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Trajectories of prenatal alcohol exposure and behavioral outcomes: findings from a community-based sample

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Abstract

Objective.—To characterize patterns of prenatal alcohol exposure (PAE), and determine whether PAE trajectories were associated with behavior from a community-based sample of first-grade children.

Methods.—Using data collected as part of the Collaboration of Fetal Alcohol Spectrum Disorders Prevalence study (n=1,663), we performed longitudinal cluster analysis on prenatal alcohol use reported for four time points around conception and pregnancy. From the sample, 638 respondents reported any alcohol use in pregnancy and were included in trajectories for average daily and maximum drinks per drinking day (max DDD). We then estimated the association with behavioral problems measured by the Child Behavior Checklist (CBCL) and Teacher Report Form (TRF) with multivariable linear regression. The reference group had 1,025 children with no reported PAE.

Results.—Five trajectories were selected to describe max DDD patterns: very low/discontinuing (n=186), low/discontinuing (n=111), very low/continuing (n=47), med/high (n=245), and high (n=49). Six trajectories best described average daily alcohol use: very low/discontinuing (n=378), very low/continuing (n=98), low/continuing (n=56), low/discontinuing (n=37), medium/high (n=35), and high (n=31). When assessing max DDD trajectories for both the CBCL and TRF, individuals with PAE in the two highest trajectories and the very low/continuing trajectory had more behavioral problems relative to children with no PAE, although confidence intervals for most estimates included the null. PAE modeled as average drinks per day did not predict behavior in any consistent pattern.

Conclusions.—In this community-based sample, select PAE trajectories were associated with behavior, even at relatively low levels of PAE that continued later in gestation.

Keywords

prenatal alcohol exposure; trajectory models; behavioral outcomes

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1. Introduction

Neurodevelopmental deficits have been consistently associated with prenatal exposure to heavy or binge alcohol (Bay and Kesmodel, 2011; Conover and Jones, 2012; Flak et al., 2014; May et al., 2013). Findings regarding low to moderate levels of prenatal alcohol exposure (PAE) have been less consistent, with some systematic reviews and meta-analyses reporting no deficits in functional domains (Bay and Kesmodel, 2011; Flak et al., 2014; Henderson et al., 2007; Kesmodel et al., 2012), while other studies have suggested effects even at lower levels of consumption (Flak et al., 2014; Sood et al., 2001; Willford et al., 2004). This heterogeneity in findings contributes to inconsistency in advice offered to women regarding prenatal alcohol consumption (Anderson et al., 2014; Niclasen, 2015).

Some of the discrepancies in previous findings are likely due to methodologic issues arising from traditional methods of exposure classification (Bandoli et al., 2019; Niclasen, 2015). Previous studies have typically classified PAE using dichotomous categories or as a cumulative count of drinking days across gestation (Bay and Kesmodel, 2011; Henderson et al., 2007; Kesmodel et al., 2012; Skogerbø et al., 2012). However, PAE patterns are highly variable within pregnancy and between individuals. Given that dose, frequency and gestational timing of PAE all contribute to the etiology of PAE-related outcomes, failure to incorporate each and their combined variation over time (May et al., 2013; Niclasen, 2015) will lead to misclassification and potential attenuation of risk estimates, resulting in poor prediction of risk. Weak effect estimates associated with low levels of PAE may be particularly vulnerable to this attenuation.

Two recent studies (Bandoli et al., 2019; Dukes et al., 2017) have used longitudinal cluster analysis methods to summarize complex individual level alcohol use trajectories across pregnancy and estimate offspring outcomes. Such methods classify individuals with similar patterns of alcohol dose and frequency over a specified period into distinct groups. These studies were performed on high-risk samples from Ukraine (Bandoli et al., 2019) and South Africa/Northern Plains, US (Safe Passage Study; Dukes et al., 2017) specifically recruited for their level of alcohol consumption around the time of conception or early pregnancy. Both studies found nuance in risk estimates when assessed by pattern of PAE, particularly with respect to the timing of reduction or cessation of alcohol. However, it is unclear what the patterns of PAE look like in a community-based sample, and whether those patterns are also associated with behavioral outcomes. We hypothesized that, similar to the high-risk samples, patterns of PAE in a community-based study would also differentiate risk of behavioral outcomes in children.

The objective of this study was to characterize prenatal alcohol consumption self-reported in the Collaboration on Fetal Alcohol Spectrum Disorders Prevalence (CoFASP) study. Given the uncertainly around whether the modeled consumption (max drinks per drinking day vs. average drinks per day) differentially predicts outcomes of interest, we modeled both. We then determined whether trajectories of PAE were associated with behavioral outcomes.

