Prenatal exposure to alcohol can damage the developing fetus and is the leading preventable cause of birth defects and intellectual and neurodevelopmental disabilities. In 1973, fetal alcohol syndrome was first described as a specific cluster of birth defects resulting from alcohol exposure in utero. Subsequently, research unequivocally revealed that prenatal alcohol exposure causes a broad range of adverse developmental effects. Fetal alcohol spectrum disorder (FASD) is the general term that encompasses the range of adverse effects associated with prenatal alcohol exposure. The diagnostic criteria for fetal alcohol syndrome are specific, and comprehensive efforts are ongoing to establish definitive criteria for diagnosing the other FASDs. A large and growing body of research has led to evidence-based FASD education of professionals and the public, broader prevention initiatives, and recommended treatment approaches based on the following premises:

- Alcohol-related birth defects and developmental disabilities are completely preventable when pregnant women abstain from alcohol use.
- Neurocognitive and behavioral problems resulting from prenatal alcohol exposure are lifelong.
- Early recognition, diagnosis, and therapy for any condition along the FASD continuum can result in improved outcomes.
- During pregnancy:
  - no amount of alcohol intake should be considered safe;
  - there is no safe trimester to drink alcohol;
  - all forms of alcohol, such as beer, wine, and liquor, pose similar risk; and
  - binge drinking poses dose-related risk to the developing fetus.

HISTORY AND TERMINOLOGY

Fetal alcohol spectrum disorders (FASDs) is an overarching phrase that encompasses a range of possible diagnoses, including fetal alcohol syndrome (FAS), partial fetal alcohol syndrome, alcohol-related birth defects (ARBD), alcohol-related neurodevelopmental disorder (ARND),...
and neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE). FAS refers to a clinical diagnosis based on a specific constellation of physical, behavioral, and cognitive abnormalities resulting from prenatal alcohol exposure (PAE).\(^1\) By 1973, sufficient research evidence had accrued to devise basic diagnostic criteria such that FAS became established as a diagnostic entity.\(^1\) The US Surgeon General issued the first public health advisory in 1981 (reissued in 2005) that alcohol during pregnancy was a cause of birth defects.\(^2,3\) In 1989, Congress mandated that alcohol product labels include a warning about potential birth defects. Nineteen states and the District of Columbia have now enacted laws requiring these warnings at the point of sale, including bars and restaurants.\(^4\)

As it became evident that PAE resulted in a spectrum of lifelong manifestations, varying from mild to severe and encompassing a broad variety of physical defects and cognitive, behavioral, emotional, and adaptive functioning deficits, the term “fetal alcohol effects” was adopted to describe children who had PAE manifestations yet did not meet the FAS diagnostic criteria, primarily by lacking physical abnormalities associated with FAS. Because the term was too broad and vague for practical clinical or epidemiologic use, it was retired from use in 1996 and replaced with 2 pathophysiologically based diagnostic categories: ARBD and ARND.\(^5-7\)

Despite greater public awareness, improved terminology, and an accruing body of research, the lack of uniformly accepted diagnostic criteria for FAS and other related disorders has critically limited efforts to determine accurate prevalence figures, expand awareness and prevention campaigns, actuate early identification and intervention programs, and delineate the full continuum of alcohol-related conditions. As part of the fiscal year 2002 appropriations legislation, Congress mandated that the Centers for Disease Control and Prevention (CDC) develop diagnostic guidelines for FAS and related disorders and integrate them broadly across medical and allied health professions’ training curricula. Under the auspices of the CDC, acting through the National Center on Birth Defects and Developmental Disabilities FAS Prevention Team, in conjunction with the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effects, a multidisciplinary scientific working group of key national experts engaged in an intensive collaborative effort to draw conclusions about PAE effects. This collaborative conducted a comprehensive review of scientific and clinical evidence and extensively consulted with clinicians, experts, and families to delineate clear diagnostic criteria for FAS on the basis of a combination of 3 cardinal facial features, growth problems, and central nervous system abnormalities qualified by confirmed or unknown PAE (Fig 1).\(^8\) Through this effort, practical clinical approaches were endorsed so that those children with PAE could be more readily identified, the condition could be diagnosed with greater accuracy, and children could be referred for appropriate services.\(^9,10\)

