschfeld et al., 1989; Bruce et al., 2005) and specific social difficulties (Merikangas et al., 1998b; Swendsen and Merikangas, 2000; Davis et al., 2008; Kessler and Wang, 2008b; Jaworski et al., 2011).

Comorbid alcohol and mental health problems are also prevalent in the general population: in 2007, 22% of the Australian population with a lifetime alcohol use disorder (AUD) (Teesson et al., 2010) also reported a co-occurring mental health disorder (Teesson et al., 2009). Similar findings are seen elsewhere (Merikangas et al., 1998b). In the National Longitudinal Alcohol Epidemiologic Survey (NLAES), those with comorbid depression and alcohol problems tended to have more severe alcohol use disorders (AUD) than those without depression (Grant et al., 1996). At population level, it is unclear whether alcohol and mental health comorbidity is linked with poorer functioning in other areas although some initial evidence suggests this is the case. The Australian National Survey of Mental Health and Wellbeing (NSMHWB) and US national studies showed that those with comorbid anxiety and alcohol disorders experienced significantly more days out of role as a result of their illness than those without comorbidity (Merikangas and Kalaydjian, 2007; Kessler and Wang, 2008a; Slade et al., 2009). More recently, longitudinal studies have suggested that social functioning may also be affected, manifesting as relationship difficulties and intimate partner violence (Boden et al., 2012; 2013; Heron et al., 2013).

One marker of decreased functioning which may be associated with CAMHD is behaviour problems. This area has been less examined to date. Yet individuals with problematic behaviour such as
aggression and delinquency experience substance use and mental health disorders during their lifetime as well as poorer social and economic position (Achenbach et al., 1995; Bor et al., 2010). Additional evidence suggests that behaviour problems often cluster with substance use disorders (Helstrom et al., 2004; Heron et al., 2013), as do personality disorders (PD) such as Antisocial PD (Regier et al., 1990) and Borderline PD (Bornovalova et al., 2005) although this may be due in part to diagnostic overlap (Regier et al., 1990) or shared traits such as impulsivity and disinhibition (Bornovalova et al., 2005). In contrast however, latent class analysis of disorders in the National Comorbidity Study – Adolescent Supplement (NCS-A) (Kessler et al., 2012b) ascribed behaviour disorders and substance disorders to separate classes, with the suggestion that the two have unique underlying psychopathological processes in younger persons, and that these may vary across the life course (Kendler et al., 2008). Existing studies have tended to focus on childhood or adolescent behaviour problems, as predictors of later substance use or mental disorders (Becker et al., 2012; Kessler et al., 2012a), and suicidal behaviours (Matsumoto et al., 2011). As to comorbid mental health and alcohol problems, most (Regier et al., 1990; Merikangas et al., 1998b; Teesson et al., 2009), though not all (Kessler et al., 2012b) population studies have investigated CAMHD in adults, therefore describing comorbidity years after its initial development. Occurring on a backdrop of anxiety and behaviour problems in childhood and adolescence, with depression developing through late teenage years to early adulthood (Merikangas et al., 1998b; Marquenie et al., 2007; McEvoy et al., 2011), early adulthood is arguably a sensitive period for the development of CAMHD (Cerda et al., 2010), as well as for determining trajectories of social functioning. In this respect, it is surprising that little research attention has been paid to the role of behaviour problems and how these may be associated with CAMHD in young adults.

Finally, methodological weaknesses in the existing literature are worth noting. Firstly, assessment of CAMHD has often relied on lifetime diagnoses, with little validation of disorder overlap to ensure co-occurrence of the disorders of interest (Grant et al., 1996; Kessler, 2004; Kessler et al., 2012b). The use of shorter diagnostic periods (i.e. last twelve months (Hall et al., 2009; Teesson et al., 2009)) has
been advocated, but this method also has disadvantages as it may miss earlier co-occurrences. Secondly a dimensional approach to behaviour problem assessment, using continuous rather than categorical diagnostics, is not typically used in studies of adults despite being common in studies of children. Yet treating each behaviour problem dimension as a continuum is arguably a more powerful approach. Compared to a categorical diagnostic approach, a dimensional approach permits identification of sub-threshold behaviour patterns and provides more information on wellbeing, with details of behaviour problems, severity and impact on functioning that are more indicative of the range of issues experienced by the general population (Achenbach, 2005; Brauner and Stephens, 2006; Hudziak et al., 2007).

