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Fetal Alcohol Spectrum Disorders in a Southeastern County of the United States: Child Characteristics and Maternal Risk Traits

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Contributors' Statement:

Philip A. May was the Principal Investigator who designed and directed the overall study, received the NIH funding, directed all operations in the local site and all interaction with the school administrators. He wrote the majority of the first and last drafts of the manuscript. Julie Hasken was the Program Manager for both samples at this site. She oversaw all data and logistical matters locally, performed much of the data analyses and along with Dixie Hedrick, constructed the graphics, tables and figures. Heather Mastro and Julie Stegall were local field coordinators and maternal interviewers who provided constant liaison with school administrators, individual schools, and organizers for all participants in both samples. Each contributed programmatic data, written text and edited various drafts of the manuscript. Wendy Kalberg, David Buckley, Marian Ortega, and Marita Brooks designed, oversaw and performed various data management tools and files, data entry, and IRB activities at the central data repository. Wendy Kalberg, with input from Claire Coles of Emory University, designed the neurobehavioral battery of tests and checklists. Also, Ms. Kalberg trained local school psychologists and oversaw the implementation of neurobehavioral testing and data collection. Amy Elliott served as an advisor, evaluator in the neurobehavioral domain with the final case conferences for each child for each child. Barbara Tabachnick served as the statistical advisor for the manuscript, designed and performed the advanced statistical procedures. Omar Abdul-Rahman, Margaret Adam, Luther Robinson, Tamison Jewett, and Melanie Manning were project dysmorphologists who performed dysmorphology examinations on all children, generated clinical dysmorphology data in field clinics, and made the final diagnoses of all children in the multidisciplinary case conferences. H. Eugene Hoyme was the chief dysmorphologist supervising all of the clinical, medical team members, provided clinical exams, and generated a substantial portion of the pediatric data. He contributed written material and edited various drafts of the manuscript. Each co-author read drafts of the manuscript and contributed to the writing and editing.

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Abstract

Objective—Detail the characteristic traits of children with fetal alcohol spectrum disorders (FASD) and maternal risk factors in a Southeastern U.S. County.

Methods—Independent samples were drawn from two different cohorts of first grade students. All consented children (49.8%) were measured for height, weight, and head circumference, and those ≤ 25th centile entered the study along with a random sample drawn from all enrolled students. Study children were examined for physical growth, dysmorphology, neurobehavior and their mothers were interviewed.

Results—Total dysmorphology scores discriminated well the physical traits of children across the FASD continuum: fetal alcohol syndrome (FAS) =15.8, partial FAS (PFAS) = 10.8, alcohol-related neurobehavioral disorder (ARND) = 5.2 and typically-developing controls = 4.4. Additionally, a neurobehavioral battery distinguished children with each FASD diagnosis from controls. Behavioral problems qualified more children for FASD diagnoses than cognitive traits. Significant proximal maternal risk variables were: reports of pre-pregnancy drinking, drinking in any trimester, and co-morbid use of other drugs in lifetime and during pregnancy, especially alcohol and marijuana (14.9% among mothers of children with FASD vs. 0.4% for controls). Distal maternal risks included reports of: other health problems (e.g., depression), living unmarried with a partner during pregnancy, and a lower level of spirituality. Controlling for other drug use during pregnancy, having a child diagnosed with a FASD was 17.5 times greater for women who reported usual consumption of three drinks per drinking day prior to pregnancy than for non-drinking mothers (p<.001, 95% CI = 5.1 – 59.9). There was no significant difference in prevalence of FASD by race, Hispanic ethnicity or socioeconomic status. The prevalence of FASD was not lower than 17.3 per 1,000 and weighted estimated prevalence was 49.0 per 1,000 or 4.9%.

Conclusion—This site had the second lowest rate in the CoFASP study, yet children with FASD are prevalent.

Keywords

fetal alcohol spectrum disorders; prevalence; alcohol use and abuse; women; prenatal alcohol use; children with FASD; maternal risk traits for FASD

INTRODUCTION

Previous Epidemiology Studies of Children with FASD

The specific traits of children with fetal alcohol syndrome (FAS) were first delineated by Jones and Smith (1973) from a dozen clinical cases, and in the next decade other clinical case descriptions of FAS appeared in the literature. A United States (U.S.) Institute of Medicine (IOM) study (Stratton et al., 1996) put forth guidelines for diagnosing four clinically-significant outcomes of prenatal alcohol exposures: FAS, partial fetal alcohol syndrome (PFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD). These diagnoses were referred to as a continuum and later named fetal alcohol spectrum disorders (FASD) as an umbrella term (Calhoun et al., 2006).

Several diagnostic systems were developed in North America and used globally with minor variations (Astley and Clarren, 2000; Chudley et al., 2005; Cook et al., 2016; Hoyme et al., 2005). The strengths and weaknesses of these systems have been described, debated, and evaluated (Coles et al., 2016), but all utilize similar: physical features and measurements, anomalous features, and neurobehavioral traits and assessments to evaluate children for FASD. The categories within FASD, names of the categories, and cut-off points for particular domains and traits have varied over the years. While some differences exist, all agree on the concept of a spectrum of damage, which is primarily attributed to quantity, frequency, and timing of prenatal alcohol exposure (May et al., 2013b).

Prior to 2000, few publications provided a population-based understanding of the prevalence of FAS or FASD, and therefore, no firm understanding of prevalence and variation of FASD physical and neurobehavioral traits among the general public. Active case ascertainment (ACA) methods emerged as a promising method for prevalence studies, for surveillance through registries and most clinic-based studies were found to be gross undercounts of total cases, were selective in whom was studied, and understanding of the prevalence and characteristic traits of children on the full continuum of FASD had not emerged (May et al., 2009). ACA studies in elementary schools emerged as an effective approach to fill this knowledge gap. Studies of whole communities were published from South Africa, Italy, Croatia, and Canada (May et al., 2017a, 2016a, 2016b, 2013a, 2011a, 2007, 2006, 2000; Okulicz-Kozaryn et al., 2017; Petkovic and Barisic, 2010, 2013; Popova et al., 2019; Urban et al., 2008, 2015; Viljoen et al., 2002, 2005). Rates of FAS and FASD varied in these studies by county and over time. However, total FASD was consistently found to be higher than older estimates of 1% and ranged from 1-5% in Croatia, Canada, and the United States to highs of 23-28% in five South African communities.

When samples in schools participating in ACA studies are representative, they establish the lower bound (lowest possible) FASD prevalence, an estimate of the true prevalence of FASD, and a representative description of the common traits (and their variability) of children with FASD. Furthermore, these studies can also establish the traits of typically-developing children in a population. In such studies few children are identified who were previously diagnosed with FASD (Clarren et al., 2001; May et al., 2018), indicating that FASD is under diagnosed (Chasnoff et al., 2015).

Associating Specific Maternal Risk Factors to Children with FASD

Identifying maternal risk factors for FAS and FASD has a long history. From clinical studies (Aase, 1994; Abel and Hannigan, 1995; Blume, 1985; Esper and Furtado, 2014; Jones and Smith, 1973) to basic science investigations (Balaraman et al., 2016; Sulik, 2014) a number of maternal risk factors have been identified in drinking prevalence studies (Denny et al., 2019, 2009; Hasin et al., 2019). Furthermore, an understanding of drinking quantity and frequency reported by women of childbearing age and pregnant women has been well covered (Denny et al., 2019; Grant et al., 2017; Green et al., 2016; Hasin et al., 2019; Keyes et al., 2011; Keyes and Miech, 2013; Roozen et al., 2018; Shmulewitz and Hasin, 2019). However, in such studies drinking patterns or quantities cannot be matched to specific child outcomes, because they do not have the link to a formal diagnosis of children on the continuum of FASD as do ACA studies.

Since it is standard procedure to interview all mothers of study children in ACA studies, maternal traits are matched with child outcomes (e.g., diagnosis and traits) (Ceccanti et al., 2014; May et al., 2013b, 2011b, 2009, 2008, 2005; Viljoen et al., 2002). A major goal is to understand particular quantity (Q), frequency (F), and gestational timing (T) of exposures associated with specific outcomes and diagnoses (May et al., 2013b).

The Collaboration on FASD Prevalence (CoFASP) was funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in 2010 to provide solid prevalence data on FASD in the U.S. (May et al., 2018). CoFASP investigators sought to expand knowledge of the full continuum of effects of prenatal alcohol consumption on children. Population-based research was undertaken in four sites, each in different regions of the U.S.: Rocky Mountain, Midwest, Southwestern Pacific, and Southeast. This paper describes the Southeast regional site, a county that is representative of this large and populous region. It is a comprehensive summary and analysis of the domains covered in a CoFASP study: physical growth, dysmorphology, neurobehavior, and maternal risk factors.

The Study Community

One-hundred-sixty thousand persons reside in the study county. The county is designated by the U.S. Census as part of a Standard Metropolitan Area that is among the 15 most populous in the country and has been growing steadily for decades. The County has several major, incorporated urban areas (cities and towns), suburban bedroom communities, and rural areas where a variety of small agriculture enterprises are practiced. Small manufacturing and distribution businesses are prevalent, as are health care clinics, a major tertiary care hospital, and retail businesses. The population of the county was 68.2% White, non-Hispanic, 17.8% Black, non-Hispanic, and 10.8% Hispanic (U.S. Census, 2015) (see Table 1). The residents had per capita income of $25,544 and median household income of $47,694, both slightly below U.S. averages. Fewer people were below the poverty level than the U.S. average (U.S. Census, 2015). Religious survey data (Pew Research Center, 2015) indicate that 77% of the people in this state identify themselves as Christian, 3% Jewish, Muslim, Buddhist or Hindu, and 20% unaffiliated ("nones"), higher than U.S. averages. Also, 84% said that religion is very, or somewhat important, in their lives. Per capita alcohol consumption in this state was 2.02 gallons (7.65 liters) of ethanol per year in 2009, lower than the U.S. average of 2.3 gallons (8.71 liters) (LaVallee and Yi, 2011). The health ranking of this state falls between 30 and 34th of 50 states (America's Health Rankings Annual Report, 2015). Almost 14% of adults in this county reported binge drinking, and excessive drinking was 15.1% in the state, both lower than the U.S. average (vs. 17.4%) (Tan et al., 2015).

METHODS

Diagnostic Procedures

Revised IOM diagnostic guidelines for FASD (Hoyme et al., 2005) were used and consensus cut-off values were established by the investigators and CoFASP advisory group (Hoyme et al., 2016). Classification of children was based on blinded assessments of: (1) physical growth, (2) dysmorphology, (3) cognitive and behavioral assessments, and (4) maternal risk interviews of the participant's mothers. Other recognizable malformation syndromes were ruled out, and final diagnoses were made for each child in formal, data-driven case conferences.

