SEED Study to Explore Early Development

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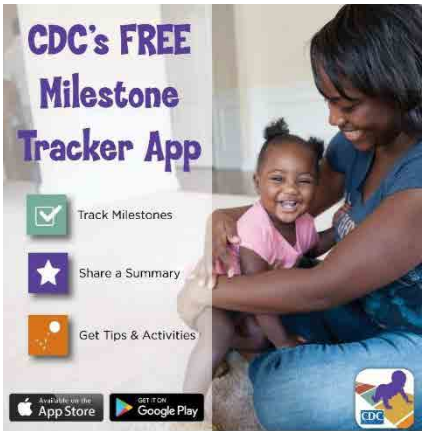


A New Way to Keep Track of Your Child's Progress

Every new parent looks forward to their baby's first step or first words. Now, parents can track their child's progress with a free Milestone Tracker app from the Centers for Disease Control and Prevention (CDC). Use this free, parent-friendly app to track and celebrate your young child's development from ages 2 months through 5 years. See photos and videos that illustrate milestones. Try new activities to support your child's early development. Get helpful reminders for appointments, and more!

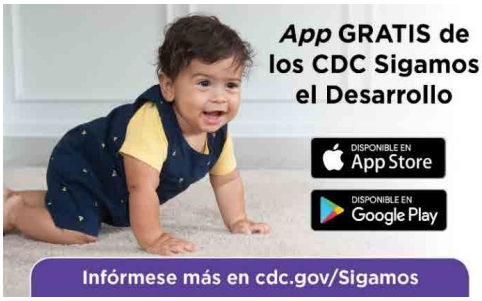
Although it's packed with parent-friendly features, this app is not just for parents! Healthcare providers can use it to help with developmental surveillance (regularly monitoring a child's development to identify problems with development early), as recommended by the American Academy of Pediatrics. Early care and early education providers can use the app to better understand their students' skills and abilities and to engage families in monitoring developmental progress.

The app is available in both English and Spanish. It has been culturally adapted for Spanish-speaking parents of young children, as *Sigamos el Desarrollo*.

To get the app, go to www.cdc.gov/MilestoneTracker, or click here to download from the App Store or here to download from Google Play.

"I love the photos and videos on Milestone Tracker. It helps me to know exactly what milestones my son should be reaching."

Jasmine B., mother of 1-year-old, Atlanta, GA



Inside this issue ...

Autism and Genetics

Autism spectrum disorder (ASD) is a complex condition that affects social skills, communication, and other behaviors. Despite improvements in our understanding of ASD, we still have a lot to learn about its causes and treatment. Studies indicate ASD has both environmental (meaning exposures, like a person's diet, medicines, or pollutants, which are external) and genetic causes.

Many types of genetic mutations (meaning changes in a person's genes) are linked with ASD. Because of these genetic changes, some people are more likely to have ASD. For example, families who have one child with ASD have an increased risk of having a second child with ASD. Similarly, if one twin is diagnosed with ASD, the other has a higher likelihood of having ASD.

However, genetics do not account for all ASD risk. Things in the environment may also contribute to ASD risk for some children. Researchers are examining whether environmental factors might interact with a person's genetic makeup to elevate ASD risk. The interaction between genes (made up of DNA within each cell in the body) and the environment is a major focus of the Study to Explore Early Development (SEED).

SEED is one of the largest studies designed to compare children with ASD and other developmental disabilities to children without these conditions. SEED has sites in California, Colorado, Georgia, Maryland, Missouri, North Carolina, Pennsylvania, and Wisconsin. Each SEED study site collects information on risk factors, including family members' health, experiences of mothers during pregnancy, and children's health and development during infancy and the first few years of life. In addition, SEED has collected blood and saliva, which give us genetic information about parents and children. Research using SEED's data will contribute to our understanding of how genetics and environmental factors contribute to the development of ASD.

Identifying the genetic causes of ASD can help us understand who may be at risk for ASD. This information can help doctors and caregivers diagnose ASD at earlier ages. Being able to diagnose ASD earlier allows children to begin ASD treatment at a younger age. Early treatment can help reduce how severe some ASD symptoms can be.