In summary, there is a notable gap in research on the relationship between behaviour problems and the highly prevalent combination of alcohol problems and common mental disorders in young adults. We hypothesize that comorbidity of alcohol and mental health disorders is associated with greater behaviour problems compared with single disorder types. The purpose of this study was to evaluate this association, accounting for early individual and environmental factors, and using both categorical and dimensional diagnostic instruments to assess disorders and behaviours at age 21.
2. Methods

2.1 Study design and participants

The Mater University Study of Pregnancy (MUSP) is a birth cohort study of mothers and their children, enrolled at the mothers’ first clinical visit during pregnancy to the Mater Misericordiae Hospital in Brisbane during the 1980s. Both dyads were followed up at birth, 5 days and 6 months, then 5, 14 and 21 years after birth. At the time of enrolment and at follow ups, all participants gave their signed, informed consent. The MUSP study was approved by the Behavioural and Social Sciences Ethics Review Committee at the University of Queensland and has been extensively described elsewhere (Najman et al., 2005). At the 21–year follow up, 3801 members of the offspring cohort participated; 3778 completed a self-report questionnaire including the Young Adult Self Report (YASR) (Achenbach, 1997). Of these, 2539 participants (67%) were also administered the mental health and substance use disorders modules of the Composite International Diagnostic Interview (CIDI). Only participants for whom complete data on mental health, substance use and behaviour disorders are available (2314) were included in the current analyses.

2.2. Measures

2.2.1: Comorbidity categories

Data from CIDI responses were coded to yield DSM-IV disorder diagnoses for occurrence over the lifetime (LT) of the participant. For the purpose of this study, both alcohol abuse and dependence were included in ‘any alcohol use disorder’ (AUD). Participants diagnosed with any DSM-IV disorder/s were defined as having ‘any mental health disorder’ (MHD) (including any anxious, affective, psychotic or eating disorder).

A four-category variable “Comorbidity Type” was created. Participants were classified as having ‘no (DSM-IV) disorder’; a ‘mental health disorder only’ (MHD only, i.e. no alcohol disorder); an ‘alcohol use disorder only’ (AUD only, i.e. no mental health disorder) or ‘comorbid (CAMHD) alcohol and mental health disorders’ (i.e. ‘any alcohol use disorder’ plus ‘any mental health disorder’). Rather
than using last-12-month diagnoses to ensure temporal overlap of disorders for comorbidity (Hall et al., 2009; Teesson et al., 2009), which missed earlier disorder episodes, we examined ages of onset of most recent episodes for the disorders comprising each individual’s lifetime comorbid status. All participants within this classification were found to have episodes of the alcohol use disorder and the mental health disorder occurring within 12 months of each other, indicating temporal overlap of these disorders.

2.2.2: Behavioural problems

The YASR is a self-report scale developed for use with young adults aged 18-30 years in clinical settings (Achenbach, 1997) but validated in large population samples (Achenbach et al., 1995). It comprises 114 items describing a range of behaviour problems experienced over the previous 6 months using eight subscales. It has achieved internal reliability scores of 0.91 in this sample (Dingle et al., 2011). The Total Problems score comprises the Internalizing (anxiety/depression and withdrawn) and Externalizing (intrusive, aggression and delinquency) scales plus the somatic, thought and attention subscales. For the main regression models, each scale or subscale was used as a continuous variable. For supplementary analyses, the dimension score was categorised, using a 90th percentile cut-off to indicate case-ness for each dimension (Achenbach, 1997; Dingle et al., 2011).

2.2.3: Covariates

Covariates included participants’ demographics (age, gender, maternal marital status and maternal education) and factors previously found to be associated with CAMHD and behaviour problems in adults. Maternal smoking, drinking, anxiety, depression were also included in the multivariable models, since previous studies have shown these factors to be associated with development of both mental health and substance use problems in their offspring (Merikangas et al., 1998a; Alati et al., 2006; Saraceno et al., 2009). Maternal education level was recorded at the first clinic visit during pregnancy (FCV) and was categorised to less than high school, completed high school or completed post-high school study. Maternal marital status, drinking and smoking at the 14-year follow up were
assessed using maternal self-reports; these were categorised as partner (married/living together) or no partner (single, divorced, or separated); smoker or non-smoker; and non-drinker, occasional drinker (less than weekly) or regular drinker (weekly or more). Maternal anxiety and depression were assessed at the 14-year follow-up using the Delusions-Symptoms-States Inventory (DSSI; (Bedford and Foulds, 1977)). The DSSI contains both anxiety and depression subscales; the depression subscale has been found to correlate strongly with other scales of depression, including the Beck’s Depression Inventory (Najman et al., 2000) and achieved Cronbach’s α values of 0.88 in the maternal sample at the 14-year follow up. The internal consistency of the anxiety subscale reached 0.84 in this sample. Maternal anxiety and depression were recorded as a case if the individual was positive for at least four of the seven symptoms from that subscale (Bedford and Foulds, 1977).