Each of the four diagnostic categories of FASD was carefully considered for the CoFASP study, and specific cut-off criteria are summarized in Figure 1. Diagnosis of FAS and PFAS without a confirmed history of alcohol exposure is permitted by the original and revised IOM criteria (Hoyme et al., 2016; Stratton et al., 1996) when other anomalies with similar phenotypes are ruled out. Other evidence of alcohol exposure of prenatal drinking is often used in clinical work, but the diagnosis of a FASD in epidemiology studies is rarely made without direct maternal reports of alcohol use reported: immediately prior to pregnancy, prior to pregnancy recognition, in any trimester, or collateral reports. In many populations a substantial number of women may underreport alcohol use or their levels of drinking during pregnancy (Alvik et al., 2006; Bakhireva et al., 2017; Wurst et al., 2008); yet in other populations, accurate reports of drinking and levels of drinking are the norm (Fortin et al., 2017; May et al., 2016b). An ARND diagnosis always requires direct confirmation of prenatal alcohol use in the index pregnancy.

Sampling of First Grade Children

The sampling process and combined numbers of children and mothers participating from two independent cohorts are documented in Figure 2. There were two public school districts with a total of 24 elementary schools in this county. Consent forms were sent to the parents/ guardians of all first-grade students in all five elementary schools in the independent city school district for two consecutive cohorts (2013 – 2014 and 2014 – 2015). In the county school district, 7 (cohort 1) and 9 (cohort 2) schools were chosen by random selection from the 19 schools in this administrative district. Therefore, in Cohort Sample 1, 12 schools participated and in Cohort Sample 2, 14 schools were studied. No schools refused participation, and total consent for both Cohorts was 49%.

Consented children entered the study primarily via one or both of two criteria: 1) oversampling of all children who were ≤25th centile on height or weight or head circumference and 2) selection by a simple random sample drawn from the entire first grade class roles (50.5% of the randomly-selected children were consented). Children selected at random and confirmed by the research team as not FASD (or as having another known anomaly) constituted the final comparison/control group. Additional children entered the study (n=26) either because a teacher or parent had concerns about their development or they were a twin to a participating child. Children entering the study via non-random selection routes and determined not FASD, did not default to the control group. Identical exams and testing were performed on all children who participated through all of the study (Figure 2).

Study Procedures: Screening in Tiers I and II

In Tier I, the research team measured all consented first grade children in both cohort samples (*n*=1,439) on height, weight, and occipitofrontal (head) circumference (OFC). Any consented child ≤25th centile on OFC or height or weight, or referred by teachers, or twins of a selected child, or selected randomly was included in Tier II physical exams (Figure 2). Four teams, each headed by a pediatric dysmorphologist, provided brief, structured examinations blinded to background information about the child or mother. Examinations assessed: growth, multiple anthropometric measurements, and minor anomalies of the craniofacies, limbs, skin, hair, hands, and heart. Each child was then assigned a "dysmorphology score," an objective quantification of growth deficiency and minor anomalies (Figure E1) (Hoyme et al., 2016). Although not directly used for an assignment of FASD diagnoses, the score is a useful research tool, correlating well with extent of maternal drinking and learning/behavior difficulties in affected children (Ervalahti et al., 2007). Inter-rater reliability of key measurements required by the revised IOM criteria has been good when tested. Evaluation in previous studies produced acceptable correlation coefficients and Cronbach's alpha coefficients of: 0.993 for OFC, 0.957 for inner canthal distance (ICD), 0.951 for palpebral fissure length (PFL), and 0.928 for philtrum length (May et al., 2011b, 2000; Viljoen et al., 2005). This examination and assessment system balances sensitivity and specificity in order to capture the full continuum of FASD for epidemiological studies (Hoyme et al., 2016).

After dysmorphology findings were reviewed for each child, a preliminary diagnosis was assigned: a) not-FASD, b) diagnosis deferred – rule out a specific FASD diagnosis or a related disorder, or c) probable FAS or PFAS. All randomly-selected children and those in categories b and c were advanced to Tier III.

Study Procedures: - Tier III: Neurobehavioral Testing and Maternal Risk Questionnaires

Development and behavior were assessed by licensed school psychologists with the CoFASP-endorsed battery which took 1.5 - 2 hours to administer (Figure 3). The battery evaluated the following domains: cognitive, academic achievement, behavior, and adaptive skills. Instruments included were: Differential Abilities Scale (DAS-II) (Elliott, 2007) to assess general intelligence; NEPSY-II (Korkman et al., 2007) to assess executive functioning, memory, and visual spatial integration; Developmental Test of Visual-Motor Integration (VMI) (Beery and Beery, 2004) to assess eye-hand coordination; and Bracken Basic Concepts Scale (Bracken, 1998) to assess basic concept development in math, reading, and spelling. Teachers and parents also completed behavior assessments: Achenbach (Achenbach and Rescorla, 2001) Child Behavior Checklist (CBCL) and Teachers Report Form (TRF); and Vineland Adaptive Behavior Scales (Sparrow et al., 2005).

All consenting mothers of children in Tier III (potential cases and potential controls), who could be scheduled successfully, were provided face-to-face interviews by experienced project staff. Sequencing of questions was designed to maximize accurate reporting of: general health, reproduction, nutrition, alcohol and drug use, socioeconomic status (SES), and maternal height, weight, and OFC were measured. Drinking questions employed a timeline, follow-back sequence, (Sobell et al., 2001, 1988) and Vessels alcohol quantity methodology for accurate calibration of standard alcohol units (Kaskutas and Graves, 2001, 2000; Kaskutas and Kerr, 2008). The American "Standard Drink" was used, where one drink was equal to consuming 14 grams of absolute alcohol: 12oz. (350mL at 5% alcohol by volume) of beer; 5oz. (150mL) of wine (12% by volume); and 1.5oz. (44mL of 40% alcohol by volume) liquor ("What Is A Standard Drink? | National Institute on Alcohol Abuse and Alcoholism (NIAAA)," n.d.). Current alcohol consumption for the week preceding the interview was embedded into dietary intake questions (King, 1994) to aid accurate calibration of drinking quantity, frequency, and timing of alcohol use before and during the index pregnancies (Alvik et al., 2006; May et al., 2013b, 2008, 2005). Retrospective reports of alcohol use have been found to be accurate in some populations when designed and administered properly (Czarnecki et al., 1990; Fortin et al., 2017; Hannigan et al., 2010; May et al., 2018).

Maternal risk data were gathered for 380 mothers in the cohorts combined (see Figure 2). Drinking during pregnancy was confirmed with the CoFASP criteria if at least one of these measures were reported: a) six or more standard drinks per week for two or more weeks during pregnancy; b) a binge of 3 or more drinks per occasion on two or more occasions during pregnancy; or c) documentation of social or legal problems in proximity to the index pregnancy (e.g. treatment of alcohol abuse or infractions of driving under the influence). These criteria were not intended to reflect a threshold for damage associated with FASD. Rather cut-off levels were based on previous experience with responses in previous self-reported drinking surveys that were associated with dysmorphology and neurobehavioral impairment characteristic of a FASD.

Multidisciplinary Case Conferences for Final Diagnoses

Following data collection, final diagnoses were made in confidential, multidisciplinary case conferences. The findings for each child in each domain were discussed in a structured manner where summary results were presented by the research team members who produced them. While findings were being presented and discussed, two-dimensional, digital photos of the child's face (frontal and profile views) were projected to contextualize the discussion. Findings from each domain and examiner were weighed throughout the presentation and the final diagnosis was made by the examining dysmorphologist with the consensus of the group. In rare cases there was lack of agreement among participants; the final diagnosis was delayed until clarification or additional data were brought to the group.

In classifying children, consistency and quality assurance were enhanced by strict application of the CoFASP criteria preparing for and during case conferences. Final diagnoses were double-checked for consistency and accuracy by the data management teams headquartered at the University of North Carolina, University of California, San Diego, and the University of New Mexico. Classifications were then triple-checked by CoFASP investigative teams by reciprocal exchange of diagnostic data for all cases and a sample of non-cases. Each team was blinded to the other team's classification and was asked to determine whether criteria had been applied accurately.

Data Analysis and Final Prevalence Rates

Data analyses were performed with Excel (Microsoft Excel, 2016) and SPSS (IBM, 2017). Child physical, cognitive/behavioral, and maternal risk findings were compared across diagnostic groups using chi square, t-tests, and one-way analysis of variance. With statistically significant ANOVAs, post-hoc analyses were performed using Dunnett's correction pairwise comparisons (α=.05).

In calculating the partial correlations, transformations were undertaken for most measures due to skewness. Transformations were undertaken for most measures due to skewness. Logarithmic transforms, square root transformations, and other appropriate data analysis techniques were applied where appropriate to individual variables. Logarithmic transformations were applied to usual number of drinks per drinking day before pregnancy (DDD), number of weeks before mother's recognition of the index pregnancy, and the teacher's reports of rule-breaking and attention problems. Square root transformations were applied to the child's total dysmorphology and general abilities scores. Although highly unbalanced, transformations could not be applied to "yes/no" items: maternal reports of drinking during pregnancy trimesters, and the covariate, whether mother had used drugs during the index pregnancy. Use of pairwise deletion ensured that all available data were included. A statistical criterion of p<.0017 was set to control for Type I familywise error rate.

The lower prevalence rates reported in this paper represent the minimum prevalence possible given the total children meeting CoFASP criteria (numerator) at this site, over a denominator of total children enrolled in these first grade cohorts (consented or not). The higher prevalence rates employed a weighted correction factor for each specific diagnosis based on the proportion of diagnoses made within the subsample of randomly-selected entrants. These corrections were projected to the unconsented portion of the students for a final estimated prevalence. Calculation methods employed in the CoFASP initiative were published as an e-appendix of May et al. (2018).

RESULTS

Child Demographic, Growth and Cardinal Features of FASD, and Other Minor Anomalies

Final cases diagnosed in the two cohorts are presented in Table 2. There were eight children with FAS, 16 with PFAS, 25 with ARND, and 413 randomly-selected, typically developing controls. ARBD has been found to be rare in any population (May et al., 2016b, 2015, 2014; May and Gossage, 2001), and no cases of ARBD were found at this site. Racial composition at this site was diverse: 46.7% were non-Hispanic White, 21.9% were of Hispanic ethnicity, 23.9% were non-Hispanic African American, and 7.5% were Other. Racial make-up did not differ significantly between the children with FASD and the randomly-selected controls, whether analyzed by specific diagnosis ($\chi^2(9) = 8.204$, p=0.514) or by FASD vs. controls ($\chi^2(3) = 4.252$, p=0.235).