2. Methods

2.1 Study population

In 2010, National Institutes on Alcohol Abuse and Alcoholism (NIAAA) initiated the CoFASP study (May et al., 2018). The consortium used an active case-ascertainment approach with data collection in four communities between 2010 and 2016 to estimate the prevalence of fetal alcohol spectrum disorders (FASD). Assessments were targeted based on four domains assessed in the diagnosis of FASD: dysmorphology (via a 60-item dysmorphology examination), a neurodevelopment battery (conducted by school psychologists or study psychometrists), growth (current percentile for height, weight and head circumference) and PAE. PAE during the time around conception and at three timepoints during pregnancy was assessed through maternal or collateral questionnaires and administered by trained interviewers. In total, 35 collateral reporters (2% of full sample) were able to provide sufficient information on maternal alcohol use. The corresponding children were included in the sample to be consistent with clinical diagnoses where collateral reports of prenatal alcohol exposure are accepted in evaluating sufficient alcohol exposure. More details on study design and enrollment are available in the original study publication (May et al., 2018).

This study was approved by the University of California San Diego Human Research Protections Program.

2.2 Prenatal alcohol exposure

The mother or collateral source responded to questions about alcohol consumed before and during pregnancy, as well as usual drinking patterns. The questions were designed to enhance recall and elicit accurate reporting of alcohol and other drugs consumed from a variety of sources and beverage types (Jacobson et al., 1991; King, 1994). Usual drinking patterns and drinking before pregnancy recognition were used to more accurately calibrate quantity and frequency of drinking during the index pregnancy (Czarnecki et al., 1990; May et al., 2013, 2000).

Prenatal alcohol consumption was queried for: the period before recognition of pregnancy, after recognition of pregnancy, the second trimester and the third trimester. A drink was defined as ‘a 12-ounce glass of beer or wine cooler, a 5-ounce glass of wine, or a drink containing 1 shot (1 ½ ounce) of liquor). The respondent was first asked, on average, how much alcohol they consumed in each period. They were then asked if they ever drank more than that, and if so, what was the largest number of drinks in a 24-hour period during that time period. For each response, they were also asked the frequency of that consumption. Women were also asked the gestational week that they became aware of their pregnancy.

2.2.1 Maximum drinks per drinking day—When asked about average alcohol consumption and if they ever consume more, the greater of the two responses was assigned as the maximum drinks per drinking day for that period.

2.2.2 Average number of drinks per day—For the average drinks per day, the average drinks per occasion were multiplied by the frequency of the drinking days, and

then converted into an average daily amount. If the respondent endorsed days of drinking more than the average amount, the largest number of drinks during that period and the frequency of that consumption were converted to daily consumption and added to the initial daily consumption estimate.

From this information calculated in each period, a weekly pregnancy diary was created for both maximum drinks per drinking day and average drinks per day by the following:

1. Conception through pregnancy recognition: 'before recognition' drinking estimates were carried forward until pregnancy recognition. If frequency was reported as 1–2 times/3 months) or less and pregnancy recognition was less than 12 weeks, then 'before recognition' exposure was assigned as 0.
2. Post pregnancy recognition through week 13: 'after recognition' drinking estimates were assigned, with the caveat that if pregnancy recognition occurred after the end of the 1st trimester, then the 'before recognition' quantity was carried forward until the week of pregnancy recognition, when second trimester estimates were then assigned.
3. Weeks 14–26: 'second trimester' drinking estimates were assigned, with the caveat that if recognition occurred after the beginning of week 14, then 'before recognition' estimates were carried forward until the week of recognition, when 'second trimester' estimates were then assigned.
4. Weeks 27-delivery: 'third trimester' drinking estimates were assigned, with the caveat- that if recognition occurred after the beginning of week 27, then 'before recognition' estimates were carried forward until the week of recognition, when 'third trimester' estimates were then assigned.

For each individual, self-report of pregnancy recognition was used unless the variable was missing (n=33 with enough information to construct trajectories). For those cases, the median gestational week of pregnancy recognition for the sample (6 weeks) was imputed.

2.3 Outcome measures

Behavior was measured with the Child Behavior Check List (CBCL) (Achenbach and Rescorla, 2001). The CBCL has eight syndrome scales which group into two sub-scales for internalizing and externalizing behaviors. For this analysis, we assessed the total score, externalizing score and internalizing score. In addition, teachers of children in the study were asked to complete the Teacher Report Form (Achenbach and Rescorla, 2001), from which we assessed the same domains.

2.4 Covariates

Covariates for the analysis were selected from the maternal and collateral surveys, and included maternal education (current), maternal employment (during pregnancy), marital status (during pregnancy), pregnancy smoking, pregnancy drug use (marijuana, heroin/opiates, crack cocaine, methamphetamine, hallucinogens, non-medical inhaled substances, other drugs), gestational age at delivery for the index child (preterm (<37 weeks) vs. term), race of the index child, maternal age at delivery, maternal body mass index (current),

parity (current), and the gestational week of pregnancy recognition for the index child. We also assessed 'sufficient PAE' for FASD diagnosis, defined in the CoFASP study as ≥6 drinks/week for ≥2 weeks in pregnancy or ≥3 drinks/occasion on ≥2 occasions in pregnancy or documentation of alcohol related social or legal problems prior or during pregnancy (May et al., 2018). Finally, the CoFASP study evaluated the data for all participants in case conferences, and fetal alcohol spectrum disorder status was assigned. The CoFASP designated assignments were categorized into no FASD diagnosis, (partial) fetal alcohol syndrome (FAS/pFAS), alcohol related neurodevelopmental disorder (ARND), and undetermined.