2.3. Statistical analyses

2.3.1: Main analysis
Although both major measures (DSM-IV diagnoses and YASR behaviour problems) were assessed at the 21-year follow up, for the purposes of these analyses, DSM-IV diagnosed comorbidity categories were used as the outcome variable. To discern whether worse behaviour was more likely to indicate comorbid alcohol and mental health disorders, we generated a mean score, by comorbidity category, for each YASR subscale. Variation of subscale scores across the comorbidity categories was tested using ANOVA, with post-hoc paired t-tests used to examine differences between categories. To account for skewed distribution, ANOVAs were performed using transformed scores (square root of score). The results did not differ significantly from those for untransformed scores, so the latter are presented here for ease of interpretation. In order to compare the magnitude of change across comorbidity categories between YASR dimensions, change as a percentage of the total score range was calculated for each dimension (data not shown).
Multinomial logistic regression analyses were performed to examine the relationships between comorbidity category and YASR subscale scores, with the No Disorder category as reference. Models were adjusted for covariates as described above. Regressions were then repeated with the AUD and MHD categories as reference in order to establish differences between these and the CAMHD group.

To assess the association of comorbidity class with severe behaviour problems, we examined the number of individuals whose YASR behaviour problem reached case level. As a measure of behaviour problem complexity, we then assessed the number of case-level behaviour problems per individual, by comorbidity category. For each, we used multinomial regressions and adjusted for covariates as described above. Regressions were performed with alternate reference groups as described above to compare comorbidity categories with the no-disorder control, and to describe differences between single-disorder groups and the CAMHD group.

In sensitivity analyses, to ascertain the specificity of alcohol effects versus other substances, we adjusted for offspring smoking (smoker or non-smoker) and regular marijuana use (occasional/no use or use every day/few days), self-reported at the 21-year follow-up (data not shown).

2.3.2: Attrition analysis
Finally, we used two methods to assess how loss to follow up (LFU) may have affected our results.

Firstly, to determine whether differential attrition introduced bias to our results, we fitted a multivariate logistic regression model to compare a number of baseline factors between those retained and those lost to follow up. Secondly, starting from a missing at random assumption (Sterne et al., 2009), we used the STATA procedure of multiple imputation, using 10 cycles of regression to generate 10 data sets; our analysis was repeated using these data. Variables used for the imputation models included maternal age, education, marital status, anxiety and depression at first clinical visit during pregnancy and maternal pre-pregnancy drinking and smoking, in addition to
those listed above. All analyses were undertaken using the STATA 11 statistical package (StataCorp, USA).
3. Results

Of the original birth cohort (7223), 3801 MUSP offspring completed the YASR at age 21, with 2515 providing complete information on both CIDI and YASR. Some differences emerged between those lost to follow up (LFU) and those included in this study. In the multivariate model of loss to follow up, participant male gender, maternal anxiety, depression and smoking, un-partnered marital status and lower education significantly predicted loss to follow up (Table 1). These factors were then used in the multiple imputation process.

Of those remaining in the study, 48.7% had no lifetime DSM-IV disorder, 23.3% had a lifetime mental health disorder but no alcohol disorder (MHD only), 16% had a lifetime alcohol disorder but no mental health disorder (AUD only), and 12% had comorbid lifetime alcohol and mental health disorders (CAMHD) (Table 2). Analysis of episode recency for each individual’s disorders showed that all members of the CAMHD group experienced co-occurrence of the disorders within 12 months, allowing the disorders to be considered comorbid. Although the MHD only group comprised more females (75%) and the AUD only group more males (80%), both the no-disorder and CAMHD groups had similar proportions of male and female members (Table 2).

In exploratory analyses, significant differences were found by ANOVA between disorder groups for the total problems scale; paired t-tests showed the mean score was significantly higher for the CAMHD group than for either single-disorder group (). We therefore examined each subscale separately. Similar results were seen for all but the withdrawn and anxiety/depression subscales (Table 2). Considering the score difference between the CAMHD group and the single-disorder groups as a proportion of score ranges, the greatest increments were seen for aggression and delinquency subscales (data not shown).

All covariates found to be related to at least one disorder category (Table 3) were retained in the final models (Table 4). After excluding individuals with data missing for variables of interest, a final sample of 2314 remained. Participants’ age, smoking, regular marijuana use, lower maternal
education, and maternal smoking, depression, anxiety and un-partnered marital status were all associated with CAMHD, but only participant and maternal smoking and depression were more strongly associated with CAMHD than with either single disorder (P-value for all covariates <0.05). No gender interactions were found for the behaviour problems in the comorbid group.

