Current considerations for fetal alcohol spectrum disorders: identification to intervention

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Purpose of review
This review highlights recent findings regarding the prevalence, public health impact, clinical presentation, intervention access and conceptualization of fetal alcohol spectrum disorders (FASDs). Despite ongoing work in prevention and identification of this population, the rates of drinking during pregnancy have increased and significant gaps remain in diagnosis and intervention.

Recent findings
Prenatal alcohol exposure is the most common preventable cause of developmental disability in the world. Research has focused on improving diagnostic clarity, utilizing technology and neuroimaging to facilitate identification, engaging broader stakeholders (including self-advocates) to inform understanding and needs, and increasing access to effective interventions. There is an emerging focus on developmental trajectories and experiences in young and middle adulthood. Public policy advocacy has also made great strides in recent years.

Summary
Increases in public awareness, greater concordance of diagnostic schema, leveraged use of novel technology, and the development of targeted interventions within a holistic, strengths-based conceptualization are important considerations for this population.

Keywords
fetal alcohol spectrum disorders, neurodevelopment, prenatal alcohol exposure

INTRODUCTION

Alcohol exposure *in utero* produces by far the most serious neuro-behavioral effects compared with other substances of abuse including heroin and cocaine [1]. Fetal alcohol syndrome (FAS) was first diagnosed 50 years ago, and the broader effects of alcohol exposure on brain and behavior have been conceptualized under a nondiagnostic umbrella term of Fetal Alcohol Spectrum Disorders (FASDs). FASD captures the wide continuum of physical, neurological, cognitive, adaptive functioning and behavioral that can occur following prenatal alcohol exposure. Although there is a large body of evidence that alcohol use during pregnancy can lead to significant negative outcomes, prevention and mitigation efforts have been difficult to implement and the rate of drinking has increased [2,3].

Over the past decade, the rate of reported drinking during pregnancy as tracked by the CDC has increased by 50%, and binge drinking has doubled. On the basis of the most recent United States reported data, in 2020, 14.3% of pregnant people reported current drinking (at least one drink in the past 30 days while pregnant) compared with 9.2% in 2011. Further, 6.1% of pregnant people reported binge drinking (four or more drinks per occasion at least once in the past 30 days), compared with 2.5% in 2011 [2]. Almost half of all pregnancies are unplanned and there has been an increase in women with alcohol use disorders and related problems during the pandemic [4], leading this to be a public health priority.

Understanding specific maternal risk factors (e.g. mental illness, exposure to abuse and alcohol consumption of partners) may also inform successful prevention efforts [5]. There are some programs

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KEY POINTS

- Fetal alcohol spectrum disorders are a significant public health concern.
- There is a need for increased public awareness and diagnostic clarity to better identify and support those affected by prenatal alcohol exposure.
- Leveraged use of technology can assist with identification and intervention.
- Utilizing a holistic and strengths-based approach can facilitate positive outcomes.
- Consultation across settings and stakeholders is paramount to effective assessment and treatment across the lifespan.

in place aimed to reduce drinking during pregnancy (e.g. CDC CHOICES [6]), though additional brief, evidence-based interventions to treat active substance use disorders in pregnant women are needed. Although there is standard public messaging that the safest choice would be to abstain from alcohol during pregnancy, women still encounter mixed information. Further, it is difficult to determine why some children are affected more than others. There are a variety of potential variables to consider, including amount of drinking, timing and pattern of drinking, genetics, prematurity or gestational age, polysubstance use, nutritional status, maternal weight and other preexisting risk and resilience factors that have been targets of recent investigations [7,8▪,9,10].

In light of the well-documented increase in drinking during pregnancy, it has been difficult to track the prevalence and incidence of FASD. Accurate identification has been difficult in part due to no clear consensus for diagnostic criteria as well as other factors including lack of awareness and stigma. Further, although there are physical manifestations of FAS, the majority of individuals affected by prenatal alcohol exposure do not show clear facial dysmorphology (Fig. 1). Despite these challenges, prevalence estimates have been attempted though various methodologies. Recent studies using a random sample and active case ascertainment reported the prevalence rates of FASD to range from 1 to 7% [11,12].