In Table 3, no significant difference in age was found by diagnosis. A difference in sex was due primarily to excess males with ARND, and all eight cases of children with FAS were female. Even though the mean values of the diagnostic groups fell within the normal range, virtually all physical variables differed significantly across diagnostic categories, indicating the discriminatory power of the CoFASP criteria. Child birthweight, height, weight, and OFC/head circumference centiles were all significantly different among groups, with post-hoc analyses indicating significant pairwise differences: FAS groups vs. controls on mean birthweight; FAS different than PFAS, ARND, and controls on height; FAS different than ARND and controls on weight; and FAS and PFAS different than all other groups on OFC. Mean OFC percentile of children with FASD was 5.3, and 50% of children with FAS were below the 3rd centile. Twelve and one-half percent (12.5%) of children with PFAS, and 20% of children with ARND were below 3rd centile (see Figure 3). The FAS group had the lowest body mass index (BMI). In keeping with diagnostic criteria, palpebral fissure length (PFL) centile differed by group, with significant post-hoc analysis differences among FAS and ARND, and FAS vs. controls. A higher frequency of smooth philtrum was confirmed among children with FAS than among children with PFAS, ARND, and controls. The vermilion border rank of the upper lip was also significantly different between all FASD groups and controls. Other minor anomalies found to differ significantly among groups were: inner pupillary distance, outer canthal distance, maxillary arc, mandibular arc, ptosis (droopy eyelid(s)), and hypoplastic fingernails. Post-hoc analyses indicated smaller maxillary arcs for children with FAS vs. ARND and FAS vs. controls and smaller mandibular arcs for FAS vs. controls. Finally, all groups differed significantly by mean total dysmorphology score (Figure 4). The children with FAS had the highest mean (15.8), followed by PFAS (10.8), ARND (5.2), and controls (4.4). In post-hoc analysis, total dysmorphology score significantly discriminated the individual FASD groups from one another and controls except for FAS vs. PFAS and ARND vs. controls.

Child Performance on Neurobehavioral Measures

Performance centiles on virtually every cognitive and behavioral measure in Table 4 were significantly lower for children with a FASD diagnosis than controls. Highlighted in Figure 5 are four of the specific tests by specific FASD diagnoses. On the general abilities test, the children with ARND performed the worst, children with FAS next, then PFAS, and controls performed the best. The INN score refers to a naming task where the child must name shapes or the direction of arrows as quickly as possible. The INI task is an inhibition task that requires a child to say the opposite shape name or arrow direction as quickly as possible. The INN vs. INI Contrast Scaled Score compares the naming speed score and the inhibition score. On this difficult task the children with FAS performed most poorly, ARND next, then PFAS, and controls the best. For the Teacher Report Form (TRF) on attention problems, control children had the best attention scores and children with ARND the poorest, followed by children with FAS and PFAS also poorer than controls. Children with FAS and controls had the fewest problems with rule-breaking behavior and children with ARND and PFAS had the most. For the breakdown of neurobehavioral measure by specific diagnosis see Table E1 in the Appendix.

Maternal Risk Factors – Proximal

While 50% of the mothers of typically-developing children (controls) reported drinking three months prior to pregnancy, significantly more mothers of children with FASD reported drinking pre-pregnancy (83%) (Table 5). Mothers of children with FASD consumed significantly more drinks per drinking day (DDD) pre-pregnancy than controls. As presented in Appendix Table E2, only half of the mothers of children with FAS reported drinking pre-pregnancy, and mothers of children with FASD diagnoses reported higher mean DDD prior to pregnancy than controls: (4.3 vs. 2.6), with mothers of children with ARND reporting the highest average (4.6). Median drinking values in Table 5 did not differ much from the mean values, indicating minimal skewing from extremely high values reported. Mothers of children with FASD drank more frequently prior to pregnancy than controls, with 71.5% drinking once a week or more and 23.7% reporting drinking three times a week or more compared to 37.2% and 13.2% for controls. Mothers of children with a FASD were more likely to report drinking during pregnancy than controls: 24.4% vs. 4.4%, 17.6% vs. 1.6%, and 17% vs. 3.2%, respectively, in first, second and third trimesters. Mothers of children with ARND were most likely to report drinking in each trimester: 39%, 26%, and 24% in each. Among those mothers who drank during pregnancy, DDD did not differ significantly between groups in any trimester, although control mothers reported a higher DDD than mothers of children with FASD in each trimester, but lower percentage of control mothers drank at all.

Per CoFASP criteria, maternal alcohol use during the index pregnancy was confirmed for all children diagnosed with ARND. For more dysmorphic forms of FASD, direct alcohol use confirmation is sought, but not required. At this site, 50% of FAS cases and 78.6% of PFAS cases were confirmed by direct maternal reports on one or more of the multiple alcohol variables (Figure 6).

Other drug use distinguished significantly the two maternal groups; drug use was uniformly and significantly higher for mothers of children with FASD for all categories of drugs. In Table 5, mothers of children with FASD report a significantly higher frequency of use during pregnancy for any drug use, tobacco, prescription drugs, marijuana, co-morbid use of alcohol and marijuana, and cocaine. For lifetime use, any drug use, tobacco, marijuana, cocaine, heroin, club drugs, crack cocaine, and pain killers were all higher for mothers of children with FASD than controls. Co-morbid use of alcohol and marijuana during pregnancy was significantly higher among mothers of children with any FASD (14.9%) than controls (0.4%), especially for mothers of children with ARND (28%).

Maternal Risk Factors - Distal

There were no significant differences in maternal physical variables among the groups: age, height, weight, BMI, or head circumference (Table 6). Mothers of children with FASD reported more negative lifetime health indicators than did mothers of controls: depression, liver problems, and neurological conditions. Mothers of children with FASD reported significantly later recognition of pregnancy than controls (p=.022). Average recognition of the index pregnancy was 7.7 weeks gestation for mothers of all children with FASD compared to 5.7 weeks for mothers of typically-developing controls. For mothers of children with FAS and ARND, the average was 8.3 and 8.0 weeks respectively (Figure 7).

There were no differences in prenatal care variables. Compared to controls, children with FASD were significantly lower in birth weight (p=.005) and gestational age at birth when measured across the four specific diagnostic groups (Table E3). Children with FASD were also less likely to have been breastfed or live with the biological mother, and more likely to receive baby formula supplementation. A common practice in the U.S. today among alcohol-using mothers is expression and disposal of breastmilk when drinking, a practice called "pump and dump". All (100%) mothers of children with FASD who drank during the breastfeeding period report having used "pump and dump" with the index child, but none of the mothers of a child with FAS reported drinking while breastfeeding or us of "pump and dump" use (Table E3).

Some socioeconomic variables did not discriminate significantly among maternal groups on any variable: education completed or household income at pregnancy or at interview. Marital status during the index pregnancy was significantly different between groups: mothers of children with FASD were less likely to be married and more likely to be living with a partner. Spirituality was reported to be significantly higher among the mothers of controls (6.9 v. 5.6), but memberships in a formal religion (Christian, Jewish, or Muslim) was not different among groups nor was frequency of service attendance (not in Tables).

Correlation Analyses – Linking Selected Child and Maternal Traits to a FASD Diagnosis

Partial correlation analysis measured associations between maternal and cognitive/behavioral measures, FASD diagnosis, and total dysmorphology scores after adjusting for whether mother had used drugs other than alcohol during the index pregnancy (Table E4). All four measures of maternal alcohol use correlated significantly with FASD diagnosis: usual DDD consumed three months prior to pregnancy, and whether the mother drank during any of the trimesters. None of these statistically significant partial correlations were particularly strong once adjusted for drug use, with absolute values of r ranging from .11 to .36. Thus, each maternal variable accounted for no more than about 13% of the variance in the child's diagnosis. Note, however, that correlations may be attenuated due to non-normality remaining even after transformation and to highly unbalanced frequencies in dichotomous yes/no categories. Thus, there was a suggestion of a link between mother's late recognition of pregnancy and lower general abilities score. Also, late recognition of pregnancy may have been associated with lowered INN vs. INI (naming vs inhibition) Contrast Scaled Score. Drinking in the third trimester may also have been linked with teacher reports of more attention problems. There also was an unexpected possible link between drinking in the first trimester and lower total dysmorphology score.

Further correlation analysis was undertaken to define the association of alcohol use to final diagnosis via binary logistic regression. Adjustments were again made to control for any tobacco and illicit drug use during pregnancy. Table 7 presents adjusted results for reported DDD three months prior to pregnancy to a FASD diagnosis. Reporting of three DDD prior to pregnancy is significantly associated (p<0.001) with an odds ratio of 17.5 (95% CI = 5.1-59.9). Therefore, the likelihood of an FASD diagnosis in this community, controlling for other diagnosis, is approximately 18 times greater for a child of a woman who drinks three drinks or more prior to pregnancy. Furthermore, the probability is estimated to be 12.7 times greater (95% CI = 3.4 – 46.5) for women who reported drinking four or more DDD, and 7.8 (95% CI = 2.6 – 24.1) for those reporting five or more DDD prior to pregnancy. The decline in odds for the higher DDD amounts is likely due to under-reporting by respondents who consumed substantially more (e.g., five DDD) yet reported three DDD.

Prevalence of FASD

Figure 8 presents the Southeastern site prevalence based on the combined findings (mean) from both cohort samples. FAS prevalence cannot be calculated lower than 2.7 per 1,000 from diagnosed with CoFASP criteria, for this low rate is calculated as the number of cases as the numerator over the total children enrolled in first grade classes. The rate is more accurately estimated as 3.2 per 1,000 first grade children in this county (see formula and weighing techniques in May et al. (2018)). PFAS is not lower than 5.7 and is estimated to be 11.4 per 1,000. ARND is at least 8.9 per 1,000 and estimated at 34.4 per 1,000. Total FASD in this county is not lower than 17.3 per 1,000 but is more accurately estimated as 49.0 per 1,000.

DISCUSSION

ACA epidemiology of FASD studies provide much data to digest and summarize. But for prevalence, the combined cohort rate for total FASD was estimated as 4.9% of the first-grade population in this County. This is the second lowest rate of FASD of the four CoFASP sites.

Physical Growth and Development

By definition, and as applied here, average growth and physical traits of the children with FASD differed significantly from controls on all cardinal criteria and many other minor anomalies at this site. Revised IOM diagnostic criteria and CoFASP cut-off criteria differentiated the physical attributes of the cases well from the randomly-selected, typically-developing, community comparison group. The physical traits form a continuum on most variables in which children with FAS have the most suppressed growth and more characteristic traits of FASD, followed by children with PFAS, ARND, and controls. Interestingly, all cases (n=8) of FAS were females and males were overreported among cases of ARND (see May et al. 2017b).

The neurobehavioral test battery also discriminated well FASD cases among diagnostic groups and children with any FASD from controls. Total dysmorphology, specific neurobehavioral tests and final diagnosis are associated with various alcohol exposure variables. We suspect that there is substantial under reporting of the quantity of alcohol use, especially the quantity consumed during pregnancy. This may be reflected by the logistic regression where the drinking data clustered to produce a higher odds ratio for a FASD diagnosis at three DDD than at higher DDD (four DDD and above). Nevertheless, reported pre-pregnancy quantity of DDD and drinking in each trimester were significantly different between mothers of children with FASD and controls indicating risk to the fetus for both structural growth and dysmorphology in the first trimester and for brain development throughout pregnancy. Furthermore, mothers of children with FASD reported recognizing that they were pregnant significantly later, on average, than other mothers, indicating possible exposure in the most critical period for structural effects that occur in the first 45 to 90 days of fetal development (Lipinski et al., 2012; Parnell et al., 2014; Sulik et al., 1981;

Sulik, 2014). By definition, all children diagnosed with FAS and PFAS met the facial criteria for FAS with at least two of the three cardinal features (palpebral fissure ≤10th centile, smooth philtrum and/or thin vermilion border of the upper lip), and they had significantly smaller heads and BMI than normal controls. Although the physical growth of children with ARND was similar to that of other first graders, they have a higher occurrence of suppressed head growth and a non-statistically significant higher total dysmorphology score than controls. Minor anomalies other than the cardinal FAS features also play an important role in identifying affected children, as reflected in the dysmorphology score differences among the diagnostic groups. Total dysmorphology scores reflect a continuum of FASD diagnoses, for children with FAS had a total score of 15.8, PFAS = 10.8, ARND = 5.2 and controls a score of 4.4.

