The Association Between Prenatal Alcohol Exposure and Behavior at 22 Years of Age

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Background: Prenatal alcohol exposure (PAE) affects central nervous system development, growth, and morphology at higher exposure levels. Little is known about the effects of PAE at lower exposure levels or in young adults. Research on children with higher levels of PAE has shown that PAE predicts behavior problems. The question remains whether these effects are permanent or ameliorated by maturation into adulthood.

Methods: These data are from a longitudinal study of PAE. Mothers were recruited from a prenatal clinic and interviewed during their fourth prenatal month, seventh month, and delivery. In the postpartum, mothers and offspring were seen at 8 and 18 months, and 3, 6, 10, 14, 16, and 22 years.

Results: At 22 years, PAE significantly predicted behavior as measured with the adult self-report. These findings were significant controlling for covariates. Exposure at each trimester predicted increased behavior problems on the Total Score, Internalizing, Externalizing, Attention, and Critical Items scales. Use across pregnancy predicted a higher rate of behavior problems compared to no use and use in the first trimester only.

Conclusions: The effects were dose-response and significant at each trimester of pregnancy. However, duration across pregnancy was a better predictor than drinking during the first trimester only. Binge drinking was not a better predictor of outcome compared to average daily volume (ADV), and within categories of ADV, binge drinking did not predict more problems than nonbinge drinking. Thus, there is no safe level or safe time during pregnancy for women to drink. These data demonstrate that the effects of PAE, even at low to moderate levels, extend into young adulthood and are most likely permanent.

Key Words: Fetal Alcohol, Behavior, Young Adults.

A lcohol use during pregnancy is associated with physical, behavioral, and cognitive abnormalities in the offspring and can result in a diagnosis of fetal alcohol syndrome (FAS), which is characterized by deficits in 3 domains: growth retardation, facial anomalies, and central nervous system deficits (IOM, 1996). FAS, however, is far outweighed by the subdiagnostic effects of prenatal alcohol exposure (PAE). Among those with PAE but not FAS, deficits comparable to the diagnostic criteria of FAS are found but the presentation does not reach diagnostic level. Numerous studies have reported effects of PAE on growth deficits (Day et al., 2002), academic difficulties (Coles et al., 1991; Goldschmidt et al., 1996), behavior and emotional problems (Brown et al., 1991; Walthall et al., 2008), IQ deficits (Olson et al., 1997; Willford et al., 2006), and deficits in learning and memory (Richardson et al., 2002).

Despite the established negative consequences, alcohol use during pregnancy is not uncommon. Data from the 2009 Survey on Drug Use and Health (SAMHSA, 2010) found that approximately 10% of pregnant women aged 15 to 44 years old reported alcohol use and 4.4% reported binge drinking in the past month. Given the high prevalence of drinking during pregnancy and the potential for adverse health outcomes, it is important to explore the long-term consequences of PAE.

This paper addresses the effects of PAE on behavior problems in offspring who are young adults at age 22. It is well known that individuals with FAS are at an increased risk for behavioral and emotional problems (IOM, 1996), but there is less research examining behavior problems among offspring with PAE who do not have FAS. Sood and colleagues (2001) addressed this question among a sample of 506 African American parent–child dyads recruited from an urban maternity clinic. Women reported prepregnancy alcohol consumption at their first prenatal visit and during the prior 2 weeks at every subsequent visit. Mothers completed the Child Behavior Checklist (CBCL; Achenbach, 1991) when their children were 6 to 7 years old. PAE was associated with higher mean CBCL scores on the Total Score, Externalizing, and Internalizing scales after controlling for child’s custody status, current lead level, maternal smoking during preg-
nancy, maternal education, and characteristics of the home environment.

D’Onofrio and colleagues (2007) used data from the National Longitudinal Survey of Youth (Baker and Mott, 1989) and the Children of the National Longitudinal Survey of Youth (Chase-Lansdale et al., 1991) to examine the association between PAE and offspring externalizing problems, assessed by the CBCL, in the 4- to 11-year-old offspring of 4,912 women. Controlling for demographic factors, gender, and prenatal nicotine exposure, PAE was associated with significantly more externalizing problems compared to offspring who were not exposed. Similar outcomes have been reported by a number of studies (Brown et al., 1991; Carmichael-Olson et al., 1992; Sampson et al., 1989; Streissguth et al., 1989).