2.5 Statistical analysis

2.5.1 Exposure trajectory modeling—In order to model PAE trajectories, we performed K-means longitudinal (kml), an unsupervised, group-based trajectory modeling technique (R package *KML* (Genolini and Falissard, 2016)). K-means does not require any normality or parametric assumptions within clusters, is robust to numerical convergence, and requires no assumptions about the shape of the trajectory (Genolini and Falissard, 2011).

2.5.1.1 Maximum drinks per drinking day: Due to the heterogeneity in distribution and compression of lower values, the sample was stratified at a maximum value of drinks per drinking day in the 'before recognition' period of 2. Kml was then performed twice, first on the 'lower consumption' strata and then again on the 'higher consumption' strata (10>x>2). Seven individuals had maximum drinks per drinking day greater than 10, which were removed from the high consumption strata due to disproportionate influence on trajectory assignment and were manually assigned into the highest trajectory.

2.5.1.2 Average drinks per day: Due to the heterogeneity in distribution and compression of lower values, the sample was stratified at a maximum value of average drinks per day in the 'before recognition' period of 2. Kml was then performed twice, first on the 'lower consumption' strata and then again on the 'higher consumption' strata. One outlier (>20 drinks per day before recognition) was removed from the high consumption strata due to disproportionate influence on trajectory assignment and was manually assigned into the highest trajectory.

In all analyses, we allowed k-means to run for 2 to 6 clusters 1000 times each. Selection of the number of clusters was based upon sample size in each cluster with an effort to retain 5% of the trajectory sample within each trajectory.

2.5.2 Analytic models—We first described the population stratified by maximum drinks per drinking day PAE trajectory. We then performed linear regression analysis, with individual models for each of the three scales on the two behavioral assessments (CBCL and TRF). Multivariable models were adjusted for maternal age, smoking or other substance use during pregnancy. Models were constructed for trajectories from maximum drinks per drinking day, as well as average drinks per day. No PAE served as the reference category in all models. All analyses were performed in SAS 9.4, with the exception of k-means longitudinal analysis, which was performed in R 4.1.0.

3. Results

The mother/caregiver/collateral source of 1,704 individuals provided sufficient alcohol exposure information (known quantity of alcohol at the four time points) to be included in the study (Supplemental Figure 1). From the sample, 41 children were diagnosed with FAS with no maternal endorsement of alcohol use during pregnancy. These subjects were removed from the sample due to demonstrably unreliable exposure information. This resulted in 638 participants (37%) with documented alcohol exposure during pregnancy whose exposure information was included in maximum drinks trajectory analysis. Two individuals reported the number of drinks prior to pregnancy recognition, but not the frequency, and thus were not included in the average drinks per day trajectories (n=636). Individuals with no reported alcohol exposure (n=1,025) were assigned to the 'no alcohol' trajectory.

3.1 PAE trajectories

3.1.1 Maximum drinks per drinking day—Maximum drinks per drinking day was best described by five trajectories (Figure 1): max A: very low/discontinuing (n=186; mean drinks per drinking day trimesters 1–3: 1.2/0.0/0.2), max B: low/discontinuing (n=111; mean drinks per drinking day trimesters 1–3: 2.1/0.1/0.0), max C: very low/continuing (n=47; mean drinks per drinking day trimesters 1–3: 1.2/1.2/0.5), max D: med/high (n=245; mean drinks per drinking day trimesters 1–3: 4.6/0.3/0.2), and max E: high (n=49; mean drinks per drinking day trimesters 1–3: 10.8/1.4/0.6).

3.1.2 Average drinks per day—Six trajectories best described average daily alcohol use (Supplemental Figure 2): avg F: very low/discontinuing (n=378; mean drinks per day trimesters 1–3: 0.1/0.01/0.01), avg G: very low/continuing (n=98; mean drinks per day trimesters 1–3: 0.5/0.03/0.01), avg H: low/continuing (n=56; mean drinks per day trimesters 1–3: 1.4/0.03/0.01), avg I: low/discontinuing (n=37; mean drinks per day trimesters 1–3: 0.6/0.04/0.02), avg J: medium/high (n=35; mean drinks per day trimesters 1–3: 2.2/0.1/0.04), and avg K: high (n=31: mean drinks per day trimesters 1–3: 7.1/1.4/0.6).

