

# SEED Study to Explore Early Development

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Dr. Jenny Radesky

## Experts advise limits on children's media use

Children today have more media choices than ever, with new options introduced all the time. Traditional TV, desktop

computers, and in-home DVD players seem almost quaint compared with the array of content available through tablets, in-vehicle players, smart phones, and gaming devices. Without limits, overuse of media can negatively impact young children's social, emotional, and physical development. Experts say it is particularly important to monitor media use for children with developmental challenges.

In 2016, the American Academy of Pediatrics (AAP) released its newest advice on children's media use, encouraging caregivers to put hands-on playtime first for babies, toddlers, and preschoolers. Young children need "unplugged" playtime in which they can physically explore their surroundings and interact socially with their caregivers, the AAP advised. The first AAP guidelines, from 1999, called for no digital media use for children under 24 months. The newer advice suggests that children ages 2-5 have no more than 1 hour a day of screen time with high-quality content such as Sesame Street or other PBS children's programming. The AAP also says that caregivers should watch with children, to help them understand the content and apply it in real life.

The media landscape has changed drastically since the AAP first offered screen time advice in 1999, said Dr. Jenny Radesky, a University of Michigan behavioral pediatrician who was the lead author of the new AAP policy statement about media use by babies, toddlers and preschoolers. While prior guidelines focused only on time spent using media, the 2016 update is more nuanced. It still addresses time, but also addresses the type of media, the content, and whether the media use is shared between child and caregiver. For example, a caregiver helping a child visit with her grandparents via Skype is different than having that child spend time alone watching a video.

The rapid spread of media options is startlingly evident in data released in fall 2017 by Common Sense Media.

The nonprofit group surveyed a nationally representative group of 1,400 U.S. parents about their children's media use in 2011, 2013 and 2017. These children's ages were from birth to 8 years. Common Sense Media found that 95 percent of children live in a home with a mobile device, up from 41 percent in 2011.

Kids spend an average of 2 hours and 20 minutes a day on screen media, with 48 minutes of that time on mobile devices.

Dr. Radesky treats young patients with autism and other developmental disabilities. "I started to get very interested in digital media use by young children because I saw how much, in clinic, it was being used as a behavior management tool," she said. Some parents offered a child a digital device as a planned strategy to pass time in the waiting room or to occupy the child while the parent and doctor spoke. Others, however, offered a device as a last-ditch effort to calm an upset child. Dr. Radesky believes that it's better to help a child build internal regulation strategies, rather than calm the child with distraction after a tantrum has begun. However she understands that parents at times may need to use a device to reduce distress. "We've all been there," she says, thinking about times when a parent needs help getting their child through a traffic jam or worship service without a meltdown. But she hopes that parents will become more aware of when and how their children access media -- and that they will avoid using it as a default. Children need opportunities to interact with others and to learn to self-regulate their emotions and behavior. In the midst of a tantrum, giving a child a mobile device misses a key chance to coach a child to control himself.



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Children 18 months and younger	Avoid screen media other than video chatting. If you do introduce digital media, choose high-quality programs that you watch with your child to help them understand.
Children ages 2 to 5 years	Limit screen use to 1 hour a day of high-quality programs that you watch with your child to help them understand what they're seeing and how to apply it to the world.
Children age 6 and older	Be consistent about media time limits and types of media. Ensure media use doesn't interfere with sleep and physical activity.
All children	Create media-free times such as dinner and media-free areas, such as bedrooms.

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## More Information:

To learn more about ASD, please visit: [cdc.gov/autism](http://cdc.gov/autism)

To learn more about SEED, please visit: [cdc.gov/SEED](http://cdc.gov/SEED)





## 10 Years of SEED: Moving from Data Collection to Analysis...

In December 2007, SEED enrolled its first study participants. From 2007 to 2012, more than 3,000 children and their caregivers enrolled in the first phase of SEED (SEED 1), and over 2,500 of them completed most study steps.

Once data collection was finished, the SEED Data Coordinating Center at Michigan State University, the CDC, and researchers from all SEED sites carefully reviewed the data to get them ready for study analyses. The full set of SEED 1 data files were ready by 2015 and researchers began working on many different studies to:

- better understand risk factors for autism spectrum disorder (ASD)
- assess the health of children with ASD and other developmental disabilities
- explore the range of developmental characteristics among children with ASD.

More than 20 SEED studies have now been published. We have compiled brief summaries of all of the published studies in a special supplement to this newsletter. Additionally, we have chosen two studies for special focus articles in this newsletter:

- how self-injurious behaviors impact children with ASD.
- how the SEED data on biomarkers provides insight into the effects of smoking in pregnancy.

