

Italian Guidelines for the diagnosis and treatment of Fetal Alcohol Spectrum Disorders: multimodal approaches of treatment and intervention

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Summary. Fetal Alcohol Spectrum Disorders (FASD) are pervasive disorders that impact various domains of functioning, including self-esteem, familial and peer relationships, and academic success. The high rate of comorbidity may contribute to delayed diagnosis and treatment. Early diagnosis and intervention that aim at primary symptoms may prevent secondary disabilities and improve the outcomes. No intervention emerged as maximally effective across all symptoms and domains. Consequently, the complex pathophysiology of FASD emphasizes the need for individualized assessment and treatment by using a multimodal approach to intervention.

Key words. Adoption, fetal alcohol spectrum disorders, fetal alcohol syndrome, intervention, prenatal alcohol exposure, treatment.

Linee guida italiane per la diagnosi e il trattamento dei disturbi dello spettro feto-alcolico: approcci multimodali di trattamento e intervento.

Riassunto. Il disturbo dello spettro feto-alcolico (FASD) è un disturbo pervasivo che colpisce vari ambiti del funzionamento, tra cui l'autostima, le relazioni familiari e tra pari e il successo accademico. L'alto tasso di comorbidità può contribuire a ritardare la diagnosi e il trattamento. La diagnosi precoce e l'intervento mirato ai sintomi primari possono prevenire le disabilità secondarie e migliorare i risultati. Nessun intervento è emerso come massimamente efficace in tutti i sintomi e in tutti gli ambiti. Di conseguenza, la complessa fisiopatologia del FASD enfatizza la necessità di una valutazione e di un trattamento individualizzati utilizzando un approccio multimodale all'intervento.

Parole chiave. Adozione, esposizione prenatale all'alcol, intervento, disturbo dello spettro feto-alcolico, sindrome feto alcolica, trattamento.

Introduction

When a pregnant woman drinks alcohol, it enters the bloodstream and reaches the fetus by crossing the placenta, interfering with the growth and development of all fetal body systems, especially the developing central nervous system (CNS)^{1,2}. Fetal Alcohol Syndrome Disorder (FASD) refers to the range of mental and physical problems caused by prenatal alcohol exposure (PAE). The problems caused by fetal alcohol syndrome may vary from child to child, and as brain and body damage is permanent, defects caused by fetal alcohol syndrome are not reversible³⁻⁸ and the only suggestion for pregnant women is to quit alcohol drinking while having a health gestation⁹⁻¹². FASD has been recognized in the DSM-5 as a Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure" (ND-PAE)" and placed in the section regarding 'conditions needing further study'¹³.

The aim of this work is, within the scope of the Italian Guidelines for the diagnosis and treatment of FASD, to describe the different types and approaches to the treatment of FASD patients depending on their age.

Primary and secondary disabilities

The signs and symptoms of FASD can be broken down into primary and secondary disabilities (figure 1). Primary disabilities reflect inherent CNS dysfunctions¹⁴. This damage manifests itself in a range of impairments in three core areas including neurocognitive, self-regulation, and adaptive functioning¹⁵. Secondary disabilities are not evident since birth but result from the primary disabilities as well as limited understanding (and availability) of effective interventions. They include poor mental health, disrupted school experiences due to difficulties in learning and/or behavioral problems; negative involvement with the law (troubles with authorities, including being charged and/or convicted of a