Overall, the effects of alcohol remain missed and are often misdiagnosed, and individuals who are identified have difficulty accessing effective interventions and navigating support systems [13]. Increased awareness, standardized diagnostic criteria and leveraging technological advances can help improve identification. In addition, use of a strength-based framework and greater involvement of various stakeholders (including self-advocates) can also help in both increasing understanding and improving outcomes in a variety of settings and across the lifespan [14▪,15▪▪].

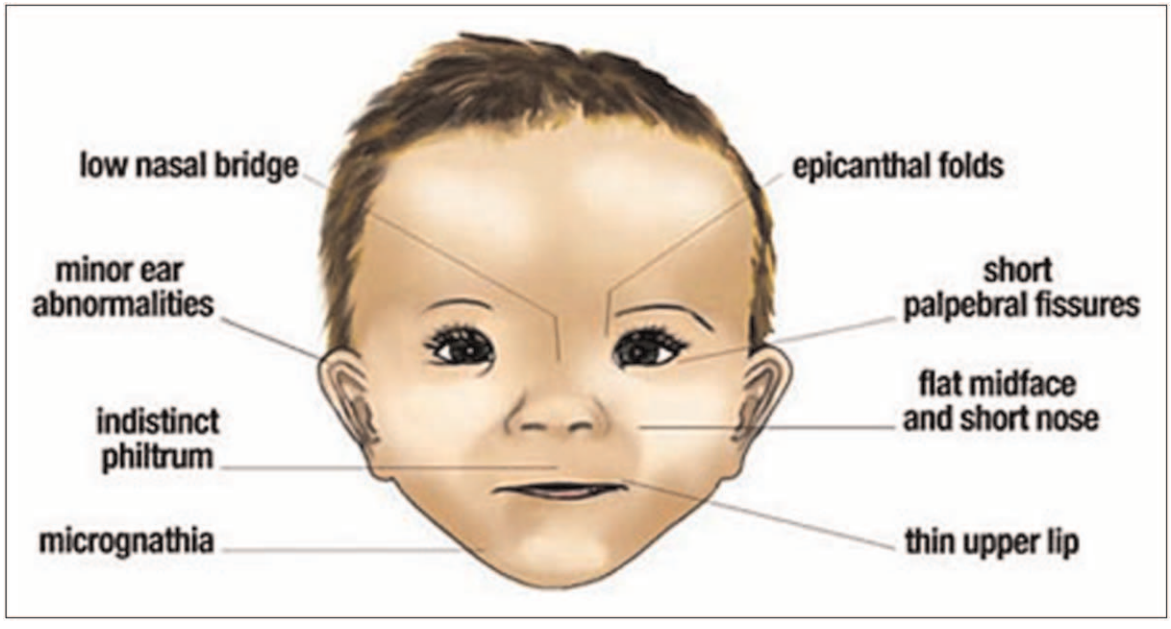

FIGURE 1. Facial characteristics that are associated with fetal alcohol exposure. Figure in public domain - https://pubs.niaaa.nih.gov/publications/aa82/aa82.htm.

IDENTIFICATION

Efforts are underway to increase access to diagnostic services, improve early intervention and FASD-informed care across the lifespan [16–18]. Despite attempts to standardize and formalize diagnostic schema to capture the spectrum of potential effects of prenatal alcohol exposure, there continues to be discordance in research and clinical communities [19]. The Diagnostic and Statistical Manual, 5th Edition (DSM-5) lists Neurobehavioral Disorder associated with Prenatal Alcohol Exposure (ND-PAE) as a condition under further review, though also notes alcohol exposure as a model modifier for Specified Neurodevelopmental Disorder [20], see Table 1. The ICD codes used by medical professionals also have different codes that can be used for FAS/FASD, whereas the American Academy of Pediatrics (AAP) has a number of different diagnostic schema for paediatricians to consider (Institute of Medicine guidelines and 4-digit code).

Without clear and consistent diagnostic criteria, not only is it hard to identify those in need, but it is also difficult to educate providers, teachers and parents about the importance of screening for potential areas of concern related to FASD, especially compared with other neurodevelopmental conditions (e.g. autism, attentional disorders). Other complicating factors that limit identification include the wide spectrum of cognitive, behavioral and adaptive function, ongoing stigma related to FASD, and high rates of comorbidity and adverse childhood experiences [21], see Table 2 for more detail.

