## Title

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## Journal

Alcoholism Clinical and Experimental Research, 44(6)

## ISSN

0145-6008

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## Publication Date

2020-06-01

## DOI

10.1111/acer.14325

Peer reviewed

HHS Public Access

Author manuscript

*Alcohol Clin Exp Res*. Author manuscript; available in PMC 2022 June 09.

Published in final edited form as:

*Alcohol Clin Exp Res*. 2020 June ; 44(6): 1245–1260. doi:10.1111/acer.14325.

# Characterizing Alcohol-Related Neurodevelopmental Disorder (ARND): Prenatal Alcohol Exposure and the Spectrum of Outcomes

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## Abstract

**Background:** Effects of prenatal alcohol exposure (PAE) are conceptualized as fetal alcohol spectrum disorder (FASD), with fetal alcohol syndrome (FAS) as the most severe. Many find it more difficult to characterize behavioral and cognitive effects of exposure on the central nervous system when physical signs are not present. In the current study an operational definition of Alcohol Related Neurodevelopmental Disorder is examined to determine its usefulness in discrimination of children classified as ARND based on behavior (ARND/B) and cognition (ARND/C) from children in four contrast groups, 1) Children exposed to study-defined "risky drinking"; 2) Children with any reported PAE; 3) Children classified as "Higher Risk" for developmental problems; and 4) Children classified as "Lower Risk".

**Method.—**1842 children seen as part of a surveillance study (May, Chambers, et al., 2018) were evaluated for alcohol exposure, physical characteristics of FAS, and completed neurodevelopmental testing. Ninety one were identified as either ARND/B or ARND/C and contrasted with other groups to further identify distinguishing patterns. Multinomial Logistic Regression (MLR) was used to examine accuracy of classification and to identify factors contributing to such classification.

**Results:** Children described as ARND/C were distinct from other groups based on cognition and behavior as well as demographic factors (e.g., age, race, SES) child characteristics (e.g.,

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The authors have no conflicts of interest to report.

gestational age; sex) and other drug exposures while those described as ARND/B differed only on behavior and other drug exposures. MLR models successfully discriminated ARND groups from children in other groups with accuracy ranging from 79% (Higher Risk) to 86.7% (Low Risk).

**Conclusions.—**ARND has been a subject of debate. This analysis suggests effects of alcohol on behavior and cognition even in the absence of the characteristic facial features and growth deficiency that can be identified. Results also indicate that it may be possible to distinguish such children from those in other high risk groups.

### Keywords

Prenatal alcohol exposure; fetal alcohol spectrum disorders; diagnosis; Alcohol Related Neurodevelopmental Disorder

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Prenatal alcohol exposure (PAE) results in a spectrum of outcomes in exposed children ranging from Fetal Alcohol Syndrome (FAS) at the most severe end, through milder expressions, and finally to what appears to be a lack of measurable effects. There has been ongoing discussion about how to characterize and diagnose conditions that may make up these fetal alcohol spectrum disorders (FASD). It is frequently argued, by both professionals and families, that the most important teratogenic outcome of prenatal alcohol exposure is on neurobehavior through its impact on the central nervous system. Nevertheless, physical features are considered the hallmarks of FAS and partial fetal alcohol syndrome (pFAS), and it is growth deficiency and facial and other physical features that are most often identified by physicians. Neurobehavioral deficits, in the absence of physical features, are often overlooked or attributed to other causes, including environmental factors and other conditions that affect behavior. Thus, it can be difficult to identify non-dysmorphic, alcohol-affected children either by surveillance or in clinical settings.

Those individuals who are prenatally exposed and have neurobehavioral effects in the absence of the characteristic facial features and growth deficiency have been described as having an Alcohol-Related Neurodevelopmental Disorder (ARND) (Stratton et al, 1996). Neurodevelopmental disorders can involve cognitive deficits and/or behavioral deficits. In longitudinal exposure samples where maternal alcohol use is known and information about potentially confounding factors collected, observed differences in cognition and behavior in offspring can be attributed to prenatal exposure with some confidence (Brown, et al, 1991; Day, et al, 2013; Hendricks, et al., 2019; Streissguth, et al, 1999). It is also from such studies that we have confirmed that behavioral and mental health effects of PAE can exist in the absence of cognitive deficits (e.g., Lynch et al, 2016). There has been less certainty, however, about the use of ARND in clinical situations since information about maternal alcohol use is often lacking and it is very difficult to account for the effects of other variables that also are known to affect outcomes. Such difficulty can lead to an inability to identify and treat those children referred for care who are affected by alcohol but do not meet diagnostic criteria for FAS or pFAS.

Although some criteria have been proposed, (e.g., see, Johnson, et al, 2018), the construct of ARND remains somewhat theoretical, as it has not been rigorously evaluated and there is no agreement on its characteristics. To address this problem, we use the results of an active case ascertainment prevalence study of 3,397 first grade children in 4 sites in the United States (May, Chambers, et al., 2018) to examine factors associated with ARND and to determine whether it is possible to identify such children reliably and to discriminate them from those in various contrast groups. The Collaboration on Fetal Alcohol Spectrum Disorders Prevalence research consortium (CoFASP) was created to estimate the prevalence of the full range of FASD specifically including ARND within 4 regions of the United States, (May, Chambers, et al., 2018). To do so, CoFASP developed a set of criteria to operationalize the identification of FAS, pFAS and ARND for this study based both on previous research and clinical experience. For the purposes of the surveillance study, ARND was operationalized to include children with deficits in cognitive functioning or those with specific weaknesses in behavior as both of these domains are associated with teratogenic exposures (Brown, et al, 1991, Day, et al, 2013, Streissguth, et al, 1999). Subsequently, a more generalized version of these criteria was proposed by Hoyme et al (2016) for use in the diagnosis of FASD in clinical settings.

Data from the CoFASP prevalence study provided several advantages for the exploration of ARND in the current paper where the classification of ARND was operationalized as noted in figure 1 and applied consistently. Secondly, these data provide the opportunity to compare those classified as ARND with children in various different groups similar to those encountered in clinical settings and schools. A criticism of some FASD clinical studies is that children identified as ARND may be distinguished only from typically-developing children and not from other high-risk groups like those with Attention Deficit, Hyperactivity Disorder (ADHD) (although see, Barrett, et al, 2019; Coles, et al, 1997, Ware, et al , 2012). In the absence of control over social and caregiving factors that can affect development of any child, it is not always clear that those with FASD are different from other children with problematic caregiving histories, from other high-risk groups or other neurodevelopmental disabilities (McLennan & Braunberger, 2017). The current study addressed this question by examining of the characteristics of those classified as ARND in comparison to four other groups of children. These other groups included two groups with PAE who did not meet the CoFASP criteria for ARND. They included: 1) children of mothers who reported drinking at a risky level, but who did not meet criteria for neurobehavioral impairment and 2) children of mothers who had reported some alcohol exposure in pregnancy but did not meet the study's Alcohol Criteria for risky drinking. The Alcohol Criterion group (Group 1) is necessarily a subset of the Any Alcohol Group (Group 2). The study also compared those classified as ARND to: 3) children at risk due to developmental concerns and/or smaller size on growth measures ("Higher" Risk) (Group 3) and to 4) typical community controls (Low Risk) (Group 4). Children of women who used alcohol were not excluded from these last two contrast groups to more closely replicate real world situations in which children would be identified. Finally, the study collected information about other factors that might be associated with the behaviors of interest (e.g., demographic information, birth characteristics, other substance use) and allowed examination of the contribution of these other factors to the classification of ARND within these different groups.

Importantly, the current analysis was not designed to identify the "base rate" of ARND in the population, or within these samples, as this was done by the prevalence study itself (May, Chambers, et al, 2018). Our goal was to provide an understanding of the characteristics of children identified as ARND using these methods to determine if there were reliable patterns associated with this classification and if these were meaningful in relation to the characteristics of other children who may be considered at risk.

## Methods

The collaborative prevalence study (May, Chambers, et al., 2018), supported by the National Institutes of Health, National Institute of Alcohol and Alcohol Abuse (NIH/NIAAA) was designed to research the prevalence of FASD among typical first grade classrooms in 4 diverse regions of the United States. Two study teams investigated FASD through similar sampling methods and a standardized study protocol that included the application of agreed-upon classification criteria and evaluation protocols for dysmorphology, neurobehavioral ability, and determination of evidence of prenatal alcohol exposure. ARND was identified when, in the presence of known prenatal alcohol exposure at a defined level, children met a set of functional criteria on a specific neurobehavioral testing protocol. In the current paper, children were categorized as ARND based on either Behavior (ARND/B) or Cognition (ARND/C). (See Figure 1 for these criteria). While it is possible that a child might meet both criteria, this was not required for classification.

### Study Design

This was the first large study in the United States to gain access to a general community population and comprehensively evaluate children to estimate the prevalence of FASD. An active case–ascertainment approach was used in four regional study sites; Rocky Mountain, Midwest, Southeast and Pacific Southwest. Due to confidentiality agreements with some of the study sites, specific community names were not made available for publication. The case-finding process identified potential FASD cases within first grade classrooms in public and private schools. Methods included detailed instructions and standardized case-finding processes for collection of the data and assignment of diagnoses based on the agreed-upon criteria.

Although data collection protocols were identical across the study sites, recruitment of participants used the following three similar, but slightly different, sampling methods (see Figure 2): 1) Sampling Method One recruited children whose height, weight, and/or head circumference were ≤25$^{th}$ percentile plus a group of participants selected randomly from the general school rolls (the over-sampling of smaller children was used because growth deficiency is one of the hallmarks of children affected with FAS, thereby, potentially recruiting children who may be at greater risk of a diagnosis of FAS or pFAS); 2) In Sampling Method Two, a simple random sample of children was pulled from the school rolls; 3) In Sampling Method Three a sample of children whose height, weight and/or head circumference were ≤25$^{th}$ percentile or children with developmental concerns, as reported by the parent or caregiver, as well as randomly selected children with neither small size nor developmental concerns were recruited. The group considered Higher Risk in the current analysis included those children whose growth was ≤25$^{th}$ percentile or who were identified as having developmental risk using a screening questionnaire (PEDS: Parents Evaluation of Developmental Status, Glascoe, 2013). The Low Risk group included randomly sampled children who did not meet any of the risk criteria. All study procedures were approved by the institutional review boards of the participating research institutions. Approval for the study was secured from all school districts with which the study teams interfaced. All parents and caregivers provided written informed consent to participate in the study, and children seven years of age or older provided written assent.

Standardized growth and dysmorphology examinations were completed for each child as well as maternal interviews with core questions about the mother's drinking prior to and during pregnancy. Alcohol information was obtained from all *consenting* mothers of study participants or from collateral reporters if the birth mother was not available. Timeline follow back methods were employed to assure that this retrospectively-collected information was as accurate as possible (Sobell, et al., 2001). In this way, information about alcohol exposure was obtained from 54.5% of the total sample. The neuropsychological testing battery was carried out in a proportion of the study children by psychologists or trained psychometrists using standardized procedures. Detailed information about the structure of the surveillance study and overall study results can be found in the Journal of the American Medical Association (May, Chambers, et al., 2018).

## Maternal Drinking Criteria

Known prenatal alcohol exposure that met certain criteria was required for there to be an assignment of ARND for any given child. Although some women reported drinking at lower levels, for ARND to be diagnosed in this study, the following criteria were required (See also Figure 1):

One or more of the following conditions must be met to constitute documented prenatal alcohol exposure during pregnancy. The information must be obtained from the biological mother or a reliable collateral source (e.g., family member).