Table 4 shows the unadjusted and fully adjusted models of comorbidity class with individual problem subscales as predictors (composite scales are not shown). The adjusted models differ little to the univariable analyses. Other than the anxiety/depression and withdrawn subscales, for each subscale, those with higher behaviour problem scores were more likely to be in the CAMHD group than to have single disorder types only. Further adjustment for participant smoking and marijuana use produced negligible change (data not shown). When we repeated the regressions using the MHD or AUD group as reference, odds ratios showed that, for each point increase in YASR behaviour score, there was roughly a 10% increase in the likelihood of the person having comorbid alcohol and mental health disorders over a single disorder. Aggression, somatic, thought and attention disorders appear to contribute more through the mental health disorders, whereas delinquency associates more strongly via the alcohol disorders. Multiple imputation analysis yielded very similar results to those shown here (Supplementary Table 3).

In additional analyses, we found that those in the CAMHD group were more likely to have a subscale score reaching case level for somatic, thought, intrusive, aggression or delinquency problems than those with single disorders (Supplementary Table 1). Individuals with comorbid alcohol and mental health conditions also tended to have more case-level problem behaviours (Supplementary Table 2). Having a larger number of case-level problem behaviours was associated with a significant increase in the likelihood of comorbidity, a trend which was unaltered by adjustment (Supplementary Table 2).
4. Discussion

In this research we aimed to investigate whether behaviour problems were more strongly associated with comorbid alcohol and mental health problems than they were in those with the constituent disorder types alone. This study extends clinical evidence, confirming that CAHMDs emerge early in adulthood, suggesting that the associated behaviour problems are likely to be more complex and more severe than in those with either single disorder type.

We found that the significant comorbidity between alcohol and mental health disorders, reported in adults by a number of large population studies, is apparent by early adulthood. Any functional deficit will thus affect a crucial developmental stage in the life course. Although some identification of the functional impact of comorbidity in younger people was undertaken in the National Comorbidity Study Replication – Adolescents (NCS-A) (Merikangas et al., 2009), these specific analyses have not yet been published. We provide the first report of population-level associations with behaviour at age 21; those in the CAMHD group experienced significantly more numerous and more severe problems than those with alcohol or mental health disorders alone. Within this, our study found that the relationship of comorbidity with internalizing behaviour problems was no stronger than that reported with constituent disorders. However, this may be due to a ceiling effect, whereby the constructs measuring the internalising disorders and internalising behaviour problems overlap such that the addition of AUD contributes little extra to the internalising behaviour problem score in those with internalising disorders. More importantly, those with CAMHD were more likely to externalize their distress. Behaviour scores on the aggressive, intrusive and delinquent subscales were more elevated for the CAMHD group, consistent with extensive evidence associating externalizing, conduct and disruptive behaviour problems separately with alcohol (Fergusson et al., 1993; Alati et al., 2005; Boden et al., 2012; Heron et al., 2013) and mental health disorders (Alegria et al., 2010).
Some links between behaviour problems and comorbidity have been reported in clinical samples (Fazel et al., 2009), but these focused on severe disorders such as schizophrenia and other psychoses. This is the first study suggesting that the same associations are found to be true for more common mental health disorders, such as mood and anxiety disorders. It is likely that similar associations may be found with other substance use disorders, potentially via the associated disinhibition (Bornovalova et al., 2005). This is beyond the scope of this paper, but future studies should expand our findings to other, less prevalent, substance use disorders to investigate possible links with behaviour. The increases in severity of behavioural problems for those with CAMHD (10-15% over single disorder groups) are smaller than those observed in clinical samples (Swendsen and Merikangas, 2000; Davis et al., 2008), but this is to be expected; firstly because our study is based on a population rather than a clinical sample, and secondly because participants are young adults, who are likely to have been assessed at early stages of their disorders. What is however notable is that even by this early stage, important increases in severity of behaviour problems are already apparent.