Table 1. Overview of criteria for neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE)

A. More than minimal exposure to alcohol during gestation
B. Impaired neurocognitive functioning (one or more of the following):
1. Impairment in global intellectual performance
2. Impairment in executive functioning
3. Impairment in learning
4. Memory impairment
5. Impairment in visual-spatial reasoning
C. Impaired self-regulation (one or more of the following):
1. Impairment in mood or behavioral regulation
2. Attention deficit
3. Impairment in impulse control
D. Impairments in adaptive functioning (two or more of following, must include (1) or (2)):
1. Communication deficit
2. Impairment in social communication and interaction
3. Impairment in daily living skills
4. Impairment in motor skills
E. The onset of the disorder occurs in childhood
F. The disturbance causes clinically significant distress or impairment in social, academic, occupational, or other important areas of functioning
G. The disorder is not better explained by other causes

Note: ND-PAE is listed as a condition for further study in the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5), American Psychiatric Association. (2013). https://doi.org/10.1176/appi.books.9780890425596.

Table 2. Considerations underlying missed or misdiagnosis of fetal alcohol spectrum disorders

• High rate of comorbidity with other neurodevelopmental and psychiatric diagnoses
• Lack of consensus for standard assessment or diagnostic criteria
• Stigma related to biological parents, adoptive/foster care and individuals with prenatal alcohol exposure
• Heterogenous clinical presentation
• Lack of awareness and minimal training for medical providers and educators
• Lack of an accurate, sensitive, and specific biomarker or blood test
• Minimal access to multidisciplinary teams to ensure accurate diagnosis
• Often inadequate or missing histories of prenatal alcohol exposure for children or adults
• Other confounding factors such as polysubstance use, poor nutrition or other maternal risk factors

Neurobehavioral profile and other considerations

Another barrier to the development and use of a robust and comprehensive diagnostic schema is the ongoing refinement of the neurobehavioral profile associated with prenatal alcohol exposure and raising awareness in the community [22,23]. The wide spectrum and heterogeneity of cognitive, behavioral and adaptive skills can further make it difficult to accurately identify individuals in need. Even within a domain of strength, there are variations in the profile; for example, an individual with strengths in language can show wide variation in regards to receptive versus expressive and functional communication versus social communication [24].

There are a number of attempts to help improve screening and identification, such as the development and validation of a postnatal risk score that helps accurately identify children with prenatal alcohol exposure [25▪▪] as well as a clinical decision tree [26]. Further, there are promising results found

using telemedicine to improve access and accuracy of physical, and cognitive examinations of children with FASD [27,28], which can improve access. Use of initial screenings can indicate that an individual requires a broad multidisciplinary assessment to confirm the diagnosis [29,30]. However, even within broad, comprehensive assessments, there are continued debates over the threshold of what would qualify as a weakness (1 or 1.5 SD), how to best address not knowing a prenatal alcohol exposure history and how to achieve the best sensitivity and specificity in identifying those in need [25▪▪,26,31]. A recent study described the validation of the FASD-Tree as a screening tool for FASD. This tool incorporates readily accessible parent questionnaires and a physical examination and provides two metrics: a numeric risk score and a dichotomous (yes/no) outcome indicating the screening outcome. The FASD-Tree was effective as a screening tool, with accuracy rates of 75–84% and fair to good discrimination [32].

The lack of education of providers and stigma associated with prenatal alcohol exposure can also hinder those screened or referred for an assessment or services. Unfortunately, FASD has often not been a primary consideration in healthcare settings (paediatricians, primary care, OB-GYN, social workers, psychologists, psychiatrists) and has significantly less funding and attention than other less prevalent neurodevelopmental disorders. There have been small steps of improvement. For example, the AAP recently released a new, free online course covering 'Fetal Alcohol Spectrum Disorders: Recognition and Management' to provide paediatric professionals to increase awareness and empower them to recognize and determine a coordinated referral and treatment approach.

Neuroimaging and other potential biomarkers

Over the past few decades, there has been a growing base of research literature describing the structural and functional changes associated with prenatal alcohol exposure to help differentiate those with alcohol exposure from typically developing youth [33] and identify potential clinical correlates that may be provide cause of deficits or targets for intervention [34]. Smaller overall brain size is among the most reported findings, underscoring alcohol's global teratogenic effect on the brain; however, this is not specific to prenatal alcohol exposure, as it also occurs in other disorders. However, there does appear to be some selectivity to alcohol's effects on the brain. Some regions appear to be more negatively affected by alcohol than others, evidenced by structures that are smaller than one would expect given the total brain size (i.e. disproportionately smaller regions). The corpus callosum, basal ganglia and cerebellum are all regions that have rather consistently been found to have disproportionately smaller volumes among individuals with prenatal alcohol exposure [35].