In April 2004, the National Institutes of Health, CDC, and the Substance Abuse and Mental Health Services Administration, along with additional experts in the field, were convened by the National Organization on Fetal Alcohol Syndrome to develop the following consensus definition of FASD: “FASD is an umbrella term describing the range of effects that can occur in an individual whose mother drank alcohol during pregnancy. These effects include physical, mental, behavioral, and/or learning disabilities with possible
lifelong implications. The term FASD encompasses all other diagnostic terms, such as FAS, and is not intended for use as a clinical diagnosis.”11

Research continued to accrue about ARND, that is, individuals with PAE-associated neurodevelopmental and behavioral abnormalities yet without the FAS facial phenotype, so that in late 2011, the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders organized a consensus conference to define ARND diagnostic criteria and related screening and referral needs.7 As an outgrowth of this conference, a subcommittee collaborated with the American Psychiatric Association in preparing the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, reorganized on a neurologic disorders framework. The manual includes FASD under the term “FAS (ND-PAE).”12 FASD terminology continues to evolve, and research evidence suggests that ARBD may be declining in use while ARND/ND-PAE terminology remains incompletely defined. ND-PAE may become the accepted diagnostic term for moderate PAE findings, and “static encephalopathy” associated with PAE is a suggested diagnostic term for severe PAE effects.13

**EPIDEMIOLOGY**

FASDs remain among the most commonly identifiable causes of developmental delay and intellectual disability yet are generally accepted to be vastly underrecognized. FAS, ARBD, and ARND prevalence rates and occurrence patterns have been the subject of many studies since the late 1970s. The wide variance in reported rates reflects the specific diagnoses studied and the different research methodologies used, the 3 most common methodologies being clinic-based studies, passive surveillance of existing records often limited to a geographic area, and active case ascertainment studies.14,15 Although the prevalence of FAS in the United States during the 1980s and 1990s was reported as 0.5 to 2 cases per 1000 live births, recent studies aggressively diagnosing FASD have reported FAS rates and FASD estimates of 6 to 9 cases and 24 to 48 cases per 1000 children (or up to 5%), respectively, while continuing to consider these rates underestimates.14–16 Rates as high as 9 cases per 1000 live births have long been documented among vulnerable populations, usually related to isolation and socioeconomic impoverishment, such as can be more often found among certain American Indian and other racial/ethnic minority populations.17–19 An FAS prevalence of 1.0% to 1.5% has been reported among children in foster care.20

A recent study among a population of foster and adopted youth referred to a children’s mental health center reported a FASD misdiagnosis rate of 6.4% and a missed diagnoses rate of 80.1%.21 FAS is the FASD with the most explicit diagnostic criteria, so it only represents a fraction of individuals affected by PAE. FASDs other than FAS are more challenging to diagnose, so the true FASD prevalence remains unknown and the actual impact underappreciated.14–16

Approximately half of all US women of childbearing age have reported past month alcohol consumption, and use ranged from sporadic intake to 15% reporting binge drinking.22 Binge drinking is a pattern of drinking that raises a person’s blood alcohol concentration to 0.08% or greater and was originally defined as 5 or more standard drinks per occasion (generally within 2 hours).23 A “standard drink” contains approximately 0.5 fluid oz of pure ethanol, which is the amount found in a 1.5-oz shot of distilled spirits, 5 oz of wine, or 12 oz of beer. In 2004, the National Institute on Alcohol Abuse and Alcoholism changed the binge drinking definition for women to “the ingestion of 4 or more drinks per occasion” to account for known physiologic gender-related differences affecting alcohol absorption.24 Setting this lower threshold for binge drinking among women also served to increase prevalence.25 Binge drinking in the preconception period is associated with unintended pregnancy and a higher likelihood of risky behaviors, including drinking during pregnancy.26 Often, PAE is unintentional, occurring before the woman knows that she is pregnant. Women continue to drink alcohol and binge drink during pregnancy despite the US Surgeon General’s warnings and their awareness that risk for potential harm exists.27–29 Although most women report cutting down or abstaining from alcohol use during pregnancy, 7.6% of pregnant women report continued alcohol use, and 1.4% report binge drinking.22