In general, most alcohol consumption during pregnancy was sporadic or of low frequency (data not shown). Approximately 8% of women who consumed alcohol before pregnancy recognition reported 5–6 days/week or more; 9% reported use 3–4 days/week; 33% reported use 1–2 times/week; and 42% reported use as 1–3 times/month. The remaining 8% were using alcohol 1–2 times or less/3 months. Approximately 33% of women who used any alcohol during gestation abstained from alcohol upon pregnancy recognition, which increased to 95% after the first trimester.

When comparing the two trajectory models, there was relatively high concordance between the lowest and highest trajectory assignments for the maximum drinks and average drinks per day (Supplemental Table 1). There was less concordance between trajectory assignments in the middle trajectories. Additionally, while the assigned trajectories for max drinks per drinking day were fairly concordant with assigned trajectories for average drinks per day, the same was not true of the reciprocal association, particularly in the lower trajectories for average drinks per day. This is likely because of the relatively low frequency of alcohol

consumption, causing some individuals in high max drinks per drinking day to drop into low average drinks per day trajectories once frequency was incorporated into the measure.

3.2 Population characteristics by maximum drinks per drinking day trajectories

Women in the highest two alcohol use categories (max D: medium-high and max E: high) were more likely to be single, divorced or widowed during pregnancy, to smoke and use other substances during pregnancy (Table 1). There were more likely to have delivered the index child prematurely, to have offspring who identified as Black or Native American, have younger age and higher BMI, and become aware of the pregnancy later in gestation compared to women who reported the lowest amounts of alcohol (max A,B: very low/low discontinuing). Women who drank very low amounts but continued drinking longer in pregnancy (max C: very low/continuing) had profiles more similar to women with higher alcohol consumption (smoking, other substance use, offspring who identified as a minority, later pregnancy recognition) compared to women with the same initial consumption but earlier pregnancy cessation (max A,B). However, the continuing trajectory also had the highest proportion of women with more than a high school education, were most likely to have worked full time during pregnancy, were no more likely to deliver the index child prematurely, and had the highest mean age at birth.

3.3 Maximum drinks per drinking day and FASD diagnosis

As expected, the proportion of children diagnosed with FASD increased with increasing alcohol exposure trajectory (Supplemental Figure 2).

3.4 Behavioral outcomes

3.4.1 Maximum drinks per drinking day—

For all outcomes, Figures 2–3 display the beta estimates and 95% confidence intervals from adjusted models while unadjusted and adjusted estimates are noted in Supplemental Table 2.

In general, higher PAE trajectories were associated with worse performance on the CBCL, although confidence intervals were wide and often included the null (Figure 2, Supplemental Table 2). Notably, the very low/continuing trajectory (max C) was associated with the highest endorsement of behavioral problems on the CBCL, while the low/discontinuing trajectory (max B) had the lowest endorsement of behavioral problems compared to no PAE. There was little difference on internalizing and externalizing scales, with the exception of the highest PAE trajectory (max E), which was only elevated on the externalizing scale.

Approximately 90% of teachers in the sample completed the TRF. The highest trajectories were again associated with higher total scores, although again, confidence intervals often included the null (Figure 3, Supplemental Table 2). On this assessment, there was little difference on internalizing vs. externalizing scales, although percentiles were slightly higher on the externalizing scale. Interestingly, when assessed by teachers, the reduction in scores for the low/discontinuing PAE trajectory (max B) observed on the CBCL was not replicated. Instead, this group performed the same as the no PAE trajectory. Finally, similarly to the CBCL, the very low/continuing PAE trajectory (max C) had estimates more similar to the highest trajectories than to the lowest (max A,B: very low or low/discontinuing) trajectories.

3.4.2 Average drinks per day—

In general, average drinks per day trajectories were poor predictors of performance on the CBCL or the TRF (Supplemental Table 3). Once again, a trajectory in the low range (avg G: very low/continuing) performed better than all other groups on the CBCL, including the no alcohol group. However, like the maximum drinks per drinking day trajectories, these findings attenuated on the teacher-rated scale. There were no other notable patterns in the findings, and confidence intervals were very wide for all estimates.

4. Discussion

Here, we described two types of PAE trajectories in a community-based sample and estimated the association with behavior in first-grade. When modeled as maximum drinks/drinking day, higher PAE trajectories were generally associated with more behavioral disturbance on both caregiver and teacher-rated behavioral problem scales. However, the estimates were imprecise and often contained the null. We observed low levels of PAE with discontinuation (max B) had lower behavioral problem scores on the CBCL than the very low PAE trajectory (max A) or the no PAE reference. This observation has been made before (Flak et al., 2014), although interestingly this effect was not seen on the teacher rated version. In addition, the trajectory with longer continuation of PAE (max C: very low/cont) had risk estimates as strong or stronger than the higher trajectories, despite having initial consumption levels similar to the lowest PAE trajectories. This pattern is similar to our findings from a cohort in Ukraine (Bandoli et al., 2019), where low, continued PAE conferred greater risk of adverse neurodevelopmental outcomes than higher initial PAE with earlier discontinuation. Finally, when PAE was summarized by average drinks per day, trajectories were not associated with behavioral problems in first-grade children.