Our finding that comorbid alcohol dependence is associated with increased externalising behaviour problems among individuals with mental health problems has several implications. For individuals, the presence of externalizing behaviour problems in particular may exacerbate the severity of alcohol problems and hasten progression from the alcohol abuse disorders that are typical of this age group, to alcohol dependence (Behrendt et al., 2011), or further undermine chances of recovery from CAMHD (Grella and Stein, 2013). The complexity of problems may explain the increased days-out-of-role reported by comorbid persons (Slade et al., 2009; Teesson et al., 2009), and dovetails with reports of increased disorder severity for comorbid groups (Merikangas and Kalaydjian, 2007; Kessler and Wang, 2008a). More importantly, it is possible that higher externalizing behaviour problems will increase the risk of exposure to the criminal system for individuals with CAMHD. There are well-documented links between alcohol, violence, involvement with the justice system and recidivism (Sly et al., 2009; Boden et al., 2012; O'Driscoll et al., 2012) and the economic costs of these (Bouchery et al., 2011). Younger persons engage less with treatment services, whether for
alcohol or mental health disorders (Cohen et al., 2007), so these associated behaviour problems are likely to manifest as public order problems (Hingson et al., 2009; Laslett et al., 2011). As a result, comorbid conditions may be highly prevalent in those engaged with the criminal system, and conversely, behaviour problems may act as indicators of underlying alcohol/mental health disorders in offenders. Co-occurrence of mental health disorders has been noted in reoffending substance users (O'Driscoll et al., 2012), but the full impact of comorbid disorders on rehabilitation and reoffending in offenders is unknown. Future research should investigate this likelihood and any associated social and individual implications.

Finally, our findings may also have implications for early intervention. The externalizing behaviour problems associated with CAMHD are likely to be challenging in mainstream service environments and hence alienate this group of people from care when they do present for treatment (Alegria et al., 2010). Although current service-level initiatives regarding comorbidity recommend routine screening for both substance and mental health disorders on presentation (Mills et al., 2009), our findings suggest that the presence of externalizing behaviours on presentation should highlight the need for dual disorder screening, and management practices should be implemented for the externalizing behaviours associated with this comorbidity. Our findings underline the need for adequate measures to be routinely employed in expectation of such behaviour problems, as opposed to being regarded as an extreme and uncommon occurrence.

This paper has significant strengths. It describes effects in a large and non-selected community sample, allowing conclusions to be generalized to the population, and is able to adjust the associations seen for a number of relevant longitudinal covariates. Ours is one of the first studies to use a rigorous method to assess comorbidity. Using the onset of most recent episodes, we were able to demonstrate that the entire group reporting comorbid alcohol and mental health disorders showed co-occurrence of the two classes within a 12 month period. Most previous large scale national studies have used lifetime reporting of two disorders as their criterion for comorbidity.
(Swendsen and Merikangas, 2000; Kessler, 2004). With variation in ages of onset (Merikangas et al., 1998b; McEvoy et al., 2011), and the episodic rather than chronic nature of such disorders during youth development, our more stringent approach gives us greater confidence that the constituent disorders were temporally comorbid, in order to show the impact of their co-occurrence. Additionally, we have been able to provide more detailed information on the range of behavioural problems associated with CAMHD by using continuous measures rather than categorical diagnostics.

Our findings should be seen in the context of some limitations. Firstly, our data were cross-sectional, and so have limited predictive value. However, the reporting periods for behaviour and CIDI-diagnosed comorbidity may not overlap. Behaviour problems are reported for the six months immediately prior to interview, whereas 69% of comorbidity cases were not within the 12 months preceding interview, so may have preceded the behaviour problems. From this information we may suggest that, for those in whom the comorbid disorder episodes may have subsided, the more severe behaviour problems with which they are associated persist.

Secondly, the loss to follow up in our study may have introduced bias to our results. Only 2575 of the original birth cohort were administered the CIDI at the 21-year follow up, resulting in 32% of the original birth cohort being available for this analysis. Some differences have emerged between those represented her and the original sample. Those lost to this group were more likely to have mothers who smoked and were depressed. Maternal smoking remained a significant factor in the relationships between the externalizing behaviour problems and comorbidity, and maternal depression in the relationship between aggression and comorbidity, as well as with single disorders. Thus, the relationship strengths described here may have been underestimated as a result of loss to follow up. In addition, despite the limitations of imputations analysis in dealing with attrition bias, the results of our MI analysis were virtually identical to those in our main analysis, giving further confidence to the robustness of our findings in the face of attrition.
In conclusion, we found that CAMHD emerge at young adulthood in significant numbers in the general population, and that this comorbidity is strongly associated with increases in internalising and externalizing behaviour problems. If our findings are replicated in similar studies, future intervention strategies will need to include behavioural management practices.

Author disclosures

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Contributors

Authors Salom, Alati, Williams and Scott designed the study; author Salom wrote the protocol and managed the literature searches. Authors Salom and Betts undertook the statistical analysis. Author Salom wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare there are no conflicts of interest.

