

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Report to Congress:

Pediatric Research in Fiscal Year 2019

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PEDIATRIC RESEARCH AT THE NATIONAL INSTITUTES OF HEALTH

Research advances supported by the National Institutes of Health (NIH) have transformed the diagnosis, treatment, and prevention of disease. Children have benefitted greatly from revolutionary progress in biomedical research. Taking folic acid before and during pregnancy prevents most neural tube defects. Survival rates for preterm infants have increased substantially. The genetic causes of several disorders have been identified, such as Fragile X syndrome and Rett syndrome. Several conditions that once caused intellectual disability, like congenital hypothyroidism or phenylketonuria (PKU), are no longer major threats. Scientists' understanding of how children grow and develop has grown immensely and informed early intervention efforts that have dramatically improved the lives of millions of children worldwide.

Pediatric research continues to be an NIH priority. NIH's strong basic and clinical research portfolio provides the foundation for pediatric research in a variety of scientific areas, including neurodevelopment, cardiology, cancer, pharmacology, and behavioral and social sciences. In fiscal year (FY) 2019, NIH funded research grants and projects directed specifically at pediatric research for a total of \$4,922,180,825, as detailed in Table 1 in the Appendix. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) funds the largest portion of pediatric research among the NIH institutes, centers, and offices (ICOs), taking a leadership role in many pediatric research efforts that involve trans-NIH collaborations. For example, NICHD leads the Trans-NIH Pediatric Research Consortium (N-PeRC), which was established in June 2018 to coordinate pediatric research programs, best practices, and training opportunities across all NIH ICOs. All the ICOs support pediatric research; NICHD alone accounts for only 18 percent of the total NIH support for pediatric research. This reflects the breadth of the research portfolio at NIH dedicated to improving the health of children everywhere.

NEW IN FY 2019

In FY 2019, several new technologies for pediatric populations emerged from NIH-supported research. For example, NICHD-supported researchers applied artificial intelligence techniques to diagnose newborn screening results more rapidly, providing timely information to inform treatment decisions. A new handheld imaging tool, supported by National Eye Institute (NEI) researchers, improved diagnostics for infants with vision impairment. A wearable tool supported by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and the NICHD, coupled with standard therapy, increased socialization skills in children with autism spectrum disorder more than children who received only the standard therapy. Several interventions, initially supported by NIH funding, were approved by the Food and Drug Administration (FDA). For example, the first gene therapy approved for treating spinal muscular atrophy (SMA) was originally supported by the National Institute of Neurological Disorders and Stroke (NINDS). In another example, based on the promising results of a phase II multicenter trial, the Food and Drug Administration (FDA) awarded selumetinib with a breakthrough therapy designation.¹ This designation allows the FDA to speed up the review process and possible approval of this drug. Selumetinib is being used to treat symptomatic and/or progressive neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN) in children age 3 and older. In NF1, a signaling pathway that causes tumor growth is turned on. The researchers found that selumetinib blocks a protein in this signaling pathway and reduces the size of tumors. The researchers also found that NF1 patients who were treated with selumetinib experienced improvements in clinical outcomes, such as less pain, more strength,

¹ On April 10, 2020, the FDA approved Koselugo (selumetinib) for the treatment of pediatric patients with NF1. Koselugo is the first drug approved by the FDA for the treatment of NF1.

and better quality of life. After a year of treatment, most patients (or their parents) reported improved pain scores, strength, and range of motion.

NIH also launched several initiatives that will provide insight into child development and childhood disorders. The NIH Baby Toolbox (NBT) is a comprehensive developmental assessment tool for infants and toddlers ages 1 month to 42 months that allows researchers and clinicians to evaluate brain development in infants and toddlers using a computer tablet. Supported by the trans-NIH Helping to End Addiction Long-termSM (HEAL) initiative, the HEALthy Brain and Child Development Study will follow a large population of children from the prenatal period to age 10 to examine the impact of early exposure to opioids, other substances, and social stressors on brain development in children. In 2019, the Trans-NIH Fragile X Coordinating Committee published the NIH Strategic Plan for Research on *FMR1*-Associated Conditions, recognizing gaps and opportunities in studying a gene that plays an important role in the development and function of the brain and nervous system. Pediatric research at NIH has made great progress in characterizing typical development, diagnosing potential disorders, and designing interventions to improve overall health.

THE PEDIATRIC RESEARCH INITIATIVE

In the Public Health Service Act (the Act), Congress directed the Secretary of Health and Human Services (HHS) to establish a Pediatric Research Initiative (PRI) in the NIH Office of the Director (OD). The Act also directed the OD to

“... annually report to Congress and the public on the extent of the total funds obligated to conduct or support pediatric research across the National Institutes of Health, including the specific support and research awards allocated through the Initiative.”

– Section 409D(c)(3), Public Health Service Act

In response to this directive, NIH has prepared the following report for FY 2019. The overall purpose of the PRI is to “conduct and support research that is directly related to diseases, disorders, and other conditions in children” (Section 409D(a), Public Health Service Act). More specifically, the purpose of the PRI is

(1) “to increase support for pediatric biomedical research within the National Institutes of Health to realize the expanding opportunities for advancement in scientific investigations and care for children;

(2) to enhance collaborative efforts among the Institutes to conduct and support multidisciplinary research in the areas that the Director deems most promising; and

(3) in coordination with the Food and Drug Administration (FDA), to increase the development of adequate pediatric clinical trials and pediatric use information to promote the safer and more effective use of prescription drugs in the pediatric population.”

– Section 409D(b), Public Health Service Act

NIH has funded the initiative through (1) a one-time, \$5 million distribution from the NIH Director’s Discretionary Fund (FY 2002) and (2) individual and collaboratively funded ICO grants and contracts (FY 2002 and thereafter). Therefore, rather than restricting the report to research associated with the PRI, this Pediatric Research Report highlights research advances and ongoing programs in pediatric research at NIH. Table 1 in the Appendix of this report shows the funding amounts for the NIH’s total investment in pediatric research by ICO in FY 2019.

A core component of the NICHD’s mission is to improve and promote children’s health and development. Therefore, the NIH Director requested that the NICHD Director oversee and coordinate the preparation of the Pediatric Research Report.

Additionally, the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act of 2018 (Public Law 115–180) directs NIH to ensure that the childhood cancer research projects it conducts and supports are included in appropriate reports to Congress, noting that this may include the Pediatric Research Report. Accordingly, this report includes selected NIH-supported pediatric cancer research efforts throughout its main sections: research advances, new and expanded efforts, major ongoing programs, and additional collaborations.

SELECTED SCIENTIFIC RESEARCH ADVANCES IN PEDIATRICS

Selected recent advances in pediatric research are described below. Each of these advances has resulted from NIH-supported studies. Although these advances are by no means a comprehensive compilation, they represent the wide range of the NIH’s scientific portfolio in pediatrics, including advances in child and adolescent development, rare diseases, treatment of serious pediatric illnesses, prevention, and global health research. Many of these advances resulted from programs that are supported by multiple NIH components.

Pregnancy and Newborn Health

Common Chemicals Linked to Preterm Births

Preterm birth is a global public health issue, and preterm birth rates in Puerto Rico are consistently among the highest in the United States. This study found that pregnant women in Puerto Rico with higher urine concentrations of phthalate metabolites had a 42 percent greater chance of a preterm (less than 37 weeks) delivery. Phthalates are common environmental chemicals found in food, medications, perfumes, deodorants, lotions, adhesives, vinyl flooring, plastic shower curtains, and other products.

P30ES017885; P42ES017198

<https://www.ncbi.nlm.nih.gov/pubmed/31430608>

[NIEHS]

Prenatal Exposure to Common Chemicals Linked to Lower IQ

Phthalates and bisphenol A—which can be found in plastics, deodorants, and lotions—are known to interfere with hormone function and neurodevelopment. Scientists compared prenatal exposure to a mixture of common chemicals with neurodevelopment in Swedish children. By age 7, early prenatal exposure was associated with a lower intelligence quotient (IQ) in children, especially boys. The researchers noted that bisphenol F was particularly concerning.

R01ES028811

<https://www.ncbi.nlm.nih.gov/pubmed/31668669>

[NIEHS]

Early Haptoglobin Production Protects Preterm Infants Against Brain Injury

Preterm birth after the uterus has been inflamed can cause infant brain injury, cerebral palsy, or death in the first year of life. Some, but not all, preterm infants who are born in this environment begin early production of haptoglobin, an antioxidant molecule that prevents cell damage and is usually not produced until 6 months of age. Scientists analyzed umbilical cord blood and compared outcomes between infants who did and did not produce haptoglobin. The researchers discovered that fetal ability to produce haptoglobin in response to inflammation was associated with a reduction in brain injury, cerebral palsy, and/or death. Infants who do not produce haptoglobin early may need therapies that protect them from these types of neurological injury.

UG1HD027915; UG1HD040485; U10HD053097; U10HD036801; UG1HD040544; UG1HD034208

<https://www.ncbi.nlm.nih.gov/pubmed/31143877>

[NICHD]

Zika Virus Abnormalities Correlate with Maternal Antibodies

Zika virus infection during pregnancy causes congenital abnormalities, including small head size, but rates vary widely and contributing factors remain unclear. To determine whether maternal antibodies were associated with small head size, researchers analyzed biological samples from Brazilian women who gave birth during the 2015–2016 outbreak and Zika-infected pregnant macaques. When a mother had a Zika virus antibody titer that measured as intermediate or higher, her infant had an increased risk for small head size (or brain damage in macaques), revealing a connection between Zika antibodies and fetal abnormalities. If confirmed, this discovery could inform vaccine development.

P51OD011092; P51OD010425; P51OD011106; P51OD011107; U19AI083019; R01AI133976; R25TW009338; R01AI100989; R01TW009504; R01AI121207; R01AI104002; R21AI129479; R01AI145296; U19AI111825

<https://www.ncbi.nlm.nih.gov/pubmed/31413072>

[ORIP, FIC, NIAID, OD]

Birth Defects from an Anti-Nausea Drug

Ondansetron is an anti-nausea medication commonly administered after cancer chemotherapy, radiation therapy, or surgery. Although safety evidence is limited, some physicians prescribe it for extreme and persistent nausea and vomiting during pregnancy. To investigate whether ondansetron is associated with an increased risk of birth defects, scientists analyzed first-trimester data from more than 1.8 million women enrolled in Medicaid. The study found no association between ondansetron exposure and cardiac or other malformations but noted a small increased risk of cleft lip and cleft palate. However, the increased risk was smaller than previous research suggested.