FASD as such is not heritable, and having a FASD does not increase a woman’s risk of having a child with FASD. No genetic factors are known to be predictive of which particular children with PAE will have FASDs or the extent of effects. Multiple studies and meta-analyses have focused on how various patterns of drinking during pregnancy might affect fetal and child development.30–40 Mills et al prospectively studied approximately 31 000 pregnancies to determine how much alcohol pregnant women could safely consume and found increased risk of infant growth retardation even when consumption was limited to 1 standard drink daily.30 Although a consensus is still lacking about the effects of low levels of PAE, harmful effects are well documented related to moderate or greater PAE and to binge drinking.32–40 The potential for fetal harm increases as maternal alcohol consumption rises.32,40 Despite methodologic differences, potentially confounding factors, and variable sensitivity among the detection methods applied, these studies support advising that the
healthiest choice regarding alcohol use during pregnancy is to abstain.

**FASD DIAGNOSIS**

Ongoing work seeks to define specific diagnostic criteria for each of the FASD conditions along the continuum, such as has been possible for FAS. The FAS diagnosis is made only when an individual meets all 3 diagnostic criteria: prenatal and/or postnatal growth deficiency, the 3 cardinal facial features (reduced palpebral fissure length, smooth philtrum, and thin upper vermilion lip border [Figs 2, 3, 4A, 4B and 5]), and any of a range of recognized structural, neurologic, and/or functional central nervous system deficits.8–10 Confirmed PAE strengthens the evidence, but FAS can be diagnosed without this history when all of the specific FAS diagnostic criteria have been met. Diagnosing FAS also means a comprehensive history has documented any other in utero substance exposures, including tobacco, medications, or illicit substances of abuse, and that other possible genetic and environmental etiologies have been excluded, specifically Williams, Noonan, 22q deletion syndromes, trisomy 21, and fetal toluene embryopathy, because some dysmorphological features are shared with FAS.41 All other FASD conditions have a range of PAE-associated findings that meet only some of the FAS diagnostic criteria. A computer-based 3-dimensional facial image analysis is showing promise in identifying PAE-affected children who have cognitive impairments but lack the FAS diagnostic facial features.42 ARBD refers to children with confirmed PAE and certain physical findings related to congenital structural malformations and dysplasias affecting organ systems and/or specific minor anomalies but normal neurodevelopment.10,13,31 A confirmed history of PAE should also prompt careful developmental screening and assessment for ARND/ND-PAE, which is among the possible diagnoses when there are no physical stigmata of FAS, yet evidence of brain abnormalities, and either structural or functional neurocognitive disabilities manifest as problems with neurodevelopment, behavior; adaptive skills, and/or self-regulation.7,9,10 Other individuals whose features meet most but not all of the diagnostic criteria for FAS are described as having partial fetal alcohol syndrome. Fetal exposure to alcohol and to one or more additional substances complicates the causal explanation of clinical findings because the potential teratogenic, fetal growth, and neurobehavioral effects might be attributable to exposure to the other drug(s) alone, or to multiple different exposures, or to drug combinations, including alcohol.