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Figure Legends

Table 1: Multivariable attrition analysis showing the likelihood of being lost to follow up (LFU) according to baseline factors, expressed as Odds Ratios (OR) with 95% Confidence Intervals (CI95)

$^5$ FCV = first clinic visit during pregnancy

Model is fully adjusted for all covariates; significant (P<0.05) ORs are shown in bold

Reference categories for the covariates above are: male; completed post-Year 12 study; married/living together; non-smoker; non-drinker; not depressed; not anxious

Table 2: Mean YASR dimension scores for MUSP offspring participants at age 21, by comorbidity category

$^a$ Mental Health Disorders (MHD) included any lifetime DSM-IV disorder; psychoses, eating disorders and substance use disorders were included.

$^b$ Alcohol Use Disorders (AUD) included lifetime DSM-IV alcohol abuse and alcohol dependence disorders.

$^c$ CAMHD participants were diagnosed with any lifetime MHD plus any lifetime AUD.

$^d$ ANOVA results confirmed significantly different mean scores between the categories

$^6$ Post-hoc paired T-tests showed that mean score for dimension was significantly higher for the comorbid group than for either AUD or MHD (p<0.05)

Table 3: Univariate relationships between covariates and comorbidity categories
a Multinomial logistic regression models, unadjusted, using No Disorder as reference

b Measured at first clinical visit during pregnancy (FCV)

c Measured at 14 year follow up

d Measured at 21 year follow up

§ Association of covariate with comorbid group is significantly greater than with either single disorder group (P<0.005)

Table 4: Multinomial logistic regression models of comorbidity category at age 21, with YASR dimensions as predictors

a Regressions performed using No-Disorder group as reference; significant ORs (P<0.005) are in bold type

b Models adjusted for participant gender and age, plus maternal education, drinking, depression, anxiety and marital status as per Table 4; No Disorder group used as reference

c Fully adjusted regressions were repeated, using MHD as reference (CAMHD vs MHD) and using AUD as reference (CAMHD vs AUD), to allow comparison between ORs for comorbid and single disorder types

§ Odds Ratio for the CAMHD group was significantly higher (P<0.05) than that for either single-disorder group as determined above
Table 1: Multivariable attrition analysis showing the likelihood of being lost to follow up (LFU) according to baseline factors, expressed as Odds Ratios (OR) with 95% Confidence Intervals (CI95)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Category</th>
<th>Odds of being LFU at 21 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OR</td>
</tr>
<tr>
<td>Participant gender</td>
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<tr>
<td>Mother’s education at FCV§</td>
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<tr>
<td></td>
<td>Less than Year 12</td>
<td><strong>1.21</strong></td>
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<td></td>
<td>Regularly</td>
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<tr>
<td>Mother anxious at FCV§</td>
<td>Anxious</td>
<td><strong>1.29</strong></td>
</tr>
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</table>
Table 2: Mean YASR dimension scores for MUSP offspring participants at age 21, by comorbidity category