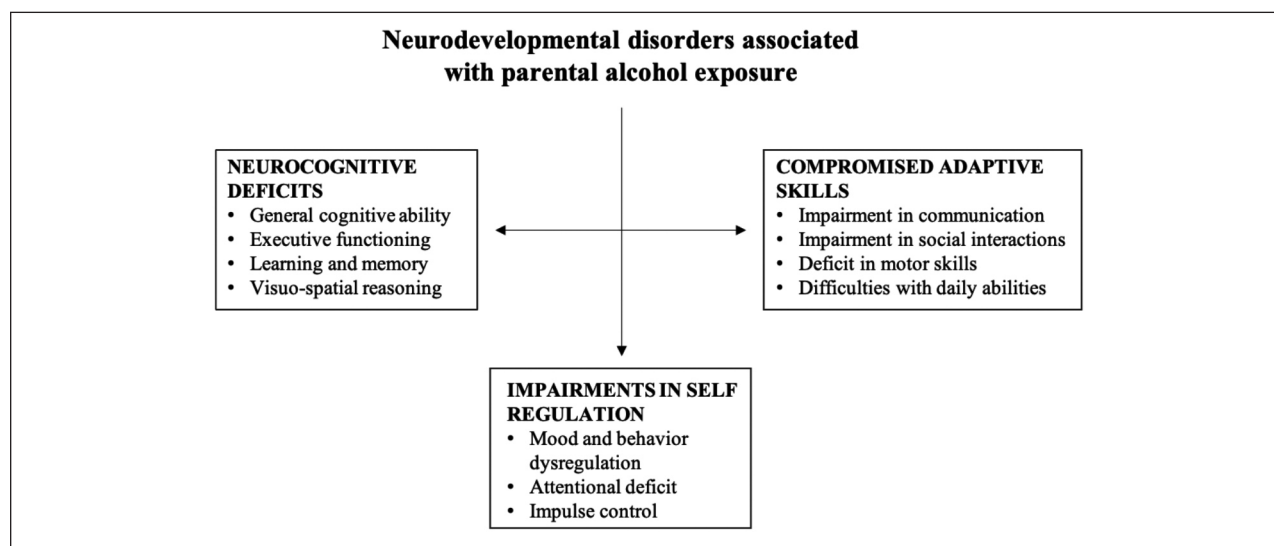


Figure 1. The three core areas including neurocognitive, self-regulation, and adaptive functioning impaired by PAE.

crime), confinement (inpatient treatment for mental health and/or alcohol/drug use, incarceration), substance abuse or addiction, sexually inappropriate behaviors, problems with gaining and retaining employment and issues with independent living¹⁶⁻¹⁸. When the needs of children with FASD are not recognized and the primary disabilities are not adequately treated, is most likely to develop more severe secondary conditions¹⁹.

Petrenko has proposed a model describing the characteristics of intervention to prevent secondary conditions in people with FASD: 1) first of all, the model considers that FASD is a life-long condition and therefore appropriate services are needed across the lifespan; 2) it recommends proactive or preventive approach; 3) due to the variability in the functioning of people with FASD and their families, it suggests that interventions should be individualized or tailored on a person's pattern of strengths and weaknesses and family or living environment; 4) it recommends comprehensive interventions that account for the complex needs and diverse experiences of people with FASD and 5) finally, it emphasizes the importance of central coordination of services that work together to follow the individual with FASD through their developmental stages (figure 2)²⁰.

Comorbidities

Beyond the primary cognitive and behavioral deficits, over 90% of individuals with FASD experience co-occurring mental health problems²¹⁻²⁴. It has been shown in a systematic review published in 2016, that there are over 428 comorbid conditions linked to FASD²⁵⁻²⁷ (figure 3).

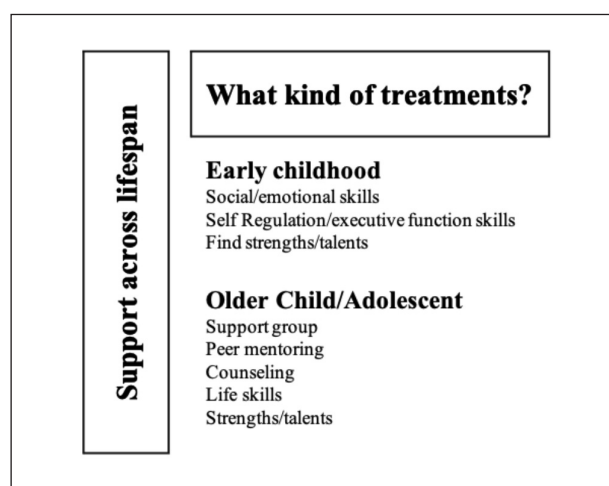


Figure 2. Neurocognitive and behavioral domains primarily treated in individuals with FASD.