Many more SEED 1 studies are currently underway and are expected to be published soon. We will continue to provide summaries of all of our published studies in future newsletters.

And, that's just the beginning. The second phase of SEED data collection (SEED 2) took place from 2012 to 2016. The numbers of families who enrolled in and completed SEED 2 study steps were about the same as for SEED 1. Thus, over 5,100 children and caregivers are included in the combined SEED 1+2 data files. These data files were recently prepared for data analyses, and many new studies are now being initiated. With the expanded SEED 1+2 sample, researchers can conduct more detailed assessments of some risk factors. They will also be able to assess some risk factors and health conditions that occur fairly infrequently and thus, were not possible to look at before.

It's been 10 years, and SEED is still going strong. Our third phase of data collection (SEED 3) is underway, and we are seeing the fruits of our labors with the many studies already published or soon to be published. We thank all the participants for their efforts. Because of you, we are learning so much about how ASD affects families.

## What to know when children injure themselves

Some children with autism or intellectual disabilities may hurt themselves by engaging in different types of behaviors, such as head-banging, hair-pulling, arm-biting, scratching and hitting themselves. These "self-injurious behaviors" (SIB) are different from the harmless head banging and rocking that some young, typically developing children engage in to help themselves fall asleep. In typically developing children, these harmless SIB generally disappear by age 3 years.

For most children with developmental disabilities, SIB is mild. But for some children, SIB can be severe and result in cuts, bruises, concussions, and infections. Children with severe SIB may miss out on educational and social activities. SIB can also be very upsetting for the child's family. Parents of children with SIB may feel that they are unable to take their child anywhere or to have visitors.

A recent study by a group of SEED investigators led by Dr. Norbert Soke looked at parent-reported SIB among children with autism spectrum disorder (ASD) and examined different characteristics that may be more common in children who display SIB. Dr. Soke found that the parents of about 28% of children with ASD said their children currently displayed some forms of SIB and 47% reported that their child had SIB now or in the past.

There are many reasons why children may engage in SIB. In SEED, Dr. Soke found that both having current SIB and ever having SIB were associated with problems performing activities of daily living, as well as gastrointestinal, sleep, and behavioral problems (e.g., aggression, hyperactivity). These findings have also been reported by others in the past.

The causes of SIB are not fully understood. Both biological (e.g., genetics and illness) and non-genetic factors (e.g., difficulty interacting and communicating with others) may be involved. Children who have trouble coping with frustration because of their inability to perform routine activities and who have limited communication skills may use SIB to express frustration. Similarly, some children may use SIB to express pain, such as when a child pinches his stomach in response to abdominal pain. SIB may also occur when a child hurts himself in order to avoid something he doesn't want to do or to get something he wants. Children who are tired or distressed may be prone to SIB.

Identifying and treating SIB early may reduce the likelihood of more severe problems later. However, parents and professionals may not recognize early signs of SIB as a potential problem. Some parents have told us that when their child's SIB is frequent but not severe, they can lose track of how often it occurs.



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Because medical providers who see the child infrequently may not be aware of the problem, it is important for parents to let their children's providers know SIB is occurring. It's also worth asking staff at children's educational and therapy programs if they also see the behavior. Sometimes parents are worried that calling attention to their child's self-inflicted injuries may result in them being viewed as negligent or abusive. However physicians, educators and therapists who know about autism are not always aware that SIB is a common problem among children with ASD.

The treatments for SIB vary depending on its cause. Treating an underlying medical problem (e.g., gastrointestinal, sleep, and sensory issues) may reduce SIB. If the cause is emotional or behavioral, a behavior therapist can suggest ways to limit the behavior. Typically the behavior therapist will conduct a functional analysis to uncover relationships between the SIB and the child's physical and social environment. If a child is responding to an aspect of the physical environment such as a noisy room, steps can be taken to reduce the noise and possibly increase the child's ability to tolerate the activity around him. Where frustration or anxiety are found to contribute to SIB, a calming activity may be helpful. Developing strategies that prevent the SIB can also be valuable. For example, when a child reacts with SIB to certain types of situations, finding strategies to minimize the emotional reaction can be helpful. In addition, psychiatric medications may help reduce irritability and anxiety, which can reduce emotional upsets and SIB. Interventions that focus on improving the child's communication skills or the use of alternative ways to communicate may also reduce SIB in some children.

Advice for parents about SIB ---

When are Head Banging and Rocking a Problem?