<table>
<thead>
<tr>
<th>Comorbidity category</th>
<th>No disorder</th>
<th>MHD only (^a)</th>
<th>AUD only (^b)</th>
<th>CAMHD (^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of participants:</td>
<td>1226 (49%)</td>
<td>589 (23%)</td>
<td>398 (16%)</td>
<td>302 (12%)</td>
</tr>
<tr>
<td>Male</td>
<td>606</td>
<td>146</td>
<td>319</td>
<td>152</td>
</tr>
<tr>
<td>Female</td>
<td>620</td>
<td>443</td>
<td>79</td>
<td>150</td>
</tr>
<tr>
<td>YASR dimension</td>
<td>Mean score ((CI_{95}))</td>
<td>Mean score ((CI_{95}))</td>
<td>Mean score ((CI_{95}))</td>
<td>Mean score ((CI_{95}))</td>
</tr>
<tr>
<td>Total problems</td>
<td>22.05 ((21.28, 22.81))</td>
<td>36.27 ((34.74, 37.79))</td>
<td>27.84 ((26.18, 29.49))</td>
<td>42.76(^\delta) ((40.42, 45.10))</td>
</tr>
<tr>
<td>Internalizing</td>
<td>8.17 ((7.80, 8.54))</td>
<td>14.77 ((14.05, 15.50))</td>
<td>8.12 ((7.47, 8.78))</td>
<td>14.76 ((13.76, 15.77))</td>
</tr>
<tr>
<td>Anxiety/depression</td>
<td>6.08 ((5.80, 6.37))</td>
<td>11.53 ((10.95, 12.11))</td>
<td>5.89 ((5.38, 6.39))</td>
<td>11.43 ((10.64, 12.21))</td>
</tr>
<tr>
<td>Withdrawn</td>
<td>2.10 ((1.98, 2.21))</td>
<td>3.22 ((3.01, 3.42))</td>
<td>2.23 ((2.03, 2.44))</td>
<td>3.31 ((3.02, 3.59))</td>
</tr>
<tr>
<td>Externalizing</td>
<td>7.33 ((7.03, 7.62))</td>
<td>10.37 ((9.83, 10.91))</td>
<td>11.45 ((10.74, 12.16))</td>
<td>14.95(^\delta) ((14.01, 15.88))</td>
</tr>
<tr>
<td>Intrusive</td>
<td>2.49 ((2.36, 2.61))</td>
<td>3.12 ((2.92, 3.32))</td>
<td>3.07 ((2.83, 3.31))</td>
<td>3.69(^\delta) ((3.38, 4.00))</td>
</tr>
<tr>
<td>Aggression</td>
<td>3.29 ((3.13, 3.45))</td>
<td>5.24 ((4.94, 5.53))</td>
<td>4.55 ((4.18, 4.91))</td>
<td>6.83(^\delta) ((6.33, 7.33))</td>
</tr>
<tr>
<td>Delinquency</td>
<td>1.60 ((1.50, 1.70))</td>
<td>2.02 ((1.85, 2.19))</td>
<td>3.80 ((3.52, 4.07))</td>
<td>4.41 ((4.07, 4.75))</td>
</tr>
<tr>
<td>Somatic</td>
<td>3.43 ((3.27, 3.60))</td>
<td>6.13 ((5.81, 6.44))</td>
<td>4.12 ((3.79, 4.45))</td>
<td>6.87(^\delta) ((6.36, 7.38))</td>
</tr>
<tr>
<td>Thought</td>
<td>0.45 ((0.40, 0.50))</td>
<td>1.02 ((0.91, 1.13))</td>
<td>0.76 ((0.64, 0.87))</td>
<td>1.40(^\delta) ((1.21, 1.59))</td>
</tr>
<tr>
<td>Attention</td>
<td>2.82 ((2.70, 2.94))</td>
<td>3.91 ((3.70, 4.11))</td>
<td>3.37 ((3.13, 3.62))</td>
<td>4.54(^\delta) ((4.25, 4.83))</td>
</tr>
</tbody>
</table>

Behaviour in comorbid alcohol/mental problems

TABLES 26
Table 3: Univariate relationships between covariates and comorbidity categories

<table>
<thead>
<tr>
<th>Covariate</th>
<th>No of cases (%)</th>
<th>MHD only OR (CI95)</th>
<th>AUD only OR (CI95)</th>
<th>CAMHD OR (CI95)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>1790 (47%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>1988 (53%)</td>
<td><strong>2.97</strong> (2.38, 3.69)</td>
<td><strong>0.24</strong> (0.18, 0.32)</td>
<td>0.96 (0.75, 1.24)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>3778</td>
<td>1.05 (0.93, 1.18)</td>
<td><strong>1.26</strong> (1.10, 1.44)</td>
<td><strong>1.30</strong> (1.11, 1.52)</td>
</tr>
<tr>
<td><strong>Maternal education</strong> b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post Year 12 study</td>
<td>1252 (17%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed Year 12</td>
<td>689 (10%)</td>
<td>0.99 (0.66, 1.49)</td>
<td><strong>1.58</strong> (1.01, 2.48)</td>
<td><strong>1.85</strong> (1.09, 3.13)</td>
</tr>
<tr>
<td>Did not complete Year 12</td>
<td>5229 (73%)</td>
<td><strong>1.31</strong> (1.02, 1.68)</td>
<td><strong>1.62</strong> (1.20, 2.20)</td>
<td><strong>2.07</strong> (1.44, 2.98)</td>
</tr>
<tr>
<td><strong>Maternal drinking</strong> c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-drinker</td>
<td>2436 (47%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occasional drinker</td>
<td>1657 (32%)</td>
<td>1.02 (0.81, 1.27)</td>
<td><strong>1.35</strong> (1.03, 1.76)</td>
<td>0.84 (0.62, 1.14)</td>
</tr>
<tr>
<td>Regular drinker</td>
<td>1079 (21%)</td>
<td>0.88 (0.67, 1.15)</td>
<td><strong>1.48</strong> (1.10, 1.99)</td>
<td>1.23 (0.89, 1.69)</td>
</tr>
<tr>
<td><strong>Maternal smoking</strong> c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>3570 (69%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>smoker</td>
<td>1602 (31%)</td>
<td><strong>1.51</strong> (1.21, 1.89)</td>
<td><strong>1.46</strong> (1.13, 1.88)</td>
<td><strong>2.19</strong> $^f$ (1.67, 2.87)</td>
</tr>
<tr>
<td><strong>Maternal depression</strong> c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-depressed</td>
<td>6789 (94%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed</td>
<td>434 (6%)</td>
<td>1.15 (0.75, 1.78)</td>
<td>1.35 (0.85, 2.16)</td>
<td><strong>2.62</strong> $^f$ (1.71, 4.02)</td>
</tr>
<tr>
<td><strong>Maternal anxiety</strong> c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not anxious</td>
<td>6250 (86%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td>973 (14%)</td>
<td><strong>1.44</strong> (1.11, 1.87)</td>
<td>1.21 (0.89, 1.65)</td>
<td><strong>1.75</strong> (1.28, 2.41)</td>
</tr>
<tr>
<td><strong>Maternal marital status</strong> c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/living together</td>
<td>4184 (81%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No partner</td>
<td>983 (19%)</td>
<td><strong>1.52</strong> (1.17, 1.97)</td>
<td>1.18 (0.86, 1.62)</td>
<td><strong>1.43</strong> (1.03, 1.99)</td>
</tr>
<tr>
<td><strong>Participant smoking</strong> d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>2396 (64%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>smoker</td>
<td>1362 (36%)</td>
<td><strong>1.90</strong> (1.54, 2.34)</td>
<td><strong>2.87</strong> (2.27, 3.36)</td>
<td><strong>4.95</strong> $^f$ (3.79, 6.46)</td>
</tr>
<tr>
<td><strong>Participant marijuana use</strong> d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non/occasional use</td>
<td>3289 (88%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular use</td>
<td>465 (12%)</td>
<td><strong>1.56</strong> (1.07, 2.28)</td>
<td><strong>5.95</strong> (4.28, 8.28)</td>
<td><strong>6.68</strong> (4.72, 9.47)</td>
</tr>
</tbody>
</table>
Table 4: Multinomial logistic regression models of comorbidity category at age 21, with YASR dimensions as predictors