Neurobehavioral Characteristics

Although there were significant differences in virtually all areas of testing between children with a FASD vs. controls, intellectual, executive functioning, visual precision, and behavioral deficits were most markedly seen between the children diagnosed with ARND and controls. In the cognitive domain, significant differences were seen in general intellectual ability (GCA percentile), nonverbal reasoning and spatial skills percentiles (as assessed using the DAS-II). Similarly, executive functioning abilities were significantly lower for the ARND group compared with randomly selected controls in Naming and Inhibition (using the NEPSY-II). Behaviorally, the most significance between ARND and control children was seen in externalizing problems, including conduct problems, assessed by the Achenbach Teacher Report Form. While children with ARND are less affected by prenatal alcohol exposure in growth and dysmorphology, this study (and other CoFASP samples) indicate they are often as impaired or more impaired in the neurobehavioral domain as the other FASD groups.

Maternal Risk

Over 80% of mothers with children with FASD reported drinking prior to pregnancy, drinking 4.3 DDD. But only 24% of the mothers of a child with FASD directly reported first trimester drinking and 18% and 17% reported second and third trimester drinking. Average pregnancy recognition was at 7.7 weeks gestation among mothers of children with FASD significantly different from 5.7 for mothers of typically-developing controls. And fewer mothers of children with FASD report for prenatal care in the first trimester (although this later prenatal care is not statistically significant).

Other drug use was common among all groups of mothers, even controls. Thirty-eight percent (38%) of mothers of children with FASD smoked tobacco during the index pregnancy, compared to 13.2% of mothers of controls. And 17% used other drugs during the index pregnancy, compared to 4% of the mothers of controls. After tobacco, marijuana was the most frequently used other drug, used by 28% of mothers of a child with FASD and 2.8% of controls. Co-morbid use of alcohol and marijuana during pregnancy was 14.9% for mothers of children with FASD, and 28% of the mothers of children with ARND. Other drug use in pregnancy was highest among the mothers of children with ARND and higher lifetime use was highest among mothers of children with FAS and PFAS. The former use may account for the poorer neurobehavioral performance of the ARND group (Fish et al., 2019).

Reports of drinking three months prior to pregnancy were the most accurate measures in the domains relevant to FASD: quantity and frequency. Given the diagnostic outcomes of the children, direct reports of drinking during pregnancy may be unreliable. For example, alcohol use reported for first trimester seem to be much less accurate when compared with reports of pre-pregnancy drinking. By triangulating quantity and frequency of drinking prior to pregnancy with gestational week of pregnancy recognition, the reports of drinking during first trimester, more accurate estimates of maternal risk may be ascertained in this population. Therefore, it is not surprising that reports of three drinks or more prior to pregnancy and late recognition of pregnancy best predict risk for FASD in this population, even when smoking and other drug use are controlled in regression analysis.

Making Sense of the Prevalence Findings

The prevalence of total FASD found in this Southeastern site, both the low and the high estimates, exceed the old estimate of 1% (Sampson et al., 1997), and recent estimates from meta-analyses (Lange et al., 2017; Roozen et al., 2016). ACA methods were used consistently and recorded higher rates of FASD, in this case with revised IOM criteria and CoFASP cut-off criteria. Chasnoff and colleagues (2015) reported that 80% to 87% of children with FASD may be undiagnosed or mis-diagnosed in the first years of life, and therefore ACA brings forth a higher prevalence than other methods of prevalence estimations.

Unlike our studies of less economically developed communities in South Africa where a larger percentage of cases are full-blown FAS, the large proportion of PFAS and ARND cases to FAS cases in this population is notable. It may indicate that in this U.S. community many children are negatively affected by prenatal drinking by three DDD both in the critical period of the first trimester, but throughout pregnancy. The high proportion of less dysmorphic cases (PFAS and ARND) diagnosed seems indicative of: 1) a community with a range of drinking styles, as opposed to a dominance of chronic alcohol consumption, 2) a population that has norms allowing, or encouraging, drinking, at least until official recognition of pregnancy, and 3) co-morbid drug use before and during the index pregnancies. And if similar trends are at work in this community to that reported for the U.S. in the past 20 years, these FASD rates may be higher than 20 years ago (Grant et al., 2015; Hasin et al., 2019; Shmulewitz and Hasin, 2019). Furthermore, the rates of alcohol use reported by controls at this site parallel those of the U.S. Centers for Disease Control (Denny et al., 2009; Tan et al., 2015) where 50 to 54% of women of childbearing age drank alcohol, 18% binge drank and 7% of pregnancies were alcohol exposed. Therefore, a rate of FASD of 4.9% in this site is generally supported by other maternal drinking data. Furthermore, SES variables of maternal risk in this community did not differentiate significantly among the FASD and control groups. The risk of FASD is spread throughout various SES strata of the community. The CDC and others also report that half of all pregnancies are not planned in the U.S. population today (Green et al., 2016), which further supports the findings of late pregnancy recognition and continued pre-pregnancy drinking patterns.

One unique variable that distinguished mothers of children with FASD from controls, at this site, was spirituality, where the former group rated themselves as 5.6 on a scale of spirituality compared to 6.9 for the latter (p<.001). Furthermore ecological data presented in Table 1 indicate that this state is one: with a high percentage of the population that is affiliated with a formal religion (Christian, Jewish, or Muslim = 80%), that rates religion as very or somewhat important (84%), and the percentage reporting “no formal religion” is lower than the overall U.S. population (20% vs. 22.8%) (Pew Research Center, 2015). This community is in the changing, but historical “Bible Belt” of the U.S. The community with the lowest prevalence rate in CoFASP had a similar spirituality profile (Midwest site), and the two CoFASP sites with the highest rates had the highest percentage of “unaffiliated” people /those who report no religious affiliation, who are referred to as “nones” (Rocky Mountain, 30% and Pacific Southwest, 27%). Each of the three formal religions most practiced in America have historical normative orientation which encourages abstinence from alcohol, or at least moderation of use (Fjær et al., 2016; Meyers et al., 2017; Room et al., 2016). Norms emanating from a formal affiliation with an established religion promote abstinence or moderation of drinking during pregnancy. This may play a role in regulating the prevalence of FASD at this site.

Limitations

The consent rate for this site was slightly lower (50%) than other samples that we have collected in the U.S.; but it is similar to samples we completed in Italy (May et al., 2011a, 2006), and higher than most attempted elsewhere by other researchers in Europe and North America. Often when one or two teachers or key administrators in one or more schools are not enthusiastic, lower consent rates result. But there was also a relatively high non-completion rate from maternal interviews. Scheduling issues for two income families and that was encountered as the deadline for completing this study approached, emphasis of the staff was focused on completing interviews for those with preliminary diagnosis of “rule out” an FASD. A second limitation is suspected underreporting of prenatal drinking. The experienced interviewers did an exceptional job of interviewing all but two mothers of the children diagnosed with a FASD, at this site, but only 50% of the mothers of the children with FAS directly admitted to drinking during the pregnancy, 12.5% reported drinking during the first trimester, and none reported drinking during the second and third trimesters. Similarly, drinking reports of quantity, frequency, and timing from mothers of children with PFAS seem quite low given the amount of dysmorphology recorded in their children. Even though blinded, the interviewers had estimated at interview completion, that at least three-fourths of the mothers of a child with FAS and PFAS were not fully forthcoming regarding their quantity or frequency of alcohol use in pregnancy. Third, by initiating this study in both cohorts with screening of child physical growth and head circumference, the number of children with ARND (less dysmorphic) may have been under identified, especially given the reluctance of some mothers to report prenatal alcohol use. Therefore, the rate of ARND may be somewhat higher than reported here. ARND cases may be most accurately estimated from methods that utilize a very large random sample and can obtain more accurate data on alcohol use in the index pregnancy.

CONCLUSION

This site had the second lowest rate of FASD of the CoFASP sites. There was no difference in the prevalence of FASD by race, Hispanic ethnicity, or socioeconomic status. Over 80% of all mothers with children with FASD reported drinking prior to pregnancy at a usual level of pre-pregnancy drinking of 4.3 DDD. Pregnancy recognition was later among mothers of children with FASD than controls, and co-morbid use of other drugs were common during pregnancy and lifetime, especially alcohol and marijuana during pregnancy for mothers of children with FASD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ACA	active case ascertainment
ARBD	alcohol-related birth defects
ARND	alcohol-related neurodevelopmental disorder
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CoFASP	Collaboration on Fetal Alcohol Spectrum Disorders Prevalence
DDD	drinks per drinking day
FASD	fetal alcohol spectrum disorders
FAS	fetal alcohol syndrome

ICD	inner canthal distance
IPD	inter pupillary distance
IOM	Institute of Medicine
OFC	occipitofrontal (head) circumference
NIAAA	National Institute on Alcohol Abuse and Alcoholism
PFAS	partial fetal alcohol syndrome
PFL	palpebral fissure length
SES	socioeconomic status

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What's Known on This Subject: There are few studies of the characteristics of children with FAS and FASD and their mothers within the general population of the United States. Additionally, most studies of FASD prevalence and maternal and child characteristics have been undertaken using passive methods of case ascertainment or methods which are selective and underestimate the rates of FASD. Furthermore, most clinical and epidemiological studies of FASD do not provide a detailed description and overview of child physical and neurodevelopmental traits. Furthermore, maternal risk factors are rarely associated with fully diagnosed children with FASD. Here, children with FASD are described and compared to normally-developing children and their mothers in the same population.

What This Study Adds: Using active case ascertainment (ACA) methods among children in a representative, ethnically and racially diverse county in the Southeastern United States, child traits of all diagnoses within the continuum of FASD are described and compared to typically-developing children from the same community and cohorts. The results of two ACA cohort samples in two different cohorts of first grade students from the same county are presented here. The traits provide clear differentiation of the diagnostic groups. The prevalence of FASD in this community was found to be substantially higher than most previous estimates for the general U.S. population, and lower than two other sites in the same study in the USA.