<https://my.clevelandclinic.org/health/articles/pediatric-body-rocking>

Challenging Behavior in Autism

<https://iancommunity.org/aic/challenging-behavior-autism-self-injury>

Applied Behavior Analysis (ABA)

<https://www.autismspeaks.org/what-autism/treatment/applied-behavior-analysis-aba>

Medicines for Treating Autism's Core Symptoms

<https://www.autismspeaks.org/what-autism/treatment/medicines-treating-core-symptoms>

Soke, GN., Rosenberg, SA., Rosenberg, C., Vasa, Roma, Lee, L-C, and DiGuseppi, C. (2017). *Self-injurious behaviors in children with autism spectrum disorder enrolled in the Study to Explore Early Development*. Autism, 1-11.

## SEED Results: Preschoolers' DNA reflects moms' smoking in pregnancy

A study of SEED data published in the Journal of Environmental Research found that certain markers on preschoolers' DNA hint at whether their mothers smoked during pregnancy. These are called epigenetic biomarkers. The point of the study was not to assess whether smoking raises the risk for ASD, but rather to develop a way to measure things that happened during pregnancy.

In the study, Dr. M. Daniele Fallin, the lead investigator at the Maryland SEED site, co-investigator Dr. Christine Ladd-Acosta and their colleagues tested the DNA of 531 SEED preschoolers. They compared epigenetic biomarkers in the DNA to mothers' answers about smoking in pregnancy. They found the biomarkers could predict mothers' smoking 81 percent of the time.

The research focused on smoking for two reasons. First, moms generally recall if they smoked during pregnancy, even years later. Second, past studies using DNA obtained from babies at the time they were born had found evidence that prenatal smoking leaves epigenetic marks. The SEED study took this a step further by showing that those markers were still present years later. Thus, it is possible to predict whether a mother smoked during pregnancy based on the DNA of a child as old as 5 years.

"If you have a blood sample, you may be able to ask research questions that you could never ask before," Fallin says. For example, it may be possible to tell whether a child's mother was exposed to unknown infections or toxic chemicals during pregnancy – such as chemicals in drinking water or from materials such as plastics. These types of exposures can be difficult or costly to obtain using existing research methods. Ladd-Acosta says, "If we can use this method to learn about past exposures, we may be able to better understand how diseases develop and help to prevent them."

The journal's editors chose the study as their top paper for 2016. The study is Ladd-Acosta C, Shu C, Lee BK, Gidaya N, Singer A, Schieve LA, Schendel DE, Jones N, Daniels JL, Windham GC, Newschaffer CJ, Croen LA, Feinberg AP, Daniele Fallin M. Presence of an epigenetic signature of prenatal cigarette smoke exposure in childhood. *Environmental Research* 2016 Jan;144(Pt A):139-148.







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## Highlights of SEED Progress

### SEED 3 is beginning to grow!

The families joining SEED 3 are adding to the knowledge gathered in SEED 1 and SEED 2! More than 5,100 families finished the first two phases of the Study to Explore Early Development. The data from new families who finish SEED 3 will help us get a better idea of what puts children at risk of developing autism spectrum disorder.



**SEED 1**

**SEED 2**

**SEED 3**

Goal = 21 leaves

**1 leaf = 100 families  
who finished**

Watch for future newsletters to see how SEED grows and visit [www.cdc.gov/seed](http://www.cdc.gov/seed) to see all the editions of the SEED newsletter.



Researchers working on the Study to Explore Early Development (SEED) have recently published many studies reporting on important findings related to autism spectrum disorder (ASD). These studies used data collected from the first phase of SEED (SEED 1). The scientific findings for all SEED studies published to date are summarized below.

Many additional studies are underway. We will provide summaries of those studies in the future.

## Reports Outlining SEED Methods and Descriptions of the SEED Study Sample

SEED investigators have prepared several reports detailing the study methods and describing the children enrolled in the SEED sample. These reports provide foundational information about SEED for other researchers, policymakers, and clinicians.

### **The Study to Explore Early Development (SEED): a multisite epidemiologic study of autism by the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) network.**

Schendel DE, Diguiseppi C, Croen LA, Fallin MD, Reed PL, Schieve LA, Wiggins LD, Daniels J, Grether J, Levy SE, Miller L, Newschaffer C, Pinto-Martin J, Robinson C, Windham GC, Alexander A, Aylsworth AS, Bernal P, Bonner JD, Blaskey L, Bradley C, Collins J, Ferretti CJ, Farzadegan H, Giarelli E, Harvey M, Hepburn S, Herr M, Kaparich K, Landa R, Lee LC, Levenseller B, Meyer S, Rahbar MH, Ratchford A, Reynolds A, Rosenberg S, Rusyniak J, Shapira SK, Smith K, Souders M, Thompson PA, Young L, Yeargin-Allsopp M.