CS302357-A

Centers for Disease Control and Prevention
National Center on Birth Defects and Developmental Disabilities

Sharing Data on ASD: Opportunities for Research

Do you ever wonder if scientists around the country who study ASD pool their resources to better understand it? It turns out they do. Data, or information, collected from different ASD studies are combined on an ongoing basis into a database for researchers to access. By combining smaller studies into one database, scientists can have more information to study questions they couldn't look at before.

Q: How are scientists working together to study ASD?

A: Two big projects are underway that allow scientists to share data for research. Data from different projects are combined at a repository (a place where de-identified data are kept all together). The two big projects are called the National Database for Autism Research (NDAR) and the Database of Genotypes and Phenotypes (dbGaP). The data in NDAR and dbGaP are managed by the National Institutes of Health (NIH), which is part of the U.S. Department of Health and Human Services.

Q: What information is included in NDAR and dbGaP?

A: NDAR and dbGaP include information about study participants' genes, health, and health behaviors. Researchers can use this information to see if certain genes are linked with the risk of ASD as well as explore how genes and health factors combined might be related to autism.

To protect privacy, information that can be used to identify an individual person, such as names, addresses, birthdates, and other personal information, is not included in NDAR or dbGaP.

Q: Why are scientists sharing data this way?

A: By sharing data from smaller studies, researchers hope to learn about autism more quickly and at lower costs than they could if they worked separately. Sharing data also allows scientists to study genetics and ASD more easily.

Q: Will SEED share my data with NDAR or dbGap?

A: SEED will only share data if the family has given us permission to do so. If you participated in SEED between 2007 and 2011, you may be contacted by SEED study staff in the future to ask if you are willing to have your own or your child's information sent to NDAR or dbGaP. Beginning in 2012, families participating in SEED were asked specifically if they were willing to have their information shared with these databases. We will only share information for those families who gave us written consent to do so.

Q: What information will SEED send to NDAR or dbGaP?

A: If permission is granted, SEED scientists will share genetic and other health data. We will not share any private information, such as names, addresses, birthdates, or phone numbers with NDAR or dbGaP.

Q: If my own or my child's data are sent to NDAR or dbGaP, will I get genetic results back?

A: No, genetic data are being used for research purposes only. We will not send the results of any genetic testing to families.

Q: Will I be asked for more specimens (such as blood, cheek brushes, or saliva) for NDAR or dbGaP?

A: No. You will not be asked for additional specimens. We have finished collecting the specimens needed from all families who have completed their participation in SEED. Additional specimens are not needed even if you participate in NDAR or dbGaP.

Q: Is there a risk that my child could be identified if his or her information is sent to NDAR or dbGaP?

A: Because everyone's genetic information is different, there is a very small chance that someone with access to the databases could trace an NDAR or dbGaP participant's genetic data back to the participant or biological relative. The risk of this happening is very small, as NIH has safeguards in place to protect participants' privacy.

Q: How do NDAR and dbGaP protect participants' privacy?

A: Only scientists approved by the NDAR Data Access Committee may obtain research data from NDAR. Scientists who have approval to analyze data must protect the data using standard procedures. Similarly, scientists who want to analyze data in dbGaP must get authorization from dbGaP's Data Access Committee.

Q: Can I change my mind about sharing my own or my child's information with NDAR or dbGaP?

A: If a participant decides later not to share his or her information with NDAR or dbGaP, that participant can request that it not be shared any longer. However, any data already shared with NDAR cannot be taken back.

Q: How can I find out more about NDAR and dbGaP?

A: For more information on these projects, go to:

NDAR: http://ndar.nih.gov/index.html

dbGaP: http://www.ncbi.nlm.nih.gov/gap

Meet Colorado SEED

In Colorado, the University of Colorado School of Medicine (UCSOM), the Colorado School of Public Health (CSPH), and the Colorado Department of Public Health and Environment (CDPHE) work together to invite families to participate in the SEED study and to collect and analyze the data.

Situated in the Front Range of the Colorado Rockies, JFK Partners, on the University of Colorado Anschutz Medical Campus, houses the Colorado SEED. The Colorado SEED site is led by two professors:

- Cordelia Robinson Rosenberg, PhD, RN, a professor of pediatrics and psychiatry at UCSOM and
- Carolyn DiGuiseppi, MD, MPH, PhD, a professor of epidemiology at CSPH

JFK Partners is designated as Colorado's University Center of Excellence in Developmental Disabilities (UCEDD) and Leadership Education in Neurodevelopmental Disabilities (LEND) Program. They have collaborative relationships with many organizations that are a part of Colorado's developmental disability and special healthcare needs communities.