Prenatal Alcohol Exposure	FAS Facial Features [a]	Growth Restriction [b]	Deficient Brain Growth [c]	Neurobehavioral Impairment (< 3yo)[d]	Neurobehavioral Impairment (> 3yo)[e]		Structural Birth Defects [f]
FAS (Fetal Alcohol Syndrome)							
Confirmed/ Unconfirmed Alcohol Exposure	X	X	X	X	X	1.Global impairment 2. Cognitive Deficit (1) 3. Behavioral Impairment (1)	
PFAS (Partial Fetal Alcohol Syndrome)							
Confirmed Alcohol Exposure	X			X	X	1.Global impairment 2. Cognitive Deficit (1) 3. Behavioral Impairment (1)	
Unconfirmed Alcohol Exposure	X	X ⟺ *OR*	X	X	X	1.Global impairment 2. Cognitive Deficit (1) 3. Behavioral Impairment (1)	
*ARND (Alcohol-Related Neurodevelopmental Disorder) ***							
Confirmed Alcohol exposure				N/A	X	1.Global impairment 2. Cognitive Deficit (2) 3. Behavioral Impairment (2)	
ARBD (Alcohol-Related Birth Defects)							
Confirmed Alcohol exposure							X

a: Characteristic pattern of facial anomalies characterized by ≥ 2 of the following: 1) Short palpebral fissures (≤ 10th centile), 2) Thin vermilion border (rank of 4 or 5 on racially normed lip/philtrum guide), 3) Smooth philtrum (rank of 4 or 5 on racially normed lip/philtrum guide).

b: Prenatal and/or postnatal growth deficiency: height and/or weight ≤ 10th centile on gender specific population normed growth curves.

c: Deficient brain growth/ morphogenesis/neurophysiology characterized by ≥ 1 of the following: 1) Head circumference ≤ 10th centile, 2) Structural brain abnormalities, 3) Recurrent non-febrile seizures.

d: Evidence of developmental delay ≥1.5 SD below the mean.

e: 1) Global impairment: general conceptual ability, performance IQ (PIQ), visual IQ (VIQ) or spatial IQ ≥1.5 SD below the mean;
2) Cognitive deficit in 1 domain ≥1.5 SD below the mean (executive function, specific learning impairment, memory impairment or visual spatial impairment;
3) Behavioral impairment without cognitive Impairment: behavioral deficit in 1 domain ≥1.5 SD below the mean in areas of self-regulation (mood or behavioral regulation impairment, attention deficit or impulse control).
: For ARND, ***2 domains* of impairment are required for EITHER cognitive deficit without behavioral impairment, OR behavioral impairment without cognitive deficit.

f: One or more major malformations demonstrated in animal models and human studies to be related to prenatal alcohol exposure, including *cardiac defects* (e.g., atrial septal defects, ventricular septal defects, aberrant great vessels, conotruncal heart defects); *musculoskeletal defects* (e.g., radioulnar synostosis, vertebral segmentation defects, large joint contractures, scoliosis); *renal anomalies* (e.g., aplastic/ hypoplastic/ dysplastic kidneys, "horseshoe" kidneys, ureteral duplications); *eye anomalies* (e.g., strabismus, ptosis, retinal vascular anomalies, optic nerve hypoplasia), and/or *hearing impairment* (e.g., conductive or neurosensory hearing loss)

Figure 1.

Collaboration on FASD Prevalence (CoFASP) Consensus Clinical Diagnostic Guidelines

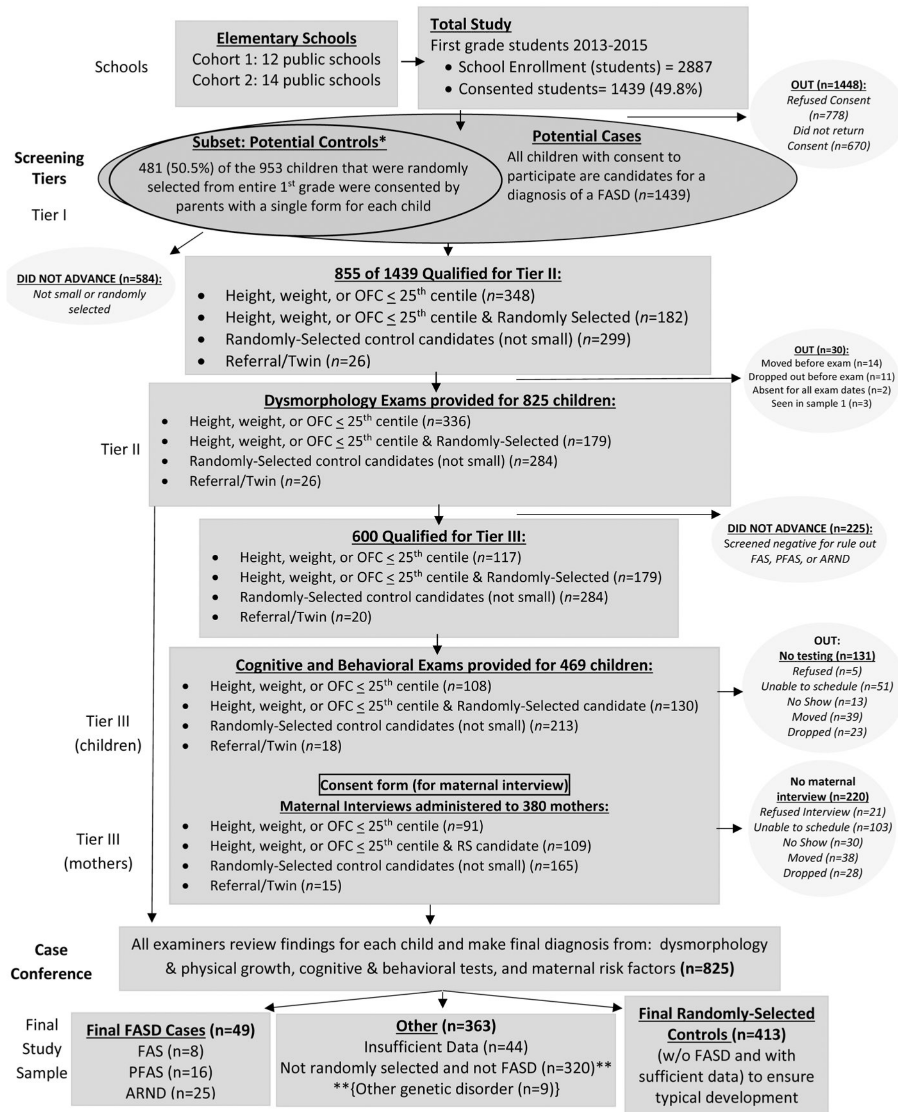


Figure 2. Sampling Methodology for Prevalence of FASD in a Southeastern City and County: Cohorts 1 and 2 Combined

*All potential controls were randomly-selected and became part of the control group if found to be not-FASD and within parameters of typical development. **Children not-randomly-selected or found to have another disorder did not default to the control groups.

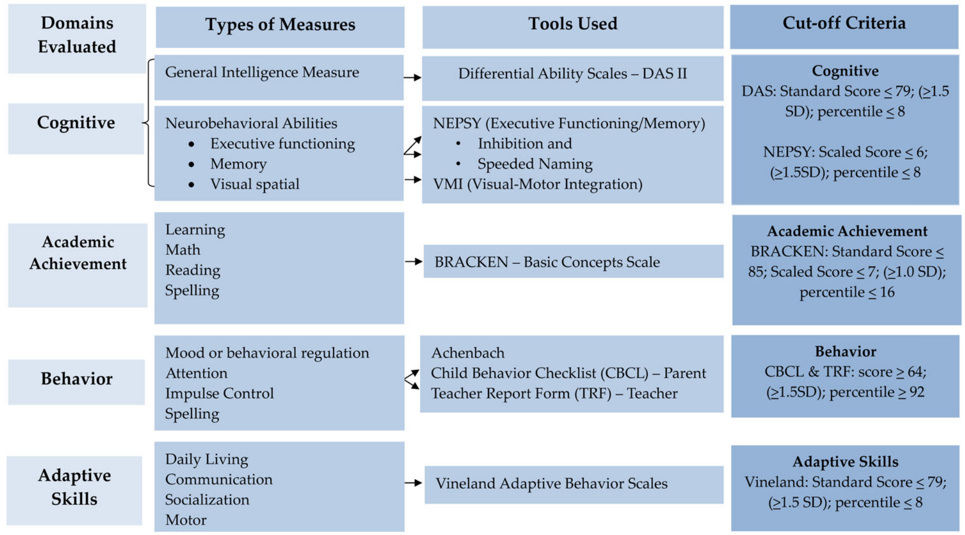


Figure 3.

CoFASP Cut-Off Criteria: Neurobehavioral Testing Battery

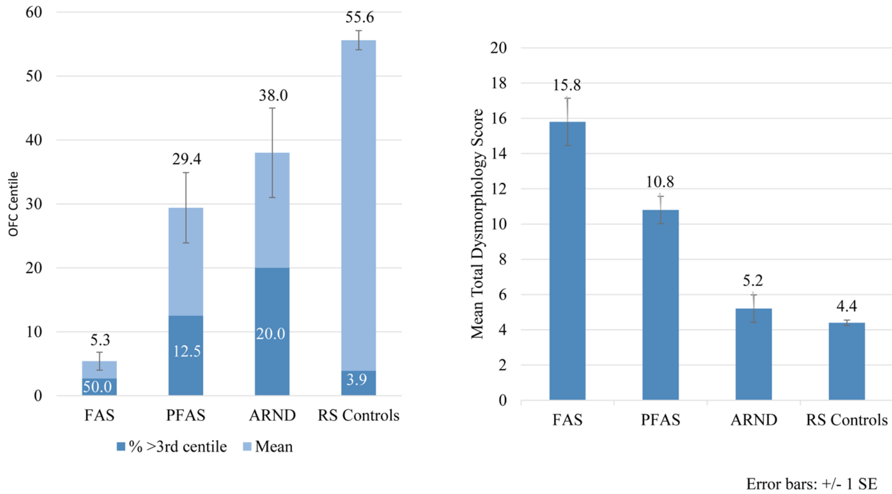


Figure 4.

Occipitofrontal Circumference (OFC) and Total Dysmorphology Score by FASD Diagnosis, Southeastern County

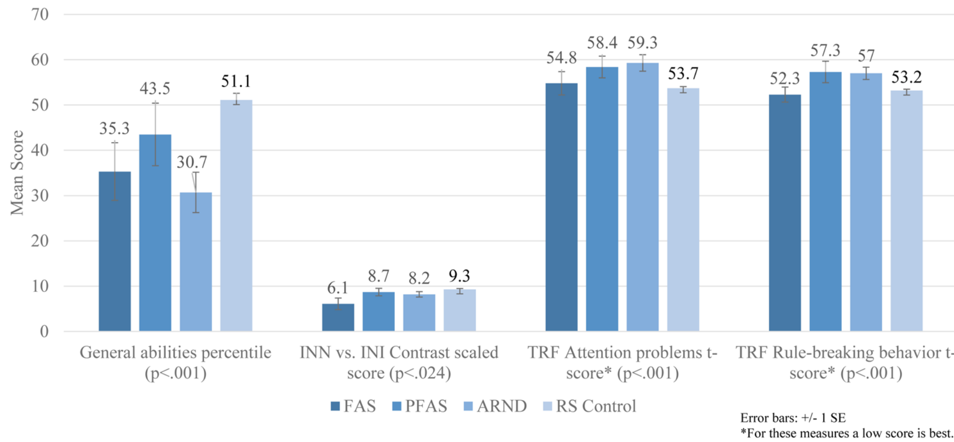


Figure 5.