FASD has been linked with more self-control, reasoning, problem-solving and planning issues than ADHD²⁸. The attentional deficit in individuals with FASD persists into adolescence and adulthood, and differently from idiopathic ADHD the severity of the symptoms increases with aging²⁹. Moreover, memory deficits in FASD individuals depend on encoding difficulties, while in ADHD those depend on information retrieval problems⁶.

Children with FASD have an increased risk of developing comorbid neurodevelopmental disorders. Comorbid neurodevelopmental disorders most frequently occurring are attention-deficit/hyperactivity disorder (ADHD), present in 50% of persons with FASD³⁰ and Autism Spectrum Disorders (ASD), occurred in a range from 2.6% to 72% of persons with

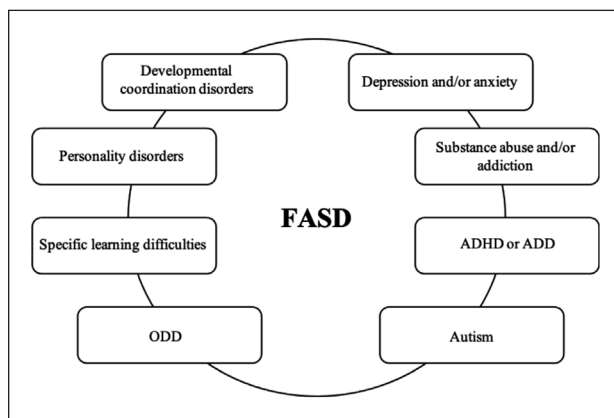


Figure 3. Neurodevelopmental disorders and mental health comorbidities with FASD.

FASD^{27,31}. Many efforts are being made to differentiate idiopathic disorders from those occurring in FASD^{15,31-34}. Anyway, when people have both FASD and ADHD or ASD at the same time, it is very important to consider both diagnoses when planning and implementing treatment keeping in mind that treatment responses for people with ADHD and FASD are different from those who only have ADHD or FASD^{35,36}.

Challenges with mood disorders (i.e., depression and bipolar), anxiety, psychosis (i.e., schizophrenia), and suicidality are very common in FASD^{24,37,38}. Depression and anxiety are among the most common, affecting 45%-50% and 20%-40% of individuals with FASD, respectively³⁹⁻⁴¹. Internalizing disorders, such as depression and anxiety, in adolescents have a large prevalence in FASD^{25,42,43}. Among articles published on the topic, many are focused on supporting early child development by supporting regulation, social skills, attachment, and positive child-caregiver interactions within the family context⁴⁴.

People with FASD are at high risk for developing alcohol and substance disorders⁴⁵. One study found that 38% of people with FASD were using or misusing alcohol and 46% other substances^{46,47}. As almost everyone has also neurocognitive deficits, it is likely that many of them enter treatment with few abilities to learn and benefit from treatment. As undiagnosed cognitive deficits and associated learning problems do in fact play a significant role in treatment failure, it will be important for treatment programs to screen for such factors during intake and modify therapeutic approaches accordingly⁴⁵. Unfortunately, many people who have FASD have never been diagnosed⁴⁸ and some who go through treatment aren't recognized as having FASD disorders⁴⁵ further contributing to the thwarting of treatment attempts. In a recent review study on the possible interventions to improve mental health and substances use in individuals with FASD a total of 33 articles were identified, most of

which were focused on building skills or strategies that underlie the well-being of children with FASD and their families⁴⁴. Nevertheless, a meta-analysis study reviewed 15 clinical trials examining the efficacy of an integrated cognitive-behavioral intervention (CBI) and found variable and very few effects when delivered in a comorbid condition rather than in an idiopathic condition confirming an increased clinical complexity when comorbidity is present⁴⁹.

Outcomes and protective factors

There is no known cure that leads to complete recovery for babies born with fetal alcohol spectrum disorders (FASD). While the physical, mental, and behavioral deficits caused by brain damage usually last a lifetime, the development of secondary disabilities is the result of the complex interaction of factors across ecological levels (e.g., individual, family, care systems, and culture) influencing positively or negatively the outcomes for individuals affected by FASD^{50,51}. Risk factors are conditions that increase the likelihood of maladjustment and/or psychopathology⁵² or, in the case of FASD, of the secondary conditions and family, school and healthcare environments play a key role in reducing risk factors and in improving the developmental outcomes of children with FASD^{16,53}.