By working together, UCSOM, CSPH, and CDPHE have also been able to conduct other multi-site CDC projects. One of these projects, which is led by CDPHE, is the Autism and Developmental Disabilities Monitoring (ADDM) Network. ADDM has the important task of monitoring the frequency of ASD in communities across the United States. In addition to the SEED and ADDM projects, several other research studies are ongoing at JFK Partners:

- Colorado Project LAUNCH (Linking Actions for Unmet Needs in Children's Health)
- SPARK (Simons Foundation Powering Autism Research for Knowledge)
- FORWARD (Fragile X Online Registration with Accessible Research Database)

Results Corner

Several SEED articles have recently been published. Below is a brief summary of each. Please see our website for a full listing of SEED publications. https://www.cdc.gov/ncbddd/autism/seed-research.html.

Demographic and Operational Factors Predicting Study Completion in a Multisite Case-Control Study of Preschool Children

Bradley CB, Browne EN, Alexander AA, Collins J, Dahm JL, DiGuiseppi CG, Levy SE, Moody EJ, Schieve LA, Windham GC, Young L, Daniels JL

American Journal of Epidemiology, 2018

This report describes study completion among 3,769 families who enrolled in the first phase of SEED between 2007 and 2011. Families were asked to complete multiple steps for SEED, including phone interviews, filling out forms, participating in an in-person visit to check a child's development, and providing biological specimens (such as cheek swabs and blood). Researchers found that completion was generally 70% or higher for each study step and 58% of participants completed all key study steps. Researchers found that completion rates varied by families' demographic characteristics and also the distance they had to travel to the study clinic. This information is important in helping researchers understand the SEED data already collected and in planning future SEED phases. These study findings also inform researchers on possible ways to improve participation in other future studies.

Family History of Immune Conditions and Autism Spectrum and Developmental Disorders: Findings from the Study to Explore Early Development

Croen, LA, Qian Y, Ashwood, P, Daniels JL, Fallin D, Schendel D, Schieve LA, Singer AB, Zerbo O

Autism Research, 2018

This study examined the relationship between autism spectrum disorder (ASD) and other developmental disorders (DDs) and having a family history of conditions related to immune system functioning. Such conditions include asthma, allergies, and autoimmune disorders such as eczema or psoriasis. Previous studies have suggested some association, but the results about specific conditions varied. SEED's large sample size and detailed data on specific types of immune disorders allowed researchers to conduct an in-depth analysis on this topic and examine the associations with ASD alongside associations with other DDs. The study findings show that maternal history of eczema or psoriasis and asthma are associated with both ASD and other DDs in children. Researchers also found that children with ASD are more likely to have eczema or psoriasis and allergies than children without ASD. Autoimmune disorders were not notably increased among children with other DDs. This study highlights the relationship between maternal health before and during pregnancy and ASD and other DDs, and provides researchers more information about the health of children with ASD.

Continued on pages 4-5

Case-control Meta-analysis of Blood DNA Methylation and Autism Spectrum Disorder

Andrews SV, Sheppard B, Windham GC, Schieve LA, Schendel DE, Croen LA, Chopra P, Alisch RS, Newschaffer CJ, Warren ST, Feinberg AP, Fallin MD, Ladd-Acosta C

Molecular Autism, 2018

In this study, researchers used SEED data and data from another study of children and adolescents with and without ASD to learn more about how genes are regulated in children with ASD. Many genes are turned on or off by a process called "methylation." Although methylation does not change a person's actual genes (or genetic code), methylation helps different types of cells do their specific jobs by affecting which genes are turned on and which genes are not. The researchers examined children's DNA to look for differences in the methylation of genes between children with and without ASD. Previous studies of methylation in relation to ASD were limited by small sample sizes. This study is one of the largest so far to look broadly at methylation patterns in children with and without ASD. The study showed several potential differences in methylation between children in the two groups. Some of the differences suggest links to brain function, and they were consistent with results from previous studies. These findings provide clues as to how genes might be related to ASD in children.