K01MH099141; K08AG055670; K08HD075831; R03HD091699

<https://www.ncbi.nlm.nih.gov/pubmed/30561479>

[NICHD, NIA, NIMH]

Artificial Intelligence Can Speed Diagnosis of Genetic Diseases in Newborns

Genetic diseases cause the deaths of about 15 percent of U.S. infants admitted to neonatal and other intensive care units. Because many of these diseases progress rapidly, timely diagnosis is extremely important to inform treatment decisions. Interpreting the results of a genomic sequencing test is time-consuming and must be done by experienced geneticists. Scientists who wanted to find a way to test more rapidly used an automated system to rapidly sequence the baby's genes from blood used for routine newborn screening. Then, using artificial intelligence, they matched the sequencing results to automated descriptions of genetic diseases obtained from patient records. The new method correctly identified 105 genetic conditions that had previously been diagnosed in 101 children. In another sample of children, the approach correctly identified 95 of 97 conditions that had been diagnosed earlier. This new method can help diagnose rare genetic disorders more rapidly than traditional methods, providing timely information to inform treatment decisions.

U19HD077693; U01TR002271; UL1TR002550

<https://www.ncbi.nlm.nih.gov/pubmed/31019026>

[NICHD, NCATS]

The Microbial Environment and Preterm Birth

Microbial communities are groups of microorganisms that share a common living space. The interaction between microbial communities and their host has been found to be involved in disease pathogenesis across many areas of medicine. To determine whether the maternal microbiome is a factor in preterm birth, scientists analyzed the vaginal and cervical microbial environment of women with spontaneous preterm births and compared it against that of women who delivered at full term. Seven types of bacteria

significantly increased the risk of preterm birth, especially in African American women. Conversely, higher levels of an antimicrobial produced by the immune system lowered the risk of preterm birth.

F32AI136400; R01NR014784

<https://www.ncbi.nlm.nih.gov/pubmed/30899005>

[NINR, NIAID]

Delayed Cord Clamping May Benefit Brain Development

Practitioners have traditionally clamped the umbilical cord immediately after birth. Previous studies have shown that delaying cord clamping increases an infant's blood volume, potentially lowering the risk of iron deficiency and improving the flow of red blood cells to the kidneys and brain. To follow up on a study of delayed cord clamping in infants, scientists obtained magnetic resonance imaging (MRI) brain scans taken 4 months after birth from 44 of the original newborns. The researchers used the scans to assess and compare levels of myelin, a substance that accelerates communication in the brain. Infants who underwent delayed cord clamping had higher levels of myelin in brain regions associated with motor, visual, and sensory functioning and processing, along with higher serum levels of ferritin, a protein that stores iron. Researchers found no difference between the two groups in visual, gross and fine motor, and language skills. Delayed cord clamping may benefit long-term brain development.

K99MH110596; R01HD076589; T32HD007489; R01MH087510; U54GM115677

<https://www.ncbi.nlm.nih.gov/pubmed/30473033>

[NICHD, NIMH, NIGMS]

Genes Related to Sudden Infant Death Syndrome

Sudden Infant Death Syndrome (SIDS), the sudden, unexplained death of a baby less than 1 year old, is the most common cause of sudden death of babies in the United States. Scientists suspected that changes in some genes might increase a baby's risk of SIDS. Previous research had identified 61 genes that might be linked to SIDS, so scientists compared the noncardiac genes in babies who died of SIDS against those of healthy people and found no significant differences. Because the genes studied were found to be unlikely to play a role in SIDS, the researchers suggested a shift in focus to other factors that cause SIDS.

R01HD042569

<https://www.ncbi.nlm.nih.gov/pubmed/30139991>

[NICHD]

Comparing Blood Protein Levels, Pregnancy, and Fetal Complications in Women with Lupus

Because women with systemic lupus erythematosus (lupus) are at increased risk for preeclampsia, miscarriage, and premature birth, studying their pregnancies can provide information that could help predict complications in all pregnant women. Researchers examined gene expression patterns of immune cells in blood samples collected over the course of pregnancy and the postpartum period from women with lupus, healthy women, and women undergoing assisted reproductive therapy. Data analysis identified a unique immune signature that appeared to be a better predictor of preeclampsia than existing clinical factors. Lupus patients with fetal complications demonstrated the highest levels of the immune signature and also had a higher number of activated immune cells. Monitoring the lupus-related immune signatures in the blood could help predict adverse pregnancy outcomes.

R01AR049772; P50AR070594; R01AR043727; R01AR069572; U19AI082715

<https://www.ncbi.nlm.nih.gov/pubmed/30962246>

[NIAMS, NIAID]

Doctors Typically Do Not Ask Mothers About Unsafe Infant Sleep Practices

Rates of infant sleep-related deaths have fallen over the last 30 years, but African American babies from low-income families are still at high risk. Safe sleep practices, such as putting babies to sleep on their backs, can help reduce sleep-related death rates. Researchers wanted to know whether doctors ask parents about unsafe sleep practices. In this study, 46 African American mothers were asked about their infants'

sleep practices during three separate encounters on the same day: a survey administered by a research assistant, a well-baby visit with the pediatrician, and a safe sleep discussion with a health educator. The mothers generally did not tell their pediatricians about unsafe habits. The doctors did not ask detailed questions about specific sleep practices, but instead asked general questions—if they asked any. Using a standardized survey tool to ask parents about specific infant sleep practices could help doctors quickly get accurate information so that they can help parents keep their babies safe.

R01HD072821

<https://www.ncbi.nlm.nih.gov/pubmed/31260002>

[NICHD]

Quitting Smoking Earlier in Pregnancy Lowers the Risk of Preterm Birth

Smoking during pregnancy leads to many newborn health problems, including preterm birth, low birth weight, and infant mortality. Researchers sought to determine whether the probability of preterm birth among pregnant women who had smoked cigarettes before pregnancy varied by the timing of when they quit. This cross-sectional study of more than 25 million pregnant women found that quitting smoking earlier in pregnancy reduced the risk of preterm birth. The study also confirmed that pregnant women who smoked more frequently had a higher risk for preterm birth. Quitting smoking—and quitting early in pregnancy—was associated with reduced risk of preterm birth, even for high-frequency cigarette smokers.

P2CHD041022

<https://www.ncbi.nlm.nih.gov/pubmed/31002320>

[NICHD]

Better Tracking of Growth Differences in Twin Pregnancies

In twin pregnancies, sometimes one fetus grows more quickly than the other. When the weight difference between twins is above 18 percent, there is a greater risk for stillbirth, neonatal mortality, respiratory distress, and infections. Researchers monitored 140 women carrying dichorionic twins. The researchers used ultrasound imaging to estimate the fetal weights at up to six timepoints, then they measured the infants' weights at birth. The number of twins with weight differences greater than 18 percent increased as the pregnancies progressed, and twins with greater differences in fetal weights had greater differences in birth weights. Having one or both twins with small size for a pregnancy timepoint was more common within twin pairs with greater differences in birth weight. Using different cutpoints to compare the weights of dichorionic twin fetuses at different points during pregnancy might help identify higher-risk pregnancies that need closer monitoring.

Intramural Research, ZIAHD008956

<https://www.ncbi.nlm.nih.gov/pubmed/31454510>

[NICHD]

Child Development

Sex-Based Differences in the Development of Brain Hubs Involved in Memory and Emotion

The amygdala and the hippocampus are structures in the brain that play key roles in processing emotion, learning, and memory. To advance understanding of the normal pattern of growth and development of these brain structures in males compared with females, intramural scientists used magnetic resonance imaging (MRI) to track changes in brain shape and volume in a cohort of 792 healthy, typically developing people between ages 5 and 25. The researchers identified sex-based differences in the rate at which these regions developed. A particularly striking finding was that the amygdala matured later and more slowly in males than in females. The researchers concluded that sex-based differences in the rate at which these brain components mature may contribute to differences in adolescent behavior and in the occurrence of conditions such as autism, attention-deficit/hyperactivity disorder, anxiety, depression, and schizophrenia during adolescence.

Intramural Research, ZIAMH002949
<https://www.ncbi.nlm.nih.gov/pubmed/31470127>
[NIMH]

Assessing How Distinct Gene Mutation Types Affect Brain Development

The protein made by the *KMT2E* gene is important for controlling how the body reads information from DNA to make proteins. Changes in this gene can affect brain development and cause brain disorders. Research had previously identified symptoms of brain disorders in three patients with changes in the *KMT2E* gene. To better understand the effects of these changes, researchers examined 38 patients from 36 families with various changes in the *KMT2E* gene. These changes led the patients' bodies to produce nonfunctional or altered KMT2E protein. Most of the changes were not inherited from their parents. In general, the patients had similar facial features, larger- or smaller-than-average head size, muscle weakness, digestion problems, and mostly mild developmental delays. Most patients with a change that resulted in a shorter KMT2E protein had mild intellectual disability. Male patients—who made up 70 percent of the group—were more likely to have autism; female patients were more likely to have epilepsy. It appeared that the type of change to the *KMT2E* gene affected the severity of developmental delay. The findings can help scientists better understand the genes that control brain development and may help them develop new treatments for brain disorders.

UM1HG008900; K12HD052896; R01HG009141; R01HD091846; R01HD073104
<https://www.ncbi.nlm.nih.gov/pubmed/31079897>
[NHGRI, NICHD]

Effects of Secure Attachment in Early Childhood

Early experiences with parents are believed to shape children's long-term health outcomes. Scientists assessed the long-term effects of a program designed to increase parents' sensitivity to their children's needs. The study participants were parent-child pairs from families with a history of involvement with Child Protective Services. Half had been randomly assigned when the children were infants to the parent-sensitivity program and the other half to a control program in which the parents were taught about milestones in children's development. The children's body mass index (BMI) was assessed annually until the children were 4 years old. Participation in the parent-sensitivity program did not show a direct effect on BMI; however, children with a secure parental attachment had significantly lower BMI at age 4 than those with an insecure attachment. Subsequent follow-up when the children were 9 years old found that children whose parents had participated in the parent-sensitivity program performed better on measures of the body's response to stress compared with children who had participated in the control program.

R01MH074374; R01MH052135; R01MH084135
<https://www.ncbi.nlm.nih.gov/pubmed/30772404>
<https://www.ncbi.nlm.nih.gov/pubmed/30659782>
[NIMH]

Social and Environmental Influences

Effects of Stress in Early Childhood

A study of a diverse group of 306 young children explored how negative experiences early in life (e.g., poverty, family instability, abuse) may affect child development. Beginning when the children were around age 3 and continuing to about age 5.5, the researchers collected data on the children's executive control, such as the ability to follow directions and take actions contrary to impulse. With parents' help, the researchers also measured children's levels of cortisol, a stress hormone that typically reaches its peak level in the body about 30 minutes after waking and then decreases throughout the day. Data on family income, stressful experiences such as divorce and residential instability, and children's behaviors were also collected. Results showed that children living in families with lower income and more adversity

tended to have both reduced executive control and an atypical pattern of cortisol levels throughout the day, compared with their peers who lived in less-stressed families. Moreover, each factor worsened the adverse impact of the other factor on the children's development.