There are also negative reports. Kelly and colleagues (2012) reported that 5-year-olds exposed to light levels (1 to 2 drinks per week or per occasion for less than weekly drinkers) during gestation had fewer behavior difficulties than did offspring of the abstainers and the heavier drinkers. Robinson and colleagues (2010) found the same association between PAE and behavior using data from the Western Australian Pregnancy Cohort. In a series of papers from the Lifestyle During Pregnancy Study (Kesmodel et al., 2010), the authors found that factors that contribute to the development of problem behavior such as executive functioning (Skogerbo et al., 2012), IQ (Falgreen Eriksen et al., 2012), and attention (Underberg et al., 2012) were not affected by low to moderate levels of gestational alcohol exposure at age 5.

Few studies have examined the effects of PAE on adult offspring who do not have FAS, and those that have focused on more severe outcomes related to either substance abuse or psychiatric diagnoses. Controlling for covariates, PAE has been associated with increased symptoms of nicotine, alcohol, and illicit drug dependence among adult adoptees aged 18 to 45 years old (Yates et al., 1998), offspring alcohol problems at 21 years of age (Baer et al., 2003), and DSM-IV alcohol use disorders between the ages of 13 to 21 years (Alati et al., 2006). A study from the Maternal Health Practices and Child Development Study also found that after considering all significant covariates, PAE, dichotomized at the level of ≥1 drink per day and <1 drink per day, was significantly associated with a higher rate of conduct disorder at age 16 (Larkby et al., 2011). A report from the Minnesota Twin Family study (Disney et al., 2008) reported similar findings with 17-year-olds.

Considered together, the weight of evidence demonstrates that there is an association between PAE and behavioral problems among children and adolescents. The effects of PAE, particularly at light and moderate levels, are not well studied in adulthood. In this study, we examine the effects of PAE on behavior at 22 years of age in a cohort that has been followed since the fourth gestational month. Based on the relationship between PAE and childhood behavior problems, we hypothesized that PAE would be associated with a higher rate of problem behaviors in young adulthood.

**MATERIALS AND METHODS**

**Sample Selection and Study Design**

Subject recruitment for this study began in 1983 and was completed in 1986. Women who were at least 18 years of age were recruited from a prenatal clinic in their fourth or fifth prenatal month. A total of 1,360 women completed an initial interview in which prenatal alcohol and other substances were assessed. Two cohorts were selected from that subject pool. One cohort was composed of all women who drank 3 or more alcoholic drinks per week during their first trimester and a random equal-sized sample of women who drank less than that amount or not at all. The other cohort was all women who reported using marijuana at least 2 times per month and an equal-sized random sample of women who reported they used marijuana less often or abstained. Women were eligible for either or both of the cohorts and the methods of both studies were identical.

The cohorts are combined for these analyses. There is a 47% overlap between the cohorts. There were no significant demographic differences between cohorts. The nonoverlapping groups differed by their level of alcohol and marijuana use, but not cigarette smoking or behavior problems. The women who were selected for the study were interviewed again in their seventh prenatal month and at delivery. The combined birth cohort consisted of 763 live singleton infants. Subsequent interviews were conducted at 8 and 18 months and at 3, 6, 10, 14, 16, and 22 years. Growth, cognitive and physical development, mental health, and behavior were measured at each of the follow-up times, as were demographic characteristics and maternal psychological, social, and environmental factors.

At the 22-year phase, 80% (n = 608) of the birth sample was interviewed. Missing were 30 who refused to participate, 3 were adopted, 18 were institutionalized, 56 were lost to follow up, 29 moved out of the Pittsburgh area, 11 died, and 8 were unable to participate due to low cognitive functioning. One offspring did not complete his/her behavioral assessment, resulting in a sample of 607 offspring for analysis. There were no significant differences between those included in the 22-year analyses (n = 607) and those who were not (n = 156) when maternal socioeconomic status, race, prenatal alcohol, marijuana, or tobacco exposures were considered.