The very early detection of FASD remains the best protective factor allowing intervention to begin even before a formal diagnosis is made, at a critical time in neurodevelopment, which consequently causes better outcomes and prognosis^{16,54} (figure 4).

Approach to the treatment

Randomized-controlled trials regarding therapy research for children and adolescents with FASD⁵⁵ indicate that the combination of parents, child and school interventions represents the best way to treat FASD⁴². As FASD is a multifaceted disability, characterized by exceptional clinical complexity and wide-ranging impacts on individuals and their families, a multimodal treatment that involves parents, child and school and that combines medical interventions, pharmacological, cognitive behavioral, and psychoeducational treatment is strongly recommended⁵⁶. The approach involves individuals with FASD, schools and families and combines pharmacological treatment, cognitive behavioral treatment, and psychoeducational treatment⁵¹.

An individual with cognitive deficits and poor social and emotional skills may require a more orientated therapy such as Applied Behaviour Analysis (ABA) to improve functional behavior and reduce

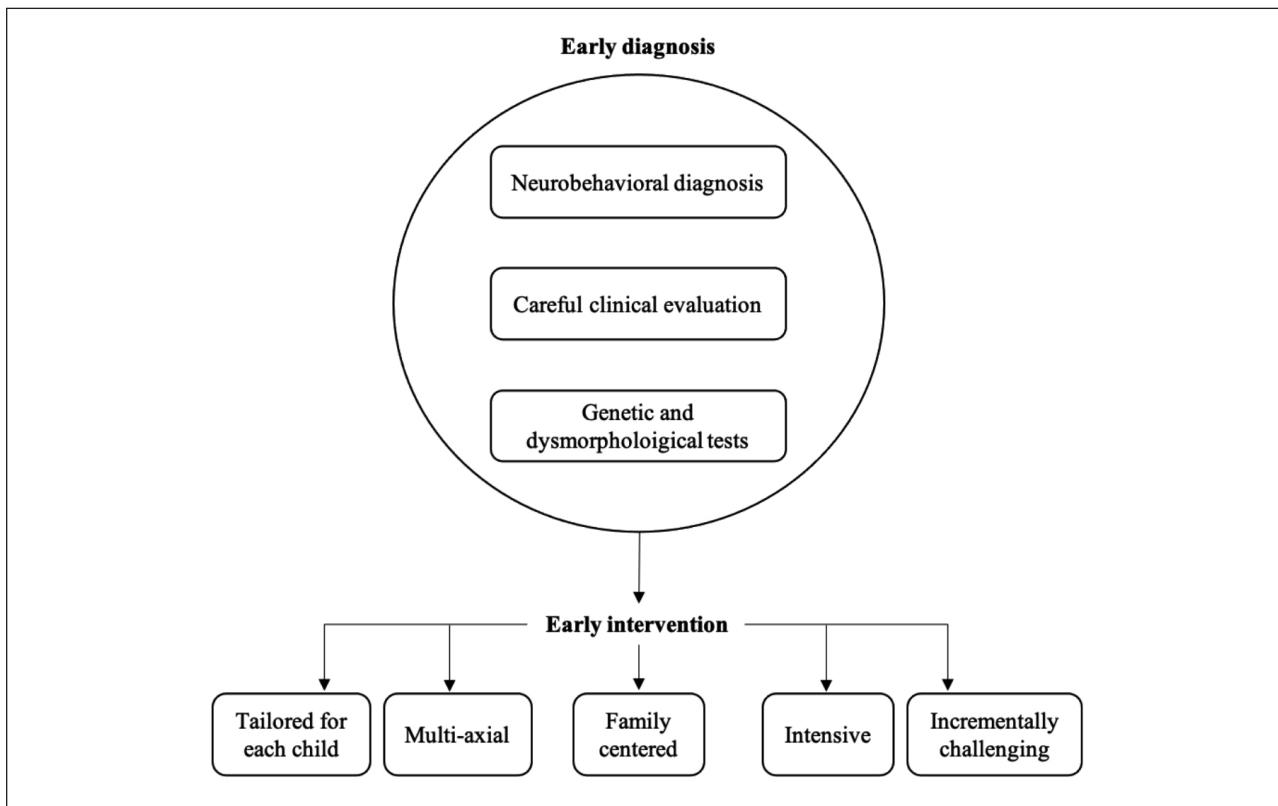


Figure 4. Early diagnosis facilitates the provision of intervention.

dysfunctional ones. Otherwise, an individual without severe cognitive deficits and social and emotional impairment would benefit from dialectical behavior therapy (DBT)^{57,58}.