**A.** 6 or more standard drinks per week for 2 or more weeks during pregnancy

**B.** 3 or more standard drinks per occasion on 2 or more occasions during pregnancy

**C.** Documentation of alcohol-related social or legal problems in proximity to (prior to or during) the index pregnancy (e., history of multiple citations for driving while intoxicated or history of treatment for an alcohol-related condition) (Hoyme et al, 2016).

Children whose mothers met these criteria comprised the **Alcohol Criteria Met** Group and children whose mothers reported **any** drinking in pregnancy, comprised the **Any Alcohol** group.

## Neurobehavioral Testing Battery

The following criteria were used in selection of tests for the battery: 1) Empirically shown to reflect effects of PAE on development, 2) Must be valid, reliable, and available in English and Spanish, 3) Total battery limited in time (1.5 to 2 hours), 4) Administered by professional psychologists/ psychometrists to ensure reliability in administration and future replication.

Global and specific intellectual abilities were tested and cognition sampled in neurobehavioral domains known to be sensitive to effects of PAE: executive functioning, learning, memory, and visual-motor abilities. Assessment of some of these constructs had to be limited due to the time constraints of the surveillance study. Intellectual ability was assessed using the Differential Ability Scales, Second Edition (DAS-II) (DAS-II, 2007), an individually administered battery for ages 2 years 6 months to 17 years 11 months. Both the Upper Early Years battery (3:6 −6:11 years) and the School-Age battery (7:0 – 17:11) were used due to the age of these first graders. The overall General Cognitive conceptual and reasoning ability score is the GCA with cluster scores including Verbal, Nonverbal Reasoning, and Spatial Abilities.

NEPSY-II (NEPSY-II, 2007) subtests were selected to sample executive functioning, language, and sensorimotor abilities. The Inhibition (INI) subtest was used to assess attention, processing speed, inhibitory control and cognitive flexibility. The Speeded Naming subtest was used to assess potential issues with expressive language, lexical access, processing speed and cognitive control. The Visuomotor Precision subtest was chosen to assess psychomotor processing speed, visual attention, motor control and coordination. In addition to the NEPSY-II Visuomotor Precision subtest, the Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI) (Beery and Beery, 2004) was used to assess eye-hand coordination and graphomotor skills.

The Bracken Basic Concepts Scale – Revised (BBCS-R) (BBCS-R, 1998), was used to assess basic concept development of the children in the study. A School Readiness Composite Score (SRC) is derived from foundational and functionally relevant educational subscales important for early learning.

Behavioral data were collected using caregiver and teacher questionnaires, the Child Behavior Checklist (CBCL) and the Teacher Report Form (TRF) (Achenbach and Rescorla, 2001). In addition, the Vineland Adaptive Behavior Scales, 2$^{nd}$ Edition (VABS-II) (Sparrow et al, 2005) was used to assess adaptive skills of the children through an interview with the caregiver.

Setting of “cut off” scores to meet classification criteria was determined based on previous research with FASD. The deficits in neurobehavioral functioning resulting from PAE may not be extreme enough to qualify for special education placement or for a diagnosis of disability. Often children with an FASD have cognitive abilities within the average or low average range, but have specific executive functioning, memory, attention, visual-perception impairments that may deter or limit their success (Streissguth et al, 1999; Mattson et al, 2013; Mattson et al, 2011; Ware et al, 2012). In addition, while maintaining overall intellectual skills within the average range, children prenatally exposed to alcohol frequently have behavioral concerns related to attentional abilities, impulse control and mood or self-regulation (Howell et al, 2006; Glass et al., 2017; Glass et al, 2013; Mattson et al, 2013; Ware et al, 2013; Rasmussen et al, 2013; Crocker et al, 2015). Based on our understanding of these patterns of functioning, the decision was made to set qualification criteria for classification at the 8$^{th}$ percentile below the mean or at the 92$^{nd}$ percentile above the mean for all testing done with the exception of BBCS-R (the early learning measure). Because the children were so early in their school careers when potential foundational skills were still being developed, a cut off of ≥1 standard deviation below the mean was used as criteria for the BBCS-R. See Figure 1 for detailed information regarding criteria used to determine whether a child could be classified as either ARND/C or ARND/B.

## Data Analysis

**Subject selection:** From a sample of 3,397 children originally recruited across sites, 1,842 were eligible for inclusion in this analysis because there was reliable information obtained about alcohol use in pregnancy and ARND requires that information about PAE be available. Of these, 635 (34.5%) reported any alcohol use and 198 (10.7%) reported using at levels that met the CoFASP criteria for risky alcohol use. Of these 1,842 cases, 1,023 were recruited as "higher risk" for alcohol effects, based on growth measurements for current weight, height or head circumference ≤25$^{th}$ percentile for age and sex, or 2 or more developmental problems on the PEDS screening measure; and 819 were recruited as randomly-selected controls. Groups were further refined by excluding children who had not completed neurodevelopmental testing. Thus, the final n for each contrast group minus any children with FASD diagnoses was: Any Alcohol Exposure=531; Higher Risk=805; Low Risk=750. Of the cases that met the Alcohol Criterion for risky drinking, 62 were classified as FASD other than ARND. Removing these individuals yielded a total of 140 cases. Of the 140 cases, forty nine were children who could not be classified as ARND despite their mothers' use of alcohol meeting study criteria, while 47 met criteria for ARND/B and 44 for ARND/C. Of the 44 children classified ARND/C, 27 also met the ARND/B classification.

Traditional descriptive and inferential statistics (Chi Square, Analysis of Variance) were used to compare the two ARND groups, ARND/B and ARND/C , to each other as well as to each of the four contrast groups, on demographic, physical and neurodevelopmental outcomes. This was done separately in each of the four contrast groups. The ARND groups were evaluated in comparison to each of the contrast groups individually as the contrast groups were not independent of each other.

**Classification.—**Effectiveness of identification and classification of ARND in relation to individuals in contrast groups was evaluated using multinomial logistic regression (MLR). This procedure allows evaluation of a number of variables in a model for classification of individuals into discrete categories such as those required for diagnosis. The regression procedure also allows the evaluation of the relative contribution of selected variables to the model. It is important to keep in mind that classification rates are subject to inflation because some of these factors were used as part of the original diagnostic procedure.

**Selection of random samples.—**Logistic regression does not yield accurate classification when there is a large discrepancy in the size of sample groups. That is, when the cases (i.e., ARND) are "rare events" in comparison to the size of the contrast group (see King & Zeng, 2001, for a discussion). Therefore, for several of the analyses, 12 to 20% of the contrast group was selected randomly (using a feature included in SPSS 26, 2016) for inclusion in the analysis. This was done with the Any Alcohol group as well as the Higher Risk and the Low Risk groups. The group that met the CoFASP criteria for risky alcohol use did not require this procedure since the three outcome groups were approximately equal in size. To ensure the representativeness of the selected sample, the randomization procedure was carried out several times for each group and the analyses repeated to assure that similar results were obtained. Bootstrapping was also employed to confirm results. Reported results represent the final random sample generated for each group.

Given that the MLR was carried out in a reduced sample, it was necessary to correct the intercept for the parameters (see Supplemental Tables S2-S5) consistent with the recommendations in King and Zeng (2001). The following formula was used to identify the correct intercept for each of the three analyses that employed the reduced sample, where Tau ($\tau$) is the proportion of ARND in the larger sample. Mean of y($\bar{y}$) is the proportion of ARND randomly sampled from the contrast group. The intercept from the randomly sampled data is $\hat{\beta}_0$ and the equation solves for the corrected intercept: $\beta_0$.

$$\beta_0 = \hat{\beta}_0 - \ln[((1-\tau) / \tau)(\bar{y} / (1-\bar{y}))]$$

**Missing Data and Data Reduction.—**Not all individuals had information for all variables. Therefore, to avoid reducing sample size, missing data were replaced with their predicted values in the various data sets using the linear trend at point method (SPSS 26, 2016) that replaces the missing value with the linear trend for that point by regressing the series on the index variable. This strategy was employed only when the data were missing for that variable in less than 10% of the total number of subjects. The few subjects with more extensive missing data were excluded from the sample. In addition, to reduce collinearity that could invalidate the procedure, the following variables (mother's education, income and marital status) were submitted to a factor analytic procedure and the resulting single factor representing socioeconomic status (SES) was used in the regression procedure.

**Models.—**To examine factors that are associated with a classification of ARND within each comparison, we employed MLR to create models to classify individuals as "Not FASD", ARND/B or ARND/C, with "Not FASD" as the Reference group. In creating the models to be tested, a Main Effects regression procedure was employed in which the following 15 variables were entered: 1) Cognitive and behavioral outcomes that measure the constructs that were used in the initial classification. For these models, only summary scores from outcome measures were used, including: DAS-II GCA, the NEPSY-II Visuomotor Precision score, VMI, Vineland ABC, school readiness standard score (BBCS), the CBCL and TRF Total Problems T-Scores; 2) Demographic factors including child's age and biological sex, height percentile, racial identification, gestational age at birth and socioeconomic status (SES) (based on maternal characteristics); and 3) Drug use reported in pregnancy, specifically tobacco and marijuana use. Other drug use was less frequent and did not contribute significantly to models in preliminary analyses. Inclusion in the model followed the default values provided by SPSS 26 (IBM, 2016). A Likelihood Ratio Test was used to determine the contribution of factors to the model and, after the initial analysis, those that had significance levels of less than $p<.20$ were retained in the model for the purposes of classification. A second model was then done and those results retained as a final model.

Models were tested independently for the four comparisons: ARND vs all children whose mothers reported drinking met the criterion for risky drinking; ARND vs all children whose mothers with any reported drinking in pregnancy; ARND vs Higher Risk contrast group and ARND vs Low Risk contrast group.

## Results

### Demographic Measures and Outcomes.

Descriptive information is presented in Table 1 in which ARND/B and ARND/C groups are compared with children in the four contrast groups. The two ARND groups are shown in the shaded area with results of comparisons between those two groups only. Note that the contrast groups are not compared with each other in Table 1, so the significance statistics indicate only the differences between each contrast group and one or both of the two ARND groups. The ARND groups both demonstrate elevations in behavior problems while those in the ARND/C group are different on cognitive measures as would be expected. This group also differs significantly in many of the child physical characteristics. For many of the characteristic assessed, the ARND groups, and particularly the ARND/C group, are significantly different from those in the contrast groups. Those in the ARND/B group are distinguished by their behavior only. For more information about drug use in pregnancy see Supplemental Table S1.

### Multinomial Regression Models.

For all models, the same set of variables was included. These were: 1) Cognitive and behavioral outcomes reflecting constructs used in group classification: General Cognitive Ability (GCA) on the DAS-II, Visuomotor Precision from the NEPSY-II, the Beery VMI, Total Problems T-score on the CBCL, and Total Problems T-score on the TRF, Adaptive Behavior Composite on the Vineland, and the Bracken School Readiness Composite, Revised.; 2) Child personal and demographic characteristics: child sex, child age, racial category, height, gestational age, SES; 3) Other drug exposure in pregnancy, particularly cigarette and marijuana use.

**ARND and No Diagnosis in Group that met Alcohol Criterion. (N=140)—**Using a data set (N=140) that included all of the individuals whose mothers were reported to meet study alcohol exposure criteria (see Methods) for use in pregnancy and who were diagnosed as: 1) Not FASD (n=49), 2) ARND/B (n=47); 3) ARND/C (n=44), multinomial regression was used to identify models that accurately classified individuals as either ARND/B or ARND/C, versus those who were not.