R01HD054465

<https://www.ncbi.nlm.nih.gov/pubmed/31072416>

[NICHD]

Early Life Adversity and Adult Mortality

Poverty, family instability, abuse, and other negative experiences in childhood—collectively referred to by researchers as early life adversity—may affect health across the lifespan. Researchers studied how childhood adversity affected later-life events, including health outcomes, substance abuse, and mortality. Results showed that both men and women who experienced low socioeconomic status (a measure of income, education level, and occupation) combined with frequent abuse during childhood had the highest risk of death from any cause. For women, but not men, frequent abuse increased the risk of death even if they grew up in middle- or high-socioeconomic status families. Individuals of both sexes who had faced early life adversity had lower levels of financial security, well-being, and social support, as well as less-healthy lifestyles and more substance abuse. The scientists concluded that early life adversity is an important determinant of mortality for both men and women, but traumatic early life experiences may compromise later health more for women than for men.

K99AG052458; P30AG017266; R00AG052458; P01AG020166; U19AG051426

<https://www.ncbi.nlm.nih.gov/pubmed/31585378>

[NIA]

Puberty May Be a Period for Positive Intervention Following Early Life Adversity

Children who experience chronic stress due to early life adversity (e.g., poverty, family instability, abuse) may have abnormally low levels of the stress hormone cortisol and therefore may have a reduced response to stress than children who did not experience early life adversity do. In previous studies, low cortisol levels had been linked to aggressive behavior in childhood and adolescence. Recent work by NIH-funded researchers has indicated that children who spent their infancy in institutional care exhibit a reduced stress response in childhood, even after being adopted into a supportive family environment. However, when these children reach puberty, their stress response normalizes to levels comparable to those seen in children who have always lived in supportive environments. The researchers concluded that outcomes for children who have experienced early life adversity could be improved by focusing interventions on the period immediately before and during puberty.

T32MH015755; R01HD075349

<https://www.ncbi.nlm.nih.gov/pubmed/31712449>

[NIMH, NICHD]

Early Adversity May Affect DNA Methylation and Genetic Activity

Genes, which carry the instructions for all the activities of human life, are regulated by being turned on or off. One of the major processes by which genes are turned on and off is known as DNA methylation (DNAm). Recent studies have suggested that early life adversity (e.g., poverty, abuse, family instability) can lead to changes in DNAm, while other studies have shown that early life adversity may more than double an individual's risk for developing a psychiatric illness. However, it is not known whether adversity at any time during childhood contributes to changes in DNAm or whether there are periods of sensitivity when adversity has particularly strong effects on DNAm. Using data from a long-term study of parents and children, researchers found that, at age 7, children's experience of adversity corresponded with altered DNAm at 38 DNA locations; of these, 35 locations were predicted by having experienced adversity before the age of 3. These findings suggest that very early childhood may be a sensitive period during which adversity is particularly influential on DNAm.

K01MH102403; R01MH113930

<https://www.ncbi.nlm.nih.gov/pubmed/30905381>
[NIMH]

Pollution May Partly Explain Association Between Urban Living and Psychosis in Teens

Previous research suggests that the risk for developing psychotic disorders such as schizophrenia in adulthood is twice as high for people who grow up in urban areas as it is for those who do not. Research into possible reasons for this has mostly examined social factors such as rates of crime and poverty in urban areas. At the same time, a growing body of evidence has linked air pollution—a worldwide health issue—to mental illnesses such as anxiety and depression. To examine the association between exposure to outdoor air pollution and psychotic experiences in adolescence, researchers analyzed data for 2,066 youth (age 18) who had been followed since childhood in a study of environmental risks. Participants who had been exposed to high levels of air pollution, such as nitrogen oxides and particulate matter, were more likely to report psychotic experiences in adolescence. The scientists concluded that higher levels of outdoor air pollution could partly explain the association between urban residence and psychotic experiences in adolescence.

R01HD077482

<https://www.ncbi.nlm.nih.gov/pubmed/30916743>
[NICHD]

Kids Living Near Major Roads at Higher Risk of Developmental Delays

Researchers found that young children who live close to a major roadway were twice as likely to score lower on tests of communication skills compared with children who live farther away. Children born to women exposed during pregnancy to higher-than-normal levels of two traffic-related pollutants—ozone and fine particles—were also slightly more at risk of developmental delays during infancy and early childhood.

Intramural Research, ZIAHD008889

<https://www.ncbi.nlm.nih.gov/pubmed/30979514>
[NICHD]

Pesticide Exposure Linked to Childhood Depression and Anxiety

Past studies have suggested that organophosphate pesticides are cholinesterase inhibitors that increase depression and anxiety symptoms in animals and humans. To investigate this connection, researchers tested Ecuadoran children living near pesticide spray sites. The scientists found a correlation between measurable increases in a pesticide exposure biomarker (acetylcholinesterase) and depression and anxiety, especially in girls and children under age 14. The researchers hypothesized that the organophosphate insecticides were likely interfering with the brain's cholinergic system, which plays a role in mood regulation.

R01ES025792; R21ES026084

<https://www.ncbi.nlm.nih.gov/pubmed/31202795>
[NIEHS]

How Fluoride Affects Adolescent Kidney and Liver Function

Fluoridated water is the main source of fluoride exposure in the United States, and approximately 74 percent of the U.S. population that relies on public water distribution systems receives chemically fluoridated water for the purpose of preventing tooth decay. To determine whether fluoride contributes to complex changes in kidney and liver function in adolescents, researchers analyzed fluoride levels in the blood ($n = 1,983$) or household tap water ($n = 1,742$) of adolescents without kidney disease and compared those levels against kidney and liver blood plasma test results. Higher plasma fluoride concentrations were associated with changes in kidney- and liver-related parameters. The researchers suggested that children with poor kidney or liver function may absorb more fluoride than healthy children do; that poorer kidney function may contribute to, rather than resulting from, increased plasma fluoride levels; or that the

relationship between fluoride exposure and kidney function may be bidirectional or cyclical in nature, with fluoride hindering kidney function, which contributes to decreased fluoride excretion, increased bodily fluoride absorption, and further decrements in kidney function. Fluoride's effects on the liver were less well-characterized.

R01ES013744; R24ES028522; R01ES014930; P30ES023515; R00ES027508

<https://www.ncbi.nlm.nih.gov/pubmed/31402058>

[NIEHS]

Nutrition and Obesity

“Night Owl” Teen Girls and Weight Gain

Many older children and teens stay awake far later on weekends than weeknights, creating a situation called “social jet lag.” Because they had found that adults with high social jet lag were more likely to gain weight than those who went to bed earlier, scientists conducted a study to determine whether the same associations were seen in children. A total of 804 adolescents (418 girls and 386 boys) ages 11 to 16 responded to questionnaires on their sleep habits and wore a wrist device that tracked movement.

Researchers measured participants' waist size and calculated their proportion of body fat. Staying up later and social jet lag were associated with increased waist size and body fat for girls. These associations were reduced—but still remained—after the researchers statistically adjusted for sleep duration, diet, physical activity, and television viewing. The associations were not statistically significant in boys. Improving sleep schedules may help prevent childhood obesity, especially in girls.

UG3OD023286; R01HD034568; U54CA116847; P30DK092924; R35HL135818

<https://www.ncbi.nlm.nih.gov/pubmed/31524936>

[NICHD, NCI, NIDDK, NHLBI, OD]

Implementing School-Based Policies to Prevent Obesity

Adolescents who are obese are significantly more likely to have prediabetes, hypertension, or hypercholesterolemia than adolescents who are a healthy weight. They are also at greater risk for bone and joint problems, sleep apnea, and social and psychological problems related to stigmatization and poor self-esteem. Researchers conducted a randomized trial in 12 urban schools and analyzed data from nearly 600 students in fifth grade through eighth grade to assess whether implementing nutrition and physical activity policies would reduce obesity. After 3 years, eighth graders in schools with nutrition interventions (with or without physical activity interventions) had a smaller increase in body mass index (BMI) than students in schools without the policies. There was no difference in student BMI percentile changes between schools with and without physical activity interventions. School-based nutrition policies could be a helpful part of efforts to reduce childhood obesity. Because more than half the students studied were already overweight or obese by fifth grade, the researchers suggested an earlier intervention timeline.

R01HD070740

<https://www.ncbi.nlm.nih.gov/pubmed/30573151>

[NICHD]

Intervention to Help Prevent Childhood Obesity

An 8-week, mindfulness-based parenting stress intervention that addressed nutrition and physical activity was developed for parents with obesity to prevent obesity in their at-risk 2- to 5-year-old children.

Researchers used a multimethod approach to assess nutrition, physical activity, and stress. The intervention group demonstrated significantly better group attendance and improvement in parental involvement and had a decreased parental emotional eating rating. The control group was associated with significant increases in child body mass index percentile during treatment. A mindfulness-based parent

stress intervention to reduce the risk of childhood obesity is feasible, requires further testing of therapeutic mechanisms in larger samples, and might help attenuate the risk of childhood obesity. R01DK099039; R01DK117651; R21AT007708
<https://www.ncbi.nlm.nih.gov/pubmed/30241766>
[NCCIH, NIDDK]

Prenatal Supplement Might Protect Obese Offspring from High Blood Pressure

Docosahexaenoic acid (DHA) is a fatty acid used for energy and tissue growth and found primarily in fish and seafood. It is important for the development of a baby's brain during late pregnancy. Studies have linked DHA consumption to lower blood pressure in adults and children. A study from the Netherlands found that babies exposed to higher levels of DHA during pregnancy had lower blood pressure at age 6 years than babies exposed to lower DHA levels. To learn if prenatal DHA supplements might also have an effect on children's blood pressure, scientists re-analyzed data from a study comparing 89 children whose mothers took 600 mg of DHA each day during pregnancy with 82 children whose mothers took a placebo. They found that children who became obese or overweight and whose mothers took DHA had lower average systolic (top number) and diastolic (bottom number) blood pressure than the obese or overweight children of mothers from the placebo group. The results suggest that prenatal DHA supplements can help mitigate high blood pressure in children who are overweight or obese. R01HD047315; U54HD090216
<https://www.ncbi.nlm.nih.gov/pubmed/30794304>
[NICHD]

Low Vitamin D Early in Life Might Increase Risk of High Blood Pressure

Vitamin D is found in some foods and is produced by the body after exposure to sunlight. Studies have linked low vitamin D levels to high blood pressure in adults and older children. Researchers analyzed data from 775 children who were enrolled at birth in a long-term study of obesity risk factors and followed until age 18. The researchers measured vitamin D levels at birth and in early childhood and took the children's systolic blood pressure (top number) annually from ages 3 through 18. Children with a low vitamin D level at birth had more risk for high systolic blood pressure at ages 6 through 18 than children with sufficient vitamin D at birth. Children with a low vitamin D level at ages 1 to 3 had a nearly 60 percent greater risk of high systolic blood pressure from ages 3 to 18. These results suggest that low vitamin D levels at birth or in early childhood increase the risk of high blood pressure later in childhood and adolescence. R01HD041702; R01HD086013; U54TR001012
<https://www.ncbi.nlm.nih.gov/pubmed/31256718>
[NICHD, NCATS]