Selected Cognitive and Behavioral Measures by FASD Diagnoses, Southeastern Site

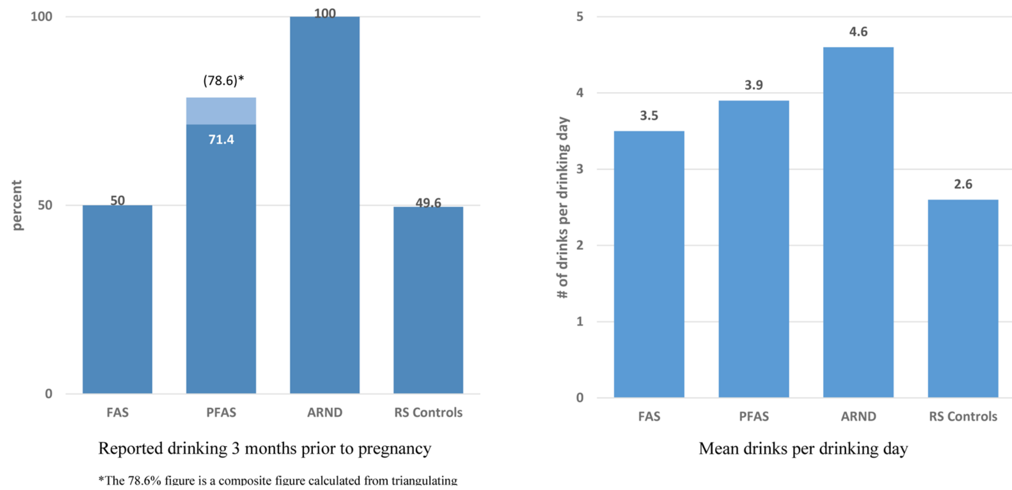


Figure 6.
Pre-Pregnancy Drinking by Percentage and Drinks per Drinking Day by Child's Diagnostic Group

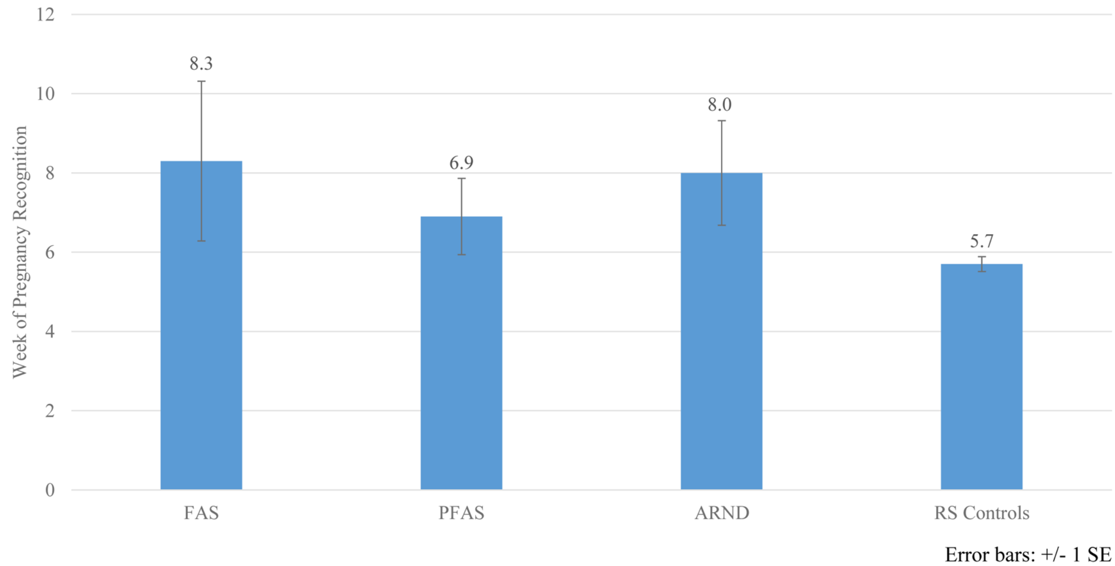
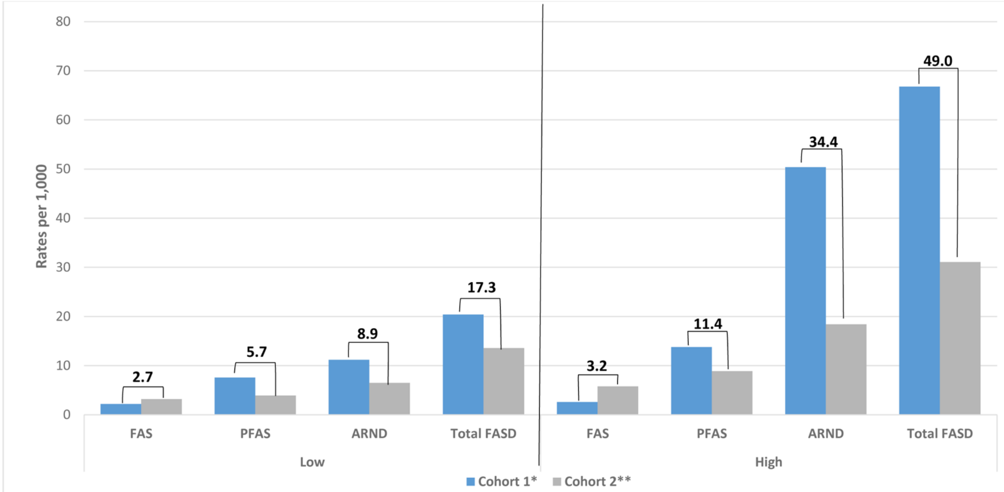


Figure 7.

Week When Pregnancy Was First Recognized by Diagnosis, Southeastern Site



* The low rate is the number of cases identified/diagnosed over the total number of first graders enrolled x 1,000.
**The high estimate is a weighted estimate that utilizes the proportion of children diagnosed with FAS, PFAS, and ARND in the randomly-selected entry group extrapolated to the total number of children who were not consented to participate in the study at this site. See the detailed calculation formula in May, Chambers, et al., 2018 and the appendix to that paper.

Figure 8.

Southeastern Site Prevalence of FASD, Low and High Estimates from Cohorts 1 and 2 Combined

Table 1.

Demographic Indicators for the Southeastern US County compared to the United States Averages

Demographic Indicator	Southeastern County	United States
Population (7/2015)[1] (percentage of US population)	206,392 (0.06%)	321,418,820 (100%)
Population change (%) since 2010[1]	9.4%	4.1%
Race/Hispanic Ethnicity (2010)[1]		
White, non-Hispanic	68.2%	63.7%
Black, non-Hispanic	17.8%	12.6%
American Indian and Alaskan Native	0.4%	0.9%
Asian	1.6%	4.8%
Two or more races	2.3%	2.9%
Hispanic or Latino	10.8%	16.3%
Foreign born persons[1]	7.5%	13.1%
Age – years (median)	36.4	37.2
Housing[1]		
Median household value	$167,700	$176,700
Education[1]		
High School graduate or higher, % ages ≥25 years	84.6%	86.3%
Bachelor’s degree or higher, % ages ≥25 years	22.1%	29.3%
Economy[1]		
Per capita income in past 12 months (2014 dollars)	$25,544	$28,555
Median household income	$47,694	$53,482
Persons in poverty	12.2%	14.8%
Religion[5]		
Composition		
Christian	77%	70.6%
Non-Christian	3%	5.9%
Unaffiliated (“nones”)	20%	22.8%
Importance of Religion		
Very important	62%	58%
Somewhat important	22%	24%
Not too important/not at all	16%	16%
Health Behavior		Median 25 (Range 1-50)
Overall state health Rank in US[2]	30-34	
Alcohol Use		
Binge drinking[^] state %, (US rank)[2]	13.6% (9)	16.8% (25)
Excessive drinking[+], state % (US rank)[2]	15.1% (9)	Median = 17.4% Mean = 16.8%
Excessive drinking, county[3]	16.0%	

Demographic Indicator	Southeastern County	United States
Heavy drinking[#], city[3]	4.9%	
State per capita ethanol consumption (2009), volume per person 14 years and older[4]	2.02 gallons 7.65 liters	2.30 gallons 8.71 liters

Sources:

[1.] ("U.S. Census Bureau QuickFacts: United States," n.d.) US Census

[2.] United Health Foundation, America's Health Rankings, 2015; comprised of scores on behaviors, community and environment, policy and clinical care; scores are ranked for each of the 50 states with better scores resulting in a higher rank among the 50 states; ranges indicate that different rankings are provided for each of the four domains named above

[3.] ("CDC - BRFSS," n.d.) BRFSS (Behavioral Risk Factory Survey data of the CDC. Reported in local city and county statistical reports

[4.] La Valle and Yi, NIAAA Surveillance Report #92

[5.] Pew Research Center. America's Changing Religion Landscape, 2015. Online. www.pewresearch.org.

[^] Binge drinking defined as: during the past 30 days, the consumption of 5 or more drinks for men or 4 or more drinks for females on an occasion

[#] Heavy drinking is defined as males having more than two drinks per day and females having more than one drink per day

[+] Excessive drinking of alcohol is defined as both binge drinking (above) and chronic drinking also referred to as heavy drinking (above)

Table 2.

Distribution of FASD Cases and Randomly-Selected Controls by Racial and Hispanic Ethnicity Categories: Southeastern US County

Southeastern			**FAS**		**PFAS**		**ARND**		**RS controls**		X^2	**p**
	n	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**		
White- non-Hispanic	213	46.7	4	50.0	8	50.0	12	48.0	190	46.6		
Hispanic	100	21.9	1	12.5	4	25.0	1	4.0	94	23.0		
African American-non-Hispanic	109	23.9	2	25.0	3	18.8	8	32.0	96	23.5		
Other	34	7.5	1	12.5	1	6.3	4	16.0	28	6.9	8.204	0.514

			FASD		**RS controls**		X^2	**p-value**
	n	**%**	***n***	**%**	***n***	**%**		
White- non-Hispanic	213	46.7	24	49.0	190	46.6		
Hispanic	100	21.9	6	12.2	94	23.0		
African American- non-Hispanic	109	23.9	13	26.5	96	23.5		
Other	34	7.5	6	12.2	28	6.9	4.252	0.235

Table 3.