Initial analyses included all factors but, as discussed above, only those factors whose p value was less than .2 were retained in calculating the final model. This final model was significant ($X^2_{(26)}$ =226.99, p<.000). Table 2 shows the Likelihood ratios and Table 2.1 the classification table for the final model. Classification was 87% accurate using these factors. In this model, VMI, gestational age and the drug variables did not contribute significantly to classification. Supplemental Table S2 shows the parameter estimates for this model.

**ARND and No Diagnosis in Group with Any Alcohol Use in Pregnancy (N=190).—**From the total pool of 635 cases in which mothers reported any alcohol use during pregnancy, a random sample was selected and combined with the ARND group. Any duplicate cases or cases diagnosed with other FASDs were removed from the data set yielding 190 unique cases.

Following the same strategy as above, all variables were entered initially. Those that did not meet the p<.20 criteria were eliminated and the model recalculated. Those eliminated included: VMI, school readiness, Vineland ABC, child sex, gestational age, height percentile, and cigarette use.

The following model was significant (Model: ($X^2_{(22)}$ =184.27, p<.000), and allowed accurate classification of 79% of cases. Table 3 and 3.1 below show results. Supplemental Table S3 shows the parameter estimates with corrected intercept.

**ARND and Higher-Risk Contrast Group (N=173)—**In the surveillance study, 805 children, who were included due to characteristics that placed them at higher risk for a diagnosis of FASD, were assessed with the cognitive battery that allowed classification of ARND. From this group, a random sample was selected and combined with the ARND group and duplicate cases were deleted resulting in a final sample of 173. Missing data were treated as discussed above and similar models created.

Selected factors were entered into the regression and those that were found to have significance levels greater than p=.20 were removed from the next analysis. These were: VMI standard score, Height percentile and SES. Other factors were retained. The subsequent model ($X^2_{(30)}$ =184.77, p<.000) classified 79% of cases accurately and is shown below in Table 4. Parameter estimates are in Supplemental Table S4.

**ARND and Low Risk Contrast Group (N=179)—**There were 750 Low Risk children who completed the neurobehavioral testing battery. From this pool, a random sample was drawn and combined with the ARND cases and duplicates were eliminated, resulting in a sample of 179 cases.

The selected factors were entered in the Main Effects model for a preliminary analysis and those exceeding the significance level of p=.20 were removed for subsequent analysis. Factors removed were: VMI, school readiness (BBCS standard score), gestational age, and race. Using the remaining variables, the classification model was significant (Model: $X^2_{(28)}$ =222.83, p<.000) and accurately classified 86.7% of cases. The final model is shown below in Table 5. Parameter estimates are in Supplemental Table S5.

## Discussion

There has long been a desire for a "behavioral phenotype" of PAE that could be used in the absence of accurate information about maternal alcohol use to identify alcohol-affected children (Kodituwakku, 2007) despite concerns that environmental and caregiving factors made it difficult to specify the characteristics of such a pattern. The results of this analysis indicate that there are, in fact, behavioral patterns that can be associated with PAE. These characteristics can be used to identify children who differ from other groups of children and, when there is some information about maternal alcohol use, can suggest that PAE contributed to these outcomes. However, given the measures used, it seems that information about maternal alcohol use will continue to be necessary to identify affected children accurately. This is true because the observed behaviors are not necessarily unique from all other conditions. Indeed, as long as the outcomes assessed and the measures used are not unique, it is unlikely that a unique ARND phenotype can be created.

These results also provide some insights into the other factors that contribute to the impact of PAE on behavior and cognition. Examination of Table 1 suggests that, as expected, there are some factors that distinguish the ARND groups and probably interact with alcohol exposure. These factors are those known to be associated with developmental risk in general and may be indicators of stress. Children classified as ARND are more likely to be from minority groups rather than from the majority population. Similarly, even when the child is prenatally exposed, family educational levels and marital status are associated with ARND classification, suggesting that higher SES and more stable caregiving may be protective in the presence of alcohol. It also appears that those identified as ARND are more likely to be male, particularly in the Higher Risk group. As males are usually more vulnerable (Schore, 2017), this finding is not surprising. In addition, those children who are classified as ARND based on their cognition are more likely to have been born preterm and to have lower birthweight than all other groups. Although these conditions are well known risk factors for developmental problems, both lower birthweight (Day et al., 1989) and preterm birth (Coles, et al, 2019) have been shown to be associated with PAE (Carter et al., 2016). Thus, prenatal exposure may be exerting an effect here even when these perinatal factors are not in a range that is typically associated with later risk. Finally, maternal use of other drugs in pregnancy, particularly cigarettes and marijuana, is associated with ARND classification. Given the well-known relationship between alcohol and other drug use, such an outcome is to be expected.

Behavioral outcomes were used to identify children as alcohol affected so it is not surprising that many of these variables distinguish ARND from other groups. However, it is also clear that while the measures of behavior (CBCL and TRF) and adaptive functioning (Vineland) are lower in both ARND/B and ARND/C groups, and while in the ARND/C group many of the cognitive outcomes are also suppressed, those in the ARND/B group cannot be distinguished based on any of the cognitive outcomes included in this analysis. Thus, it appears that these two groups may indeed represent distinct categories within the FASD spectrum.

### ARND versus ND-PAE.

Those children meeting ARND/C criteria in this sample show a similar, although not as severe a pattern of outcomes, as do children qualifying for the Neurobehavioral Disorder-Prenatal Alcohol Exposure (ND-PAE) diagnosis as described in the most recent Diagnostic and Statistical Manual, 5$^{th}$ Edition (DSM-5) of the American Psychiatric Association (APA, 2013). The DSM-5 proposed a set of criteria for Neurobehavioral Disorder-Prenatal Alcohol Exposure (ND-PAE) as a condition for further study (Doyle & Mattson, 2015; Kable &

Coles, 2018; Kable et al., 2016). This proposed disorder is different from the concept of ARND that we have outlined in this paper in that it specifies that the affected individual must meet all 4 of the following criteria: 1) Cognitive deficit, 2) Impaired self-regulation; and 3) impairment in two areas of adaptive functioning, in addition to 4) “more than a minimal exposure to alcohol during gestation.” In addition, ND-PAE can be diagnosed in the presence of FAS and pFAS and does not, therefore, necessarily represent a part of the exposure spectrum without physical features. In contrast, as defined here, ARND requires evidence of prenatal exposure, but does not require that the individual have both a cognitive and a behavioral disorder nor adaptive dysfunction and thus may be descriptive of a less disabling effect of PAE than that which is required for ND-PAE. For instance, ARND may be a way to describe a child of normal intelligence who has an alcohol-related learning disability and no behavioral disorder or the child with a behavior problem who is intellectually in the typical range. However, the response to prenatal alcohol exposure results in great variability in behavior and, in other populations, ARND might present with much more severe behavioral features.

### ARND and Self-Regulation.

In the current study, those labelled ARND/B appear unaffected except for their self-regulation of behavior. Questions do remain about the basis for such behavior problems. Difficulties in self-regulation among those with FASD are often attributed to deficits in executive functioning (EF) believed to be caused by PAE’s impact on the frontal cortex (Kable & Coles, 2017) and EF is widely regarded as central to the deficits associated with PAE (Khoury, Milligan, & Girard, 2015). In this study EF was measured using several variables including the NEPSY-II INI variables and Speeded Naming (not shown in Table 1; supplemental tables available from the authors), although these measures do not represent a comprehensive assessment of this construct and might be considered to be assessing only the “cognitive” aspects of EF. Unsurprisingly, then, outcomes for these measures are significantly lower in those who are designated as ARND/C but not different from contrast groups for those designated as ARND/B. This finding raises questions about the basis for the behavioral differences reported in those with ARND and there are several possible explanations for this finding. Given that executive function was not measured comprehensively in the surveillance study, the measures used may not have been adequate to evaluate all aspects of this construct. Parental report, which is often used to assess “behavioral” EF problems was not included. Previous research has found a lack of association between measurements of EF by direct assessment, as was done here, and through parental report (Ten Eycke & Dewey, 2015) including a recent study among children with FASD (Mohamed, et al, 2019). Thus, one possibility is that EF was not measured in a way that captured its effects in the ARND/B group. It is also possible that there are other bases for the observed effects on behavior in this group and this seems a fruitful direction for future study.

### Other factors affecting ARND classification.

The MLR models examined the factors that contribute to classification as ARND in this sample and the degree to which consideration of these factors allows accurate classification in comparison to different contrast groups. Classification was, in fact, consistently accurate using these variables as well as various other individual and social descriptors. In all of the models, cognition and behavior made the greatest contribution which was to be expected based the way in which children with ARND were identified. However, it is important to remember that children were generally not identified in this study based only on the summary scores used in the models, but could be identified based on many of the subtests that were not included in the regression models. It is also of note that the measure of adaptive function (Vineland ABC) did not contribute to these classifications to the same extent as other similarly independent factors. This finding is of interest in that Adaptive Function has often been cited as an important indicator of FASD (Doyle, et al, 2019) although some studies find that adaptive problems among those with FASD are not different from those in other clinical groups (Whaley, O'Connor & Gunderson, 2001). The current results, although limited to young children, suggest the impact of PAE on adaptive function requires more critical investigation. Previous findings of association with adaptive function could be an artifact related to environment, social factors or selection criteria and it is not clear that adaptive function, as captured through parental report, has a consistent relationship with PAE across all settings.

Although we know that academic problems are often observed in alcohol-affected individuals, in the current study, the measure of school readiness used (Bracken School Readiness Standard Score) was different only in the cognitively impacted group and was of marginal usefulness in the classification models. This may be due to the age of the children who were just beginning their academic careers or the characteristics of the test itself. Children this young may not, as yet, have encountered PAE-related academic limitation and this may be reflected in their test scores. Examination of this relationship in older children seems warranted.

Several other factors were identified by the MLR models within different contrast groups that allowed these children to be distinguished with a high degree of accuracy. These results suggest that there is validity in the idea that the effects of PAE can be understood as a spectrum of outcomes, ranging from FAS through ARND/B and that it is possible to identify those who are affected even in comparison to other groups.

### Limitations of the current study.

There are certainly some limitations to consider in interpreting these results. First, the children ascertained were first graders in school settings who, in most cases, had not been referred for assessment and probably represent a group less likely to demonstrate significant effects of exposure. Secondly, maternal alcohol use in pregnancy was ascertained many years postnatally and was by maternal or collateral report. It is unknown to what extent this information was biased due to unwillingness to report or inaccurate due to inability to recall. In addition, many women did not provide this information so that those who could be included in this study represent only a portion of the total sample. All of these factors might have reduced the likelihood of identifying affected children. Another concern is that information about child behavior was obtained through caregiver and teacher questionnaires rather than through direct observation of children's behavior. While this is a common practice, there is some opportunity for bias.

### Conclusions.

Despite these limitations, this study is one of the first to examine the construct of ARND in a systematic way. While these results do not provide the unique pattern that would be a short cut to a clinical diagnosis, they do demonstrate several other things. First, that there is, indeed, a spectrum of outcomes of PAE that includes a group of affected children who do not have the characteristic physical features and growth deficiency but who can be distinguished from other groups with reasonable accuracy. That is to say, it appears that there is evidence for ARND, and it has not always been accepted that this is the case. Second, while discrimination is greatest in comparison to "typical" Low Risk children, those with ARND can be distinguished from other groups of children even including others at high risk due to physical and developmental characteristics or due to maternal alcohol use in pregnancy. The high level of discrimination in comparison to the Alcohol Criteria group is probably an artifact of the methods used in this analysis, since those children in that group who had behavior and cognitive problems were identified as ARND and, thus, removed from the contrast group.