Early Risk Factors for Childhood Sleep Apnea

Obstructive sleep apnea, breathing that repeatedly stops and starts during sleep, is caused by relaxed throat muscles that block the airways. Sleep apnea affects between 1 percent and 5 percent of children and can lead to long-term problems, such as intellectual and behavioral deficits and reduced quality of life. To identify risk factors for sleep apnea in children, researchers analyzed the medical records of children around 6 years of age collected from a long-term study of 2,867 mother–infant pairs. The researchers found four risk factors for childhood sleep apnea: maternal obesity or diabetes during pregnancy; preterm birth or low birth weight; elevated blood levels of leptin, a protein associated with fat cells; and early childhood obesity. Children with all four risk factors were 10 times more likely to have sleep apnea than children with no risk factors and were significantly more likely to have sleep apnea than children who had only some of the risk factors. R01HD041702; R01HD086013; R01HD098232
<https://www.ncbi.nlm.nih.gov/pubmed/31253409>
[NICHD]

Diabetes

Improving the Ability to Diagnose Prediabetes in Adolescents

Prediabetes is a condition in which insulin does not break down glucose adequately, causing higher blood glucose and increasing the risk for type 2 diabetes. An early and accurate diagnosis of prediabetes allows people to take steps to lower their risk of developing type 2 diabetes. The oral glucose tolerance test, commonly used to diagnose prediabetes and diabetes, measures insulin and glucose levels over a 2-hour period after a person drinks a glucose solution. The test accurately diagnoses prediabetes in adults but is inconsistent in adolescents. To improve prediabetes testing for adolescents, scientists performed oral glucose tolerance tests in 83 adolescent girls, repeating the tests after 6 weeks and again after 1 year. The scientists found that they could diagnose prediabetes using the highest glucose level and the glucose level after 1 hour. More importantly, they could use those two glucose values to diagnose prediabetes after 1 hour of testing just as well as the standard 2 hours. These findings suggest that a 1-hour oral glucose tolerance test could be a quicker, more cost-effective way to predict or diagnose prediabetes in adolescents.

Intramural Research, ZIAHD000641; R00HD069516

<https://www.ncbi.nlm.nih.gov/pubmed/30520201>

[NICHD, NIDDK]

Drug Delays Type 1 Diabetes in People at High Risk

A clinical trial conducted by Type 1 Diabetes TrialNet demonstrated that a drug called teplizumab that targets the immune system slowed the progression to clinical type 1 diabetes in high-risk individuals. The trial enrolled 76 relatives of people with type 1 diabetes, ages 8 to 49; 72 percent were 18 years old or younger. The participants did not have clinical type 1 diabetes but were at high risk for developing it because they had at least two types of diabetes-related autoantibodies (proteins made by the immune system) and abnormal blood sugar levels. Participants were randomly assigned to receive either intravenous teplizumab for 14 days or placebo. During the trial, 72 percent of people in the placebo group developed clinical type 1 diabetes, compared with only 43 percent in the teplizumab group. The median time for people in the placebo group to develop the clinical disease was just over 24 months, compared with 48 months in the treatment group. This is the first study to show that clinical type 1 diabetes can be delayed by 2 or more years among high-risk individuals.

U01DK085476; UL1TR000445; U01DK061010; R01DK057846; U01DK1103282; UL1TR002243; UL1TR000114; UL1TR001857; UL1TR000064; UL1TR002537; U01DK085466; UL1TR001872; U01DK103153; U01DK061058; UL1TR002529; UL1001863; U01DK085453; UC4DK085466; UM1A109565; U01DK106984; UL1TR000114; U01DK085499; U01DK107013; U01DK103266; F31AI009565; UL1TR002366; UC4DK106993; P30DK045735; UL1TR000142; U01DK107014; U01DK106994; UL1TR000142; UL1TR002529; UL1TR001082; U01DK085461; UL1TR002366; UL1TR002537; UC4DK097835; UL1TR001857; U01DK103180; U01DK085465; U01DK085504

<https://www.ncbi.nlm.nih.gov/pubmed/31180194>

[NIDDK, NIAID, NCATS]

African American Youth with Type 1 Diabetes Have More Unstable Hemoglobin A1c than White Youth

Hemoglobin A1c (HbA1c) levels are higher in African Americans than in Whites even after adjusting for blood sugar levels. To better understand this difference, researchers examined the relationship of an unstable form of HbA1c with race and glucose. The researchers measured levels of unstable HbA1c, stable HbA1c, and blood sugar in African American and White teenagers with type 1 diabetes. The team found higher levels of unstable HbA1c in the African American teenagers, even after adjusting for blood

glucose levels. These findings point to early factors, prior to the formation of stable HbA1c, that might contribute to the observed higher HbA1c levels in African Americans.

U54MD008176; U54GM104940

<https://www.ncbi.nlm.nih.gov/pubmed/31038272>

[NIMHD, NIGMS]

Childhood Diseases

Predicting the Most Effective Treatment Approach for Pediatric Ulcerative Colitis

In the United States, about 2 of every 100,000 children between the ages of 10 and 19 have ulcerative colitis, and the disease is becoming more common in children younger than 5. A recent large clinical study, the Predicting Response to Standardized Pediatric Colitis Therapy (PROTECT) study, identified several patient traits, such as gene signatures, the gut microbiome, and disease severity, to help predict how well children with ulcerative colitis will respond to treatment. This study points toward a more personalized approach to treating the disease.

K08DK101753; P30DK043351; P30DK07892; T32DK007727

<https://www.ncbi.nlm.nih.gov/pubmed/30935734>

<https://www.ncbi.nlm.nih.gov/pubmed/30604764>

[NIDDK]

Five-Year Outcomes of Gastric Bypass in Adolescents as Compared with Adults

In a comparison of 161 teens with 396 adults who had a form of bariatric surgery called Roux-en-Y gastric bypass, researchers found that, even with similar weight loss, the teens were significantly more likely than the adults to have remission of type 2 diabetes and high blood pressure. This study suggests that bariatric surgery at a younger age provides significant health benefits in addition to substantial weight loss, with the potential to avoid the adverse effects of long-term severe obesity into adulthood. While this study contributes important information about the reversal of obesity-related conditions after surgery, the procedure is not without risk, and lifetime risk remains unknown.

UM1DK072493; UM1DK095710

<https://www.ncbi.nlm.nih.gov/pubmed/31116917>

[NIDDK]

Gene Associated with Hirschsprung Disease

One out of 5,000 babies is born with an incomplete nervous system in the intestines, a condition called Hirschsprung disease. It causes abdominal swelling, pain, and vomiting, along with constipation and poor weight gain. Researchers screened for mutations in zebrafish with Hirschsprung disease and identified a gene called *uhrfl*. Without this gene, newly hatched zebrafish have poor organization of their intestinal muscle, uncoordinated gut muscle contraction, bloated intestines, and many fewer nerve cells in their gut nervous systems. The *uhrfl* gene controls chemical changes to the DNA that affect gene activities. These results are the first to suggest that *uhrfl* and its partner gene *dnmt1*, which actually makes the DNA modifications, could be candidate target genes for the treatment of Hirschsprung disease.

R01OD011116; P01HD022486; R25HD070817

<https://www.ncbi.nlm.nih.gov/pubmed/31394080>

[ORIP, NICHD]

Gene Sequencing Can Help Tailor Treatments for Young People with Kidney Failure

Scientists sequenced approximately 400 chronic kidney disease (CKD)-linked genes in 104 children and young adults who developed the disease before the age of 25 and who received a kidney transplant. From their analyses, the scientists identified a genetic cause of CKD in 34 patients (32.7 percent). These findings could be clinically useful, because different types of CKD often require different patient care

approaches (e.g., early screening for anticipated health problems, treatment strategies before and after transplantation).

R01DK076683; R01DK088767; R01DK068306; UM1HG006504; T32DK007726; UM1HG008900
<https://www.ncbi.nlm.nih.gov/pubmed/30655312>

[NIDDK, NHGRI, NHLBI, NEI]

Prevention of Lower Urinary Tract Symptoms (PLUS)

From childhood to menopause and beyond, bladder health is a concern for all women. Health issues related to the bladder and/or urination range from acute infections to chronic, sometimes painful conditions and can have far-reaching negative effects on health and well-being for girls and women. The PLUS consortium is conducting transdisciplinary studies necessary to establish the evidence base that will lead to recommendations that promote bladder health and inform prevention of lower urinary tract symptoms in girls and women. Girls are included in past and planned clinical and other studies.

<https://pubmed.ncbi.nlm.nih.gov/31287183/>

<https://pubmed.ncbi.nlm.nih.gov/30957915/>

<https://plusconsortium.umn.edu/>

[NIDDK, ORWH]

X-Ray and MR Imaging Used to Guide Congenital Heart Disease Catheterizations

Researchers fused images from magnetic resonance imaging (MRI) with those from standard live X-rays to help guide cardiac catheterization for 37 patients with congenital heart disease. The patients ranged in age from 6 months to 63 years (median age, 8.7 years) and had a variety of conditions. Comparing them with matched control patients, the researchers found significantly shorter fluoroscopy times but no significant difference in radiation exposure or procedure time with the combined imaging. The operators never found the combined imagery misleading and found the MR images helpful in all cases. The researchers suggested that junior operators might find the fused imagery most useful.

Intramural Research, ZIAHL006039

<https://www.ncbi.nlm.nih.gov/pubmed/31062506>

[NHLBI]

Early Breathing Tube Removal in Infant Heart Repair Surgery

Repair surgery is sometimes a necessary treatment for congenital heart disease in very young infants. Since 2001, the Pediatric Heart Network, a consortium of more than 30 children's hospitals with specialized heart disease teams, has studied ways to improve treatment for these heart diseases. For example, through a collaborative review of surgeries for two common heart defects, network researchers developed new guidelines that cut the amount of time that infants spent on a breathing tube by 80 percent. In a comparison of the costs of these surgeries, network researchers found that using the new guidelines reduced the cost of surgery by 27 percent compared with costs for the same surgeries at care centers not using the guidelines.

U10HL109818; U10HL109741; U10HL109781; U10HL109816; U10HL109743; UG1HL135682;

U10HL068270; U10HL109737; U10HL109777; U10HL109778; U10HL109673

<https://www.ncbi.nlm.nih.gov/pubmed/27513600>

<https://www.ncbi.nlm.nih.gov/pubmed/30458158>

[NHLBI]

Udenafil Improves Exercise Ability in Children with the Fontan Procedure

Fontan surgery is the third heart repair surgery used to rebuild the heart in infants born with hypoplastic left heart syndrome. After the Fontan surgery, the heart delivers only high-oxygen blood to the child's body. However, the heart can continue to wear out over time after the surgery, leading to reduced oxygen and lowered exercise ability. Researchers tested whether the drug udenafil could help children whose hearts had been repaired but whose exercise ability had begun to deteriorate. The researchers randomly

assigned 400 teenagers at 30 centers in the United States and the Republic of Korea to treatment twice a day with udenafil or placebo. The results showed that udenafil did not significantly improve oxygen consumption at peak exercise, but several measures of exercise performance showed improvement at more routine exertion levels.