Independent examination of brain region morphology, however, may be underutilizing the vast amounts of MRI data available. Studies using multivariate analyses of brain region volumes have discriminated youth with prenatal alcohol exposure from controls, achieving 77% accuracy, 64% sensitivity and 88% specificity [36]. Further, the combination of neuroimaging with psychometric cognitive measures has been shown to be extremely effective in correctly classifying children with prenatal alcohol exposure. Using the Connors 3 Hyperactivity/Impulsivity score, magnetic resonance spectroscopy, and diffusion tensor imaging of supraventricular white matter resulted in highly accurate (92%) discrimination of children with prenatal alcohol exposure and Attention-Deficit/Hyperactivity Disorder (ADHD) from children with ADHD but without such exposure, achieving perfect sensitivity (100%) and high specificity (82%) [37]. This is particularly exciting given the high difficulty in discriminating between children with and without prenatal alcohol exposure, who may need different clinical treatments or have different trajectories or prognoses. This research suggests that neuroimaging may be beneficial in the diagnostic process.

In addition, functional MRI studies have mapped the haemodynamic response to a number of tasks among individuals with prenatal alcohol exposure, generally finding altered patterns of brain activation and/or recruitment of a broader range of brain regions when completing tasks [35,36]. Further, several studies have demonstrated that disrupted resting-state functional connectivity in children with prenatal alcohol exposure relates to poorer performance on cognitive tests [36,38,39]. These imaging studies indicate that we may have more objective methods to identify individuals with prenatal alcohol exposure and they also can help illustrate the potential relation between neurological changes and clinical presentation.

There are also new efforts underway to find biomarkers such as meconium or baby teeth to more objectively assess levels of prenatal alcohol exposure [40,41] as well as faecal microbiota in preclinical trials [42]. Although still limited, this research can help to combat the difficulty of ascertaining information about the history of prenatal alcohol exposure, which is often missing or incomplete for various reasons, despite the importance in diagnostic clarity.

CONCEPTUALIZATIONS OF FETAL ALCOHOL SPECTRUM DISORDER AND NOVEL RESEARCH AREAS

In the past few years, there has been a new movement focused on strength-based reframing and understanding the potentially modifiable factors that could improve outcomes [43]. Some argue that the lack of strength-based research has perpetuated the stress and stigma experienced by those with prenatal alcohol exposure [15▪▪]. A review of recent strength-based literature finds that individuals with FASD, particularly young adults and adults, have strong self-awareness, are receptive to support, have capacity and often seek human connection, are resilient, and have hope for the future. These strengths and a growth mindset grounded in hope and change in the future can facilitate greater quality of life. Individuals with FASD can have challenges across settings (home, school, medical system, justice system) and there is a great need for strengths-based, comprehensive, FASD-informed care that is coordinated across environments [44,45]. An additional hope of a strength-based and informed conceptualization of FASD is to reduce stigma. Stigma and shame actively impede access to diagnosis and treatment from both the provider and the patient perspective. In addition to education requirements for healthcare providers, other areas should be explored that can help birth mothers, adoptive families and self-advocates better seek treatment.

Understanding of midlife and adulthood

FASD is a lifelong condition that can have differential effects in childhood, young adulthood and middle adulthood as abilities, environment and expectations change. As FASD was first codified in 1973 by Jones and Smith ([46]), those who were diagnosed in infancy at that time are now entering midlife. Recent research has attempted to capture the areas of concern individuals are experiencing across the lifespan as well as increase understanding of their developmental trajectories (e.g. developmental delay versus stable weakness) [8▪,33,47]. On the basis of the emerging findings, prenatal alcohol exposure was associated with greater rates of mental health disorders in middle adulthood [48▪], including higher rates of depression, anxiety, bipolar disorder and attention-deficit/hyperactivity disorder, as well as increased suicidality [15▪▪]. These increased rates were mediated by greater environmental stressors, adverse childhood events and lower socioeconomic status, which are common for individuals with prenatal alcohol exposure [21]. Given these preliminary findings, more research is needed to understand the effects of prenatal alcohol exposure across the lifespan, where much remains unknown.