*Journal of Autism and Developmental Disorders, 2012*

This report describes SEED methods. SEED is one of the largest studies investigating genetic and environmental risk factors for autism spectrum disorder (ASD) and child health and behavioral traits associated with ASD. SEED enrolls preschool-aged children with ASD and other developmental disabilities and children from the general population in six sites across the United States. SEED methods focus on enrolling families from diverse populations in each area. A key strength of SEED includes the collection of in-depth information on child development, which allows researchers to more rigorously classify children into various study groups (ASD, other developmental disabilities, or population controls) than what is done in many other ASD research studies. In SEED, researchers use standardized assessment tools to determine a children's final study group and to assess specific behavioral traits among children with ASD. Another key strength is the collection of comprehensive data on child health and potential risk factors for ASD. SEED's large and diverse sample of study participants allows researchers to analyze data in greater detail than most other ASD studies and answer many important questions about ASD.

### **Using standardized diagnostic instruments to classify children with autism in the Study to Explore Early Development.**

Wiggins LD, Reynolds A, Rice CE, Moody EJ, Bernal P, Blaskey L, Rosenberg SA, Lee LC, Levy SE.

*Journal of Autism and Developmental Disorders, 2015*

This report describes the SEED process for determining whether a child enrolled in the study will be classified as an ASD case. This classification is based on an in-person assessment given by trained SEED clinicians. Children enrolled in the study are screened for autism symptoms by asking their mothers to respond to a brief questionnaire. Children with an indication of possible autism symptoms are assessed further during an in person visit. Clinicians give these children a more in-depth developmental evaluation known as Autism Diagnostic Observation Schedule and ask their mothers or other caregivers to participate in an interview known as the Autism Diagnostic Interview – Revised. Besides providing clinicians with information to determine a child's ASD classification, these assessments provide valuable information on ASD-specific behaviors and traits, allowing researchers to better understand the different characteristics among children with ASD.

### **Brief Report: The ADOS Calibrated Severity Score Best Measures Autism Diagnostic Symptom Severity in Pre-School Children.**

Wiggins LD, Barger B, Moody E, Soke GN, Pandey J, Levy S.

*Journal of Autism and Developmental Disorders, 2017*

This report describes SEED methodology for assessing autism symptom severity among children with ASD. Measuring a child's autism symptoms is often challenging because many children with ASD also have other developmental conditions. This can make it difficult to separate a child's social and communication challenges from the child's other developmental delays or conditions. Researchers evaluated several measures of autism severity and found that the Autism Diagnostic Observation Schedule (ADOS) calibrated severity score best measured the severity of core autism symptoms in a way that did not include symptoms of other developmental conditions. Because of findings from this study, the ADOS calibrated severity score will be used in other SEED research to help scientists better understand how the severity of autism symptoms relates to ASD risk factors and health outcomes.



## **Demographic Profile of Families and Children in the Study to Explore Early Development (SEED): Case-control Study of Autism Spectrum Disorder.**

DiGuseppi CG, Daniels JL, Fallin MD, Rosenberg SA, Schieve LA, Thomas KC, Windham GC, Goss CW, Soke GN, Currie DW, Singer AB, Lee LC, Bernal P, Croen LA, Miller LA, Pinto-Martin JA, Young LM, Schendel DE.

*Disability and Health Journal, 2016*

This is one of two reports that describe the characteristics of children enrolled in SEED. This report focuses on sociodemographic characteristics. SEED successfully enrolled a highly diverse sample of participants, including minorities and low socioeconomic status families. The SEED population sample represents racial, ethnic, and demographic diversity in the United States. SEED improves upon other ASD risk factor studies in that it does not rely on administrative data sources, which lack many important details of both child development and maternal risk factors. Nor does it rely on small samples from only a few clinics or schools. SEED collects detailed data in a large and diverse sample. This provides unique opportunities for researchers to learn more about how socioeconomic characteristics relate to risk factors for ASD and health outcomes in children with ASD.

## **Autism Spectrum Disorder Symptoms among Children Enrolled in the Study to Explore Early Development (SEED).**

Wiggins LD, Levy SE, Daniels J, Schieve L, Croen LA, DiGuseppi C, Blaskey L, Giarelli E, Lee LC, Pinto-Martin J, Reynolds A, Rice C, Rosenberg CR, Thompson P, Yeargin-Allsopp M, Young L, Schendel D.