Those we have called ARND/C demonstrate cognitive deficits and a significant percentage have behavioral problems, as well. In contrast, those with ARND/B do not differ from typical controls on cognitive measures, but do demonstrate significant behavioral concerns. The differences seen between those children we have called ARND/C and ARND/B indicate that there are gradations even within a general ARND classification among alcohol exposed children without physical features. These outcomes are more salient when we consider that the group that was ascertained was selected from regular first grade classrooms and, therefore, had not been identified as having significant developmental or behavioral problems by other sources.

The results suggest that there is, as has been hypothesized, a spectrum of effects of PAE that can include impact on neurocognition, behavior or both in the absence of physical features. If this is the case, future research may be able to refine these descriptions of potential phenotypes in a way that will allow more effective identification of children at risk due to PAE and identify effective directions for intervention based on how children have been affected by their exposure.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

This research was supported by the following awards from the National Institute on Alcohol Abuse and Alcoholism (NIH/NIAAA) to Christina D. Chambers (U01AA019879) and Philip May (U01 AA019894).

## References

Achenbach TM & Rescorla LA (2001). Manual for the ASEBA School-Age Forms & Profiles. Burlington, VT: University of Vermont, Research Center for children, Youth, & Families.

Barrett C, Kable JA, Madsen TE, Hsu CC & Coles CD (2019) The use of functional near-infrared spectroscopy to differentiate alcohol-related neurodevelopmental impairment. Developmental Neuropsychology, epub

Beery KE, Beery NA (2004). The Beery-Buktenica Developmental Test of Visual-Motor Integration – 5th Edition. San Antonio, Texas: Pearson Assessment.

Bracken BA (1998). Bracken Basic Concept Scale – Revised. San Antonio Texas: Harcourt Assessment, Inc.

Brown RT, Coles CD, Smith IE, Platzman KA, Silverstein J, Erickson S, & Falek A (1991) Effects of prenatal alcohol exposure at School age. II. Attention and behavior. Neurotoxicol Teratol, 13 (4), 369–376. [PubMed: 1921916]

Carter RC, Jacobson JL, Molteno CD, Didge NC, Meintjes EM, Jacobson SW (2016). Fetal Alcohol Growth Restriction and Cognitive Impairment. Pediatrics, 138(2).

Coles CD, Kable JA, Granovska IV, Pashtepa AO, Plotka LD, Dolhov VB, Wertelecki W., Jones KL, Chambers CD and the CIFASD (2019, in press) Gestational age and socioeconomic status as mediators for the impact of prenatal alcohol exposure on development at 6 months. Birth Defects Research: Special Edition on Fetal Alcohol Spectrum Disorders.

Coles CD, Platzman KA, Raskind-Hood CL, Brown RT, Falek A, & Smith IE. (1997) A comparison of children affected by prenatal alcohol exposure and attention deficit, hyperactivity disorder. Alcoholism: Clinical and Experimental Research, 21 (1), 150–161. [PubMed: 9046388]

Crocker N, Riley EP, Mattson SN (2015). Visual-spatial abilities relate to mathematics achievement in children with heavy prenatal alcohol exposure. Neuropsychology 29: 108–116 [PubMed: 25000323]

Day NL, Jasperse D, Richardson G, Robes N, Sambamoorthi U, Taylor P, Scher M, Stoffer D, & Cornelius M (1989) Prenatal exposure to alcohol: Effect on infant growth and morphologic characteristics. Pediatrics, 84, 536–541. [PubMed: 2771556]

Day NL, Helsel A, Sonon K, Goldschmidt L (2013) The association between prenatal alcohol exposure and behavior at 22 years of age. Alcohol Clin Exp Res, 37 (7), 1171–1178. [PubMed: 23442183]

Doyle LR, Coles CD, Kable JA, May PA, Sowell ER, Jones KL, Riley EP, Mattson SN and the CIFASD (2019) Relation between adaptive function and IQ among youth with histories of heavy prenatal alcohol exposure. Birth Defects Res: Special Edition on Fetal Alcohol Spectrum Disorders,

Doyle LR, & Mattson SN (2015) Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE): Review of Evidence and Guidelines for Assessment. Curr Dev Disord Rep, 2 (3), 175–186. [PubMed: 26509108]

Elliott CD (2007). Differential Ability Scales – Second Edition. San Antonio Texas: Pearson Assessment.

Gautam P, Nunez SC, Narr KL, & Sowell ER (2014) Effects of prenatal alcohol exposure on the development of white matter volume and change in executive function. Neuroimage Clin, 5, 19–27. [PubMed: 24918069]

Glascoe FP (1998) Collaborating with Parents: Using parents' evaluations of developmental status (PEDS) to detect and address developmental and behavioral problems. Ellsworth & Vandermeer, Nashville, TN.

Glass L, Moor EM, Akshoomoff N, Jones KL, Riley EP, Mattson SN. (2017). Academic Difficulties in Children with Prenatal Alcohol Exposure: Presence, Profile, and Neural Correlates. Alcohol Clin Exp Res; 41(5): 1024–1033. [PubMed: 28340498]

Hendricks G, Malcom-Smith S, Adnams C, Stein DJ, & Donald KAM (2019) Effects of prenatal alcohol exposure on language, speech and communication outcomes: A review of longitudinal studies. Acta Neuorpsychiatr, 31(2), 74–83.

Howell KK, Lynch ME, Platzman KA, Smith GH, Coles CD (2006). Prenatal alcohol exposure and ability, academic achievement, and school functioning in adolescence: a longitudinal follow-up. J Pediatr Psychol 31: 116–126. [PubMed: 15829611]

Hoyme HE, Kalberg WO, Elliott AJ, et al. (2016). Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders. Pediatrics. 138(2):e20154256 [PubMed: 27464676]

IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version, 24.0. Armonk, NY: IBM Corp.

Johnson S, Moyer CL, Klug MG, & Burd L (2018). Comparison of alcohol-related neurodevelopmental disorders and neurodevelopmental disorders associated with prenatal alcohol exposure criteria. J. Dev Behav Pediatr 39, 163–167. [PubMed: 29120886]

Kable JA, & Coles CD (2018) Evidence supporting the internal validity of the proposed ND-PAE disorder. Child Psychiatry Hum Dev 49 (2), 163–175. [PubMed: 28634776]

Kable JA, Coles CD, & the CIFASD (2017) Prefrontal cortical response in children with prenatal alcohol-related neurodevelopmental impairment: A functional near-infrared spectroscopy study. Clinical Neurophysiology, 128 (11), 2099–2109. [PubMed: 28914230]

Kable JA, O'Connor MJ, Olson HC, Paley B, Mattson SN, Anderson SM & Riley EP (2016) Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE): Proposed DSM-5 diagnosis. Child Psychiatry Hum Dev, 47, 335–346. [PubMed: 26202432]

Khoury JE, Milligan K, & Girard TA (2015) Executive Functioning in Children and Adolescents prenatally exposed to Alcohol" A Meta-Analytic Review. Neuropsychol Rev, 25, 149–170. [PubMed: 26037669]

King G, & Zeng L (2001) Logistic regression in rare events data. Political Analysis Seminar 2001: 9 (2), 137–163.

Kodituwakku PW (2007) Defining the behavioral phenotype in children with fetal alcohol spectrum disorders: A review. Neurosci Biobehav Rev, 31 (2), 192–201. [PubMed: 16930704]

Korkman M, Kirk U, Kemp S (2007). NEPSY-II. San Antonio, Texas: Pearson Assessment.

Matton SN, Roesch SC, Glass L, Deweese BN, Coles CD, Kable JA, May PA, Kalberg WO, Sowell ER, Adnams CM, Jones KL, Riley EP, and the CIFASD (2013). Further Development of a Neurobehavioral Profile of Fetal Alcohol Spectrum Disorders. Alcohol Clin Exp Res; 37(3): 517–528. [PubMed: 22974253]

Mattson SN, Riley EP (2011). The quest for a neurobehavioral profile of heavy prenatal alcohol exposure. Alcohol Res Health 34: 51–55. [PubMed: 23580041]

May PA, Chambers CD, Kalberg WO, Zellner J, Feldman H, Buckley D, Kopald D, Hasken JM, Ronghui X, Honerkamp-Smith G, Taras H, Manning MA, Robinson LK, Adam MP, Abdul-Rahman O, Vaux K, Jewett T, Elliott AJ, Kable JA, Akshoomoff N, Falk D, Arroyo JA, Hereld D, Riley EP, Charness ME, Coles CD, Warren KR, Jones KL, Hoyme E (2018). Prevalence of fetal alcohol spectrum disorders in 4 US communities. Journal of American Medical Association; 319(5):474–482. doi:10.1001/jama.2017.21896

McLennan JD, & Braunberger P (2017) A critique of the New Canadian Fetal Alcohol Spectrum Disorder Guideline. J Can Acad Child Adolesc Psychiatry, 26 (3), 179–183. [PubMed: 29056979]

Mohamed Z, Carlisle ACS, Livesey AC, & Mjkherjee RAS (2019) Comparisons of the BRIEF parent report and neuropsychological clinical tests of executive function in Fetal Alcohol Spectrum Disorders: Data from the UK nation specialist Clinic. Child Neuropsychology, 25 (5), 648–663. [PubMed: 30251596]

Rasmussen C, Tamana S, Baugh L, Andrew G, Tough S, Zwaigenbaum L (2013) Neuropsychological impairments on the NEPSY-II among children with FASD. Child Neuropsychol 19:337–349. [PubMed: 22384972]

Riniolo T (1999) Using a Large Control Group for Statistical Comparison: Evaluation of a Between-Groups Median Test. The Journal of Experimental Education, 68(1), 75–88. Retrieved from http://www.jstor.org/stable/20152616

Schore AN (2017) All our sons: The developmental neurobiology and neuroendocrinology of boys at risk. Infant Mental Health J. 38, 15–52.

Sobell LC, Agrawal S, Annis H, Ayala-Velazquez H, Echeverria L, Leo GI, Rybakowski JK, Sndahl C, Saunders B, Thomas S, & Zioikowski M (2001) Cross-cultural evaluation of two drinking assessment instruments: alcohol timeline followback and inventory of drinking situations. Substance Use & Misuse 36(3), 313–331. [PubMed: 11325169]

Sparrow AS, Cicchetti DV, Balla DA (2005). Vineland Adaptive Behavior Scales – Second Edition. Bloomington, Minnesota: Pearson Assessment

Stratton K, Howe C, & Battaglia F (Eds) (1996) Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment, Washington, DC, National Academy Press.

Streissguth AP, Barr HM, Sampson PD (1990) Moderate prenatal alcohol exposure: Effects on child IQ and learning problems at age 7 ½ years. Alcohol Clin Exp Res 14:662–669. [PubMed: 2264594]

Streissguth AP, Barr HM, Bookstein FL, Sampson PD, Olson HC (1999). The long-term neurocognitive consequences of prenatal alcohol exposure: a 14 year study. Psychol Sc 10:186–190.