**Sample Characteristics**

The mean age of the mothers in the first trimester was 23 (range, 18 to 42) years. We did not interview women below the age of 18. The sample reflects the racial composition of the clinic population: 48% Caucasian and 52% African American women. In general, the participants were of lower socioeconomic status with 61% of women reporting a family income of <$400/mo in 1982 to 1985. Their average education was 11.8 years and 26% of the women had <12 years of education. Thirty-three percent of the women were primigravidous, 32% were married, and 25% worked outside of the home. The mean alcohol use among users in the first trimester was 0.9 drinks per day (range, 0.006 to 19.6), mean marijuana use was 0.9 joints per day (range, 0.001 to 7.4), and the mean number of cigarettes was 15 per day (range, 0.5 to 50). Twelve percent of the women reported illicit drug use other than marijuana, including 4% who reported cocaine use.

Forty-eight percent of the infants were male, 8% were premature (<37 weeks gestation), and 11% were small for gestational age (birthweight less than or equal to tenth percentile for gestational age). The average birthweight in the sample was 3,199 g (range, 1,040 to 4,990). Few infants had major anomalies (1%), 8% had 2 or more minor physical anomalies.

At the 22-year assessment, the offspring were, on average, 22.8 years of age (range, 21 to 26), 47% were males, and 57% were African American. Sixty percent of the offspring worked full or part-time, 27% attended school, and 4% served in the military. 

Their average education was 12.8 years; 48% had some education past high school. Only a small proportion of the offspring were married (5.8%), 28% lived with a significant other, and 37% reported having at least 1 child.

Measures

**Offspring Behavior.** Behavior problems at age 22 were assessed with the adult self-report (ASR; Achenbach and Rescorla, 2003). The ASR is the adult continuation of the CBCL. The subjects self-reported on their behavioral, emotional, and social problems. The 126 items include Internalizing (anxious/depressed, withdrawn, somatic complaints) and Externalizing (rule-breaking, aggressive behavior, intrusive) scales. Attention problems, a Critical Items scale (sum of 19 items considered critical by majority of clinicians), and a Total Score. With regard to validity, the ASR was used because it has been shown to correlate with diagnoses of individuals who were referred for mental health or substance use reasons and with empirically based syndrome scales (Achenbach and Rescorla, 2003).

**Substance Use.** PAE for the first, second, and third trimesters was assessed at prenatal months 4 and 7 and at birth, respectively. Participants indicated their usual, maximum, and minimum quantity and frequency of beer, wine, liquor, wine, and beer coolers (Day and Robles, 1989). These were summarized as the average daily volume (ADV) of alcohol. Marijuana use was assessed using the same methodology and summarized as average daily joints (ADJ). Tobacco was expressed as the average number of cigarettes smoked per day. Offspring alcohol, marijuana, and tobacco use at 22 years was measured with the same instrument that was used for the mothers (Day and Robles, 1989). Other drugs were also assessed because their use was infrequent; they were combined into a dichotomous variable (use/no use) for these analyses.

**Other Measures.** Other covariates included in the analyses were subject’s age at assessment, gender, and race.

**Maternal Measures.** First trimester maternal depression and hostility during pregnancy were included in the model as covariates. Maternal depression was assessed using the Centers for Epidemiologic Studies-Depression Scale (Radloff, 1977). The hostility measure was from the State-Trait Personality Index (Spielberger, 1979), which contained a subset of the items from the Spielberger State-Trait Anger Scale (Spielberger et al., 1970).

Data Analysis

Stepwise multiple regressions were used to analyze the effects of PAE on the young adults’ behavior problems while controlling for other predictors. The outcome variables included the Total, Externalizing, and Internalizing T-scores, and the Attention problems and Critical Items scales from the ASR. As recommended by Achenbach and Rescorla (2003), the raw scores were used for the latter 2 scales because the T-scores for these scales are truncated. The covariates included in the model were selected based on a review of the literature and on previous experience with these data. The frequency distributions of PAE and offspring substance use (alcohol, marijuana, and tobacco) were positively skewed and were log-transformed to reduce skewness. Predictors that were significant at an alpha of 0.05 were retained in the final model. Significance level was set to 1-tailed p-value of 0.05 as we hypothesized unidirectional effects.

Regression residual diagnostics were used to identify outliers and influential cases (Stevens, 2009). The results reported here exclude influential and outlier cases (2 for externalizing and 3 for the critical items) to avoid misleading interpretations of the results.