*Journal of Autism and Developmental Disorders, 2015*

This is one of two reports that describe the characteristics of children enrolled in SEED. This report focuses on developmental characteristics. Children enrolled in SEED are divided into four groups: three with children who have varying types of developmental delays and disabilities, including ASD, and one with children from the general population. The report describes how various facets of children's development vary across these four groups and highlights the many needs of children with ASD and other developmental disabilities.

## **SEED Studies of ASD Risk Factors**

### **Maternal and Paternal Infertility Disorders and Treatments and Autism Spectrum Disorder: Findings from the Study to Explore Early Development.**

Schieve LA, Drews-Botsch C, Harris S, Newschaffer C, Daniels J, DiGuseppi C, Croen LA, Windham GC.

*Journal of Autism and Developmental Disorders, 2017*

This study examined associations between ASD and whether, prior to becoming pregnant, a child's mother had a condition that might have affected her ability to get pregnant (i.e., infertility). The study also looked at whether the mother had received any medical treatments to help her become pregnant or to prevent miscarriage during early pregnancy. SEED's detailed data on specific types of infertility disorders and treatments allowed researchers to conduct a much more in depth analysis on this topic than those that have been done previously. The study findings show that several infertility disorders in the mother -- including blocked tubes, uterine conditions such as fibroids, endometriosis, and polycystic ovarian syndrome -- are associated with ASD in children. However, treatments for infertility or to prevent miscarriage were not associated with ASD. While the reasons for the associations with infertility conditions could not be studied, possible explanations include increased inflammation during pregnancy or problems with the mother's immune system. The findings from this study add to studies of other risk factors highlighting the relationship between maternal health before and during pregnancy and ASD.

### **Prenatal Alcohol Exposure in Relation to Autism Spectrum Disorder: Findings from the Study to Explore Early Development (SEED).**

Singer AB, Aylsworth AS, Cordero C, Croen LA, DiGuseppi C, Fallin MD, Herring AH, Hooper SR, Pretzel RE, Schieve LA, Windham GC, Daniels JL.

*Paediatric and Perinatal Epidemiology, 2017*

This study examined associations between alcohol use just before and during pregnancy and ASD or other developmental disabilities (DDs). Previous studies have shown that high levels of alcohol use in pregnancy are associated with child developmental effects, such as decreased intellectual ability, hyperactivity, learning difficulties, and autism-like traits. This study investigated whether lower levels of alcohol use before and during pregnancy were associated with developmental outcomes. Most mothers of children in SEED reported no or low levels of alcohol use before or during their pregnancies. In fact, nearly all mothers reported no alcohol use in the second month of pregnancy or later (93-98% depending on month). Therefore, a main focus of the study was on alcohol use in the three months prior to pregnancy or the first month of pregnancy. The study findings show that modest alcohol use during these four months was not associated with increased risk for either ASD or other DDs. Although this study did not find an association between ASD or other DDs and modest alcohol use before or during pregnancy, women who are pregnant or planning to become pregnant should continue to follow recommendations to avoid alcohol use because of other known effects on infant and child health.



## **Autism Spectrum Disorder and Birth Spacing: Findings from the Study to Explore Early Development (SEED).**

Schieve LA, Tian LH, Drews-Botsch C, Windham GC, Newschaffer C, Daniels JL, Lee LC, Croen LA, Fallin MD.

*Autism Research, 2017*

This study examined whether the amount of time between pregnancies was associated with ASD or other developmental disabilities in children. SEED's detailed data on ASD subgroups and other developmental disabilities allowed researchers to conduct a more in depth analysis on this topic than those that have been done previously. The study findings show that both shorter and longer time periods between births are associated with having a child with ASD. Children conceived less than 18 months after their mother's previous birth and children conceived 60 or more months after their mother's previous birth were more likely to have ASD than children conceived between 18 to 59 months after their mother's previous birth. The relationship was stronger in children with more severe ASD symptoms. Also, the association between birth spacing and ASD appeared to be unique to ASD, as there was no association found between birth spacing and having children with other developmental disabilities. The association between birth spacing and ASD was not explained by unplanned pregnancy, an underlying fertility disorder in the mother, or high blood pressure or diabetes during pregnancy. The findings from this study can help healthcare providers counsel their patients on pregnancy spacing.