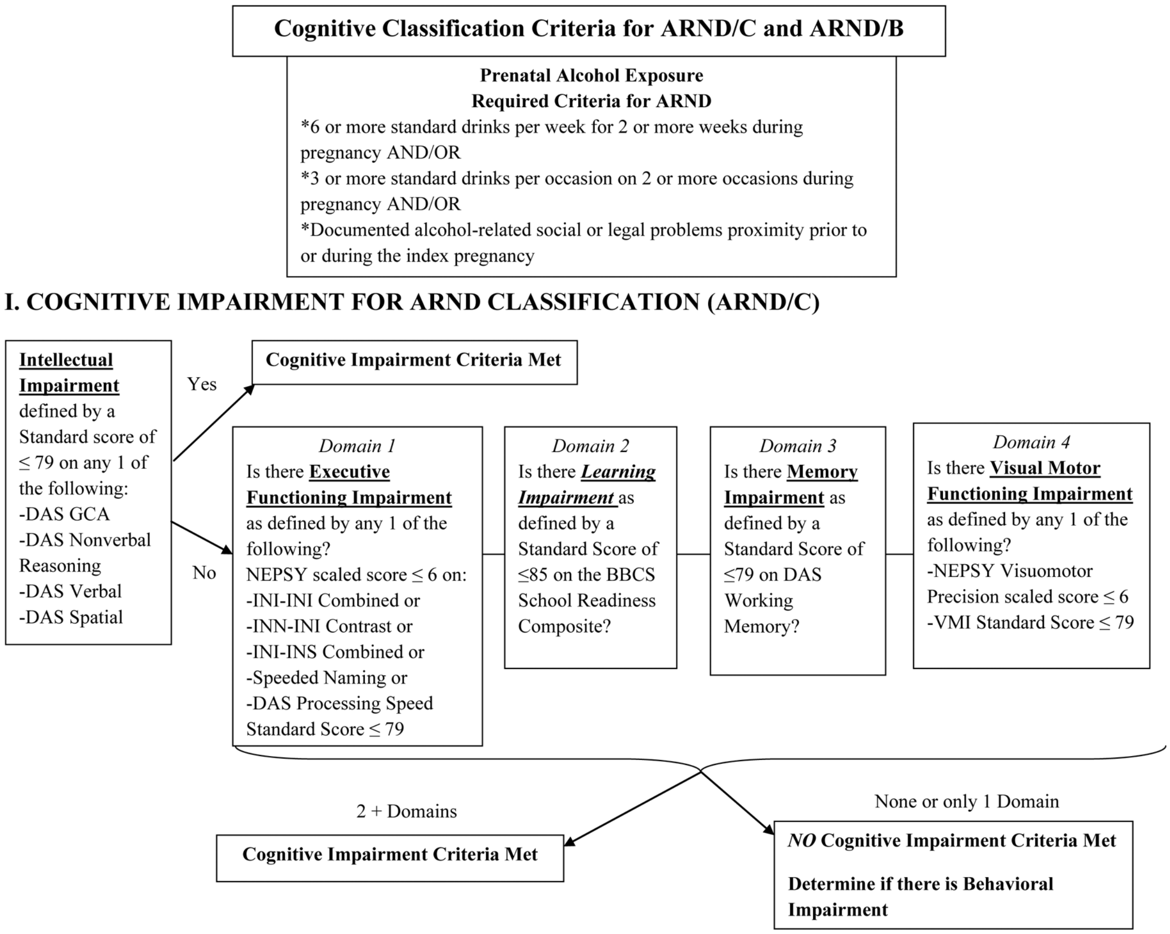
Ten Eycke KD, & Dewey D (2015) Parent-report and performance-based measures of executive function assess different constructs. Child Neuropsychology. 28 (8), 1–18.

Ware AL, O'Brien JW, Crocker N, Deweese H, Roesch SC, Coles CD, Kable JA, May PA, Kalberg WO, Sowell ER, Jones KL, Riley EP, Mattson SN, and the CIFASD (2014). The effects of prenatal alcohol exposure and attention-deficit/hyperactivity disorder on psychopathology and behavior. Alcohol Clin Exp Res: 27(3): 507–516.

Ware AL, Crocker N, O'Brien JW, Deweese BN, Roesch SC, Coles CD, Kable JA, May PA, Kalberg WO, Sowell ER, Jones KL, Riley EP, Mattson SN: CIFASD. Executive function predicts adaptive behavior in children with histories of heavy prenatal alcohol exposure and attention-deficit/hyperactivity disorder. Alcohol Clin Exp Res. 2012;36(8):1431–1441. Doi:10.1111/j.1530-0277.2011.01718.x. [PubMed: 22587709]

Ware AL, Glass L, Crocker N, Deweese BN, Coles CD, Kable JA, May PA, Kalberg WO, Sowell ER, Jones KL, Riley EP, Mattson SN, and the CIFASD (2014). Effects of prenatal alcohol exposure and attention-deficit/hyperactivity disorder on adaptive functioning. Alcoholism: Clinical and Experimental Research, 38 (5), 1439–1447. [PubMed: 24655090]

Whaley SE, O'Connor MJ, Gunderson B. (2001) Comparison of the adaptive functioning of children prenatally exposed to alcohol to a nonexposed clinical sample. Alcohol Clin Exp Res, 25, 1018–102. [PubMed: 11505027]


Cognitive Classification Criteria for ARND/C and ARND/B
Prenatal Alcohol Exposure
Required Criteria for ARND
*6 or more standard drinks per week for 2 or more weeks during pregnancy AND/OR
*3 or more standard drinks per occasion on 2 or more occasions during pregnancy AND/OR
*Documented alcohol-related social or legal problems proximity prior to or during the index pregnancy
I. COGNITIVE IMPAIRMENT FOR ARND CLASSIFICATION (ARND/C)
Intellectual Impairment defined by a Standard score of ≤ 79 on any 1 of the following: -DAS GCA -DAS Nonverbal Reasoning -DAS Verbal -DAS Spatial
Yes
Cognitive Impairment Criteria Met
No
Domain 1
Is there Executive Functioning Impairment as defined by any 1 of the following? NEPSY scaled score ≤ 6 on: -INI-INI Combined or -INN-INI Contrast or -INI-INS Combined or -Speeded Naming or -DAS Processing Speed Standard Score ≤ 79
Domain 2
Is there Learning Impairment as defined by a Standard Score of ≤85 on the BBCS School Readiness Composite?
Domain 3
Is there Memory Impairment as defined by a Standard Score of ≤79 on DAS Working Memory?
Domain 4
Is there Visual Motor Functioning Impairment as defined by any 1 of the following? -NEPSY Visuomotor Precision scaled score ≤ 6 -VMI Standard Score ≤ 79
2 + Domains
Cognitive Impairment Criteria Met
None or only 1 Domain
NO Cognitive Impairment Criteria Met
Determine if there is Behavioral Impairment