Multicollinearity was tested by tolerances to ascertain stability of the coefficients.

Separate regression analyses were run for each trimester of pregnancy to assess the effects of exposure at the different time periods. Alcohol use was correlated across trimesters: 0.44 (first to second), 0.5 (first to third), and 0.6 (second to third) although the pattern of use differed across pregnancy. To investigate the effects of duration of PAE on offspring development, 3 groups were defined using the ADV of the group: (Group 1) offspring of women who did not drink during pregnancy (n = 171), (Group 2) women who drank 1 or more drinks per day during the first trimester and did not drink during the third trimester (n = 54), and (Group 3) women who drank 1 or more drinks per day during the first and third trimesters (n = 12). Analysis of variance (ANOVA) was used to compare behavior problems among these groups.

In a separate ANOVA, we defined 3 levels of exposure (0 < ADV ≤ 0.4, 0.4 < ADV < 1; ADV ≥ 1). Within each exposure level, we categorized drinkers as binge or nonbinge drinkers. We used a 2-way ANOVA with grouping factors (binge status, level of exposure) to test for significant differences among the groups.

RESULTS

The distribution of PAE at each trimester of pregnancy is shown in Fig. 1. In the first trimester, 64% of the women drank and the median use among drinkers was 0.4 drinks per day with a range from 0.006 to 20 drinks per day; 18.3% of all women drank 1 drink per day or more. Alcohol use decreased substantially across pregnancy. The number of abstainers increased from 36 to 63% by the end of the second trimester and those who continued drinking drank less per occasion. By third trimester, 32% of the women drank, 3.6% drank 1 or more drinks per day, and the median ADV among the drinkers was 0.08 drinks per day. Defining binge drinking as consumption of 4 or more drinks/occasion, 34% of the women binged during first trimester of pregnancy and 5% binged during second and third trimesters.

Women who used alcohol heavily, an average of 1 or more drinks per day (ADV ≥ 1) during the first trimester, were significantly more likely to use marijuana and tobacco and to report a higher rate of hostility. There were no significant differences by level of alcohol use in income, education,
maternal age, maternal work, marital status, or maternal depression during pregnancy (Table 1).

At 22 years, there was a significant association between education and PAE (Table 1), but offspring were no more likely to be male, married, to have children, or to live with their parents based on PAE. There were also no significant differences in work or income status.

The results of the regression analyses are presented in Table 2. ADV was log-transformed to reduce skewness and the regression coefficients presented in Table 2 are based on this transformation. There was a significant relation between PAE and offspring behavior problems at 22 years after controlling for race, gender, maternal depression, and hostility during pregnancy, prenatal marijuana exposure, prenatal tobacco exposure, and the young adult’s substance use. First and third trimester alcohol exposures were significantly associated with all behavior problem scales: Total, Externalizing, Internalizing, Attention, and Critical Items scores. Second trimester PAE significantly predicted Internalizing behaviors, Attention problems, the Critical Items scale, and Total Score. All of these findings were significant when the current substance use of the offspring was included in the model.

In Table 3, we present a calculation of the effect size on behavior problems associated with a change in ADV from 0 to 1 drink per day. The Total Score was increased 1.3 ($t = 2.2$, $p < 0.05$), 2.9 ($t = 2.2$, $p < 0.05$), and 4.0 ($t = 3.6$, $p < 0.001$) points by a change from 0 to 1 drink per day in the first, second, and third trimesters, respectively. Other predictors of the ASR Total Score included young adult’s current substance use, age, race, and maternal depression during pregnancy. The change in variance explained ($r^2$) by the addition of PAE to the model was 1, 1, and 2% for the first, second, and third trimester exposures, respectively. These $r^2$s are small, but they are relatively comparable to other predictors in the model. The amount of change from 0 to 1 was smaller for the Attention and Critical Items scales ranging from 0.8 to 1.0 and from 0.6 to 1.3 for the first and third trimesters, respectively. In both cases, the effect size was slightly greater for the second trimester.

A change from 0 to 1 drink per day during first, second, and third trimesters predicted increases of 1.1 ($t = 1.7$, $p < 0.05$), 3.9 ($t = 2.6$, $p < 0.01$), and 5.1 ($t = 3.6$, $p < 0.001$) points on the ASR Internalizing scale, respectively. A change from 0 to 1 drink per day was associated with an increase of 1.3 ($t = 2$, $p < 0.05$) and 2.9 points ($t = 2.4$, $p < 0.01$) on the Externalizing scale for the first and third trimesters, respectively.