<table>
<thead>
<tr>
<th>YASR Dimension</th>
<th>Unadjusted models</th>
<th>Fully adjusted models</th>
<th>Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MHD only</td>
<td>AUD only</td>
<td>CAMHD D</td>
</tr>
<tr>
<td></td>
<td>OR (Cl95)</td>
<td>OR (Cl95)</td>
<td>OR (Cl95)</td>
</tr>
<tr>
<td><strong>Internalizing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety / depression</td>
<td>1.16 (1.14, 1.18)</td>
<td>0.99 (0.97, 1.02)</td>
<td>1.15 (1.13, 1.18)</td>
</tr>
<tr>
<td>Withdrawn</td>
<td>1.24 (1.19, 1.30)</td>
<td>1.03 (0.98, 1.09)</td>
<td>1.26 (1.19, 1.33)</td>
</tr>
<tr>
<td><strong>Externalizing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusive</td>
<td>1.12 (1.08, 1.17)</td>
<td>1.11 (1.06, 1.17)</td>
<td>1.23 (1.17, 1.29)</td>
</tr>
<tr>
<td>Aggression</td>
<td>1.20 (1.17, 1.24)</td>
<td>1.14 (1.10, 1.18)</td>
<td>1.33 (1.28, 1.38)</td>
</tr>
<tr>
<td>Delinquency</td>
<td>1.13 (1.07, 1.19)</td>
<td>1.52 (1.44, 1.61)</td>
<td>1.63 (1.54, 1.73)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>1.25 (1.22, 1.29)</td>
<td>1.08 (1.04, 1.12)</td>
<td>1.31 (1.26, 1.36)</td>
</tr>
<tr>
<td>Thought</td>
<td>1.67 (1.51, 1.84)</td>
<td>1.41 (1.26, 1.58)</td>
<td>1.95 (1.75, 2.18)</td>
</tr>
<tr>
<td>Attention</td>
<td>1.22 (1.17, 1.28)</td>
<td>1.12 (1.06, 1.17)</td>
<td>1.35 (1.28, 1.42)</td>
</tr>
</tbody>
</table>

Unadjusted models

Fully adjusted models

Comparisons
highlights

- Twelve percent of young adults had alcohol/mental health DSM-IV disorders with significant temporal overlap.
- The comorbid group scored significantly higher on total and externalizing behaviour problems but not internalizing behaviour problems.
- Stronger associations of aggression/delinquency with comorbidity were not fully accounted for by factors known to influence separate development of mental health and alcohol disorders.