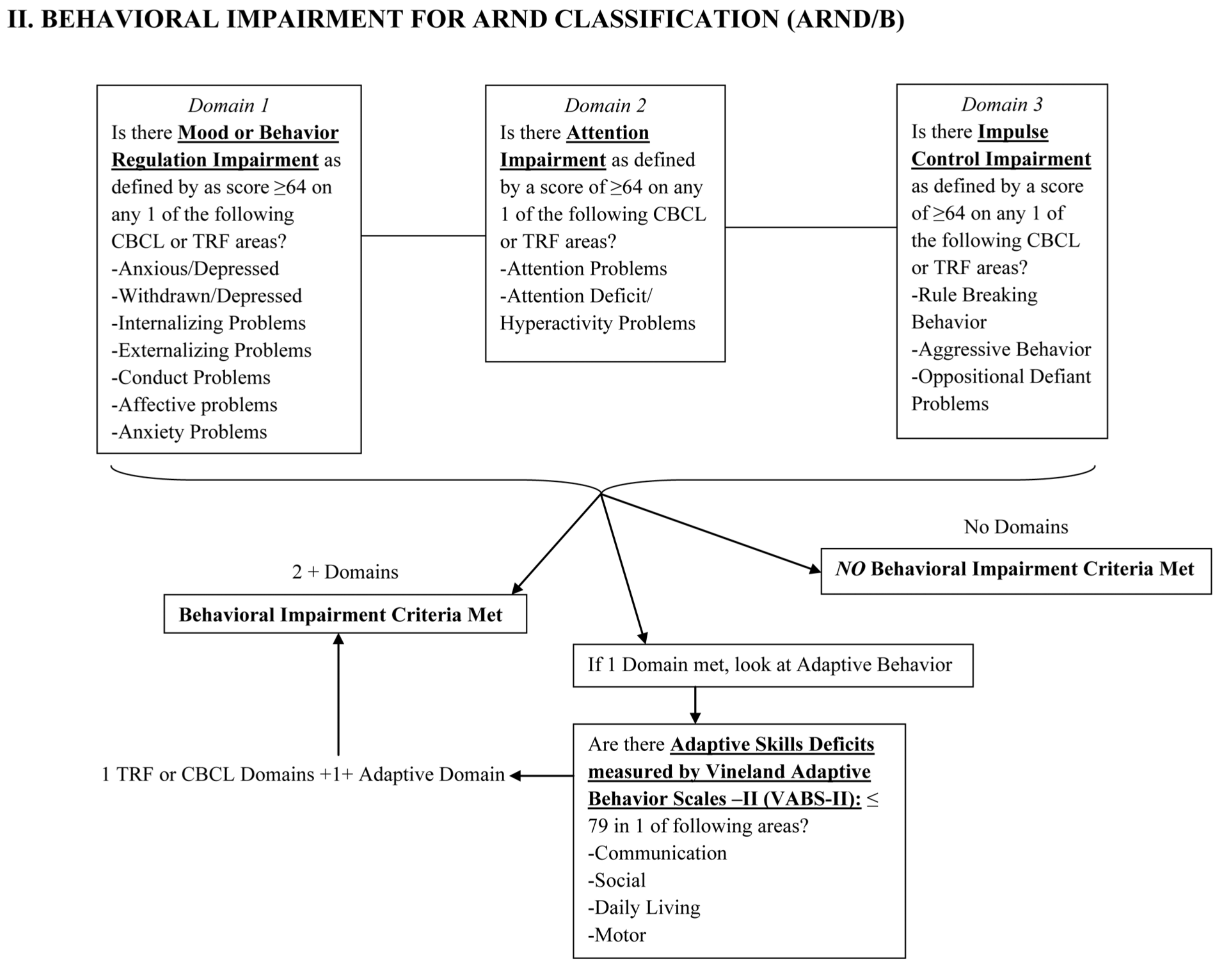



**Figure 1:**

Cognitive and Behavioral Classification Criteria for ARND/ and ARND/B

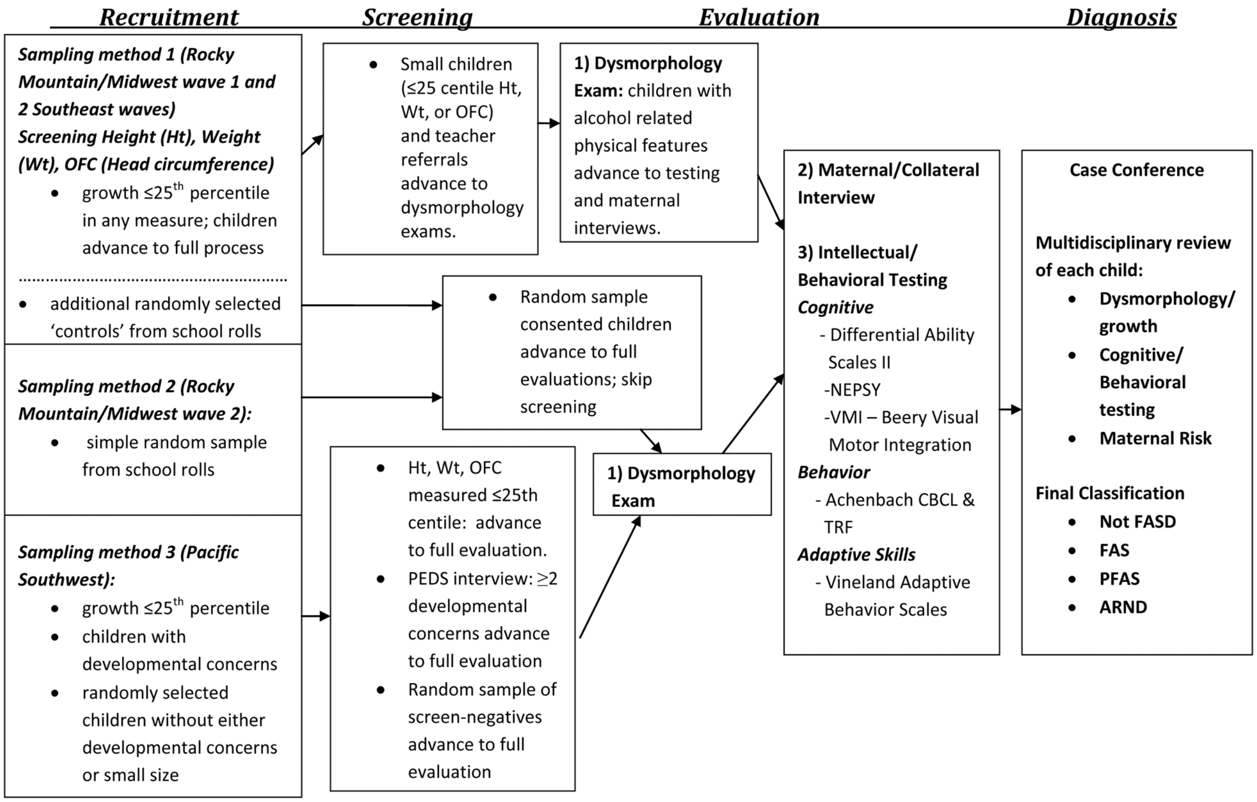



**Figure 2:**

Active Case-Ascertainment Methods Employed by Collaborative on Fetal Alcohol Spectrum Prevalence (Co FASP)

## Table 1:

ARND in Comparison to Contrast Groups on Variables Considered for Multinomial Regressions.

(Notes: ARND groups are in shaded area. Contrast groups are not compared to each other; Statistics show comparisons to ARND groups only. Group 1 is subset of the Group from which Group 2 was randomly selected. Comparisons are made without substitution for missing data.)

Table 1a: Demographic Characteristics of Caregivers

| | ARND/ Behavior | ARND/ Cognitive | 1. Alcohol Criterion Met/Not FASD | 2. Any Alcohol Use Random Sample | 3. High Risk Random Sample | 4. Low Risk Random Sample |
|---|---|---|---|---|---|---|
| **Measure** | **(n=47)** | **(n=44)** | **(N=49)** | **(N=99)** | **(N=82)** | **(n=88)** |
| Caregiver Age/Yr-M(sd) | 37.58 (8.42) | 35.61 (10.25) | 35.57 (6.53) | 36.59 (5.95) | 36.84 (6.4) | 35.53 (5.59) |
| | $F_{(1,88)}$=1.01,p=.319, NS | | $F_{(2,136)}$ <1, NS | $F_{(2,187)}$ =1.67, NS | $F_{(2,168)}$=1.45, NS | $F_{(2,160)}$=1.11, NS |
| Maternal Race % | | (n=43) | | (n=98) | (n=59) | (n=73) |
| White | 74.5% | 69.8% | 83.7% | 82.7% | 73.8% | 83.6% |
| African/American | 2.1% | 25.6% | 2.0% | 4.1% | 6.3% | 5.5% |
| Native | 10.6% | 4.7% | 2.0% | 3.1% | 1.3% | 2.7% |
| American/Alaskan | | | | | | |
| Asian/Pacific | 4.3% | 0 | 8.2% | 4.1% | 15% | 2.7% |
| Multiracial | 8.5% | 0 | 4.1% | 6.1% | 3.8% | 5.5% |
| | $X^2_{(4)}$=15.86,p<.003 | | $X^2_{(8)}$ =28.67, p<.000 | $X^2_{(8)}$ =28.52; p<.000 | $X^2_{(8)}$ =32.99; p<.000 | $X^2_{(8)}$ =24.26; p<.000 |
| Maternal Education % | | | | | (n=80) | (n=73) |
| Less than HS | 8.6% | 16.3% | 12.3% | 4.0% | 23.8% | 6.8% |
| High School/GED | 14.9% | 16.3% | 12.2% | 14.1% | 10% | 17.8% |
| Post High School | 44.7% | 34.9% | 34.7% | 34.3% | 26.3% | 32.9% |
| College Graduate | 19.1% | 25.6% | 24.5% | 19.2% | 26.3% | 23.3% |
| Graduate/Professional | 12.7% | 7% | 16.4% | 28.3% | 13.8% | 19.1% |
| | $X^2_{(6)}$=4.86,p=.561, NS | | $X^2_{(14)}$ =28.67, p<.000 | $X^2_{(14)}$ =21.9, p<.04 | $X^2_{(14)}$ =14.29, NS | $X^2_{(14)}$ =12.57, NS |
| Marital Status % | | | | | (n=80) | (n=73) |
| Married/Cohabiting | 63% | 60.5% | 57.2% | 72.7% | 82.5% | 78.3% |
| Widowed/Divorced/ Separated | 28.2% | 16.3% | 14.3% | 18.2% | 12.5% | 13.8% |
| Single/Never Married | 6.5% | 20.9% | 26.5% | 9.1% | 5% | 6.8% |
| | $X^2_{(6)}$=9.31,p=.157, NS | | $X^2_{(12)}$ =15.92, NS | $X^2_{(12)}$ =24.51, p<.02 | $X^2_{(12)}$ =23.34, p<.025 | $X^2_{(12)}$ =18.33, NS |
| **Yearly Family Income in dollars%** | | | | (n=93) | (n=71) | (n=67) |

| Measure | ARND/ Behavior (n=47) | ARND/ Cognitive (n=44) | 1. Alcohol Criterion Met/Not FASD (N=49) | 2. Any Alcohol Use Random Sample (N=99) | 3. High Risk Random Sample (N=82) | 4. Low Risk Random Sample (n=88) |
|---|---|---|---|---|---|---|
| <15,000 | 10.8% | 12.5% | 11.9% | 7.5% | 11.3% | 9% |
| 15-24,999 | 13.5% | 15.6% | 9.6% | 5.4% | 9.8% | 4.5% |
| 25-49,999 | 27% | 28.2% | 14.% | 18.3% | 18.3% | 26.8% |
| 50-75,000 | 10.8% | 15.6% | 21.4% | 17.2% | 16.9% | 13.4% |
| >75,000 | 37.8% | 28.1% | 42.9% | 51.6% | 43.7% | 46.3% |
| | $X^2_{(7)}$=0.91,p=.996, NS | | $X^2_{(14)}$ =6.85, NS | $X^2_{(14)}$ =16.79, NS | $X^2_{(14)}$ =13.43, NS | $X^2_{(14)}$ =10.57, NS |
| Cigarette Use in Pregnancy (%) | 44.4% | 44.2% | 32.7% | 21.2% | 7.5% | 8.3% |
| | $X^2_{(1)}$=0.05, p=.825, NS | | $X^2_{(2)}$=1.78, p=.4 | $X^2_{(2)}$=11.42, p<.003[1] | $X^2_{(2)}$=28.97, p<.000 | $X^2_{(2)}$=25.37, p<.000 |
| Marijuana Use in Pregnancy (%) | 15.2% | 32.5% | 20.4% | 9.2% | 6.3% | 4.1% |
| | $X^2_{(1)}$=6.85,p=.009 | | $X^2_{(2)}$=7.33, p=.39 | $X^2_{(2)}$=12.57, p<.01[#] | $X^2_{(2)}$=28.97, p<.000[*] | $X^2_{(2)}$=16.86, p<.000[*] |

[#] significantly different from ARND/C

[*] Significantly different than both other groups

**Table 1b:**

Physical Characteristics of Children

| | ARND/ Behavior | ARND/ Cognitive | 1. Alcohol Criterion Met/Not FASD | 2. Any Alcohol Use Random Sample | 3. High Risk Random Sample | 4. Low Risk Random Sample |
|---|---|---|---|---|---|---|
| **Measure** | (n=47) | (n=44) | (n=49) | (n=99) | (n=82) | (n=88) |
| Child Sex (%male) | 61.7% | 68.2% | 44.9% | 56.6% | 45.1% | 54.5% |
| | $X^2_{(1)}$=0.42,p=.518, NS | | $X^2_{(2)}$ =5.58, p=.06 | $X^2_{(2)}$ =1.75, NS | $X^2_{(2)}$ =7.17, p<.03 * | $X^2_{(2)}$ =2.36, NS |
| Gestational | (n=45) | (n=43) | | | (n=80) | (n=73) |
| Age/weeks | 38.79 (2.63) | 37.59 (3.69) | 38.89 (1.58)# | 39.16 (1.73)# | 38.98 (2.57) # | 38.90 (2.4)# |
| | $F_{(1,84)}$=3.01,p=.086, NS | | $F_{(2,132)}$=3.19, p<.04 | $F_{(2,184)}$=6.16, p<.003 | $F_{(2,165)}$=3.55, p<.03 | $F_{(2,158)}$=3.25, p<.04 |
| Birthweight/gm | (n=44) | (n=42) | | (n=98) | (n=75) | (n=73) |
| | 3264.25 (785.48) | 2912.28 (816.43) | 3302.0# (504.6) | 3352.27# (494.9) | 3168.58# (743.9) | 3241.03# (595.49) |
| | $F_{(1,84)}$=4,15,p=.045 | | $F_{(2,134)}$= 4.03, p<.02 | $F_{(2,181)}$= 6.71, p<.002 | $F_{(2,158)}$= 2.41, P=.09 | $F_{(2,156)}$= 3.47, p<.03 |
| Current Height Percentile | 55.49 (25.42) | 48.91 (32.0) | 44.06 (26.7) | 50.94 (29.05) | 45.16 (29.18) | 64.39 (25.94)# |
| | $F_{(1,88)}$=1.18,p=.281, NS | | $F_{(2,139)}$=2.00, NS | $F_{(2,186)}$<1,NS | $F_{(2,169)}$=1.9, NS | $F_{(2,175)}$=4.95, p<.008 |
| Current Weight Percentile | 56.72 (28.76) | 54.14 (33.68) | 48.90 (28.56) | 52.70 (28.73) | 51.28 (28.3) | 67.11 (25.26) * |
| | $F_{(1,88)}$=2.89,p=.093 | | $F_{(2,139)}$<1, NS | $F_{(2,186)}$<1,NS | $F_{(2,169)}$<1,NS | $F_{(2,175)}$=3.82, p<.02 |
| Current Head Circumference Percentile | 57.40 (29.94) | 43.28 (35.89) | 50.61(29.34) | 54.24 (31.56) | 38.55 (30.59) + | 65.78 (23.6)# |
| | $F_{(1,89)}$=4.72,p=.03 | | $F_{(2,139)}$=2.23, NS | $F_{(2,186)}$=2.45, NS | $F_{(2,169)}$=5.32, P<.006 | $F_{(2,175)}$=9.75, p<.000 |
| PFL 1,2-left Percentile | 27.63 (14.96) | 32.86 (14.21) | 23.08 (14.23) | 26.02 (15.2) | 25.32 (15.30)# | 32.73 (15.84) |
| | $F_{(1,88)}$=2.89,p=.093 | | $F_{(2,136)}$=5.29, p<.006 | $F_{(2,186)}$=3.22, p<.05 | $F_{(2,169)}$=3.66, p<.03 | $F_{(2,175)}$<1, NS |
| PFL 1,2-Right Percentile | 29.26 (15.37) | 33.36 (13.29) | 24.61 (13.61) | 26.79 (15.3) | 26.28 (15.16)# | 33.13 (15.95) |
| | $F_{(1,88)}$=1.83,p=.18 | | $F_{(2,136)}$=4.47, P<.013 | $F_{(2,175)}$=2.98, p=.053 | $F_{(2,169)}$=3.31, p<.04 | $F_{(2,175)}$<1, NS |
| Philtrum Code 2 | 2.72 (0.649) | 2.95 (0.785) | 2.92 (0.64) | 2.93 (0.81) | 2.95 (0.52) | 2.98 (0.71) |
| | $X^2_{(4)}$=5.41,p=.293, NS | | $F_{(2,136)}$=1.48,NS | $F_{(2,186)}$=1.37, NS | $F_{(2,169)}$=2.25, NS | $F_{(2,175)}$=2.07, NS |
| Vermilion Code 2 | 2.85 (0.691) | 2.79 (0.638) | 2.94 (0.719) | 2.98 (0.78) | 2.99 (0.71) | 2.91 (0.74) |
| | $X^2_{(3)}$=0.69,p=.877, NS | | $F_{(2,136)}$<1, NS | $F_{(2,186)}$=1.18, NS | $F_{(2,169)}$=1.33, NS | $F_{(2,175)}$<1, NS |

[*] Significantly different than both other groups

[#] significantly different from ARND/C

[+] Significantly different from ARND/B

[1] Palprebral fissure length

[2] Considered indicative of prenatal alcohol exposure.