The effects of duration were assessed by comparing 3 groups: offspring of abstainers, offspring of women who had an ADV $\geq 1$ only in the first trimester and those who had an ADV $\geq 1$ for both the first and third trimesters (Table 4). Those offspring who were exposed at both the first and third trimesters differed significantly from the offspring of abstainers on all but the Attention scale. The offspring who were only exposed to ADV $\geq 1$ in the first trimester were intermediate between the abstainers and those more heavily exposed and did not differ significantly from the nonexposed group.

The regression analyses were repeated using binge drinking as a dichotomous variable. ADV was not included in these regressions. Binge drinking during the third trimester

### Table 1. Subject Characteristics by Level of First Trimester Alcohol Use

<table>
<thead>
<tr>
<th>Variable</th>
<th>ADV = 0</th>
<th>0 &lt; ADV &lt; 1</th>
<th>ADV $\geq$ 1</th>
<th>Overall significance$^a$</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal first trimester features</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>40.2</td>
<td>41.5</td>
<td>41.3</td>
<td>Ns$^b$</td>
<td>1 and 3, 2 and 3</td>
</tr>
<tr>
<td>Hostility</td>
<td>17.7</td>
<td>19.1</td>
<td>19.8</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>23.3</td>
<td>23.0</td>
<td>22.7</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>11.8</td>
<td>11.9</td>
<td>11.8</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Work (%)</td>
<td>21</td>
<td>29</td>
<td>25</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Married (%)</td>
<td>37</td>
<td>31</td>
<td>24</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td>447</td>
<td>427</td>
<td>419</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Marijuana use (ADJ)</td>
<td>0.29</td>
<td>0.36</td>
<td>0.59</td>
<td>.02</td>
<td>1 and 3</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>6.6</td>
<td>8.3</td>
<td>11.2</td>
<td>.002</td>
<td>1 and 3</td>
</tr>
<tr>
<td>Race (% white)</td>
<td>46</td>
<td>48</td>
<td>54</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Young adult characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>52</td>
<td>43</td>
<td>50</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Married (%)</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td>12.7</td>
<td>13.0</td>
<td>12.3</td>
<td>0.0002</td>
<td>1 and 2, 2 and 3</td>
</tr>
<tr>
<td>Work (%)</td>
<td>58</td>
<td>61</td>
<td>63</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Children (%)</td>
<td>36</td>
<td>36</td>
<td>44</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Personal income</td>
<td>993</td>
<td>979</td>
<td>993</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Live with partner (%)</td>
<td>28</td>
<td>27</td>
<td>32</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Alcohol use (mean ADV)</td>
<td>1.7</td>
<td>1.8</td>
<td>2.2</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Marijuana use (mean ADJ)</td>
<td>0.9</td>
<td>1.0</td>
<td>1.1</td>
<td>Ns</td>
<td></td>
</tr>
<tr>
<td>Tobacco use (cigarettes per day)</td>
<td>4.5</td>
<td>3.9</td>
<td>4.9</td>
<td>Ns</td>
<td></td>
</tr>
</tbody>
</table>

ADJ, average daily joints; ADV, average daily volume.

$^a$Overall significance using an $F$-test for the continuous variables and chi-squared for dichotomous variables.

$^b$Not significant.
of pregnancy was a significant predictor of the Total (coefficient = 4.0, \( t = 2.1, p < 0.05, r^2 = 0.006 \)) and the Internalizing scales (coefficient = 6.0, \( t = 2.9, p < 0.01, r^2 = 0.01 \)). Binge drinking was not a significant predictor of scores on the Externalizing (coefficient = 2.3, \( t = 1.3, p = 0.1 \)), Attention problems (coefficient = 1.0, \( t = 1.1, p = 0.2 \)), or Critical Items scales (coefficient = 1.0, \( t = 1.3, p = 0.1 \)). The variance in the outcome (adjusted \( r^2 \)) was used to compare whether ADV or binge drinking was the better predictor of behavior problems. In this cohort, ADV explained more variation in behavior problems than did binge drinking.