MEDICAL INTERVENTIONS

Individuals with FASD may present higher rates of health issues compared to the general population. Some of these issues include impaired growth, defects of vision, hearing and heart function, seizures, weakened immune system, sleep and nutrition problems, elimination disorders such as enuresis or/and encopresis, and bad dental health. With interventions including medications, surgeries, nutritional supplements, health education, and exercise, individuals with FASD can manage and mitigate these health concerns⁵⁹.

PHARMACOLOGIC TREATMENT

Many children with FASD require psychopharmacological treatments for comorbid emotional and behavioral diseases. Although psychiatric symptoms are present with high prevalence and comorbidity, there is limited evidence of the use of meds in the FASD population and this raises con-

cerns⁶⁰. As said before, one of the most frequent psychiatric diseases is ADHD, diagnosed in up to 94% of individuals with FASD⁶¹. Stimulants such as methylphenidate and amphetamine derivatives are very effective medications to treat idiopathic ADHD⁶², but their effectiveness varies when used to treat ADHD symptoms in people with FASD⁶³. A recent study found that more than half of the children with a FASD diagnosis were prescribed psychotropic medications. The rates of these medications prescribed among children with co-occurring FASD and another mental disorder were higher compared to children with a mental health issue diagnosis but no FASD⁶⁴. Recently, Mela et al.⁶⁵ described four behavioral symptom clusters commonly seen in FASD associated with a suggested pharmacological treatment by using a prescription algorithm. The four clusters are: 1) *Hyperarousal*: deficits to the brain stem, midbrain, and limbic areas, resulting in mood dysregulation and impaired executive functioning. The first line treatment is adrenergic agents; the second line is Selective Serotonin Reuptake Inhibitor (SSRI); 2) *Emotional regulation*: deficits to the hippocampus, amygdala, hypothalamic-pituitary-adrenal axis (HPA axis), and prefrontal cortex, resulting in emotional dysregulation and abnormal

social behaviors. The first line treatment is mood stabilizers; the second line is SSRI; 3) *Hyperactive/Neurocognitive*: negative deficits are to the dopaminergic and noradrenergic pathways, resulting in hyperactive behavior. The first line treatment is amphetamine stimulants; the second line is other stimulants; 4) *Cognitive inflexibility*: deficits to the frontal lobe, resulting in poor adaption function. Both the lines are atypical neuroleptics. The prescription algorithm is promising but requires further refinement to accommodate the range of presentations in children with FASD⁶⁶.

BEHAVIORAL AND EDUCATIONAL INTERVENTIONS

There are a range of evidence-based approaches that aim to support individuals in developing adaptive behaviors, improving learning, and addressing emotional and behavioral challenges. Behavioral Therapy (BT) focuses on understanding and modifying behavior patterns, is grounded in the principles of learning theory, and emphasizes observable actions. Educational Therapy (ET) focuses on helping individuals with specific learning difficulties (e.g., dyslexia) and emotional or behavioral challenges. Research on Behavioral and Educational interventions for individuals with FASD has increased in recent years, providing significant inputs on how to support and address both the primary and secondary disabilities commonly experienced by people with FASD⁶⁷.