**MEDICAL, BEHAVIORAL, AND COGNITIVE PROBLEMS**

Although a classic FAS diagnostic triad has long been identified, other findings, including microcephaly, behavioral abnormalities, and “noncardinal” abnormal facial features, such as maxillary hypoplasia, cleft palate, or micrognathia, are also well recognized to co-occur with PAE.1,41,43 A wide range of developmental and/or medical problems can accompany FAS as a result of alcohol’s structural and/or functional effects on the brain and various other organs or systems, particularly the cardiovascular, renal, musculoskeletal, ocular, and auditory systems.1,41,44 A growing body of FASD research has focused on delineating how various brain volume deficits are related to neurocognitive function and facial dysmorphology, and close correlations with alcohol use in the first trimester of pregnancy have been found.45,46 Fetal death is the most extreme PAE outcome, and PAE is also associated with sudden infant death syndrome (Fig 5).33,47 Children and adolescents with known PAE experience a variety of behavioral and cognitive difficulties, ranging from subtle learning and/or behavioral problems to significant intellectual disability.10,45,48–50 PAE is associated with a higher incidence of attention-deficit/hyperactivity disorder (ADHD) and specific learning disabilities, such as mathematics difficulties.48,50–52 The neurocognitive profile associated with FASDs results from deficits in visual-spatial and executive functioning, including impaired impulse control, memory skills, and problem-solving, but also difficulties with abstract reasoning, auditory comprehension, and pragmatic language use.45,52 PAE-associated executive dysfunction is evident as slow information processing and integration, and children with FASD...
show deficits in cognitive planning, concept formation, set shifting, verbal and nonverbal fluency, social interaction skills, and peer relationships. Because attention deficits are considered a common characteristic of people with FASD, these skills have been extensively investigated. Children with FASD have demonstrated attention deficiencies with their capacity to hold information temporarily in memory while coding it or performing a mental operation on it and with the ability to shift attention flexibly compared with those with ADHD, who display greater difficulty with focus, concentration, and staying on task. Children and adolescents with PAE have difficulty rapidly processing relatively complex information and perform worse on visual than on auditory sustained attention tasks. Although a few case reports have associated extreme PAE with autism spectrum disorders, most reports have delineated qualitative differences in the social difficulties experienced by those with FAS compared with individuals with autism spectrum disorders.

SECONDARY AND CO-OCCURRING CONDITIONS

Compared with the general population, although similar to those with other intellectual disability, individuals with FASD have a higher incidence of concurrent psychiatric, emotional, and behavioral problems. Children and adolescents with FASD have a 95% lifetime likelihood to experience mental health issues, and among the most prevalent are anxiety and mood disorders, particularly depression, as well as ADHD, substance use, addiction, and suicide. Individuals with PAE have greater rates of school disruptions, trouble with the law, and under- or unemployment. Failure to achieve age-appropriate socialization and communication skills results in maladaptive and
impaired social functioning. Substance use; inappropriate sexual behaviors, such as inappropriate exposure, improper touching, and promiscuity; and consequent legal problems have been reported in adults diagnosed with FAS.\textsuperscript{50,59,60} Delayed diagnosis and misdiagnosis contribute to the higher risk for secondary and co-occurring conditions.

**TREATMENT**

An integrated multifactorial FASD model that includes genetic, PAE, and environmental factors, among others, provides an approach to understanding and assisting this complex and diverse high-risk population. FASDs have no cure, but affected individuals experience improved medical, psychological, and vocational outcomes through longitudinal intervention and treatment that maximize protective factors and build capacity in identified strengths.\textsuperscript{61–65} Multimodal symptom treatments that improve long-term outcomes include optimizing environmental modifications, parenting strategies, social support, and developmental and educational interventions that address the neurologically based problems related to FASDs.\textsuperscript{61–66} Children with FASDs prescribed neuroleptic medication have shown improved outcomes, but stimulant medication either failed to improve or worsened ADHD symptoms.\textsuperscript{67} The heterogeneity of FASD manifestations calls for tailoring treatments to meet individual needs and addressing these constellations of lifelong disabilities across the lifespan.

Washington State continues to be a national and international leader in FASD diagnostic, prevention, and intervention practices through a long-standing coordinated effort of diverse programs focused on their collective FASD-associated needs and building a strong FASD research and evidence basis. The 2014 recommendations...
from the Washington State Fetal Alcohol Spectrum Disorders Interagency Work Group highlight evidence-based practices that include identifying risk and protective factors, engaging early intervention, addressing the high FASD risk for substance abuse problems, and applying screening-informed treatment planning, including neuropsychological assessment-guided treatment plans.68

Children with FASD are not explicitly designated to receive special education services in the Individuals with Disabilities Education Act; however, some school districts serve affected children through the “Other Health Impaired” category. PAE is not specifically listed in this category but does qualify a child as “at risk” and eligible for early intervention services (Part C). The developmental and behavior difficulties in young children with FASDs qualify for special education services (Part C and Part B). Various school-based educational accommodations have been effective in helping children with FASDs reach their developmental and educational potential, but the transition to the posteducational setting and adulthood poses additional challenges where support services such as vocational training and life skills development are needed.50,63,65,66,68