UG1HL135665; UG1HL135666; U10HL109818; UG1HL135680; UG1HL135646; UG1HL135683; UG1HL135685; UG1HL135689; U10HL068270; KL2TR002367; UG1HL135678; U24HL135691; UG1HL135682

<https://www.ncbi.nlm.nih.gov/pubmed/31736357>

[NHLBI, NCATS]

Avoiding Unnecessary Bone Marrow Biopsy in Children with Mastocytosis

Mast cells are immune cells associated with allergy and inflammation. Mastocytosis is a disease in which there are too many mast cells in the skin and internal organs. In general, mastocytosis is divided into cutaneous (skin) mastocytosis (CM) and systemic mastocytosis (SM), which is diagnosed by a bone marrow biopsy. However, most patients with SM carry a mutation in the *KIT* gene, which can be detected with a relatively simple blood assay that is becoming useful in diagnosing SM in adult patients. Scientists tested whether this *KIT* mutation assay could help providers decide when to perform a bone marrow biopsy in children with symptoms of CM. The researchers found no indication of the *KIT* mutation in the blood of children with only CM but found the mutation in children with SM or both CM and SM. The results indicate that this assay is useful for identifying children who are likely to have SM and avoiding an unnecessary bone marrow biopsy in children unlikely to have SM. Researchers also published a diagnostic algorithm for mast cell activation syndrome that can be used in pediatric patients.

Intramural Research, ZIAAI001091

<https://www.ncbi.nlm.nih.gov/pubmed/30488427>

<https://www.ncbi.nlm.nih.gov/pubmed/30737190>

[NIAID]

New Prediction Rule Could Ease Diagnosis of Bacterial Infections in Infants

An estimated 8 percent to 13 percent of infants up to 2 months of age who have a fever may have a serious bacterial infection. A physician must often confirm a diagnosis by taking fluid from the spinal canal (a spinal tap). Complications of the procedure are rare but can be serious. Seeking a way to avoid a spinal tap, researchers measured the levels of bacteria in urine, the amount of procalcitonin (a response to bacterial infection) in the serum, and the number of neutrophils (a kind of white blood cell). The researchers derived and validated their prediction rule using data from over 900 infants, finding a total of 170 cases of serious infection. The rule enabled them to find all but three of the bacterial infections ultimately detected. This prediction rule could help emergency room physicians rule out life-threatening bacterial infections among febrile infants up to 2 months of age, without the need for spinal taps, antibiotic treatments, or long hospital stays.

R01HD062477

<https://www.ncbi.nlm.nih.gov/pubmed/28988964>

[NICHD]

Enterovirus Infection in Children with Acute Flaccid Myelitis

Acute flaccid myelitis is a rare but often serious condition that mostly affects children. More than 560 cases have been confirmed in the United States since 2014. Acute flaccid myelitis can lead to muscle weakness and paralysis. The cause of acute flaccid myelitis is unknown, but there is evidence that enterovirus infection is involved. Researchers studied samples from one adult and 13 children with confirmed acute flaccid myelitis, looking for evidence of enterovirus infection, including the virus itself, enterovirus RNA, or proteins that react to the virus called antibodies. The researchers found enterovirus antibodies in the cerebrospinal fluid of 11 of the 14 cases of acute flaccid myelitis but in none of the

comparison controls. These results provide further evidence that enterovirus infection is linked with acute flaccid myelitis.

U19AI109761; U54AI138370

<https://www.ncbi.nlm.nih.gov/pubmed/31409689>

[NIAID]

Rapamycin Is Not an Effective Drug for All Types of Mitochondrial Disease

Disorders of the mitochondria—the parts of a cell that make energy—affect about 1 in 8,500 people. These disorders vary in type and severity, and some cause life-threatening illness and death. Currently, there is no cure for these diseases. A mitochondrial disorder called Leigh disease causes progressive brain deterioration. Few children born with Leigh disease live beyond age 6 or 7, and none live beyond their early teens. A recent study showed that high doses of a drug called rapamycin slowed disease progression in mice with Leigh disease, and researchers wondered whether rapamycin would be effective in other types of mitochondrial diseases. The researchers used high and low doses of rapamycin to treat mice with a different mitochondrial disease that also causes brain damage and early death. Comparing treated and untreated mice with this second condition, the researchers found that mice treated with the higher dose of rapamycin were smaller and died even sooner than the other affected mice. These results show that rapamycin is not an effective treatment for all mitochondrial diseases, including those that affect the brain.

P01HD080642

<https://www.ncbi.nlm.nih.gov/pubmed/30898651>

[NICHD]

Long-Term HIV Treatment Improves the Function of Mitochondria in Children

Children who have HIV can have problems with the function of their mitochondria, the parts of a cell that make energy. To test whether long-term HIV treatment in children could help mitochondria work better, researchers examined 120 children in South Africa who were being treated for HIV. The researchers found that long-term treatment improved the function of mitochondria in children who had HIV. However, HIV treatment did not restore mitochondrial function to normal levels. The researchers also found that, regardless of how long they had been receiving treatment, children who had HIV were smaller than children who did not have HIV. This suggests that problems with mitochondria might cause growth problems in children who have HIV. The researchers concluded that, given enough time, HIV treatment might restore the function of mitochondria to normal levels. The results show the importance of long-term HIV treatment.

R01HD073952; R01HD073977

<https://www.ncbi.nlm.nih.gov/pubmed/31179720>

[NICHD]

Improvements in HIV Treatments for Children and Teenagers

Children and teenagers who have HIV need safe and effective long-term treatment options. In two separate studies, researchers tested whether two medicines, dolutegravir and raltegravir, could be used to treat HIV in this population. The researchers found that when taken as prescribed, dolutegravir effectively treated HIV in children and teenagers who had previously received other HIV treatments. Raltegravir was effective in children younger than 12 years old but might not be suitable for teenagers who have previously received other HIV treatments. These results help increase the treatment options for children and teenagers who have HIV.

UM1AI068616; UM1AI069456; UM1AI069530; UM1AI068616; UM1AI069456; UM1AI106716; UM1AI068632

<https://www.ncbi.nlm.nih.gov/pubmed/30527329>

<https://www.ncbi.nlm.nih.gov/pubmed/30951600>

[NIAID, NICHD]

Response to Previous Dengue Virus Infection Can Help Prevent the Symptoms of Zika Virus

Zika virus can cause symptoms such as fever, rash, joint and muscle pain, and headaches in children and adults. To better understand this virus, researchers examined children in Nicaragua to find out whether Zika virus infections were worse in children who had previously been infected with a similar virus called dengue virus. The researchers found that children who had recently been infected with dengue virus had fewer symptoms of Zika virus infections. These results show that the body's response to fight dengue virus infections might help protect children from the symptoms of Zika virus. The results from this study help researchers better understand how the body fights similar viruses.

P01AI106695; R01AI099631; U19AI118610
<https://www.ncbi.nlm.nih.gov/pubmed/30668565>
[NIAID]

Immunity and Allergies

Immune Responses to Malaria Infection

Malaria is caused by a parasite called *Plasmodium falciparum*, which infects red blood cells. Infected red blood cells can stick to other cells in the body, making it difficult for the immune system to clear the parasite from the body. In areas where malaria is widespread, some people have antibodies that prevent infected red blood cells from sticking to other cells. Researchers tested blood samples from children in Mali who had malaria and found that the likelihood of having this antibody increased with age. In another study, scientists found that in Tanzania, infants who got antibodies against the malaria parasite from their mothers during pregnancy had fewer serious symptoms of malaria. These results might help researchers find new ways to protect young children from malaria. A separate 3-year study of Malian children showed that a specific molecule, p53, in white blood cells was associated with lower fever and more control of parasites and inflammation.

K08AI100997; K24AI112964; R01AI076353; R01AI110699; T32DA013911; Intramural Research, ZIAAI001155
<https://www.ncbi.nlm.nih.gov/pubmed/30165569>
<https://www.ncbi.nlm.nih.gov/pubmed/30971252>
<https://www.ncbi.nlm.nih.gov/pubmed/31492649/>
[NIAID, NIDA]

Bacteria in the Gut Affect Malaria Infection and Pregnancy Outcomes in Mice

Malaria can cause pregnancy complications and health problems for babies after birth. Recent research has found that a specific type of mouse is resistant to malaria infection because of the bacteria and other microbes in its gut. Using these mice as a model, researchers tested whether malaria-resistant microbes in the gut can reduce malaria infections during pregnancy. The researchers found that the mice had less severe malaria infections during pregnancy, and their offspring had fewer complications from malaria. These results could lead to new treatment options for malaria in humans.

R01DK109560; R01HD046860; R21AI111242; T32AI060546
<https://www.ncbi.nlm.nih.gov/pubmed/31160271>
[NICHD, NIAID, NIDDK]

Development of a Respiratory Syncytial Virus Vaccine

Respiratory syncytial virus (RSV) is a common cause of serious breathing problems, such as bronchiolitis and pneumonia, in young children. To develop a vaccine for RSV, scientists examined the characteristics of a protein on the virus, called the RSV attachment protein G, and determined that including this protein in the design of an RSV vaccine could help the vaccine work better.
Intramural Research, ZIAAI000326

<https://www.ncbi.nlm.nih.gov/pubmed/30651356>
[NIAID]

Lung Disease in Systemic Juvenile Idiopathic Arthritis Patients

Systemic juvenile idiopathic arthritis (sJIA) is a condition that causes arthritis, fevers, and rashes in young children. sJIA can also cause serious lung diseases in some children. Researchers studying the complications of sJIA found that these serious lung diseases are more common in patients who have an overactive immune system and in patients who had previously used certain types of medicines called biologics to treat sJIA. This study helps lay the foundation for further research into lung diseases in children who have sJIA.

K08AR072075; R01HL085453; R01AR059049; P30AR070549

<https://www.ncbi.nlm.nih.gov/pubmed/31379071>

[NIAMS, NHLBI]

Dietary Fatty Acids May Affect Childhood Asthma

Asthma in children can be worsened by indoor air pollution. A study of children in Baltimore added to evidence that diet can help prevent the effects of air pollution. This study showed that having more omega-3 fatty acids in a child's diet led to fewer asthma symptoms caused by indoor air pollution. The same study suggested that higher amounts of dietary omega-6 fatty acids may have the opposite effect, causing more severe asthma. The findings suggest that in children who have asthma, dietary fatty acids can affect how the body responds to indoor air pollution.