**Table 1c:**

Cognitive and Academic Outcomes of Measures Included in Multinomial Regression

| | **ARND/ Behavior** | **ARND/ Cognitive** | **1. Alcohol Criterion Met/Not FASD** | **2. Any Alcohol Use Random Sample** | **3. High Risk Random Sample** | **4. Low Risk Random Sample** |
|---|---|---|---|---|---|---|
| **Measure** | (n=47) | (n=44) | (n=50) | (N=99) | (n=82) | (n=88) |
| ABC[1] M (SD) | (n-=40) 93.78 (9.54) | (n=36) 95.78 (19.24) | 102.70 (11.34) $^{*}$ | (n=78) 100.92(11.8) $^{*}$ | (n=77) 101.26 (11.44) $^{*}$ | (n=62) 106.77 (12.14) $^{*}$ |
| | $F_{(1,79)}=0.34, p=.561$, NS | | $F_{(2,122)}=5.85, p<.004$ | $F_{(2,151)}=4.30, p<.015$ | $F_{(2,150)}=4.84$ $p<.009$ | $F_{(2,135)}=13.32, p<.000$ |
| DAS II GCA[2] | 103.60 (10.23) | 86.79 (10.19) | 105.12 (9.46)$^{\#}$ | 104.8 (9.98)$^{\#}$ | 100.32 (10.07)$^{\#}$ | 107.44 (11.71)$^{\#}$ |
| | $F_{(1,88)}=60.87, p<.000$ | | $F_{(2,136)}=46.67, p<.000$ | $F_{(2,186)}=50.9, p<.000$ | $F_{(2,169)}=12.43, p<.000$ | $F_{(2,175)}=52.35, p<.000$ |
| DAS-II Verbal | 103.4 (12/29) | 89.88 (1289) | 104.49 (12.67) $^{\#}$ | 105.40 (11.42) $^{\#}$ | 101.48 (14.76) $^{\#}$ | 108.19 (14.5) $^{\#}$ |
| | $F_{(1,88)}=22.24, p<.000$ | | $F_{(2,136)}=16.78, p<.000$ | $F_{(2,186)}=23.96, p<.000$ | $F_{(2,169)}=26.01, p<.000$ | $F_{(2,175)}=24.66, p<.000$ |
| DAS-II NonVerbal | 101.38 (11.32) | 86.16 (10.75) | 103.20 (8.82) $^{\#}$ | 101.55 (10.32) $^{\#}$ | 98.49 (10.43) $^{\#}$ | 103.89 (12.58) $^{\#}$ |
| | $F_{(1,88)}=42.59, p<.000$ | | $F_{(2,136)}=36.75, p<.000$ | $F_{(2,186)}=34.28, p<.000$ | $F_{(2,169)}=12.43, p<.000$ | $F_{(2,175)}=33.75, p<.000$ |
| DAS-II Spatial | 104.43 (9.29) | 90.42 (11.29) | 104.88 (9.29) $^{\#}$ | 105.1 (10.72) $^{\#}$ | 100.43 (9.78) $^{\#}$ | 106.52 (9.85) $^{\#}$ |
| | $F_{(1,88)}=39.76, p<.000$ | | $F_{(2,136)}=29.48$ $p<.000$ | $F_{(2,186)}=30.82, p<.000$ | $F_{(2,169)}=23.09, p<.000$ | $F_{(2,175)}=37.73, p<.000$ |
| Bracken[3] School Readiness | 110.76 (9.50) | 93.81 (16.46) | 111.74 (10.23) $^{\#}$ | 113.52 (10.66) $^{\#}$ | 106.27 (14.79) $^{\#}$ | 111.67 (9.73) $^{\#}$ |
| | $F_{(1,79)}=33.74, p<.000$ | | $F_{(2,125)}=27.05, p<.000$ | $F_{(2,177)}=37.67, p<.000$ | $F_{(2,166)}=15.71, p<.000$ | $F_{(2,166)}=33.51, p<.000$ |
| INI[5] inhibition | (n=47) | (n=42) | | (n=57) | (N=32) | (n=54) |
| Combined (N=109) | 9.87 (2.97)) | 7.59 (3.57) | 10.04 (3.58) $^{\#}$ | 9.79 (3.63) $^{\#}$ | 9.03 (3.29) $^{\#}$ | 9.04 (3.24) $^{\#}$ |
| | $F_{(1,87)}=43.65, p<.000$ | | $F_{(2,77)}=33.05, p<.000$ | $F_{(2,109)}=16.58, p<.000$ | $F_{(2,84)}=14.71, p<.000$ | $F_{(2,106)}=15.36, p<.000$ |
| INS[5]Switching | (n=23) | (n=32) | 9.20 (3.16) )$^{\#}$ | 9.72 (3.29) )$^{\#}$ | 8.47 (3.37) )$^{\#}$ | 8.94 (2.49)$^{\#}$ |
| Combined (N=80) | 9.26 (2.93) | 6.63 (2.84 | | | | |
| | $F_{(1,53)}=11.25, p<.001$ | | $F_{(2,77)}=7.39, p<.001$ | $F_{(2,109)}=10.64, p<.000$ | $F_{(2,84)}=5.54, p<.006$ | $F_{(2,106)}=9.19, p<.000$ |
| Visumotor[6] Precision | 10.06 (2.92) | 6.75 (2.17) | 11.02 (3.48) $^{\#}$ | 10.16 (3.59) $^{\#}$ | 10.11 (3.39) $^{\#}$ | 10.10 (3.23) $^{\#}$ |
| | $F_{(1,89)}=37.33, p<.000$ | | $F_{(2,137)}=26.68, p<.000$ | $F_{(2,187)}=19.49, p<.000$ | $F_{(2,170)}=20.36, p<.000$ | $F_{(2,176)}=21.66, p<.000$ |

$^{*}$Significantly different than both other groups

$^{+}$Significantly different from ARND/B

[#] significantly different from ARND/C

[1] Adaptive Behavior Composite, Vineland Adaptive Behavior Scales, 2nd Edition. (M=100, sd=15)

[2] General Cognitive Ability Standard Score on the Differential Ability Scales, 2nd Edition (M=100, sd=15)

[3] Bracken Basic Concepts Scale, 3rd Edition, Standard Score (M=100, sd=15)

[4] Bracken Basic Concepts Scale, 3rd Edition, Scaled Score (M=10, sd=3)

[5] NEPSY Inhibition/Attention Subtest (n=80) (M=10, sd=3)

[6] Scaled score (M=10, sd=3)

**Table 1d:**

Emotional/Behavioral Outcomes of Measures in Children: Child Behavior Checklist[1]

| Measure | ARND/ Behavior | ARND/ Cognitive | 1. Alcohol Criterion Met/Not FASD | 2. Any Alcohol Use Random Sample | 3. High Risk Random Sample | 4. Low Risk Random Sample |
|---|---|---|---|---|---|---|
| | (n=46) | (n=42) | (n=50) | (n=97) | (N=80) | (n=70) |
| CBCL[1] Internalizing T | 57.37 (10.57) | 56.26 (11.49) | 50.46 (7.32)* | 49.12 (9.90)* | 51.33 (10.37)* | 47.84 (8.47)* |
| | FF$_{(1,86)}$=0.222,p=.639, NS | | $F_{(2,133)}$=6.63, p<.002 | $F_{(2,182)}$=12.72, p<.000 | $F_{(2,165)}$=5.67, p<.004 | $F_{(2,155)}$=16.03, p<.000 |
| CBCL! Externalizing T | 62.39 (9.12) | 58.21 (12.61) | 48.23 (8.87)* | 49.61 (10.22)* | 52.69 (9.08)* | 47.39 (9.61)* |
| | F$_{(1,86)}$=3.21,p=.077 | | $F_{(2,133)}$=23.73 p<.000 | $F_{(2,182)}$=25.8, p<.000 | $F_{(2,165)}$=14.14, p<.000 | $F_{(2,155)}$=32.55, p<.000 |
| CBCL[1] Total T (N=136) | 62.65 (8.04) | 59.31 (12.32) | 49.90 (6.91)* | 49.91 (10.03)* | 53.16 (10.07)* | 47.39 (8.92)* |
| | F$_{(1,86)}$=2.31,p=.132 | | $F_{(2,133)}$=24.05, p<.0 00 | $F_{(2,182)}$=28.97, p<.000 | $F_{(2,165)}$=13.75, p<.000 | $F_{(2,155)}$=41.07, p<.000 |
| CBCL[1] Attention Problems | 63.59 (9.21) | 63.12 (12.21) | 53.98 (4.25)* | 54.84 (7.17)* | 56.71 (7.25)* | 53.34 (5.14)* |
| | F$_{(1,86)}$=.042, p=.839, NS | | $F_{(2,133)}$=16.91,p<.000 | $F_{(2,182)}$=20.57, p<.000 | $F_{(2,165)}$=10.89, p<.000 | $F_{(2,155)}$=25.84, p<.000 |
| CBCL[1] Rule- Breaking | 58.98 (7.50) | 58.24 (8.69) | 53.02 (3.87)* | 53.96 (5.37)* | 54.83 (5.15)* | 53.09 (4.74)* |
| | F$_{(1,86)}$=.184,p=.669, NS | | $F_{(2,133)}$=10.37, p<.000 | $F_{(2,182)}$=11.02, p<.000 | $F_{(2,165)}$=6.59, p<.002 | $F_{(2,155)}$=13.04, p<.000 |
| CBCL[1] Aggression | 64.63 (9.09) | 61.60 (11.36) | 53.10 (4.74)* | 54.35 (7.95)* | 55.58 (6.68)* | 53.09 (4.78)* |
| | F$_{(1, 86)}$=1.93,p=.168 | | $F_{(2,133)}$=22.17, p<.000 | $F_{(2,182)}$=22.93, p<.000 | $F_{(2,165)}$=17.28, p<.000 | $F_{(2,155)}$=30.57, p<.000 |

* Significantly Different than both other groups

[1] Achenbach Child Behavior Checklist. Scores are T-scores with a mean of 50 and a standard deviation of 10.