Few studies incorporate timing, dose and duration of PAE into exposure measures, and this study expands the use of PAE trajectories in a few ways. First, unlike the previous two studies of PAE trajectories (Bandoli et al., 2019; Elliott et al., 2020), we assessed behavioral outcomes in first-grade children as opposed to infant outcomes. This is relevant, as it is unclear the extent to which behavioral problems identified early in life endure, particularly that which does not rise to the level of FASD.

In addition, the previous trajectory studies were done in high-risk populations, offering a stark contrast between PAE trajectories and those unexposed to PAE. In our study from Ukraine, the exposure categories (modeled as average drinks per day) ranged from 1 drink per day in lower trajectories to approximately 5 drinks per day in higher trajectories, with consumption continuing at higher levels longer into the gestations (Bandoli et al., 2019). In the Safe Passage study (modeled as maximum drinks per drinking day), the trajectories ranged from <1 drink per drinking day in the low consumption groups to 6–8 drinks per drinking day, again with continuation at higher levels longer into the gestations (Dukes et al., 2017). In our models of average drinks per day, 94% of the sample (avg F-K) ranged from <1 to 1.5 mean drinks per day in the first trimester. Further, by the second trimester, only the highest trajectory had a meaningful difference on alcohol consumption. This likely resulted in attenuated and imprecise confidence intervals for behavioral outcomes in the average drinks per day models. When modeled as maximum drinks per drinking day, there was

more contrast between PAE exposure in each trajectory, and that contrast extended further in gestation. There, we were able to see patterns of risk emerge in the higher or continuing trajectories, even at this relatively low level of PAE compared to previous high-risk samples. Notably, these patterns were also observed on teacher-rated scales, indicating the results are not solely a function of the characteristics of individuals reporting PAE and the CBCL. Estimates of the effects of low to moderate levels of PAE are often inconsistent, and the more precision we are able to offer about the patterns of PAE that increase risk of adverse outcomes, particularly at lower levels of consumption, the better informed women and clinicians will be.

Finally, our study is novel in the comparison of maximum drinks per drinking day and average drinks per day trajectories. When drinking during gestation occurs at high frequency, there may be little difference in effect estimates between the models. However, when exposure is sporadic, there can be differences in effect estimates between the models, as we observed when comparing trajectory group membership and results. Therefore, researchers may want to consider modeling both when assessing the impact of PAE on offspring outcomes, particularly when estimating outcomes in relatively low-risk populations where alcohol consumption, particularly at high levels, occurs with low frequency.

It is important to view this work in light of the limitations. First, we relied on PAE recalled from mothers or collateral sources 6–7 years after pregnancy. As there are no validated biomarkers that reflect prenatal exposure 6–7 years after birth, maternal recall is the predominant method in the FASD research field. Critically, recalled alcohol exposure is strongly predictive of pregnancy, dysmorphic and neurodevelopment outcomes (Jacobson et al., 2002; May et al., 2013, 2008). However, there is stigma associated with alcohol use in pregnancy, and we did observe a few cases of FAS in the group that endorsed no alcohol use in pregnancy. Although those individuals were removed from analyses, misclassification likely remained. However, we do not believe misclassification would be differential by child behavior, and would expect bias to be towards the null. In addition, the contrast group in this study was not representative of the general population. The original study was designed to efficiently estimate the prevalence of FASD, and thus a portion of the sample was enrolled based FASD diagnostic criteria, including small body size and physical features. These factors are correlated with behavior independent of prenatal alcohol exposure, and likely attenuated our estimates of the association between PAE and behavior. Additionally, although PAE is a necessary cause of FASD, there are other factors, including molecular pathways, genetics, epigenetics, maternal body size, maternal nutrition, and the postnatal environment that all contribute to adverse outcomes. By isolating PAE, we omit these important factors (Ehrhart et al., 2019), which are also prevention and intervention targets. In addition, although we identified numerous factors associated with the different drinking patterns, efforts to understand why individuals consume alcohol, particularly during pregnancy, would directly inform intervention efforts.

By modeling these trajectories, we aim to elucidate patterns of PAE that inform our understanding of FASD. This is our second study (Bandoli et al., 2019) that has reported that low, continuing PAE confers as high, if not higher risk for adverse neurodevelopmental

outcomes than higher PAE with earlier discontinuation. This finding reinforces the message that no matter the initial amount of consumption, cessation increases the likelihood for improved offspring outcomes. Further, women with higher or sustained levels of consumption were more likely to use other substances, which may increase the risk for FASD (Popova et al., 2020), and should also be considered when evaluating intervention targets.