We explored the relation with binge drinking in more detail because there have been reports of greater effects of binge drinking (e.g., Maier and West, 2001). We classified women into 3 levels of exposure: light (ADV < 0.4), moderate (ADV 0.4 to <1), and heavy (ADV ≥ 1) and within each of these categories we looked at the rate of behavior problems comparing those who reported binging to those who did not binge (Table 5). A 2-way ANOVA with ADV and binging as the grouping factors was used. ADV was a significant grouping factor while the binge grouping factor was not.

### DISCUSSION

In these analyses, we explored the associations between PAE and behavior problems. At 22 years of age, there were significant effects of PAE at each trimester on behavior. First and third trimester predicted the Total, Externalizing, Internalizing, Attention, and Critical Items scales of the ASR. Second trimester PAE predicted all of the outcomes but the Externalizing scale. These associations were significant after controlling for the significant covariates. These findings of behavioral effects at age 22 were significant even when current substance use was included in the model. Thus, the effect of PAE on behavior problems is independent of the effects of PAE on offspring substance use.

Prior studies have identified an association between PAE and internalizing and externalizing behaviors in childhood and adolescence (Mattson and Riley, 2000; Olson et al., 1997). This study demonstrates that the effects extend into adulthood and into lower levels of exposure. Further, the effects are wide-ranging, covering multiple domains of behavior and resulting from exposures at each of the 3 trimesters.

Two recent studies, Kelly and colleagues (2012) and Robinson and colleagues (2010), reported no association between PAE and behavior. In the U.K. study (Kelly et al., 2012), drinking was ascertained retrospectively at the ninth postnatal month and was measured as the usual amount across pregnancy. This is problematic because of the retrospective nature of the questioning. The use of usual amount under-
estimates amount and does not provide a measure of variability in intake, leading to misclassification. Further, assessing PAE without a specifier for time during pregnancy does not measure PAE accurately. The Robinson and colleagues (2010) study focused only on early pregnancy, using data from their 18 week assessment to examine the association between alcohol exposure and behavior.

The results of the Lifestyle During Pregnancy Study also had methodological problems. The cohort represented 60% of all women invited (Kesmodel et al., 2010) and 51% of mother–child pairs at age 5 (Falgreen Eriksen et al., 2012). Similar to the above-mentioned studies, the researchers measured usual use, “How many drinks on average per week?” (Kesmodel and Olsen, 2001). In addition, the assessment had a median of 17 weeks with a range of 7 to 39 weeks of gestation (Underbjerg et al., 2012).

Additionally, we looked at the effects of pattern of use across pregnancy. These results demonstrate that continued exposure predicts the greatest number of behavior problems. The significant differences were between those with no exposure compared to those offspring with exposure throughout pregnancy. However, alcohol use was highly correlated across the trimesters, and it is possible that some of the effects of duration reflected earlier and higher level of use.

We also looked at the effects of binge drinking. In these analyses, although we found significant effects for binge drinking when binge was used as the predictor in the regression analyses, when we looked within categories of exposure, we did not find that binge drinking was a significant factor at lower levels of alcohol exposure. This latter finding is counter to studies that have reported that binge drinking has a greater effect than nonbinge drinking (e.g., Carmichael-Olson et al., 1992; Maier and West, 2001). The average ADV of binge drinkers is usually higher, which may explain why binge drinking is a significant predictor when level of exposure is not controlled. However, when the level of exposure was held constant, at the lower levels of exposure, the effects of binge and nonbinge exposure on the Total Score of the ASR were similar. The results reported here need to be replicated in other studies that use the same analyses.