P50ES015903; P01ES018176; T32HL072748; K24ES021098; K23ES029105

<https://www.ncbi.nlm.nih.gov/pubmed/30922077>

[NIEHS, NCATS]

Emergency Cesarean Delivery May Increase a Child's Risk of Asthma and Food Allergies

Allergies in children have increased over the last two decades. Researchers have suggested that for infants born vaginally, exposure to bacteria and other microbes in the birth canal helps regulate the immune system and protect against allergies. Therefore, cesarean delivery may increase the risk of allergies. Other research suggests that breast milk also contains microbes that might regulate the infant's immune system. In a study, researchers found that children born by emergency cesarean had a higher risk of food allergies and wheezing, which is a symptom of asthma, than children born vaginally or by a planned cesarean did. Breastfeeding reduced the risk of wheezing, but not the risk of food allergies, in children born by emergency cesarean. The study results suggest that lack of exposure to microbes in the birth canal during labor does not cause food allergies and asthma and that babies born by emergency cesarean may be at a higher risk for these conditions.

Intramural Research, ZIAHD008949

<https://www.ncbi.nlm.nih.gov/pubmed/30475936>

[NICHD]

Diagnosing Food Allergies in People Who Have Atopic Dermatitis

Atopic dermatitis, also called eczema, is a common skin disease in children. Atopic dermatitis causes dry, red, and itchy patches of skin. Some children who have atopic dermatitis also have food allergies. In one study, researchers compared skin samples from children who had atopic dermatitis with and without food allergies. Results showed that children who had atopic dermatitis and food allergies had problems with the outermost layer of their skin that made their skin very dry, even in areas of skin that did not show signs of atopic dermatitis. These children were more likely to have a specific type of bacteria, *Staphylococcus aureus*, on their skin. In another study, researchers identified specific antibodies in children with atopic dermatitis that could be used to predict food allergies more accurately than current

tests. These findings may help doctors identify children with atopic dermatitis who are at risk of developing food allergies and lead to more accurate diagnoses of these allergies.
Intramural Research, ZIAAI001202; ZIAAI001202; UM2AI117870; R01HL128439; P01HL132821; U19AI117673; R01HL135156
<https://www.ncbi.nlm.nih.gov/pubmed/30787169>
<https://www.ncbi.nlm.nih.gov/pubmed/30639434>
[NIAID, NCATS, NCI, NHLBI]

Treatment Success in Infants with X-SCID

X-linked severe combined immunodeficiency (X-SCID) is a rare, life-threatening inherited disorder that weakens the immune system, causing repeated infections. Infants with X-SCID are typically treated with transplants of blood-forming stem cells, ideally from a genetically matched sibling, to establish a strong immune system. However, fewer than 20 percent of infants with the disease have a suitable donor. To develop a new treatment method that does not require a donor, researchers successfully used gene therapy to restore immune function using the patient's own blood-forming stem cells. These results hold promise for new treatment options for infants who have X-SCID.
Intramural Research, ZIAAI100988; P01HL053749; U54AI082973; P30CA021765
<https://www.ncbi.nlm.nih.gov/pubmed/30995372>
[NIAID, NHLBI, NCI]

Rare Pediatric Diseases

Anti-Inflammatory Drugs to Treat a Rare Disease That Causes Strokes in Children

Deficiency of adenosine deaminase 2 is a rare genetic disease that causes recurring strokes in young children. The condition causes inflammation in blood vessels, leading to stroke. Using existing drugs that were developed to treat other diseases that cause inflammation, researchers were able to prevent all strokes in a small group of patients.
Intramural Research, ZIAHG200372; ZIAHG200373
<https://www.ncbi.nlm.nih.gov/pubmed/30995379>
[NHGRI, NIAID, NINDS]

Earlier Diagnosis Improves Outcomes in All Types of Urea Cycle Disorders

Urea cycle disorders are rare genetic conditions in newborns that prevent the liver from converting ammonia in the blood into urea for excretion as urine. These disorders cause life-threatening symptoms within the early days and weeks of life and lead to brain damage in surviving infants. Researchers analyzed data from two large registries of urea cycle patients and found that the association between blood ammonia concentration and brain damage depends on the type of urea cycle disorder. They found that newborn screening helped prevent this brain damage in patients with all types of urea cycle disorders, because it led to earlier diagnosis and treatment. Researchers also found that treatment with medicines that reduce ammonia improved brain function in all disorder types; liver grafts were more helpful if done earlier rather than later. The analysis showed the importance of early screening and treatment of urea cycle disorders.
U54HD086984; U54HD061221
<https://www.ncbi.nlm.nih.gov/pubmed/31018246>
[NICHD]

Pediatric Cancer

Scientists Find a Promising Drug Combination Against Life-Threatening Childhood Brain Cancers

Scientists identified two drugs that worked together to both kill cancer cells and block the effects of a genetic mutation that causes a group of deadly childhood brain cancers collectively called diffuse midline gliomas. The researchers showed that a combination of the two drugs—panobinostat and marizomib—was more effective than either drug by itself in killing cancer cells grown in the laboratory and in animal models. The studies also uncovered a previously unrecognized trait in the cancer cells that scientists may be able to exploit to develop new strategies against the cancer and related diseases.

Intramural Research, ZIBHG200319; DP1NS111132; R01NS092597

<https://www.ncbi.nlm.nih.gov/pubmed/31748226>

[NCATS, NINDS, NIA, NCI]

Cell-by-Cell Analyses Suggest a Way to Shut Down Pediatric Brain Cancer

Glioblastomas are a highly aggressive, life-threatening, and treatment-resistant type of brain cancer. To help understand the causes of glioblastomas, scientists analyzed individual developing brain cells in newborn mice and other laboratory models of brain cancer. The scientists found a type of cell critical to the formation of glioblastomas. Researchers then blocked the function of a gene that controls how these cells grow. This significantly reduced the growth and spread of glioblastomas in the mice and increased survival for the animals. These results hold promise for new treatment options for glioblastomas in children.

Intramural Research, NIEHS; R01NS072427; R01NS078092; R01NS075243; R01HL132211; R37NS096359

<https://www.ncbi.nlm.nih.gov/pubmed/30982771>

[NIEHS, NINDS, NHLBI]

Histone Mutation May Lead to Childhood Brain Cancers

Diffuse intrinsic pontine gliomas (DIPGs) are incurable childhood brain tumors. This study provided insight into the function of a specific mutation in histone 3 protein commonly found in DIPG. In addition, researchers developed a new mouse model of spontaneous DIPG that provides a new research tool to better understand and treat the disease. Researchers found that the mutation in histone 3 promotes the expansion of neural stem cells in the hindbrain and, in combination with other specific mutated proteins, accelerates the development of brainstem gliomas such as medulloblastoma and DIPG. The researchers observed that the expansion of neural cells due to this mutation occurred for a limited time during brain development in a mouse model, suggesting that this increased pool of cells could have a high propensity for transformation into cancer cells in the presence of mutated proteins. These findings provide a possible explanation for why DIPG occurs in young children.

R50CA211481; R01CA188516; R01NS037956; P30CA021765; P01CA096832

<https://www.ncbi.nlm.nih.gov/pubmed/30595505>

[NCI, NINDS]

Blocking the Function of a Specific Protein May Stop Development of Medulloblastoma

Medulloblastoma is one of the most common malignant brain tumors in children. A subtype of medulloblastoma called group 3 is the most life-threatening form of the disease and is not well understood. Researchers found that blocking a specific protein called lysine demethylase 1 stopped the development of medulloblastoma in a mouse model. The results of this study provide new insights into the factors that control the growth of medulloblastoma and suggest that drugs designed to block the function of this protein, which are being tested in clinical trials for other cancer types, could be used to treat this type of medulloblastoma.

F31NS086367; P30CA030199; R01CA159859

<https://www.ncbi.nlm.nih.gov/pubmed/30659187>

[NCI, NINDS]

Experimental Therapy May Be a Potential Treatment for Several Types of Childhood Cancer

Chimeric antigen receptor (CAR) T-cell therapy approaches have shown success in treating relapsed pediatric acute lymphoblastic leukemia, but this has not yet translated to treating solid tumors (non-blood cancers). A new CAR T-cell therapy designed to bind to a protein called B7-H3 that is present on the surface of cancer cells in many pediatric solid tumors showed promising preclinical results. This new treatment approach eradicated tumors generated in mouse models of several different childhood cancers, including two forms of sarcoma and medulloblastoma. These results are exciting, as this single CAR T-cell treatment could be used to treat multiple cancers, including pediatric solid tumors, and thus offers a new opportunity for treatment for many cancer patients.

P01CA049605

<https://www.ncbi.nlm.nih.gov/pubmed/30655315>

[NCI]

Preserving Future Fertility in Young Boys with Childhood Cancer

Childhood cancers can lead to infertility in about 30 percent of survivors. To develop new methods to preserve fertility, researchers removed and froze tissue from the testicles of five rhesus macaques that were too young to produce sperm. When the animals approached puberty, the researchers thawed the tissue samples and implanted them back into the animals they came from. This implanted tissue produced viable sperm a few months later. This study helps establish the concept of using immature testicular tissue to preserve fertility.

P01HD075795; P51OD011092; R01HD055475; R01HD076412

<https://www.ncbi.nlm.nih.gov/pubmed/30898927>

[NICHD]

Increased Understanding of Issues That Affect Childhood Cancer Survivors

Although there are effective treatments for pediatric cancer patients, it is important to know whether these treatments can cause health problems for childhood cancer survivors later in life. Three studies provide new evidence that people who were treated for cancer as children are at risk for developing another cancer later in life. One study found that children who were given chemotherapy for any type of cancer were more likely to develop myelodysplastic syndrome/acute myeloid leukemia. The second study found that female breast cancer patients who were childhood cancer survivors were at greater risk of dying from their breast cancer than those who did not have childhood cancer. Finally, the third study focused on adults who were childhood survivors of a rare pediatric eye tumor called retinoblastoma. Children with retinoblastoma can either inherit the genetic mutation that causes retinoblastoma, which is known as hereditary retinoblastoma, or have non-hereditary retinoblastoma. Researchers studied a large cohort of childhood retinoblastoma survivors and found that hereditary retinoblastoma survivors had the highest risk for death due to cancers developed later in life than the general population and non-hereditary retinoblastoma survivors did.