5. Conclusions

In summary, we found that higher trajectories or longer continuation of maximum drinks per drinking day was associated with behavioral problems, although confidence intervals often overlapped the null. When modeled as average drinks per day, there were no notable associations with PAE trajectory. These findings support previous findings of high PAE and behavioral deficits and reinforce the important message that no matter the initial level of consumption, cessation should be encouraged to optimize outcomes. Further, methodologies incorporating timing, frequency and dose of PAE into exposure trajectories can bring insight, even in a community-based sample with relatively low levels of PAE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

ARND	Alcohol related neurodevelopmental disorder
CBCL	Child Behavior Check List
FASD	Fetal alcohol spectrum disorders
p/FAS	(Partial) fetal alcohol syndrome
PAE	Prenatal alcohol exposure
TRF	Teacher report form

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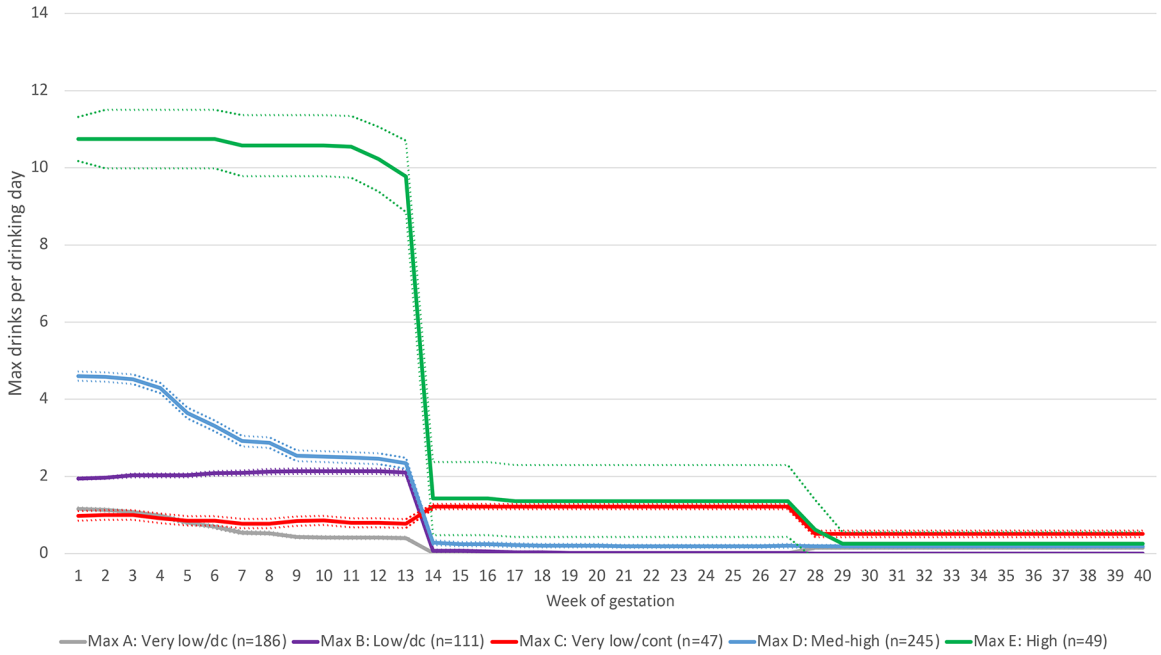

Figure 1.

Maximum drinks per drinking day (max DDD) trajectories for individuals with reported alcohol consumption during pregnancy in the CoFASP study. Trajectories modeled with k means longitudinal. Five trajectories (max a-e) best described the subgroup with any self-reported alcohol in pregnancy.