### Table 4. Effects of Duration of Exposure on the Scales of the Adult Self-Report

<table>
<thead>
<tr>
<th>Group 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Group 3&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Significance group differences at p = 0.05&lt;sup&gt;e&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ADV</td>
<td>N = 171</td>
<td>N = 54</td>
<td>N = 12</td>
</tr>
<tr>
<td>Total Score</td>
<td>51.0</td>
<td>52.1</td>
<td>60.3</td>
</tr>
<tr>
<td>Externalizing</td>
<td>54.2</td>
<td>55.5</td>
<td>62.7</td>
</tr>
<tr>
<td>Internalizing</td>
<td>51.3</td>
<td>50.3</td>
<td>61.7</td>
</tr>
<tr>
<td>Attention</td>
<td>6.9</td>
<td>7.9</td>
<td>9.1</td>
</tr>
<tr>
<td>Critical Items</td>
<td>5.1</td>
<td>5.9</td>
<td>9.3</td>
</tr>
</tbody>
</table>

ADV, average daily volume.
<sup>a</sup>Group 1: no exposure.
<sup>b</sup>Group 2: exposure to 1 or more drinks per day during the first trimester and no exposure during the third trimester.
<sup>c</sup>Group 3: exposure to 1 or more drinks per day during the first and third trimesters.
<sup>d</sup>Overall ANOVA significance using F-test.
<sup>e</sup>Tukey’s multiple comparison test comparing the largest pairwise differences.

### Table 5. Mean Behavior Scores Within First Trimester Alcohol Exposure Groups by Binging

<table>
<thead>
<tr>
<th>Light use</th>
<th>Moderate use</th>
<th>Heavy use</th>
<th>Two-way ANOVA (grouping factors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 &lt; ADV ≤ 0.4</td>
<td>0.4 &lt; ADV &lt; 1</td>
<td>ADV ≥ 1</td>
<td>Significance (p)</td>
</tr>
<tr>
<td>No binge</td>
<td>Binge</td>
<td>No binge</td>
<td>Binge</td>
</tr>
<tr>
<td>N&lt;sup&gt;a&lt;/sup&gt;</td>
<td>133</td>
<td>52</td>
<td>34</td>
</tr>
<tr>
<td>Mean ADV</td>
<td>0.11</td>
<td>0.19</td>
<td>0.62</td>
</tr>
<tr>
<td>ASR scales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score</td>
<td>48.8</td>
<td>50.5</td>
<td>53.6</td>
</tr>
<tr>
<td>Externalizing</td>
<td>51.7</td>
<td>53.2</td>
<td>57.6</td>
</tr>
<tr>
<td>Internalizing</td>
<td>49.2</td>
<td>50.8</td>
<td>53.8</td>
</tr>
<tr>
<td>Attention</td>
<td>6.2</td>
<td>6.9</td>
<td>7.4</td>
</tr>
<tr>
<td>Critical Items</td>
<td>4.4</td>
<td>4.2</td>
<td>6.4</td>
</tr>
</tbody>
</table>

ADV, average daily volume; ASR, adult self-report.
<sup>a</sup>Information about binge drinking was missing for 7 cases.
<sup>b</sup>Not significant.

ADV, average daily volume; ASR, adult self-report.
<sup>a</sup>Information about binge drinking was missing for 7 cases.
<sup>b</sup>Not significant.
The shape of the relationship between PAE and the outcome determines the public health response. In a linear association, there is no safe limit, while with a threshold there is an area of exposure that is assumed safe and a threshold past which there is an effect. Although we cannot rule out the possibility of a threshold for all associations, there is a clear dose-response pattern in the results, particularly at the third trimester of pregnancy.

This study had some limitations. First, our cohort was relatively homogeneous with respect to socioeconomic status and these findings may not generalize to exposed offspring of higher social status. Further, our reports of alcohol and other substances during pregnancy were self-reports rather than laboratory-based tests. Laboratory tests, however, only cover a small window of exposure, whereas self-reports allow a broader time frame. To offset the potential loss of precision, we developed and tested questions that were easy for the women to answer, we used a bogus pipeline to test honesty, and we selected interviewers who were comfortable asking about substance use.

These limitations are largely offset by the strengths of the study. To date, no study has evaluated the long-term effects of PAE on behavior in young adulthood using a population that represents the entire spectrum of exposure. The sample is large, has equal proportions of African Americans and Caucasians, and was not recruited from a substance abuse treatment center or from a specialized facility for PAE or prenatal care. Our follow-up rates have been very high, which gives the study a high rate of internal validity, and subject loss was independent of PAE.

In summary, there are significant long-term effects of PAE on the behavior of the exposed offspring. We have documented that these effects continue into young adulthood. The effects are dose-response and increase with duration of use, confirming that there is no safe level of drinking during pregnancy.

ACKNOWLEDGMENTS

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REFERENCES


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