Demographic, Physical Growth, Cardinal FAS Features, Other Minor Anomalies and Total Dysmorphology Scores for in a Southeastern US County

	All Children* (*n*=2558)	Children with FAS (*n*=8)	Children with PFAS (*n*=16)	Children with ARND (*n*=25)	Randomly-Selected Control Children (*n*=413)	Test-score	p-value**
Growth and Cardinal Features							
Sex (% Male)	--	0.0	50.0	60.0	52.8	χ^2=9.433	.024
Current Age (months) - Mean (SD)	-- --	82.0 (4.2)	81.8 (5.0)	81.1 (3.5)	81.6 (4.6)	*F*=.117	.950
Preterm (% Yes) ⁺	--	12.5	14.3	36.0	12.6	χ^2=10.029	.022
Birth weight (grams) – Mean (SD) ⁺	-- --	2834 (250)	3335 (780)	2801 (990)	3225 (596)	4.249	.006[C]
Height Centile – Mean (SD)	52.3 (29.0)	8.0 (9.8)	34.9 (26.5)	43.4 (26.7)	52.8 (28.2)	*F*=9.221	<.001[A,B,C]
Weight Percentile – Mean (SD)	59.6 (28.9)	15.6 (19.4)	46.3 (29.7)	51.2 (35.6)	58.6 (28.3)	*F*=7.000	<.001[B,C]
Child's BMI Percentage – Mean (SD)	-- --	38.8 (32.0)	57.1 (34.1)	56.8 (34.5)	61.3 (27.7)	*F*=1.937	.123
Occipitofrontal Circumference (OFC) Centile – Mean (SD)	55.9 (30.2)	5.3 (3.9)	29.4 (22.0)	38.0 (35.1)	55.8 (29.9)	*F*=13.50	<.001[A,B,C,E]
OFC ≤3rd centile	--	50.0	12.5	20.0	3.9	χ^2=41.652	<.001
OFC ≤10th centile	--	100.0	25.0	36.0	8.7	χ^2=77.163	<.001
Palpebral Fissure Length (PFL) Percentile – Mean (SD)	--	8.6 (9.9)	18.8 (19.1)	33.5 (13.4)	32.7 (15.3)	*F*=10.935	<.001[B,C]
PFL ≤3rd centile	--	25.0	25.0	0.0	2.2	χ^2=38.490	<.001
PFL ≤10th centile	--	75.0	50.0	0.0	7.0	χ^2=77.409	<.001
Smooth Philtrum (% Yes)	--	87.5	62.5	16.0	14.8	χ^2=51.020	<.001
Narrow Vermilion (% Yes)	--	87.5	93.8	12.0	13.6	χ^2=96.409	<.001
Other Minor Anomalies							
Inner Pupillary Distance (IPD) Percentile – Mean (SD)	--	36.9 (24.6)	47.7 (24.3)	50.3 (25.8)	57.3 (25.8)	*F*=2.694	.046
Outer Canthal Distance (OCD) Percentile – Mean (SD)	--	18.8 (14.7)	24.4 (15.1)	31.3 (17.5)	34.6 (20.2)	*F*=3.025	.029
Maxillary Arc (in cm) – Mean (SD)	--	23.0 (0.6)	24.0 (1.1)	24.0 (1.3)	24.6 (1.2)	*F*=7.323	<.001[B,C]
Mandibular Arc (in cm) – Mean (SD)	--	24.1 (1.0)	24.8 (1.2)	25.1 (1.4)	25.6 (1.4)	*F*=5.819	.001[C]
Ptosis (% Yes)		37.5	25.0	12.0	8.0	χ^2=11.144	.011
Hypoplastic Nails (% Yes)		0.0	6.3	0.0	0.5	χ^2=8.170	.043

	All Children[*] (*n*=2558)	Children with FAS (*n*=8)	Children with PFAS (*n*=16)	Children with ARND (*n*=25)	Randomly-Selected Control Children (*n*=413)	Test-score	p-value[**]
Total Dysmorphology Score – Mean (SD)	--	15.8 (3.8)	10.8 (3.1)	5.2 (3.9)	4.4 (3.1)	*F*=52.060	<001[B,C,D,E]

Post-hoc significant difference between:

[A.] FAS & PFAS

[B.] FAS & ARND

[C.] FAS & Controls

[D.] PFAS & ARND

[E.] PFAS & Controls

[F.] ARND & Controls

[+] As reported in the maternal questionnaire.

[*] All children consented to initial screening, tests of significance only compared the children with FASD and controls.

[**] Bonferroni adjusted significance level for Growth and Cardinal Features = 0.005; for other minor anomalies = .007

Table 4.

Neurocognitive Findings Among Children with FASD and Randomly-Selected Controls in a Southeastern County

	Children with FASD (*n*=49)		Randomly-Selected Control Children (*n*=444)			
	Mean	(SD)	Mean	(SD)	t-test	p-value
Intellectual Domain	(*n*=49)		(*n*=302)			
General Abilities Percentile	35.6	(23.8)	51.1	(26.0)	−3.910	<.001 **
Verbal Cluster Percentile	42.3	(26.1)	54.0	(27.5)	−2.790	.006 **
Nonverbal Reasoning Cluster Percentile	32.4	(27.1)	44.3	(26.0)	−2.694	.003 **
Spatial Cluster Percentile	40.0	(24.3)	54.9	(24.3)	−3.970	<.001 **
Executive Function	(*n*=49)		(*n*=302)			
INN (Naming) combined scaled score	8.2	(4.2)	9.7	(3.6)	2.628	.009 **
INN vs. INI Contrast Scaled Score	8.0	(3.3)	9.3	(3.3)	−2.461	.014 *
INI (Inhibition) combined scaled score	7.5	(3.3)	9.3	(3.4)	−3.338	.001 **
INS (Switching) combined scaled score	8.0	(3.0)	9.0	(3.0)	−2.062	.040 *
Speeded Naming Combined scaled score	7.8	(3.0)	9.2	(3.1)	−2.884	.004 **
Learning[1]	(*n*=43)		(*n*=249)			
BBCS School Readiness Composite Scaled Score	10.3	(2.9)	11.3	(2.6)	−2.322	.021 **
BBCS Readiness Composite Standard Score	101.5	(14.5)	106.4	(12.9)	−2.297	.022 **
Visual Spatial	(*n*=49)		(*n*=302)			
VMI Standard Score	93.6	(7.6)	95.4	(10.6)	−1.105	.270
Visuomotor Precision Combined scaled score	7.9	(3.2)	9.4	(3.3)	−2.950	.003 **
Mood Regulation[2]						
CBCL Anxious/depressed t-score	55.2	(6.1)	53.2	(5.1)	2.289	.023 *
TRF Anxious/depressed t-score	54.2	(7.2)	52.0	(4.6)	2.084	.042 *

	Children with FASD (*n*=49)		Randomly-Selected Control Children (*n*=444)			
	Mean	(SD)	Mean	(SD)	t-test	p-value
CBCL Withdrawn/depressed t-score	56.1	(7.9)	53.4	(5.2)	2.095	.041 *
TRF Withdrawn/depressed t-score	56.1	(7.7)	52.2	(4.6)	3.461	.001 **
CBCL Internalizing Problems t-score	53.7	(11.0)	48.5	(9.7)	3.132	.002 **
TRF Internalizing Problems t-score	49.7	(11.4)	44.5	(8.7)	3.022	.004 **
CBCL Externalizing Problems t-score	54.2	(10.8)	48.0	(10.0)	3.690	<.001 **
TRF Externalizing Problems t-score	53.8	(11.0)	48.9	(8.4)	2.968	.004 **
CBCL Affective problems t-score	58.5	(8.3)	53.7	(5.1)	3.614	.001 **
TRF Affective problems t-score	56.2	(7.7)	52.2	(4.9)	3.475	.001 **
CBCL Anxiety problems t-score	55.3	(6.7)	53.7	(5.6)	1.617	.107
TRF Anxiety problems t-score	54.9	(6.7)	52.2	(5.0)	2.675	.010 *
Attention[2]						
CBCL Attention problems t-score	59.3	(9.2)	55.2	(7.6)	3.135	.002 **
TRF Attention problems t-score	58.1	(8.9)	53.6	(6.5)	3.298	.002 **
CBCL Attention deficit/hyperactivity problems t-score	58.3	(8.5)	55.1	(7.3)	2.345	.023 *
TRF Attention deficit/hyperactivity problems t-score	57.9	(8.2)	54.2	(7.3)	2.895	.005 **
Impulse Control[2]						
CBCL Rule-breaking behavior t-score	55.0	(6.2)	53.8	(5.0)	1.410	.160
TRF Rule-breaking behavior t-score	56.4	(7.5)	53.2	(5.4)	2.797	.007 *
CBCL Aggressive behavior t-score	57.8	(9.1)	53.3	(5.6)	3.116	.003 **
TRF Aggressive behavior t-score	56.7	(9.3)	52.9	(5.6)	2.768	.008 *
CBCL Oppositional defiant problems t-score	58.0	(8.2)	54.3	(5.9)	2.824	.007 *
TRF Oppositional defiant problems t-score	55.8	(7.5)	52.9	(5.5)	2.528	.015 *
CBCL Conduct problems t-score	55.5	(7.2)	53.3	(5.2)	1.918	.061

	Children with FASD (*n*=49)		Randomly-Selected Control Children (*n*=444)			
	Mean	**(SD)**	**Mean**	**(SD)**	**t-test**	**p-value**
TRF Conduct problems t-score	56.5	(8.2)	52.9	(5.4)	2.9928	.005**
Adaptive Function[3]						
Vineland (Parent) VABS Communication Standard Score	90.9	(16.0)	105.1	(17.5)	−3.722	<.001**
Vineland (Teacher) VABS Communication Standard Score	91.5	(14.9)	99.7	(14.6)	−3.439	.001**
Vineland (Parent) VABS Daily Living Skills Standard Score	99.3	(21.6)	106.0	(16.9)	−1.746	.083
Vineland (Teacher) VABS Daily Living Skills Standard Score	93.0	(14.8)	100.3	(14.3)	−3.142	.002**
Vineland (Parent) VABS Socialization Standard Score	97.7	(22.3)	102.9	(17.1)	−1.328	.186
Vineland (Teacher) VABS Socialization Standard Score	96.2	(17.5)	105.4	(15.7)	−3.382	.001**

1. Children less than 7 at time evaluation did not complete a BRACKEN.

2. For CBCL: *n*=43 for FASD; *n*=232 for Controls. For TRF: *n*=47 for FASD; *n*=370 for Controls.

3. For Vineland (Parent): *n*=24 for FASD; *n*=150 for Controls. For Vineland (Teacher): *n*=43 for FASD; *n*=342 for Controls.

* Significant at <0.05

** Significant at the Bonferroni-adjusted level of significance: Intellectual: 0.0125; Executive Function: 0.01; Learning: 0.025; Visual Spatial: 0.025; Mood Regulation: 0.004; Attention: 0.0125; Impulse Control: 0.006; Adaptive Function: 0.008

Table 5.