## **Maternal Exposure to Occupational Asthmagens During Pregnancy and Autism Spectrum Disorder in the Study to Explore Early Development.**

Singer AB, Windham GC, Croen LA, Daniels JL, Lee BK, Qian Y, Schendel DE, Fallin MD, Burstyn I.

*Journal of Autism and Developmental Disorders, 2016*

This study examined whether ASD was associated with the mother's workplace exposure to certain chemicals or other substances during pregnancy. Because previous studies have shown associations between maternal asthma and allergy and ASD, researchers were particularly interested in exposure to substances that are known to trigger asthma symptoms, called asthmagens. Examples of asthmagens include latex, certain drugs and chemicals such as dyes, and some cleaning products. The findings show that mothers of children with ASD had been exposed to slightly higher levels of workplace asthmagens than mothers of children in the general population. However, the difference was small and could have been due to chance. Many gaps remain in our understanding of how environmental exposures might impact the risk for ASD, and further research is needed.

## **Associations Between the 2nd to 4th Digit Ratio and Autism Spectrum Disorder in Population-Based Samples of Boys and Girls: Findings from the Study to Explore Early Development.**

Schieve LA, Tian L, Dowling N, Croen L, Hoover-Fong J, Alexander A, Shapira SK.

*Journal of Autism and Developmental Disorders, 2018*

This study examined associations between ASD and the ratio of children's index (2nd) finger length to their ring (4th) finger length. The ratio of finger lengths (or digit ratio) has been linked to the level of sex hormones a child was previously exposed to during pregnancy. Researchers study digit ratios because they rarely have direct measurements of fetal exposure to hormones. Study findings in boys showed that digit ratio was associated with ASD, but only in certain subgroups, such as children who had ASD and also a birth defect or genetic syndrome. This suggests the association might not have been related to hormone levels, but might instead be explained by genetics. Study findings in girls showed that digit ratio was associated with ASD and that the association was not limited to certain subgroups of children. There has been little past study of the association between digit ratio and ASD, particularly in girls. The findings in this report suggest that hormone exposures during pregnancy might be related to ASD in girls, but many gaps remain in our understanding of the underlying reasons for this association and further research is needed.

# **SEED Studies of Risk Factors Associated with Adverse Child Outcomes More Generally**

## **Presence of an Epigenetic Signature of Prenatal Cigarette Smoke Exposure in Childhood.**

Ladd-Acosta C, Shu C, Lee BK, Gidaya N, Singer A, Schieve LA, Schendel DE, Jones N, Daniels JL, Windham GC, Newschaffer CJ, Croen LA, Feinberg AP, Fallin MD.

*Environmental Research, 2016*

This study examined how environmental exposures, such as smoking during pregnancy, may impact gene regulation in children. Gene regulation is the process by which genes in a cell are turned on or off, and it is important for child development. Like other studies, researchers found that smoking during pregnancy affected gene regulation in children. However, while other studies have assessed these effects in children at the time of birth, the SEED sample provided an opportunity to look at gene regulation in older children. This study showed that the same pattern of gene effects was present in older children whose mothers had smoked in pregnancy as had been previously observed in newborns. These findings suggest that the gene marks in older children may reflect their mothers' smoking during pregnancy.



# SEED Studies of the Characteristics and Health and Well-being of Children with ASD and other Developmental Disabilities

## **Injuries in Children with Autism Spectrum Disorder: Study to Explore Early Development (SEED).**

DiGuseppi C, Levy SE, Sabourin KR, Soke GN, Rosenberg S, Lee LC, Moody E, Schieve LA.

*Journal of Autism and Developmental Disorders, 2017*

This study evaluated injuries in preschool-aged children with and without ASD and other developmental disabilities (DDs). Parents of children were asked whether their child had ever had an injury that required medical attention, and what types of injuries had occurred. The study findings showed that injuries were common in all groups of children and there was little difference between groups. Parents reported injuries for 32% of children with ASD, 28% of children with other DDs, and 30% of children in the general population. The most common injuries were open wounds and fractures and the most common reason for injuries was falls. While there was a slight difference in injuries between children with ASD and other DDs, further study found that this was largely explained by a higher level of attention problems in the children with ASD.

## **Self-injurious Behaviors in Children with Autism Spectrum Disorder Enrolled in the Study to Explore Early Development.**

Soke GN, Rosenberg SA, Rosenberg CR, Vasa RA, Lee LC, DiGuseppi C.