Intramural Research, ZIACP010131; K05CA160724; K07CA134935; K08CA234232; P30CA008748; P30CA021765; R01CA134722; R01CA136783; U24CA055727

<https://www.ncbi.nlm.nih.gov/pubmed/31341236>

<https://www.ncbi.nlm.nih.gov/pubmed/31260644>

<https://www.ncbi.nlm.nih.gov/pubmed/30698734>

[NCI]

A New Treatment Approach for Rhabdomyosarcoma Shows Promising Results in a Zebrafish Model

Rhabdomyosarcoma (RMS) is a complex type of cancer whose prognosis varies greatly depending on the disease subtype, stage of disease progression, and location in the body. Surgery and radiation therapy are standard treatments for RMS that has not spread. However, there is a need for effective treatments for RMS patients for whom surgery is not an option. Using a newly developed zebrafish model of RMS, researchers identified various cell types of RMS that control tumor growth and spread. Based on the initial results, scientists tested the combination of two drugs—one that blocks DNA repair and one that

damages DNA in cancer cells—to stop RMS growth. The researchers found that this treatment eliminated RMS cells in the zebrafish model and in mouse models. This is an exciting result, as this combination treatment is being tested in a clinical trial for Ewing sarcoma. The researchers are working with the clinical trial team to redefine the existing trial to include RMS.

R24OD016761; R01CA129933; R01CA154923; R01CA215118

<https://www.ncbi.nlm.nih.gov/pubmed/31031007>

[NCI, OD]

New Treatment Targets for Malignant Rhabdoid Tumors

Malignant rhabdoid tumors are a very aggressive form of cancer that occurs mostly in young children and affects the kidneys and soft tissues. Most current cancer therapies are not successful at treating malignant rhabdoid tumors. Researchers discovered that using drugs that stop the function of two proteins, MDM2 and MDM4, caused the malignant rhabdoid tumors to become smaller in mice. These results suggest that these drugs may be effective in treating malignant rhabdoid tumors. Future studies will need to test these drugs in cancer patients.

F30CA221087; P30CA021765; P50CA101942; R00CA197640; R01CA113794; R01CA172152; R35CA197583; R35CA210030; R50CA211399; T32CA136432; T32GM007226; T32GM007753; U01CA176058

<https://www.ncbi.nlm.nih.gov/pubmed/30755442>

[NCI, NIGMS]

New Anticancer Drug Receives the Food and Drug Administration’s Breakthrough Therapy Designation to Treat Neurofibromatosis Type 1 in Children

Based on the promising results of a phase II multicenter trial, the Food and Drug Administration (FDA) awarded selumetinib with a breakthrough therapy designation. This designation allows the FDA to speed up the review process and possible approval of this drug. Selumetinib is being used to treat symptomatic and/or progressive neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN) in children age 3 and older. In NF1, a signaling pathway that causes tumor growth is turned on. The researchers found that selumetinib blocks a protein in this signaling pathway and reduces the size of tumors. The researchers also found that NF1 patients who were treated with selumetinib experienced improvements in clinical outcomes, such as less pain, more strength, and better quality of life. After a year of treatment, most patients (or their parents) reported improved pain scores, strength, and range of motion.

Intramural Research, ZIABC010801

<https://pubmed.ncbi.nlm.nih.gov/25887099/>[NCI]

New Treatment for B-Cell Acute Lymphoblastic Leukemia Receives Food and Drug Administration (FDA) Breakthrough Therapy Designation

In 2019, the FDA granted breakthrough therapy designation to an experimental cell-based immunotherapy used to treat a blood cancer called B-cell acute lymphoblastic leukemia (B-ALL). This breakthrough designation allows the FDA to speed up the review and possible approval process for this new immunotherapy. B-ALL is often treated by targeting cancer cells marked with a molecule called CD19; however, in many children and young adults with B-ALL, their cancer comes back or is resistant to these CD19-based treatments. This new cellular therapy targets cancer cells that are marked with a molecule called CD22. Researchers tested this experimental therapy in B-ALL patients, including B-ALL patients who received CD19-based treatment. The study showed that B-ALL patients who were treated with this type of immunotherapy went into remission. This experimental CD22 immunotherapy could be a treatment option for B-ALL patients who do not have success with CD19-based immunotherapy.

Intramural Research, ZIABC011295; ZIABC011565; ZIABC011734; ZIACL002120

<https://www.ncbi.nlm.nih.gov/pubmed/29155426>

[NCI]

Some Children with Liver Cancer May Need Less Chemotherapy

Liver cancer is rare in children, and only about one-third of these patients have tumors that can be removed surgically at the time of diagnosis. Approximately 90 percent of pediatric liver cancer patients whose tumors are removed at diagnosis and who receive chemotherapy survive the disease. However, some survivors develop lasting side effects of chemotherapy, including hearing loss. A phase III de-escalation clinical trial tested whether a lower dose of chemotherapy than the standard dose used in clinical practice could reduce side effects without affecting survival in children and infants with the most common type of childhood liver cancer. Results from this multicenter clinical trial showed that some children with liver cancer may need less chemotherapy than is typically used to treat the disease. In the study, children who received half the normal amount of chemotherapy survived as long as children who had received the full amount in previous trials.

KL2TR002381; U10CA029511; U10CA098413; U10CA098543; U10CA180886; U10CA180899; UL1TR002378

<https://www.ncbi.nlm.nih.gov/pubmed/30975630>

[NCI]

Increased Use of Electronic Cigarettes, Especially Flavored E-Cigarettes, Leads to Increased Tobacco Use Among Youths

The National Youth Tobacco Survey is an annual survey of middle school and high school students in the United States. Using this survey data, researchers found that use of most flavored tobacco products among young tobacco users fell from 2014 to 2016. However, from 2016 to 2017 there was a sharp increase in flavored tobacco product use among youths, likely due to the increased use of flavored electronic cigarettes. These results prompted another research team to examine whether electronic cigarette use among teenagers predicted future cigarette smoking. The study showed that young people who use electronic cigarettes are more likely to smoke combustible cigarettes in the future.

R03CA228909

<https://www.ncbi.nlm.nih.gov/pubmed/30615022>

<https://www.ncbi.nlm.nih.gov/pubmed/30689915>

[NCI]

Bone and Muscle Health

Flat Head Syndrome Severity is Associated with Long-Term Cognitive Problems

Positional plagiocephaly and/or brachycephaly (PPB), also known as flat head syndrome, is a common skull deformity in infants. Although doctors can use special helmets to correct PPB, recent work shows that PPB is more than just a cosmetic problem. There is evidence that infants with PPB can have developmental delays. Researchers wanted to determine whether these developmental delays continue into childhood and whether there is an association between the severity of the developmental delay and the severity of PPB. The researchers studied a group of infants and classified their head shape as no, mild, moderate, or severe PPB. When the children were about 9 years old, the researchers looked at cognitive testing and academic performance to assess the children's ability to learn and remember new things. The researchers found that children who had moderate or severe PPB scored lower in academic and cognitive testing than children who had mild or no PPB. Consistent diagnosis of PPB severity and early support could help children avoid any long-term issues associated with PPB.

R01HD080462

<https://www.ncbi.nlm.nih.gov/pubmed/30635350>

[NICHD]

Hormone Therapy Does Not Prevent Bone Loss in Adolescent Girls with Anorexia

Anorexia nervosa is an eating disorder that is most common in teenage girls and young women. Anorexic girls and young women typically have lower bone mass than their healthy peers. While there is no effective treatment for preventing bone loss in anorexic patients, previous research suggested that a combined hormone therapy may help anorexic patients maintain bone health. In this study, a group of girls between ages 11 and 18 with anorexia received hormonal therapy for 12 months. Unlike previous research, the combined hormonal therapy did not improve bone density in these anorexic girls. While some girls' bones did show signs of growth, those who received treatment had decreased bone density over time compared to those who did not receive treatment. The results of this study indicate that this combined hormone treatment may not help young adolescents with anorexia maintain bone health.
K23HD060066; R01AR060829; UL1RR025758
<https://www.ncbi.nlm.nih.gov/pubmed/31227390>
[NICHD, NIAMS, NCATS]

Studying Sponastrime Dysplasia in Zebrafish

Sponastrime dysplasia is a disease that causes spinal abnormalities such as scoliosis, changes in facial bone structure, short stature, weak immune system, and cloudy lens in the eyes that can decrease vision. While the disease is believed to be inherited, the specific genes and mutations that cause sponastrime dysplasia are not known. Scientists identified mutations in the *TONSL* gene in 13 children from 11 affected families. The researchers used gene editing technology to recreate these mutations in the zebrafish. Zebrafish with *tonsl* mutations were shorter, had abnormal spines, and had a lower number of the white blood cells that fight infection than their genetically normal siblings did. These *tonsl* zebrafish can be used to better understand the genetic causes of sponastrime dysplasia.
K08DK106453; R01AI120989; R01AR062651; R01AR066124; R01OD011116; T32GM007526; U01HG007709; U01HG010218; U54HD083092; U54HG006493; U54NS093793; UM1HG006348; UM1HG006493
<https://www.ncbi.nlm.nih.gov/pubmed/30773277>
[ORIP, NIAID, NIAMS, NICHD, NIDDK, NHGRI, NIGMS, OD, NINDS]

Molecules in the Blood May Predict Treatment Response in Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a genetic disease that mainly affects boys and causes progressive muscle weakness. The most common treatments are physical therapy and medications called glucocorticoids that reduce inflammation. Biomarkers are molecules that researchers can measure in the blood to show whether a person is responding to treatment. To identify DMD biomarkers, researchers measured proteins in the blood of three groups of boys with DMD: one group that had never been treated with glucocorticoids, another that started glucocorticoid treatment for the first time during the study, and a third that started treatment before the study and continued with it during the study. The researchers compared the data from these boys with data from boys without DMD. They found 17 proteins that were unique to boys with DMD and that responded to glucocorticoid treatment, meaning that the boys' blood protein levels returned to normal or near normal after treatment. These proteins could be biomarkers for predicting a patient's DMD progression or measuring the effectiveness of potential new drugs.
U54 HD090245
<https://www.ncbi.nlm.nih.gov/pubmed/31434957>
[NICHD]

New Type of Steroid Drug Improves Muscle Function in Boys with Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a genetic disease that affects the muscles. DMD affects primarily boys, beginning at 3 to 5 years old, progresses rapidly, and leads to loss of the ability to walk and, later, the need for a respirator to breathe. Glucocorticoid treatment is the standard treatment for DMD to slow muscle breakdown; however, long-term glucocorticoid treatment can have serious negative effects. In this study, researchers tested vamorolone, a new type of steroid drug, in 4- to 7-year-old boys with DMD. The researchers found that the drug was safe and well tolerated by all patients. Some doses of

vamorolone led to improved muscle function without any evidence of the negative outcomes that can occur with glucocorticoids. Additional longer-term and blinded trials are needed, but this study has demonstrated vamorolone as a potential future alternative steroid drug treatment for boys with DMD. R44NS095423; U54HD090254

<https://www.ncbi.nlm.nih.gov/pubmed/31451516>

[NIAMS, NICHD, NINDS, NCATS]

Fixing the Genetic Error in Duchenne Muscular Dystrophy with Gene Editing

Duchenne muscular dystrophy (DMD) is a genetic disorder that is caused by errors in the gene for the protein dystrophin. These errors cause the protein to be shortened and nonfunctional. Scientists are testing a variety of strategies to overcome or correct these genetic errors to treat people with DMD. Researchers have studied model animals that have the most common dystrophin error found in humans and used gene editing to restore the dystrophin protein in these animals. This study used a similar strategy to address the second most common type of DMD genetic error, which affects 12 percent of DMD patients. The scientists tested a variety of editing methods in mice and cells from DMD patients and found that the edits were able to restore dystrophin. The researchers also found that the amount of gene-editing agent they used influenced the number of cells that had restored dystrophin. This research is an important step that may lead to new ways to treat DMD.