Proximal Maternal Risk Factors for FASD: Alcohol and Drug Use a Southeastern County

	Children with FASD (n=47)		Randomly-Selected Control Children (n=251)		χ^2 or t-test	p-value
	Mean	(SD)	Mean	(SD)		
Alcohol Use – Before and During Pregnancy						
Drank before pregnancy (% Yes)	83.0		49.6		17.784	<.001**
# of drinks consumed on usual drinking day before pregnancy[1]	4.3	(2.1)	2.6	(2.8)	3.314	.001**
	Mdn = 4.0		Mdn = 2.0		—	--
Usual frequency – before pregnancy[1]						
Everyday or almost everyday	13.2		7.4			
3-4 times per week	10.5		5.8			
1-2 times per week	47.4		24.0			
3 times per month	18.4		16.5			
1 time per month or less	10.5		46.3		16.865	.002**
Days drank more than usual – before pregnancy[1] (% Yes)	22.7		15.8		1.284	.257
Drank in 1st trimester (% Yes)	24.4		4.4		22.080	<.001A,**
# of drinks on usual drinking day[1] -1st	3.4	(2.9)	5.2	(6.7)	−0.718	.483
Usual frequency[1] – 1st						
Everyday or almost everyday	18.2		10.0			
3-4 times per week	18.2		10.0			
1-2 times per week	27.3		10.0			
2-3 times per month	0.0		0.0			
1 time per month or less	36.4		70.0		2.443	.486
Drank in 2nd trimester (% Yes)	17.8		1.6		25458	<.001A,**
# of drinks on usual drinking day[1] -2nd	1.7	(1.0)	6.3	(9.2)	−0.872	.474
Usual frequency[1] – 2nd						

	Children with FASD (*n*=47)		Randomly-Selected Control Children (*n*=251)		χ^2 or t-test	p-value
	Mean	(SD)	Mean	(SD)		
Everyday or almost everyday	25.0		33.3			
3-4 times per week	12.5		0.0			
1-2 times per week	25.0		33.3			
2-3 times per month	0.0		0.0			
1 time per month or less	37.5		33.3		.497	.920
Drank in 3rd trimester (% Yes)	17.0		3.2		14.660	<.001^{A,**}
# of drinks on usual drinking day[1] - 3rd	1.1	(0.4)	2.4	(3.5)	−0.922	.373
Usual frequency[1] – 3rd						
Everyday or almost everyday	0.0		12.5			
3-4 times per week	0.0		12.5			
1-2 times per week	0.0		0.0			
2-3 times per month	0.0		0.0			
1 time per month or less	100.0		75.0		3.013	.556
Alcohol Use - Current						
Drink in past 30 days (% Yes)	59.1		52.7		.617	.432
Binge 5+ in past month (% Yes)	14.0		10.3		.494	.482
Why usually drink: because others drink	25.0		16.3		1.967	.161
Why usually drink: to feel less anxious	11.4		7.3		.837	.360
Recovering drinker (% Yes)	0.0		1.0		.362	.547
Other Drug Use						
Used tobacco – during pregnancy (% Yes)	38.3		13.2		17.521	<.001**
Used any drugs in pregnancy (% Yes)	17.0		4.0		11.562	.001^{A,**}
Abused prescription drugs – in pregnancy	8.5		1.6		7.125	.024^{A,*}
Used marijuana – during pregnancy (% Yes)	14.9		2.8		12.663	.002^{A,**}
Used marijuana & alcohol – during pregnancy (% Yes)	14.9		0.4		30.660	<.001^{A**}

	Children with FASD (*n*=47) Mean	(SD)	Randomly-Selected Control Children (*n*=251) Mean	(SD)	χ^2 or t-test	p-value
Used cocaine - during pregnancy (% Yes)	8.9		0.8		12.346	.006[A,*]
Used tobacco						
Yes, within last 30 days	40.4		18.5			
Yes, in lifetime	25.5		32.1			
Never	34.0		49.4		13.658	.001[**]
Used any drug in lifetime (% Yes)	70.2		42.3		12.331	<.001[**]
Used marijuana – in lifetime (% Yes)	70.2		41.7		12.913	<.001[**]
Used methamphetamine – in lifetime (% Yes)	6.7		2.0		3.056	.110
Used heroin – in lifetime (% Yes)	8.9		1.2		9.531	.012[A,*]
Used club drugs – in lifetime (% Yes)	30.4		7.8		19.813	<.001[A,**]
Used crack/cocaine – in lifetime (% Yes)	19.6		5.3		11.422	.003[A,**]
Abused pain killers – in lifetime (% Yes)	17.0		5.6		7.409	.013[*]

[1] Among women who drank in that specific time period.

[A] Fisher's Exact Test

[*] Significant at <0.05

[**] Bonferroni-adjusted significant levels: alcohol use -before and during pregnancy = 0.004; alcohol use – current = 0.01; other drug use = 0.004.

Table 6.

Distal Maternal Risk Factors for FASD: Physical, Demographic, and Childbearing Variables in a Southeastern County

	Children with FASD (*n*=47)		Randomly-Selected Control Children (*n*=251)		χ^2 or t-test	p-value
	Mean	(SD)	Mean	(SD)		
Physical						
Age at pregnancy (yrs)	27.6	(5.8)	28.5	(5.8)	0.675	.335
Height at interview (cm)	161.7	(6.1)	163.2	(8.0)	−1.117	.240
Weight at interview (kg)	73.9	(17.2)	78.2	(20.0)	−1.304	.193
Body Mass Index (BMI)	28.2	(6.3)	29.3	(7.0)	−0.936	.350
Head circumference	55.2	(1.9)	55.6	(2.4)	−1.072	.284
Health indicators						
Weight before pregnancy (in kg)	65.2	(17.5)	67.3	(15.8)	0.763	.401
Asthma – in lifetime (% Yes)	22.2		12.1		3.313	.069
Stomach ulcers – in lifetime (% Yes)	4.5		3.6		0.083	.675[A]
Neurological conditions/ epilepsy - lifetime	15.6		5.6		5.622	.027[A]*
Liver problems / hepatitis – in lifetime	11.1		2.4		7.915	.016[A]*
Depression – in lifetime (% Yes)	70.2		41.9		12.702	<.001**
Childbearing						
Gravidity	3.7	(2.8)	3.2	(1.7)	1.114	.270
Parity	2.7	(1.1)	2.6	(1.2)	0.419	.676
Miscarriages	0.9	(2.3)	0.5	(1.1)	1.161	.251
Abortions	0.1	(0.5)	0.1	(0.3)	0.666	.508
Stillbirths	0.0	(0.2)	0.0	(0.1)	0.940	.348
Birth order of index child	2.0	(1.1)	2.0	(1.2)	0.408	.880
Week of pregnancy recognition	7.7	(5.6)	5.7	(3.1)	2.355	.022
Prenatal Care						
Once knew pregnant, take vitamins (% Yes)	93.3		95.9		0.603	.432
# of times seen by healthcare provider						

	Children with FASD (n=47)		Randomly-Selected Control Children (n=251)		χ^2 or t-test	p-value
	Mean	(SD)	Mean	(SD)		
Never	2.3		0.4			
1-5 times	0.0		1.2			
More than 5 times	97.7		98.4		2.441	.323
When first seen by healthcare provider						
1st trimester	84.4		93.6			
2nd trimester	11.1		4.8			
3rd trimester	2.2		0.8			
Delivery only	2.2		0.8		4.500	.183
Other health problems - during pregnancy	30.4		25.1		0.574	.466
Accidents/injury – during pregnancy (% Yes)	8.7		10.8		0.190	.798[A]
Postpartum depression (% Yes)	27.3		20.2		1.101	.319
Postnatal Variables						
Child's Birth weight (grams)	2970	(864)	3225	(596)	−1.921	.060
Estimated gestation age at birth (in weeks)	37.7	(3.8)	38.7	(2.2)	−1.735	.089
COI had problem(s) at birth (% Yes)	59.6		50.0		1.450	.266[A]
Breastfed (% Yes)	55.3		76.0		8.531	.005*
Duration of breastfeeding (in months)[1]	5.5	(6.0)	7.6	(7.2)	−1.292	.198
Supplement with formula[1]	76.0		72.0		0.181	.814
Consumed alcohol in breastfeeding period	8.3		13.2		0.461	.746
Pump and dump (%Yes)[1] among mothers who breastfed	20.0		28.0		.292	.723[A]
Pump and dump (% Yes)[2] among mothers who drank during period of breastfeeding	100.0		79.2		0.516	1.00[A]
Age of biological father (in years)	28.7	(7.0)	30.4	(6.4)	−1.635	.103
Child lives with biological mother (% Yes)	76.6		93.6		13.749	.001[A]*
Child lives with:						
Foster/Adopted/Relative	9.5		4.0			
Biological mother	26.2		19.0			

	Children with FASD (*n*=47)		Randomly-Selected Control Children (*n*=251)		χ^2 or t-test	p-value
	Mean	(SD)	Mean	(SD)		
Biological father	4.8		1.6			
Biological mother and father	59.5		75.3		8.957	.023[A]**
Partner ever had a drinking problem						
Never	75.6		84.1			
In the past, but not currently	14.6		8.4			
Currently	0.0		1.3			
Both past and currently	9.8		6.3		2.923	.404
Years of Education completed	13.5	(2.8)	13.8	(3.4)	−0.578	.561
Household yearly income - during pregnancy	45549	(42587)	58256	(40656)	−1.839	.067
Household yearly income – at interview	51125	(41147)	67398	(52400)	−1.942	.053
Marital Status – Current						
Married	52.2		68.5			
Divorced/Widowed/Separated/Single	30.4		17.3			
Living with partner	17.4		14.1		5.294	.073
Marital Status – During Pregnancy						
Married	40.4		68.4			
Divorced/Widowed/Separated/Single	17.0		7.6			
Living with partner	42.6		24.0		13.758	.002[A]**
Spirituality: none [0] to high [10][1]	5.6	(2.2)	6.9	(2.3)	−3.598	<.001**

[1] Among women who breastfed.

[2] Among women who breastfed and consumed alcohol in the breastfeeding period.

[3] Among women who reported drinking in the specific time period.

[4] Pump and dump is the colloquial name for expressing breastmilk after drinking alcohol and disposing of it.

[A] Fisher's Exact Test

[*] Significant at 0.05

** Significant at the Bonferroni-adjusted level: physical = 0.01; health indicators = 0.01; childbearing = 0.007; prenatal care = 0.001; postnatal = 0.004.

Table 7.

Adjusted Binary Logistic Regression Analysis of FASD Diagnosis as a Function of Usual Number of Drinks per Drinking Day 3 Months Prior to Pregnancy: Pooled Over 25 Imputations – Southeastern County

	B	S.E.	Sig.	Odds Ratio	95% CI		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
					Lower	Upper			
1 drink per drinking day	−0.425	0.821	0.605	0.654	0.131	3.278	0.183	0.221	0.993
2 drinks per drinking day	0.311	0.635	0.624	1.365	0.393	4.738	0.043	0.044	0.998
3 drinks per drinking day	2.866	0.626	0.000	17.559	5.148	59.889	0.032	0.033	0.999
4 drinks per drinking day	2.540	0.663	0.000	12.679	3.454	46.536	0.040	0.041	0.998
5+ drinks per drinking day	2.060	0.573	0.000	7.845	2.551	24.130	0.031	0.032	0.999
Covariates									
Used tobacco during pregnancy	0.579	0.459	0.207	1.784	0.726	4.383	0.016	0.017	0.999
Used any illicit drugs during pregnancy	1.126	0.668	0.092	3.084	0.833	11.419	0.094	0.103	0.996
Constant	−2.778	0.364	0.000	0.062	0.030	0.127	0.022	0.023	0.999

Reference group: non-drinkers