Neurocognitive functioning

Several interventions have been directed towards improving neurocognitive function in FASD⁶⁸. There is a growing evidence base for cognitive interventions targeting self-regulation, memory, and attention⁶⁹. For example: a) Computerized Progressive Attention Training (CPAT) is a computer program that works to improve sustained and selective attention, spatial working memory, reading, and math fluency⁷⁰. Rehearsal training has been effective in improving working memory and may help enhance academic performance in school settings; b) Cognitive Control Therapy (CCT) teaches children how to think and engage in self-regulation and self-observation. It has been tested with children with FASD from 8-9 years old in a school setting in South Africa^{71,72}; c) GoFAR (FAR= Focus and plan, Act, and Reflect) program was developed for children with FASD (5-10 years old) and includes computerized training sessions with the child, parent training, and behavior-analogue training with parent and child. It aims to improve self-regulation, reduce disruptive behavior, and improve adaptive functioning⁷³; d) Alert Program for Self-Regulation utilizes sensory integration and cognitive strategies to help chil-

dren monitor and modify their behavior⁷⁴. The program has been evaluated in a study with children with FASD (ages 6 to 12) and improvements were found in inhibition naming, affect recognition, and parent-reported behavioral regulation⁷⁵; e) Parents and Children Together (PACT) is a group-based program for children with FASD (ages 6 to 12) and their parents. Research suggests PACT is effective in improving executive functioning and child emotional problem-solving, per parent report⁷⁶.

Adaptive functioning

People with FASD experience significant challenges, including those in adaptive functioning. Adaptive functioning refers to a person's ability to adapt to their environment, manage daily tasks, and interact effectively with others. Individuals with FASD have difficulties with various daily living skills regardless of IQ or age^{77,78}. Self-care, time management, financial management, personal safety, employment skills, risk-taking and knowing limits, social responsibility, household maintenance and problem-solving are all areas in which individuals with FASD find heavy difficulties⁷⁹. Specifically, the ability to shift skills emerged as the best predictor of adaptive functioning among children with FASD. These results highlight the possibility that targeting executive functioning domains among individuals with FASD may benefit behavior regulation, which may also extend to the other adaptive skills²³. Mentorship programs such as the WRaP (Wellness, Resilience, and Partnership) applied in Alberta schools, are proving to be a good help to children and adolescents affected by FASD. The WRaP mentors work one-on-one with individuals with FASD to guide and empower them in vocational, educational, and community support, and to help them to have good social skills. The mentors also work with educators, community agencies, and other professionals to provide them with guidance and support.

Social skills

Despite the variability, individuals with FASD consistently struggle with acquiring appropriate social skills. They can have difficulty understanding social cues, to interpret nonverbal communication, and to appropriately respond in social situations. They may have difficulties with impulse control, emotional regulation, and maintaining attention during social interactions. All of the above can adversely affect the ability to establish and maintain meaningful relationships with peers and authority figures⁸⁰. Children's Friendship Training (CFT)⁸¹⁻⁸³ is a 12-week evidence-based program for elementary school children who experience difficulties making or keeping friends.

During each group session, children are taught important social skills and are given the opportunity to practice these skills during socialization activities. Parents attend separate sessions (Families on Track Program) and are taught how to assist their children in making and keeping friends by the introduction of basic sets of social rules, to help children understand social contexts with specific guidance²⁰. Both programs have been found to increase emotional regulation and self-esteem and to decrease anxiety and disruptive behavior^{20,84}.

Academic issues

Learning requires the interactions of multiple cognitive processes including controlled attention, executive functioning, and memory⁸⁵. As mentioned before, impairments in one or more cognitive processes due to FASD interfere with academic performance with deficits in reading, spelling, and math^{68,86}. Educational planning needs to be developed in accordance with the children's individual cognitive and learning profiles focusing on the habilitation of the underlying deficits that influence learning within the context of an academic or school skill. Language and Literacy Training (LLT) focused on enhancing basic literacy skills for children⁸⁷ and Math Interactive Learning Experience (MILE) programs were developed to address deficits in mathematics and learning readiness in children aged three to ten⁸⁸, and are two examples of a good program for FASD children.

Parent training

Children affected by FASD are challenging to parent because of their problematic behaviors experiencing a higher risk of depression, psychological distress, strained family relationships, and poor physical health (including chronic fatigue and disrupted sleep)⁸⁹. Frequently families need 1) emotional support, 2) help to manage conflict relationships with their children, and 3) health services where their child can find treatment for their problems. Indeed, to cope with conflictual caregiver-child relationships, positive behavior support, the help of a mentor, and finding community resources were found to be what caregivers needed⁹⁰. Interesting is the Coaching Families (CF) program, which works to educate families about FASD, help them access resources, and assist in successful advocacy. It also includes a mentor who works with individual families to help them achieve their goals.