*Autism, 2017*

This study assessed self-injurious behavior, or SIB, among children with ASD. SIB includes head-banging, hair-pulling, arm-biting, scratching, and hitting oneself. SIB is usually mild, but can be severe in some children and may result in injuries requiring medical care. Children with severe SIB may miss out on educational and social activities. This study showed that in the SEED sample, about 28% of preschool-aged children with ASD displayed SIB currently, and 47% had previously displayed SIB. Researchers found SIB was more common in children with low adaptive behavior scores and gastrointestinal, sleep, and behavioral problems. While its causes are not completely understood, identifying SIB early is helpful because it may reduce the likelihood of more severe SIB later.

## **Brief Report: Self-Injurious Behaviors in Preschool Children with Autism Spectrum Disorder Compared to Other Developmental Delays and Disorders.**

Soke GN, Rosenberg SA, Rosenberg CR, Vasa RA, Lee LC, DiGuseppi C.

*Journal of Autism and Developmental Disorders, 2018*

This study assessed self-injurious behavior, or SIB, among preschool-aged children with ASD in comparison to children with other developmental disabilities (DDs). The study showed that SIB is common in two groups of preschool-aged children – those with ASD and those for whom some autism-related symptoms are reported by their mother or other caregiver, even though they didn't meet the criteria to be classified as an ASD case. SIB was much less common in children with other DDs whose mother or caregiver did not report autism-related symptoms. These findings suggest that clinicians working with young children with DDs consider screening for SIB, even in children who do not have an ASD diagnosis.

## **Homogeneous Subgroups of Young Children with Autism Improve Phenotypic Characterization in the Study to Explore Early Development.**

Wiggins LD, Tian LH, Levy SE, Rice C, Lee LC, Schieve L, Pandey J, Daniels J, Blaskey L, Hepburn S, Landa R, Edmondson-Pretzel R, Thompson W.

*Journal of Autism and Developmental Disorders, 2017*

This study used a complex computer program to assess the wide range of developmental characteristics among children with ASD. Researchers identified four subgroups of children within the ASD group: 1) children with mild language delay and average cognitive functioning, but increased cognitive rigidity (or difficulty changing behaviors); 2) children with significant developmental delay, below average cognitive functioning, and repetitive motor behaviors; 3) children with general developmental delay, below average cognitive functioning, and moderate to highly severe autism symptoms; and 4) children with mild language and motor delays, but increased cognitive rigidity and high rates of problem behaviors. This study shows how information on developmental characteristics can be studied using advanced statistical methods to better understand ASD. This information might also be useful in understanding children's future health and development.

## **The Prevalence of Gluten Free Diet Use among Preschool Children with Autism Spectrum Disorder.**

Rubenstein E, Schieve L, Bradley C, DiGuseppi C, Moody E, Thomas K, Daniels J.

*Autism Research, 2017*

This study estimated the proportion of children with ASD who had been on a gluten free diet. Altogether, 20% of preschool-aged children with ASD were currently or previously using a gluten free diet. In contrast, only 1% of children in the general population control group were using a gluten free diet. Children with ASD who also had gastrointestinal problems or had previously had a developmental regression were more likely to use a gluten free diet. This study demonstrates that gluten free diets are commonly used among children with ASD. More research is needed on the effectiveness of a gluten free diet in managing both gastrointestinal and behavioral symptoms related to ASD.



## **Associations between Parental Broader Autism Phenotype and Child Autism Spectrum Disorder Phenotype in the Study to Explore Early Development.**

Rubenstein E, Wiggins LD, Schieve LA, Bradley C, DiGuseppi C, Moody E, Pandey J, Pretzel RE, Howard AG, Olshan AF, Pence BW, Daniels J.

*Autism, 2018*

This study assessed how the variation in developmental features among children with ASD was related to their parents' own autism-related traits. The presence of autism traits in family members of children with ASD is commonly referred to as the "broader autism phenotype" or BAP. The study findings show that if one or both parents have traits consistent with BAP, the child's ASD is more likely to fall within a certain clinical presentation than if neither parent has traits consistent with BAP. This clinical presentation in the child is characterized by average nonverbal abilities, mild language and motor delays, and increased frequency of other co-occurring developmental difficulties such as anxiety, depression, aggression, and attention difficulties. The findings reported in this study could help better our understanding of the genetics of ASD.

## **Studies that Used SEED Data to Evaluate Clinical and Laboratory Methods**

In addition to research on ASD risk factors and on the developmental characteristics and health outcomes of children with ASD or other developmental disabilities, the wealth of data collected in SEED has allowed researchers to address critical gaps in our understanding of the performance of various ASD screening and assessment tools and to contribute to the development of genetic laboratory tests.