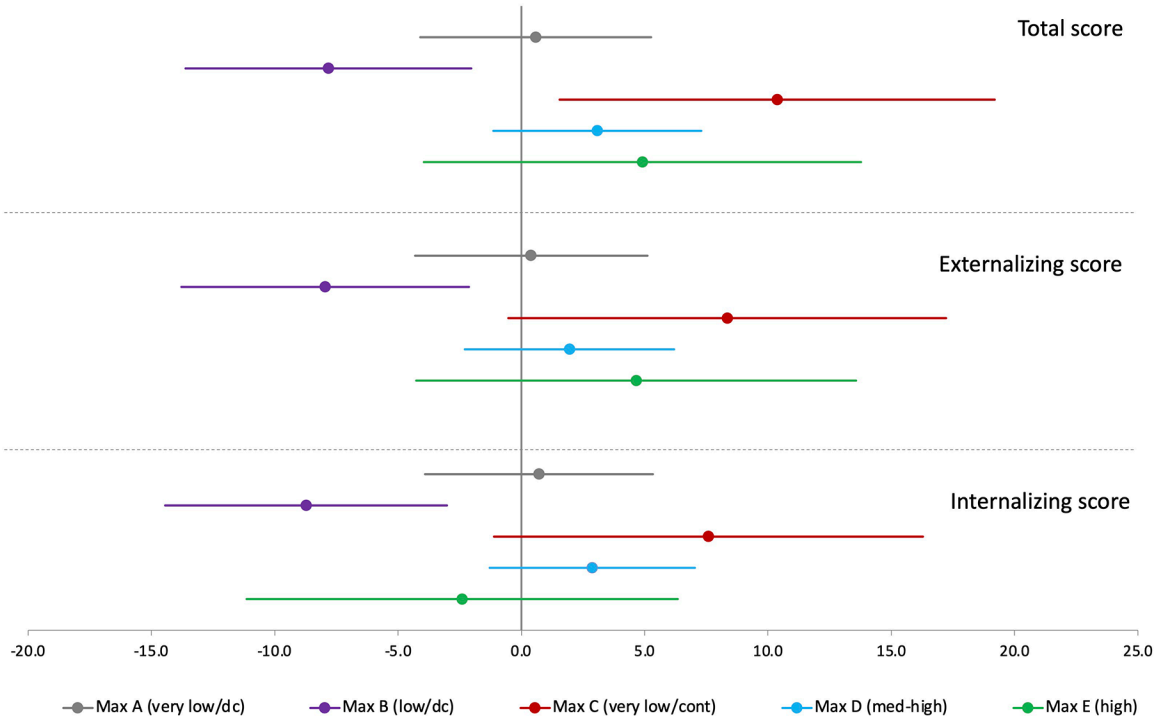

Figure 2.

Beta estimates and 95% confidence intervals for maximum drinks per drinking day trajectory (max a-e) and the Child Behavior Checklist. Models adjusted for maternal age, pregnancy smoking and other substance use. No reported PAE served as the reference group. Three models (total score, externalizing score, and internalizing score) are displayed in the figure from top to bottom. Point estimates and confidence intervals are displayed in supplemental material.

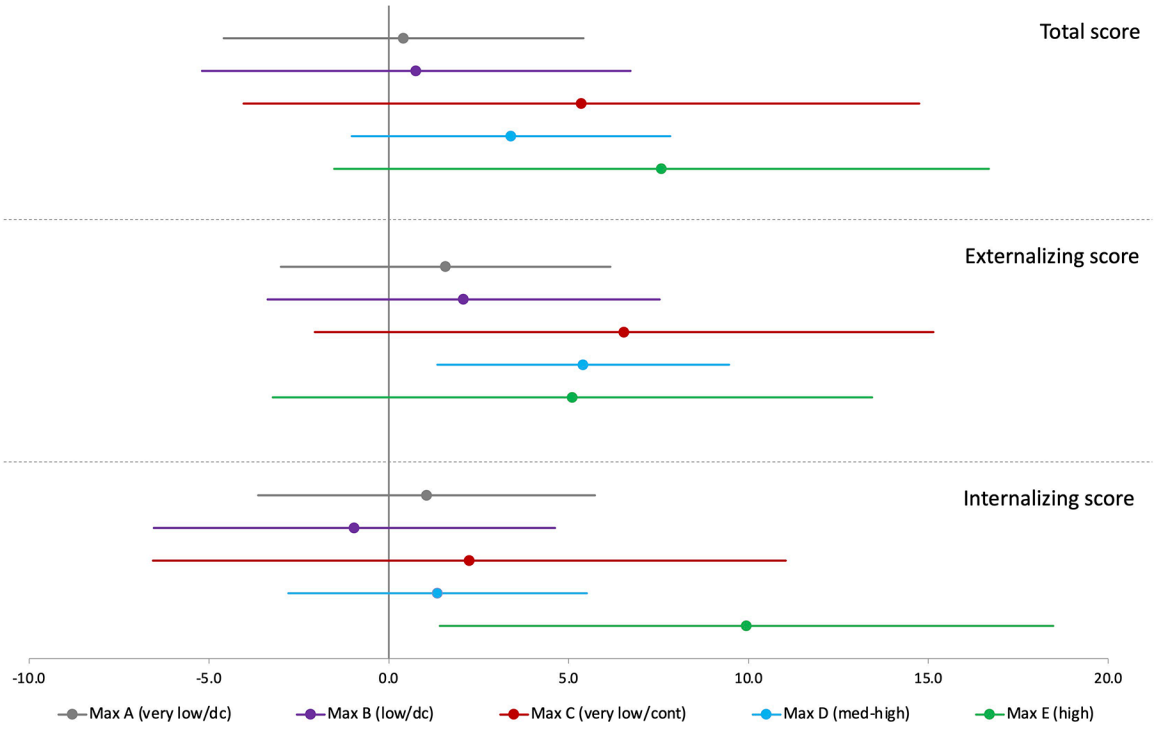

Figure 3.

Beta estimates and 95% confidence intervals for maximum drinks per drinking day trajectory and the Teacher Report Form. Models adjusted for maternal age, pregnancy smoking and other substance use. No reported PAE served as the reference group. Three models (total score, externalizing score, and internalizing score) are displayed in the figure from top to bottom. Point estimates and confidence intervals are displayed in supplemental material.