Adverse childhood experiences

Strong evidence has demonstrated that the quality of a child's parenting in the early years of life can have

a significant impact on the developing of the parent-child attachment relationship and that a secure attachment is linked to a range of positive outcomes on the child's social, emotional, and psychological outcomes⁹¹. Individuals with FASD experience high rates of prenatal and postnatal adversities, which has a significant impact on their developmental trajectories⁹². It is well-documented in this population that they are often exposed to adverse experiences such as family poverty, homelessness, marginalization, caregiving disruption, death of a parent, abuse and neglect, exposure to familial substance use, violence, mental health problems, and criminal justice system involvement⁹³.

The results of a few studies on interventions that support early parent-child relationships like Child-Parent Psychotherapy (CPP) and that promotes the development of attachment and trauma-informed parenting skills in caregivers of adolescents like The Connect Program are providing encouraging results in the direction of caring for parental relationships⁵⁶. Since the severe effects of PAE on the offspring, the focus of policy and research remains primarily on drinking during pregnancy⁹⁴. However, alcohol use in motherhood is also a significant public health concern, damaging the mother and child's health, and therefore needs to be considered and treated⁹⁵. BCTs, Brief Motivational Techniques, and personalized strategies were found to provide better outcomes for women and their families⁹⁶.

Adoption

The prevalence of FASD among adopted and foster care or orphanage children, particularly in internationally adopted children from countries with a great consumption of alcohol in the general population, such as Eastern European countries, is very high⁹⁷. It has been estimated that at least 50% of adoptees from Eastern European countries meet the criteria for a diagnosis of FASD⁹⁷. Chasnoff et al.⁴⁸ have shown evidence that in the United States up to 80% of children with FASD in the general population, referred for foster care or adoption, are undiagnosed, and 7% are misdiagnosed.

Adopting a child with complex needs, such as those of individuals with FASD, requires a depth of skills, strength and resilience as it is a lifelong disability that requires a family and constant external support in multiple areas of life for optimal outcomes to be achieved^{98,99}. Lisa Balcaen et al.¹⁰⁰, using an Interpretive Phenomenological Analysis (IPA) approach, found four main themes emerged about the adoptive parents' experiences of having a child with FASD in their family, each with several sub-themes: 1) managing individuals with FASD. This

theme is the most directly related to the individual level, namely the tasks associated with parenting, managing schools, coping with crises, and the impact of FASD on family interactions with the community; 2) navigating family cohesion. This theme refers to how family members experience their daily living environment and how certain behaviors like frustration, volatility, and 'never being relaxed' affect everyone's well-being, how living with a child with FASD impacts other children's experiences, parent relationships, and marriage and co-parenting integrity; 3) psychological warfare. This theme is especially pertinent to individual caregivers and includes how the whole FASD experience in the family impacts them emotionally, while at the same time demands that they respond in a way that maintains equilibrium for them personally and for the whole family; and 4) experiences of supports. The theme of support encompassed two subthemes covering formal and informal support. The study results emphasize that caregivers must make adaptations and accommodations over the years as they strive for well-being making internal resources and external supports necessary to help maintain such well-being (figure 5). A form of external support can be provided by family associations, created by parents of children with FASD and adults with FASD. This kind of association aims to create a support network and facilitate access to scientific information about FASD.

Future challenges

Even if the prevalence of FASD is very high rates of diagnosis stay low. Indeed, at an estimated prevalence of 4%, FASD, it is at least 2.5 times more common than autism spectrum disorder (1.52%), 19 times more common than Cerebral Palsy (0.21%), 28 times more common than Down Syndrome (0.14%), 40 times more common than Tourette's Syndrome (0.10%)¹⁰¹. Although is also associated with high rates of comorbidity, which affects parents, caretakers, schools, juvenile corrections, residential care systems, and society, the knowledge and awareness of FASD within the public and among service providers continues to lag compared with other disabilities¹⁰²⁻¹⁰⁷. It is interesting to consider that while children with neurodevelopmental disorders such as speech delay, autism, and intellectual disability have a pathway for having a diagnosis, a treatment, and economic and social help, families of children with FASD often find providers with expertise for other neurodevelopmental disorders and lack training in caring for children with FASD¹⁰⁸.