Bayesian Correction for Exposure Misclassification and Evolution of Evidence in Two Studies of the Association between Maternal Occupational Exposure to Asthmagens and Risk of Autism Spectrum Disorder

Singer AB, Fallin MD, Burstyn I

Current Environmental Health Reports, 2018

In this study, researchers used SEED data and data from another study of children with and without ASD to assess how potential errors in coding the data for certain risk factors might influence the findings of epidemiologic studies. Researchers often want to study the effects of certain exposures during pregnancy but may not have the exact data they need. It is rare to have biologic measurements of the chemicals women were exposed to during pregnancy. Therefore, studies often rely on related information to classify study participants as "likely exposed" or "not exposed" to certain chemicals. For example, studies often use information on a person's job — such as type of job and industry where the person worked — to estimate possible chemical exposures from their workplace. In this study, researchers used a statistical method to address the possibility that certain job coding schemes could result in errors when evaluating associations between workplace exposures and ASD. They propose a way researchers might use this method in future studies to assess, and possibly correct, exposure classification errors.

Sleep Problems in 2- to 5-Year-Olds with Autism and Other Developmental Delays

Reynolds AM, Soke GN, Sabourin KR, Hepburn S, Katz T, Wiggins LD, Schieve LA, Levy SE

Pediatrics, 2019

This study assessed sleep problems, such as difficulties going to sleep or staying asleep through the night, in preschool-aged children with ASD, in comparison to children with other developmental disabilities (DDs) and children in the general population. SEED's large sample and detailed data on preschoolers allowed researchers to conduct a more in-depth analysis on this topic than in previous studies. Study findings show that children with ASD and children with other DDs who have some ASD symptoms have more sleep problems than children with DDs without ASD symptoms and children in the general population. Even when researchers used a conservative definition to classify children as having sleep problems, 47% of children with ASD and 57% of children with other DDs who had some ASD symptoms were reported to have sleep problems, compared to 29% of children with DDs but no ASD symptoms and 25% of children in the general population. Sleep is important for development in young children. Addressing sleep problems among children with ASD and children with other DDs who have ASD symptoms is an important component of healthcare needs in this population.

Relationship of Weight Outcomes, Co-occurring Conditions, and Severity of Autism Spectrum Disorder in the Study to Explore Early Development

Levy SE, Pinto-Martin JA, Bradley CB, Chittams J, Johnson SL, Pandey J, Alison Pomykacz A, Ramirez A, Reynolds A, Rubenstein E, Schieve LA, Shapira SK, Thompson A, Young L, Kral TV

The Journal of Pediatrics, 2019

This study examined overweight and obesity among children with ASD, other developmental disabilities (DDs), and children from the general population. Study findings show that children with ASD or DDs were more likely to be overweight or obese than children from the general population. The proportion of children who were either overweight or obese was 28% in those with ASD, 25% in children with another DD, and 20% in children in the general population. Children with ASD or DDs were also more likely to have birth defects, medical disorders, seizure disorders, attention-deficit/hyperactivity disorder (ADHD), and psychiatric disorders than children from the general population. After controlling for these co-occurring conditions, the association between ASD and overweight or obesity was not changed, but the association between overweight and obesity and other DDs was reduced. In addition, among children with ASD, those with moderate or severe symptoms of ASD were more likely to be overweight or obese than children with mild ASD symptoms. Addressing overweight and obesity among children with ASD and other DDs is an important component of healthcare needs in this population.

Maternal Pre-pregnancy Body Mass Index (BMI) and Gestational Weight Gain in Relation to Autism Spectrum Disorder (ASD) and Other Developmental Disorders in Offspring

Windham GC, Anderson M, Lyall K, Daniels JL, Kral TV, Croen LA, Levy SE, Bradley CB, Cordero C, Young L, Schieve LA

Autism Research, 2019

This study examined the relationship between mother's body mass index (BMI) before pregnancy, mother's weight gain during pregnancy, and associations with ASD and other developmental disabilities (DDs). Although previous studies have reported an association between higher maternal BMI and ASD, having this information, along with weight gain during pregnancy in SEED, allowed researchers to conduct a more in-depth analysis on this topic than previous studies. Study findings show an association between higher pregnancy weight gain and having a child with ASD, and this association was even stronger when the mother was overweight or obese before becoming pregnant. On the other hand, while maternal BMI before pregnancy was associated with having a child with a DD, mother's weight gain during pregnancy was not. This study highlights the possible effects of maternal weight on child having ASD or DDs and the importance of maintaining a heathy weight before and during pregnancy.