ECONOMIC EFFECTS
The constellation of medical, surgical, behavioral, educational, custodial, judicial, and other services required to care for an individual with FASD results in a large economic burden to the individual, the family, and society.69 In the 1980s, the estimated annual FAS-related expenses for the United States increased from $75 million to $4 billion, with the lifetime cost of care approaching $1.4 million.50,69,70 Cost estimates are similarly high in Canada but also vary widely depending on the methodologies used.71 During 2005, children with FAS incurred average medical expenditures 9 times higher than those without FAS.72 When FAS with intellectual disability was considered in making these calculations, average expenditures increased an additional 2.8 times the costs for FAS alone.72 Because FAS is only 1 subset of FASD, the true economic effect of FASD is much larger. It has been documented in Canada that an FASD evaluation requires 32 to 47 hours for 1 individual to be screened, referred, evaluated, and given the diagnosis of an FASD, resulting in a total cost of $3110 to $4570 per person.73 On the basis of the cost of a comprehensive multidisciplinary FASD assessment in Canada, the total cost estimate of all FASD screening and diagnosis ranges from $3.6 to $7.3 million per year, excluding treatment costs.73 The estimated lifetime cost of care, including social and health care services, for each child born with FASD is up to $2.44 million.69,74 The calculated expense of raising a child with FASD is 30 times the cost of preventing the FASD.75 In 2005, the annual Medicaid cost to care for a child with FASD was 9 times that of a child without FASD.72

THE ROLE OF THE PEDIATRICIAN AND THE MEDICAL HOME
The main role of a pediatrician and the medical home regarding FASD is to be knowledgeable about the disorder to guide prevention, to suspect and screen for FASD, and to recognize, manage, and refer patients. Pediatricians, medical home team members, and other health professionals are in prime position to provide both primary and secondary FASD prevention education and counseling because young women of childbearing age are among their patient population.76 Pediatricians build trusted relationships with their adolescent and young adult patients and the parents of these patients, and a routine and expected part of medical home care is to discuss personal health responsibilities, including preventing pregnancy, alcohol, and other substance use and abstaining from sexual activity. Many women have misconceptions about the “safety” of alcohol use and as a result continue to consume alcohol during pregnancy despite the Surgeon General’s warnings.22 Refraining from alcohol use during pregnancy is an important message...
to be delivered by health care providers as a part of prenatal care and other health visits during pregnancy. Clear guidance to correct misunderstandings about the risks of alcohol use during pregnancy and educate people about the importance of abstaining from alcohol during pregnancy may prevent further PAE and related outcomes. Earlier termination of alcohol use in pregnancy is associated with fewer alcohol-related complications for the mother and her baby. Specifically, first trimester drinking (vs no drinking) produces 12 times the odds of giving birth to a child with FASD, first and second trimester drinking increases FASD odds 61 times, and drinking in all trimesters increases FASD odds 65 times.

Adolescent patient care standards include providing consistent patient and family education and anticipatory guidance about alcohol use risks, screening for alcohol use and addiction, and intervention to address use and refer patients to treatment. Because adolescents who drink alcohol while pregnant could have a child with a FASD, policies from the American Academy of Pediatrics (AAP) and public domain tools are available to promote pediatrician skills and practices related to alcohol and other drug use screening, brief intervention, and referral to treatment.

Given the prevalence in the United States of alcohol use by women who are sexually active or pregnant, pediatricians, through the medical home, should maintain a high level of suspicion for FASD, become familiar with FASD features, and conduct screening to detect PAE and FASD patients as early as possible. Maternal markers that increase the likelihood of a child having had PAE include the mother’s past history of alcohol or drug use problems, such as addiction, multiple drug use, a previous alcohol-exposed pregnancy, little or no prenatal care, unemployment, a transient lifestyle, incarceration, and/or a heavily drinking partner or family member. Primary care providers should consider the possibility for FASD whenever a child has suggestive physical stigmata and/or is being assessed for poor growth, developmental delays, or behavioral concerns, including attention deficit or school failure. Any history of adoption, especially from an environment of socioeconomic impoverishment, whether domestic or international, and any history of involvement with a US child social services system can indicate a higher likelihood of having had PAE and a need for careful screening for FASD. A history of involvement with child protective services related to parental substance use or to child neglect, abuse, or abandonment is a strong marker for risk, as is a history of any out-of-home or foster care placement, including kinship care. Many people are not aware of the requirement for health care providers to report FASD to child protective service systems. The 2010 reauthorization of the federal Child Abuse Prevention and Treatment Act legislation included specific policy revisions and mandates about FASD, including “a requirement that health care providers involved in the delivery or care of such infants notify the child protective service system,” make appropriate referrals to this system and other services, and develop a plan of safe care.