**Table 1e:**

Emotional/Behavioral Outcomes of Measures in Children: Teacher Report Form[1]

| Measure | ARND/ Behavior | ARND/ Cognitive | 1. Alcohol Criterion Met/Not FASD | 2. Any Alcohol Use | 3. High Risk Random Sample | 4. Low Risk Random Sample |
|---|---|---|---|---|---|---|
| | (n=40) | (n=41) | (n=49) | (n=90) | (N=67) | (n=79) |
| TRF[1] Internalizing T | 50.07 (9.92) | 53.80 (11.91) | 43.06 (7.04)* | 44.12 (8.33)* | 46.63 (10.29)+ | 44.72 (7.39)* |
| | $F(_{1,79})=2.34, p=.130$, NS | | $F_{(2,127)}=14.42, p<.000$ | $F_{(2,168)}=15.55, p<.000$ | $F_{(2,145)}=5.82, p<.004$ | $F_{(2,157)}=13.56, p<.000$ |
| TFR[1] Externalizing T | 56.70 (7.79) | 55.90 (11.70) | 47.98 (6.34)* | 47.64 (8.13)* | 50.69 (9.17)+ | 47.84 (7.29)* |
| | $F(_{1,79})=0.130, p=.720$, NS | | $F_{(2,127)}=13.76, p<.000$ | $F_{(2,168)}=19.6, p<.000$ | $F_{(2,145)}=6.32, p<.002$ | $F_{(2,157)}=18.82, p<.000$ |
| TRF[1] Total T (N=136) | 56.85 (7.79) | 57.63 (12.32) | 44.73 (8.14)* | 45.346 (10.1)* | 49.39 (10.75)* | 46.03 (8.77)* |
| | $F(_{1,79})=0.102, p=.751$, NS | | $F_{(2,127)}=23.65, p<.000$ | $F_{(2,168)}=26.6, p<.000$ | $F_{(2,145)}=9.53, p<.000$ | $F_{(2,157)}=25.27, p<.000$ |
| TRF[1] Attention Problems | 60.63 (9.16) | 59.54 (9.01) | 51.92 (3.10)* | 52.77 (4.39)* | 54.57 (6.96)* | 52.65 (4.42)* |
| | $F(_{1,79})=0.291, p=.591$, NS | | $F_{(2,127)}=18.69, p<.000$ | $F_{(2,168)}=23.47, p<.000$ | $F_{(2,145)}=8.47, p<.000$ | $F_{(2,157)}=21.77, p<.000$ |
| TRF[1] Rule- Breaking | 57.85 (6.48) | 57.20 (7.15) | 52.22 (3.70)* | 52.82 (4.88)* | 54.0 (5.47)* | 51.94 (3.99)* |
| | $F_{(1,79)}=0.186, p=.667$, NS | | $F_{(2,127)}=12.65$ $p<.000$ | $F_{(2,168)}=13.74, p<.000$ | $F_{(2,145)}=5.92, p<.003$ | $F_{(2,157)}=20.01$ $p<.000$ |
| TRF[1] Aggression | 57.60 (5.72) | 58.76 (10.06) | 51.82 (3.11)* | 52.26 (5.93)* | 54.13 (7.02)* | 52.51 (5.24)* |
| | $F(_{1,79})=0.402, p=.528$, NS | | $F_{(2,127)}=13.88$ $p<.000$ | $F_{(2,127)}=13.88$ $p<.000$ | $F_{(2,145)}=5.32, p<.006$ | $F_{(2,157)}=13.85$ $p<.000$ |

* Significantly Different than both other groups

+ Significantly lower than ARND/C

1 Achenbach Teacher Report Form (TRF). Scores are T-scores with a mean of 50 and a standard deviation of 15.

**Table 2:**

Main Effects Model: Likelihood Ratio Tests for First Group: ARND and Alcohol Criterion Met (N=140)

| | Model Fitting Criteria | Likelihood Ratio Tests | | |
|---|---|---|---|---|
| **Effect** | **−2 Log Likelihood of Reduced Model** | **Chi Square** | **df** | **Significance** |
| Intercept | 80.00 | .000 | 0 | - |
| GCA Standard Score | 95.49 | 19.84 | 2 | .000 |
| NEPSY Visuomotor Precision scaled score | 99.36 | 23.71 | 2 | .000 |
| CBCL Total Problems | 126.02 | 48.25 | 2 | .000 |
| TRF Total Problems | 90.17 | 14.52 | 2 | .001 |
| Adaptive Standard Score | 83.24 | 3.23 | 2 | .199 |
| School Readines Standard Score | 86.86 | 6.86 | 2 | .032 |
| Child’s Age | 106.55 | 30.90 | 2 | .000 |
| Child Sex | 85.45 | 9.80 | 2 | .007 |
| Height Percentile | 79.97 | 4.33 | 2 | .115 |
| Racial Category | 111.05 | 35.39 | 8 | .000 |
| SES* | 87.66 | 12.02 | 2 | .002 |

*Socioeconomic Status includes: Mother’s income, Education, and Marital Status;

Model ($X^2_{(26)}$ =226.99, p<.000); Factors that did not contribute significantly to model (that is p>.20), including VMI, Gestational Age, Cigarette use, and Marijuana use, were excluded from this final model.

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**Table 2.1**

Classification of Cases Based on Model (n=138)

| | **Predicted by Model** | | | |
|---|---|---|---|---|
| Observed | Not FASD | ARND/Behavioral | ARND/Cognitive | Percent Correct |
| Not FASD | 41 | 7 | 1 | 83.7% |
| ARND/Behavioral | 5 | 40 | 2 | 86.1% |
| ARND/Cognitive | 1 | 2 | 39 | 92.9% |
| Overall % | 34.1% | 35.5% | 30.4% | 87% |

**Table 3:**

Main Effects Model: Likelihood Ratio Tests for Second Group: ARND and Any Alcohol in Pregnancy (N=190)

| | **Model Fitting Criteria** | **Likelihood Ratio Tests** | | |
|---|---|---|---|---|
| **Effect** | **−2 Log Likelihood of Reduced Model** | **Chi Square** | **df** | **Significance** |
| Intercept | 183.234 | .000 | 0 | - |
| GCA Standard Score | 219.139 | 35.904 | 2 | .000 |
| NEPSY-II Visuomotor Precision scaled score | 195.728 | 12.493 | 2 | .002 |
| CBCL Total Problems | 218.442 | 35.208 | 2 | .000 |
| TRF Total Problems | 195.788 | 12.553 | 2 | .002 |
| Child’s Age | 199.544 | 16.310 | 2 | .000 |
| Racial Category | 202.573 | 19.338 | 8 | .013 |
| Marijuana use in pregnancy | 191.386 | 8.151 | 2 | .017 |
| SES* | 187.504 | 4.270 | 2 | .118 |

*Socioeconomic Status includes: Mother’s income, Education, and Marital Status

Model ($X^2_{(22)}$=184.274; p<.000); Factors that did not contribute significantly to model (that is p>.20), including Adaptive Behavior Composite (ABC); School Readines (BBCS); Child Sex; Height percentile; Gestational age; Cigarette Use in Pregnancy, were excluded from this final model.

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**Table 3.1:**

Classification of Cases Based on Model (N=181)

| | **Predicted by Model** | | | |
|---|---|---|---|---|
| Observed | Not FASD | ARND/Behavioral | ARND/Cognitive | Percent Correct |
| Not FASD | 82 | 7 | 7 | 84.4% |
| ARND/Behavioral | 14 | 31 | 1 | 67.4% |
| ARND/Cognitive | 6 | 3 | 30 | 76.9% |
| Overall % | 56.4% | 22.7% | 21% | 79% |

**Table 4:**

Main Effects Model: Likelihood Ratio Tests for ARND and High Risk Group (N=173)

| | Model Fitting Criteria | Likelihood Ratio Tests | | |
|---|---|---|---|---|
| **Effect** | **−2 Log Likelihood of Reduced Model** | **Chi Square** | **df** | **Significance** |
| Intercept | 153.02 | .000 | 0 | - |
| GCA Standard Score | 164.59 | 11.57 | 2 | .003 |
| NEPSY-II Visuomotor Precision scaled score | 162.95 | 9.93 | 2 | .007 |
| CBCL Total Problems | 160.65 | 7.63 | 2 | .022 |
| TRF Total Problems | 158.76 | 5.74 | 2 | .057 |
| Adaptive Standard Score | 159.50 | 6.48 | 2 | .039 |
| School Readiness Standard Score | 157.85 | 4.83 | 2 | .089 |
| Child's Age | 175.73 | 22.71 | 2 | .000 |
| Child Sex | 184.80 | 5.98 | 2 | .05 |
| Gestational Age | 156.45 | 3.43 | 2 | .180 |
| Racial Category | 177.43 | 24.41 | 8 | .002 |
| Cigarette Use In pregnancy | 165.01 | 11.99 | 2 | .002 |
| Marijuana Use in pregnancy | 159.40 | 6.38 | 2 | .041 |

Model ($X^2_{(30)}$ =184.771; p<.000); Factors that did not contribute significantly to model (that is p>.20), including VMI standard score, Height percentile and SES (Mother's income, Education and Marital Status), were excluded from this final model.

**Table 4.1:**

Classification of Cases Based on Model (n=162)

| | **Predicted by Model** | | | |
|---|---|---|---|---|
| Observed | Not FASD | ARND/Behavioral | ARND/Cognitive | Percent Correct |
| Not FASD | 67 | 5 | 8 | 83.8% |
| ARND/Behavioral | 12 | 32 | 0 | 72.7% |
| ARND/Cognitive | 9 | 0 | 29 | 76.3% |
| Overall % | 54.3% | 22.8% | 22.8% | 79% |

**Table 5:**

Main Effects Model: Likelihood Ratio Tests for ARND and Low Risk Group (N=179)

| | Model Fitting Criteria | Likelihood Ratio Tests | | |
|---|---|---|---|---|
| **Effect** | **−2 Log Likelihood of Reduced Model** | **Chi Square** | **df** | **Significance** |
| Intercept | 112.547 | .000 | 0 | - |
| GCA Standard Score | 161.10 | 48.56 | 2 | .000 |
| NEPSY-II Visuomotor Precision scaled score | 128.63 | 16.08 | 2 | .000 |
| Adaptive Standard Score | 117.03 | 4.49 | 2 | .106 |
| CBCL Total Problems | 155.19 | 42/65 | 2 | .000 |
| TRF Total Problems | 124.62 | 12.07 | 2 | .002 |
| Child's Age | 141.85 | 29.30 | 2 | .000 |
| Child Sex | 117.99 | 5.45 | 2 | .066 |
| Height Percentile | 115.49 | 29.30 | 2 | .230 |
| Racial Category | 133.49 | 20.94 | 8 | .007 |
| SES Factor* | 124.64 | 12.09 | 2 | .002 |
| Marijuana Use in pregnancy | 122.34 | 20.94 | 2 | .007 |

*Includes: Mother's income, Education, and Marital Status

Model ($X^2_{(28)}$ =222.83; p<.000); Factors that did not contribute significantly to initial model (that is p>.20), including VMI, School Readiness (BBCS), Gestational age and Cigarette Use were excluded from this final model.

**Table 5.1**

Classification of Cases Based on Model (n=158)

| | Predicted by Model | | | |
|---|---|---|---|---|
| **Observed** | **Not FASD** | **ARND/Behavioral** | **ARND/Cognitive** | **Percent Correct** |
| Not FASD | 65 | 5 | 3 | 89.0% |
| ARND/Behavioral | 6 | 38 | 2 | 82.6% |
| ARND/Cognitive | 2 | 3 | 34 | 87.2% |
| Overall % | 46.2% | 29.1% | 24.7% | 86.7% |