It is evident the need to create a community network of service that able to provide: 1) a child- and family-centered health and social care system that offers multidisciplinary and cross-sectorial support and services for individuals with FASD and their families; 2) an intervention or treatment plan for in-

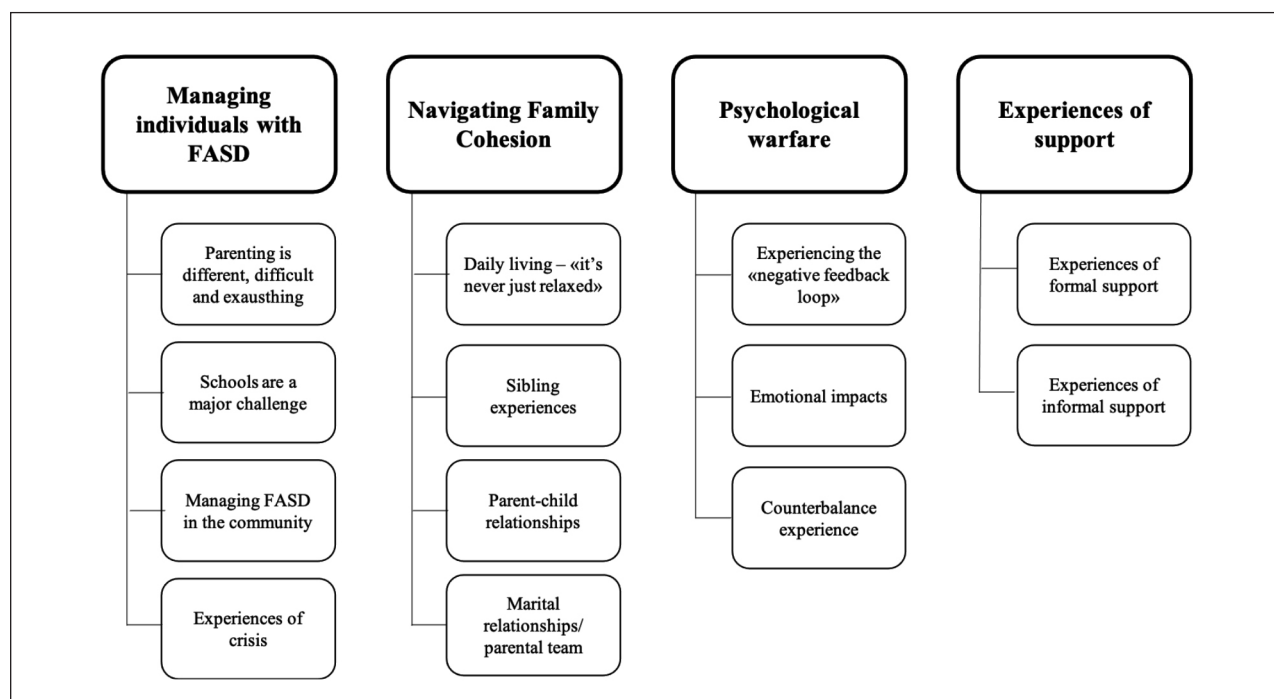


Figure 5. Themes and relative subthemes linked to parents' adoption experiences of having a child with FASD¹⁰⁰.

dividuals with FASD and their families based on their individual needs and the caregiving environment; 3) parental training to help parents better understand their child's challenges and respond to their child's needs in order to improve everyday life; 4) long-term follow-up, because the need for a support and services can continue into adulthood for many children and adolescents with FASD; 5) help to get FASD recognized as a developmental disability eligible for getting assistance for health care, support in school and for rehabilitation; 6) support for specific educational and vocational needs of children considering that adaptive function and social difficulties could exist and persist also in the presence of borderline to normal cognitive abilities, for vocational assessment and life skills training as well as support in finding employment and job coaching⁴⁶.

In conclusion, FASD is a significant social and health issue, and targeted work is needed to 1) better address the unique challenges associated with the disability, 2) recognize and build strengths and resilience, and 3) promote the long-term well-being of individuals with FASD, their families, and their communities.

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