Recent policy advances

In consideration of a continuing and clearly documented need for action, there have been a number of bills introduced to help codify access to services and recognition of FASD. A recent bill passed in California in 2022 (SB1016, [49]) which specifically includes 'fetal alcohol spectrum disorder' in the definition of 'other health impairment' that is entitled to special education and related services. In addition, there is a bipartisan bill before the US congress introduced in 2021, the FASD Respect Act (HR 4151), which would support the coordination of research, surveillance and related activities to diagnose, prevent and treat FASD, including establishing centres for excellence, implementing best practices, providing additional services and supporting the development of systems of care for those affected by FASD [50]. In September 2021, the UK government published a comprehensive health needs assessment for FASD [51].

INTERVENTION MODALITIES AND TARGETS

The wide continuum of potential outcomes associated with prenatal alcohol exposure leads to a complex clinical presentation that necessitates development of targeted evidence-based interventions [52,53]. Focus has been on cognitive (particularly executive function, inhibitory control), academic (predominately math), behavioral (mood, secondary diagnoses), legal/justice (overrepresented and prone to confabulation, [54]), adaptive function (daily living skills, social skills, care facilities) and health outcomes (sleep, nutrition, cardiac, medication). In addition to some of the few FASD-specific interventions (e.g. MILE program for math [55] and Children's Friendship Training for social skills, [56]), there are several novel interventions that are also being piloted, such as music training to increase attention [57]. Understanding the underlying cause of areas of weakness can also assist in targeted, clinical intervention. For example, understanding that behavioral regulation weaknesses are associated with poor adaptive function may point to a specific cognitive area to target for broader positive outcomes [58].

Mobile apps to support intervention have also been developed for both children [work by Dr. Christie Petrenko - Families Moving Forward (FMF) Connect for caregivers of children with FASD, ages 3–12 years] and adults (My Health Coach).

These apps were developed by working closely with individuals with prenatal alcohol exposure using theory-guided planning to increase access to care and ideally ease the barriers to effective intervention. In addition, there is active development of new resources to help children and young people with FASD understand their diagnosis and become self-advocates through Me and My FASD, which is one of the first peer-to-peer FASD resources [59].

There are still very few interventions specifically for individuals with prenatal alcohol exposure, though there have been more resources that have been made available to schools [60▪], justice systems, parents and healthcare settings to help improve outcomes. There is also great opportunity for the repurposing of interventions that can target specific behaviors associated with prenatal alcohol exposure, if they are implemented effectively (e.g. considering the full profile of functioning and environment).

Use of supplements and psychopharmacological intervention

Over the past decade, there has been a focus in both preclinical and clinical research on the use of choline to help mitigate the effects of prenatal alcohol exposure by using supplementation during critical developmental windows to enhance brain plasticity. Clinical findings indicate that young children who receive choline had higher neurocognitive skills, including nonverbal intelligence, visual spatial skills, working memory, verbal memory and fewer behavioral symptoms [61]. In addition, maternal choline supplementation may be neuroprotective [62]. In addition to human studies, preclinical data show that choline supplementation may be able to mitigate long-term effects of prenatal alcohol exposure [63]. Although additional longitudinal follow-up and study is needed, including on short and long-term risks of any treatment, based on the preliminary findings [64], choline may be a worthwhile intervention for a population that has very few options available. Preclinical data are also investigating the use of iron supplementation to improve fetal outcomes in prenatal alcohol exposure [65].

There is a dearth of research regarding the best course of action regarding psychopharmacological intervention for FASD, though many children, adolescents and adults are on various medications to manage behavioral and psychiatric symptoms. New research is trying to address this concern by understanding prior utilization of psychotropic medications in children with FASD [66] as well as evaluating the efficacy of medication management [67▪].

CONCLUSION

Although we have come a long way in the identification and intervention of FASD, there are clear ongoing documented areas of need. We need better (or better used) screening procedures that coalesce on a single diagnostic schema to assist with earlier identification. Increased access to effective intervention as well as tailored supports are required across the lifespan. Broader, holistic conceptualization of FASD, the use of a strength-based framework and encouragement of self-advocacy can also help in both increasing understanding and improving outcomes and quality of life. This is the time to increase prevention efforts and raise awareness in healthcare settings and broader policy to improve access to services to those affected by prenatal alcohol exposure.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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