Medical home care relevant to FASD patients includes documenting a PAE and other substance exposure history and other historical details as well as physical examination findings, diagnosing FAS in patients when possible, and/or referring for comprehensive FASD assessment and diagnostic evaluation for intervention. Effective medical home practices include optimizing the electronic health record use to facilitate documentation of PAE screening as a practice routine and integrating checklists or other tools to facilitate coordinated collaborative care, follow-up connections, and care transitions. Similar to other patients with complex conditions, those with FASDs are best served through periodic well-child care surveillance and coordinated collaborative patient management through referral to medical subspecialists and other health professionals to diagnose and/or manage comorbidities, facilitating access to and enrollment in developmental and educational services, consultation with social work risk assessment services, and coordination with legal and other community resources for the child and family. Partnering with the patient and family helps medical home physicians understand this lifelong diagnosis and how to manage any stigma and emotional responses, such as anger, shame, or blame that may arise from many sources, including themselves. Working closely with families to engage their child in appropriate developmental and educational services is an ongoing role, and it is important to anticipate and coordinate the eventual transition of individuals with a FASD from pediatric to adult care services. Pediatricians may also refer FASD-diagnosed patients to the Supplemental Security Income (SSI) system so they can obtain income assistance and medical insurance. Many infants and children with FASD may be eligible for SSI. Furthermore, SSI can help adolescents and young adults with income support and medical insurance beyond 26 years of age, if not available through their parents. Early referral to the SSI system is important.

Assessment of physician training needs has shown that although pediatricians are knowledgeable about FASD and PAE risks, they inconsistently provide anticipatory guidance for FASD prevention with adolescent patients and lack confidence about integrating into routine practice the care management.
and treatment coordination needed by patients affected by FASDs.

SELECTED PUBLIC DOMAIN RESOURCES

AAP FASD Toolkit. www.aap.org/fasd
Centers for Disease Control and Prevention. www.cdc.gov/fasd
National Dissemination Center for Children with Disabilities. www.parentcenterhub.org/nichcy-resources (All About the IEP—Individualized Educational Program: www.parentcenterhub.org/repository/iep/)
National Institute on Alcohol Abuse and Alcoholism (NIAAA). www.niaaa.nih.gov
• NIAAA Collaborative Initiative on Fetal Alcohol Spectrum Disorders: www.cifasd.org
National Organization for Fetal Alcohol Syndrome (NOFAS): www.nofas.org
• NOFAS National and State Resource Directory: www.nofas.org/resource-directory
Substance Abuse and Mental Health Services Administration (SAMHSA), Fetal Alcohol Spectrum Disorders (FASD) Center for Excellence: www.fascenters.samhsa.gov
SAMHSA Treatment Locator: www.samhsa.gov/treatment/index.aspx

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SUMMARY
There is no known absolutely safe quantity, frequency, type, or timing of alcohol consumption during pregnancy, but having no PAE translates into no FASD. Despite research evidence clearly documenting the spectrum of detrimental consequences of PAE, too many women continue to drink alcohol during pregnancy. Progress continues to be made in understanding the mechanisms of alcohol’s deleterious effects and identifying the most efficacious intervention strategies for preventing and ameliorating deficits associated with FASDs, but each discovery also reveals new challenges. From an economic, societal, educational, family, or health or medical home perspective, FASDs represent a major public health burden. The pediatrician and the medical home as well as cooperative care with practitioners such as obstetricians and family medicine providers play important roles in the success of FASD prevention, intervention and treatment modalities but also in the research progress needed to discover additional means to address the lifelong consequences of FASDs.

Fetal Alcohol Spectrum Disorders (FASD) represent a major economic, societal, educational, and ameliorating de...
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Fetal Alcohol Spectrum Disorders
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