### **Influence of Family Demographic Factors on Social Communication Questionnaire Scores.**

Rosenberg SA, Moody EJ, Lee LC, DiGuseppi C, Windham GC, Wiggins LD, Schieve LA, Ledbetter CM, Levy SE, Blaskey L, Young L, Bernal P, Rosenberg CR, Fallin MD.

*Autism Research, 2018*

This study assessed how the responses to a standardized questionnaire to screen for autism symptoms varied by family demographic characteristics. The study findings indicate that test performance was different in families with an indication of low versus higher socioeconomic status. These findings are important for both researchers and clinicians using autism screening questionnaires; they should be mindful that these tools might perform differently in various sociodemographic groups of children and their parents.

### **Screening for Autism with the SRS and SCQ: Variations across Demographic, Developmental and Behavioral Factors in Preschool Children.**

Moody EJ, Reyes N, Ledbetter C, Wiggins L, DiGuseppi C, Alexander A, Jackson S, Lee LC, Levy SE, Rosenberg SA.

*Journal of Autism and Developmental Disorders, 2017*

This study assessed and compared the performance of two standardized questionnaires to screen for autism symptoms. The accuracy of each questionnaire varied depending on the child's level of developmental functioning and family sociodemographic traits. For example, the instruments were less accurate when children had high levels of challenging behaviors or lower levels of developmental functioning. Test performance also varied in families with indication of lower versus higher socioeconomic status. These findings are important for both researchers and clinicians using autism screening questionnaires; they should be mindful that these tools perform differently in various sociodemographic groups of children and their parents.

### **The Broader Autism Phenotype in Mothers is Associated with Increased Discordance Between Maternal-Reported and Clinician-Observed Instruments that Measure Child Autism Spectrum Disorder.**

Rubenstein E, Edmondson Pretzel R, Windham GC, Schieve LA, Wiggins LD, DiGuseppi C, Olshan AF, Howard AG, Pence BW, Young L, Daniels J.

*Journal of Autism and Developmental Disorders, 2017*

This study assessed whether parents who have autism traits reported their children's potential autism symptoms in a similar way as parents without an indication of autism traits. The findings indicate that parents with autism traits report more autism traits in their children compared to parents without autism traits, but parent reports do not always match clinician assessments based on observed behaviors in the child. It is possible that parents with some autism traits are more adept at identifying subtle characteristics of autism in their child. Another possible explanation for the study findings is that questions on various child behaviors could be interpreted differently by parents with and without autism traits. Further study is needed. The findings reported in this study could help better our understanding of developmental assessment results in young children.

### **"Gap Hunting" to Characterize Clustered Probe Signals in Illumina Methylation Array Data.**

Andrews SV, Ladd-Acosta C, Feinberg AP, Hansen KD, Fallin MD.

*Epigenetics & Chromatin, 2016*

This study assessed new laboratory approaches to analyzing information on genetics collected through SEED. The findings contribute to the growing literature on how genes and environmental factors might interact in a way that increases the risk for ASD. While this study does not directly study these interactions, researchers describe and demonstrate how new laboratory approaches could help identify genetic associations.



# Studies that Used SEED Data in Combination with Data from Other Studies to Better Understand ASD Risk Factors

## Cross-tissue Integration of Genetic and Epigenetic Data Offers Insight into Autism Spectrum Disorder.

Andrews SV, Ellis SE, Bakulski KM, Sheppard B, Croen LA, Hertz-Picciotto I, Newschaffer CJ, Feinberg AP, Arking DE, Ladd-Acosta C, Fallin MD.

*Nature Communications, 2017*

In this study, researchers used SEED data and data from other studies to learn more about genetics and genetic regulation in children with ASD. While it is well-understood that genetics are related to ASD, many unanswered questions remain, such as how certain genes are turned on or off. The information from this study provides insights about how certain genes might be related to ASD.

## Pleiotropic Mechanisms Indicated for Sex Differences in Autism.

Mitra I, Tsang K, Ladd-Acosta C, Croen LA, Aldinger KA, Hendren RL, Traglia M, Lavillaureix A, Zaitlen N, Oldham MC, Levitt P, Nelson S, Amaral DG, Hertz-Picciotto I, Fallin MD, Weiss LA.

*PLOS Genetics, 2016*

In this study, researchers used SEED data and data from other studies to investigate sex-specific genetic effects for ASD. The findings indicate involvement of genes on the X chromosome. These findings help us better understand how ASD might differ in girls and boys.