Brief Report: Maternal Opioid Prescription from Preconception through Pregnancy and the Odds of Autism Spectrum Disorder and Autism Features in Children

Rubenstein E, Young JC, Croen LA, DiGuiseppi C, Dowling NF, Lee LC, Schieve L, Wiggins LD, Daniels J

Journal of Autism and Developmental Disorders, 2019

This study examined possible associations between prescription of opioid medications just before and during pregnancy and ASD and other developmental disabilities (DDs). Currently, the information available on this topic is very limited. SEED collects detailed information about mothers' health histories, including prescribed medication, which allowed researchers to conduct this exploratory analysis. Illicit opioid use was not included in this analysis. The study findings show that approximately 8% of mothers reported receiving an opioid prescription just before or during pregnancy; of these mothers, the majority (76%) received only one prescription. The most common reasons for opioid prescriptions were migraine headaches, injury, and back pain. Mothers who were prescribed opioids just before becoming pregnant were more likely to have a child with ASD or a child with DDs and some autism symptoms. Researchers were limited by small sample sizes; thus, they were not able to conduct a detailed assessment of whether the associations found were related to the medication itself, the reason the mother took the medication, or some other unknown factors that may be associated with opioid use. This study is among the first to assess possible associations between prescription of opioids just before or during pregnancy and ASD and other DDs. More research is needed to understand how opioid use before and during early pregnancy may impact a child's development.

Infections in Children with Autism Spectrum Disorder: Study to Explore Early Development (SEED)

Sabourin KR, Reynolds A, Schendel D, Rosenberg S, Croen L, Pinto-Martin JA, Schieve LA, Newschaffer C, Lee LC, DiGuiseppi C

Autism Research, 2019

This study evaluated the association between early childhood infections and ASD and other developmental disabilities (DDs). SEED's large sample size allowed researchers to conduct a more in-depth analysis on this topic than previous studies. The study findings show that children with ASD were more likely than children with other DDs and children from the general population to have had an infection in the first 28 days of life (early infection). Overall, 4.9% of children with ASD, 4.2% of children with other DDs, and 2.2% of children in the general population had an early infection recorded in their medical records. Children with ASD were also more likely to have an infection in the first 3 years of life than children in the general population, but children with ASD had similar rates of infection during their first 3 years as children with other DDs. This study highlights that ASD is associated with infections very early in the child's life.

A Novel Protocol for Characterizing Dysmorphology to Enhance the Phenotypic Classification of ASD in the Study to Explore Early Development

Shapira SK, Tian LH, Aylsworth AS, Elias ER, Hoover-Fong JE, Meeks NJL, Souders MC, Tsai AC, Zackai EH; Alexander AA, Yeargin-Allsopp M, Schieve LA

Journal of Autism and Developmental Disorders, 2019

This study used data from SEED to develop a new method to systematically classify certain physical features in children. The purpose of this system is to evaluate dysmorphology, which is the assessment of physical features that do not follow the typical pattern of growth and development. Children with multiple dysmorphic features often have an underlying genetic condition or had early pregnancy exposures that affected their development during the pregnancy. The SEED dysmorphology classification method is more comprehensive than that used in previous studies. The findings from this study indicate that approximately 17% of children with ASD have a high number of dysmorphic features, and hence, meet the criteria for classification as dysmorphic. In contrast, approximately 5% of children from the general population control group met the criteria for classification as dysmorphic. Some, but not all, of the dysmorphology differences between children with and without ASD were explained by previously recognized and diagnosed genetic conditions and birth defects, which both occur more commonly in children with ASD. This is the first report of dysmorphology among children with ASD in a diverse U.S. population.

Centers for Disease
Control and Prevention
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and Developmental Disabilities

CADDRE

Center for Autism and
Developmental Disabilities
Research and Epidemiology

Highlights of SEED Progress

SEED 3 is growing!

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.

1 leaf = 100 families who finished

SEED 1

SEED 2

SEED 3
Goal = 21 leaves

Watch for future newsletters to see how SEED grows and visit www.cdc.gov/seed to see all the editions of the SEED newsletter.