Table 1.

Participant and maternal characteristics in the CoFASP study by maximum drinks per drinking day trajectories (n=1663)

	No alcohol (n=1025)		Max A: very low/dc (n=186)		Max B: low/dc (n=111)		Max C: very low/cont (n=47)		Max D: med/high (n=245)		Max E: high (n=49)	
	n	%	n	%	n	%	n	%	n	%	n	%
Maternal education												
Less than high school	256	25.0	14	7.5	5	4.5	2	4.3	19	7.8	6	12.2
Highschool	180	17.6	16	8.6	12	10.8	4	8.5	35	14.3	8	16.3
More than high school	560	54.6	153	82.3	94	84.7	41	87.2	181	73.9	35	71.4
missing	29	2.8	3	1.6	0	0	0	0	10	4.1	0	0
Maternal employment during pregnancy												
Seasonal or unemployed	369	36.0	36	19.4	19	17.1	7	14.9	50	20.4	29	59.2
Part time work	120	11.7	24	12.9	20	18.0	8	17.0	32	13.1	8	16.3
Full time work	508	49.6	123	66.1	72	64.9	32	68.1	156	63.7	12	24.5
missing	28	2.7	3	1.6	0	0.0	0	0.0	7	2.9	0	0.0
Marital status during pregnancy												
Single/divorced/widowed	82	8.0	13	7.0	11	9.9	4	8.5	41	16.7	6	12.2
missing	26	2.5	3	1.6	0	0.0	0	0.0	7	2.9	0	0.0
Pregnancy smoking												
Yes/suspected	62	6.0	11	5.9	11	9.9	8	17.0	42	17.1	17	34.7
missing	16	1.6	1	0.5	0	0.0	1	2.1	1	0.4	1	2.0
Pregnancy drug use*												
Yes/suspected	17	1.7	1	0.5	3	2.7	2	4.3	17	6.9	7	14.3
missing	4	0.4	0	0.0	0	0.0	1	2.1	0	0.0	1	2.0
Participant born preterm	142	134	13.1	10.8	8	7.2	5	10.6	27	11.0	12	24.5
missing	3	0.3	0	0.0	1	0.9	0	0.0	1	0.4	0	0.0
Participant race												
White	810	79.0	151	81.2	97	87.4	33	70.2	190	77.6	38	77.6
Black	43	4.2	12	6.5	9	8.1	4	8.5	16	6.5	4	8.2
Native American	11	1.1	1	0.5	1	0.9	0	0.0	3	1.2	4	8.2
Multiracial	102	10.0	17	9.1	3	2.7	10	21.3	28	11.4	2	4.1

	No alcohol (n=1025)		Max A: very low/dc (n=186)		Max B: low/dc (n=111)		Max C: very low/cont (n=47)		Max D: med/high (n=245)		Max E: high (n=49)	
	n	%	n	%	n	%	n	%	n	%	n	%
Other	59	5.8	5	2.7	1	0.9	0	0.0	8	3.3	1	2.0
Participant gender												
Male	513	50.0	92	49.5	50	45.0	25	53.2	120	49.0	28	57.1
Collateral reporter	25	2.4	3	1.6	0	0.0	0	0.0	7	2.9	0	0.0
Maternal age at birth (mean, SD)	28.5	28.4	6.1	5.1	29.3	5.9	32.6	6.1	27.6	5.3	24.1	4.9
Maternal BMI: current (mean, SD)	28.6	28.6	6.8	6.2	28.0	7.2	26.8	5.4	27.5	6.5	29.2	7.1
Parity (mean, SD)	2.8	2.8	1.2	1.3	2.3	1.0	2.4	1.1	2.4	1.0	2.5	1.1
Gestational week of pregnancy recognition (mean, sd)	5.7	5.7	3.2	2.2	5.9	3.0	8.6	6.3	6.1	3.5	6.9	4.4
Drinks per drinking day												
Trimester 1 (mean, SD)	0.0	0.0	1.2	0.5	2.1	0.7	1.2	0.5	4.6	1.9	10.8	4.0
Trimester 2 (mean, SD)	0.0	0.0	0.0	0.1	0.1	0.3	1.2	0.5	0.3	1.0	1.4	5.0
Trimester 3 (mean, SD)	0.0	0.0	0.2	0.4	0	0	0.5	0.6	0.2	0.5	0.6	4.1
Met CoFASP alcohol criteria for FASD	1	0.1	9	4.8	6	5.4	5	10.6	119	48.6	22	44.9
Completed CBCL	999	97.5	185	99.5	109	98.2	47	100.0	240	98.0	48	98.0
Completed TRF	892	87.0	164	88.2	105	94.6	42	89.4	221	90.2	45	91.8

*Marijuana, heroin/opiates, crack cocaine, methamphetamine, hallucinogens, non-medical inhaled substances, other drugs