R01AR067294; R01HL130253; R01HL138426; U54HD087351

<https://www.ncbi.nlm.nih.gov/pubmed/30854433>

[NICHD, NHLBI, NIAMS]

Oral Health, Speech, Hearing, and Vision

Medicaid Policy and the Oral Health of Publicly Insured Children

As of 2017, all state Medicaid programs support application of fluoride varnish (FV), a coating material that prevents caries, to children's teeth by primary care doctors. Researchers examined the association between the number of years since a state implemented an FV policy and child oral health. Because states did not adopt policies at the same time, the researchers also compared children in states with FV policies and those in states without FV policies. FV policies were associated with better oral health. Children in states that had FV policies for 4 years or more were significantly more likely to have very good or excellent teeth than children in states without FV policies were.

R01DE026136

<https://www.ncbi.nlm.nih.gov/pubmed/30032444>

[NIDCR]

The Impact of Fluoride Treatment on Medicaid Spending

Untreated tooth decay in young children can cause pain and infections and can lead to expensive emergency department visits and/or hospitalizations. Silver diamine fluoride, a dental material that attacks harmful bacteria and strengthens teeth, can be used to treat active tooth decay, particularly for people who have limited access to dental care. Researchers explored the economic impact to Medicaid programs of using silver diamine fluoride rather than standard treatments to stop the progression of tooth decay in children 1 to 5 years old. The study suggests that providing silver diamine fluoride to manage tooth decay could reduce Medicaid spending on dental care and help young children avoid expensive dental treatments.

R01DE028283

<https://www.ncbi.nlm.nih.gov/pubmed/30741498>

[NIDCR]

Potential New Approach to Treat Recurrent Ear Infections

Ear infections are one of the most common reasons parents bring their child to a doctor and are the main cause of hearing loss in childhood. Scientists are learning more about how to fight recurring ear infections. Bacteria that cause the infection create a film on the surface of the middle ear, making it difficult for the immune system and antibiotic treatment to work. Researchers also found a bacterial structure that is important for creating and maintaining the films. They used that knowledge to break down the film and prevent new film from forming. Future work will show whether treatments that break down biofilms could help treat and prevent persistent ear infections.

R01DC003915; R01DC011818; R01DC015688

<https://www.ncbi.nlm.nih.gov/pubmed/31021431>

[NIDCD]

Neurodevelopmental Outcomes of Preterm Infants with Retinopathy of Prematurity

Each year, about 15,000 infants born preterm in the United States are affected by retinopathy of prematurity (ROP), a condition in which blood vessels in the eyes develop abnormally. For the 1,100 to 1,500 infants who are severely affected, ROP can cause blindness. Treatment of ROP has included either laser surgery, the medication bevacizumab, or both. Researchers recently analyzed clinical records of 405 extremely preterm infants with ROP who had been treated with either bevacizumab or surgery. When assessing outcomes in the children at 18 to 26 months, the researchers found an association between bevacizumab treatment and poor cognitive outcomes and death in early childhood. However, the authors also said that the infants who received bevacizumab may have been sicker than the surgery group. The study authors concluded that a rigorous appraisal of the risks and benefits of bevacizumab is needed.

Until then, cautious use of this therapy may be prudent.

UG1HD068263; U10HD021373; UL1TR001111; K23DK120960; UG1HD068270; U10HD040689; UG1HD027856; UG1HD034216; UG1HD027904; UG1HD027880; UL1TR001117; UG1HD027851; U10HD036790; UG1HD068278; UG1HD068244; UG1HD027853; UG1HD087229; UG1HD040689; M01RR008084; UG1HD053089; UG1HD068284; UG1HD021385; UG1HD040492; UG1HD021364; UG1HD053109; U10HD068278

<https://www.ncbi.nlm.nih.gov/pubmed/31337693>

[NICHD, NCATS, NIDDK]

New Handheld Tool Expands Use of Eye Imaging Technology

Optical coherence tomography lets doctors see tiny blood vessels in the eye to check if they are healthy. Standard devices with this technology require patients to sit in a chair and place their chin on the device. Researchers have now developed a handheld version that can be used to examine the eyes of preterm infants in intensive care nurseries, young children, patients under anesthesia, and others who cannot or should not sit up.

R01EY023039; U01EY028079; R01EY025009; R21EY029384; K23EY028227; P30EY005722

<https://www.ncbi.nlm.nih.gov/pubmed/31143506>

[NEI]

Intellectual and Developmental Disabilities, Neurological Disorders, and Mental Health

Distinct Brain Chemical Patterns in Girls with Dyslexia

Children with dyslexia, a learning disorder that affects a person's ability to read and spell, may also have challenges with other cognitive skills. The amounts of certain brain metabolites—molecules created in the brain as it functions—are associated with children's ability to see or hear words. Using brain magnetic resonance imaging and spectroscopy, researchers compared the amount of several naturally occurring brain metabolites in children with or without dyslexia. In girls with dyslexia, the amounts of two chemicals naturally found in the brain, myo-inositol and choline, were associated with challenges in the

ability to process information. This association was not seen in boys. These changes may serve as possible biological markers for children with dyslexia.

R01HD086011; T32HD049311

<https://www.ncbi.nlm.nih.gov/pubmed/30532701>

[NICHD]

Tool Helps Children with Autism Improve Social Skills

A smart eyewear system helped children with autism understand emotions through facial expressions. Combining Google Glass with games for mobile devices, researchers captured the facial expressions of a child's family member. The games reinforced the emotion associated with the expression by providing similar images and audio prompts. Children who received the intervention along with standard therapy had improved socialization skills compared with children receiving standard therapy alone. Use of this system could expand access to treatment for children with autism.

R01EB025025; R21HD091500

<https://www.ncbi.nlm.nih.gov/pubmed/30907929>

[NIBIB, NICHD]

Potential Screening for Autism Spectrum Disorders at Home Using a Video App

Autism spectrum disorder, a disorder of brain development that affects how a person perceives and socializes with others, can now be reliably diagnosed at 2 years of age. Early intervention is a known benefit for children with this disorder. Researchers created an iPhone app to test the effectiveness of collecting data at home to see whether a child needed to be referred for additional testing. The app allowed family members to complete surveys about their children and to collect data on children's behaviors while watching movies designed to elicit autism-related behaviors. The app automatically coded the videos to quantify the children's emotions and behaviors. It detected significant differences in emotion and attention by sex, age, and autism risk status. Automated digital quantification of autism symptoms could enable children to be assessed more consistently in their natural environment.

P50HD093074

<https://www.ncbi.nlm.nih.gov/pubmed/31304303>

[NICHD]

Early Detection of Motor Control Issues in Toddlers with Autism Spectrum Disorder

Evidence suggests that children with autism spectrum disorder show early signs of differences in motor function compared with children without the disorder. Using computer vision analysis, a tool that uses digital videos or images to analyze information, researchers tested postural control—a child's ability to hold their head and body steady—in children ages 16 to 31 months. The researchers found differences between typically developing children and children with autism spectrum disorder. Children with the disorder exhibited a significantly higher rate of head movement, suggesting difficulty maintaining motor control. The researchers concluded that using digital approaches to characterize early motor behaviors in children could allow for more precise, objective characterization of motor control and could lead to new, automated methods for early identification of autism spectrum disorder.

P50HD093074

<https://www.ncbi.nlm.nih.gov/pubmed/30451886>

[NICHD]

Using Functional Imaging to Track Language and Social Development in Infants

Many infants at risk for autism spectrum disorder show differences in the development of social attention and early forms of communication in the first year of life. Currently, practitioners lack reliable measures to assess these developmental delays in infants. Using functional magnetic resonance imaging, researchers found distinct neurobiology and gene expression in children who later exhibited subtypes of

autism spectrum disorder and early language delays. The differences in these biological attributes were apparent well before the classic attributes of changes in social attention were.

R01MH110558; U01MH108898; R01MH104446; R01MH036840; R01MH080134; P50MH081755; R01DC016385

<https://www.ncbi.nlm.nih.gov/pubmed/30482947>

[NIDCD, NIMH]

Nasal Spray of Neuronal Peptide May Improve Social Deficits in Children with Autism

Currently, there are no medications that treat the deficits in social characteristics apparent in autism spectrum disorder. A neuronal protein, arginine vasopressin (AVP), has been known to play a role in promoting social behaviors in mammals. Researchers conducted a controlled clinical trial with AVP in 30 children with autism spectrum disorder. Study participants received either the study drug or a placebo, administered by nose spray, for 4 weeks. Using a standard social assessment tool, the children who received the study drug were found to be more socially responsive than those in the control group. These comparisons were made by assessing the change from each child's pre-trial, baseline score. The treated children also experienced some reduction in symptoms of anxiety and in certain repetitive behaviors. These preliminary findings suggest that this treatment could improve social impairments in children with autism spectrum disorder.

UL1TR001085; K08MH111750; R21MH100387; R21HD083629; T32MH019908; R01HD091972

<https://www.ncbi.nlm.nih.gov/pubmed/31043522>

[NICHD, NCATS, NIMH]

Monitoring Brain Activity in a Mouse Model of Fragile X syndrome

Fragile X syndrome (FXS) is a neurodevelopmental disorder that is a leading inherited cause of autism and intellectual disability. Among other symptoms, individuals with FXS often have problems with sensory processing, which can lead to being oversensitive to certain sensory stimuli, such as loud noises. These sensory processing problems may, in turn, contribute to the anxiety and language delays often seen in FXS. Researchers created an FXS mouse model that displayed severe hypersensitivity to sound similar to human FXS. The researchers monitored how electrical responses to sound in different areas of the brain changed as the FXS mice grew and developed. They found that differences in the brain responses to sound were present in the FXS mice from a very young age, but these responses were different in different brain regions and changed over time. These findings suggest that studies need to examine location-specific changes in brain activity over time to better understand sensory problems in FXS.

U54HD082008

<https://www.ncbi.nlm.nih.gov/pubmed/30528856>

[NICHD]

Treatment for Tuberous Sclerosis May Improve Abnormal Development of Brain Matter

Tuberous sclerosis is a rare genetic disease that causes benign tumors in the brain and other vital organs. Abnormal white matter development in the brain has also been observed in tuberous sclerosis, which has been associated with symptoms of autism, epilepsy, and intellectual disability in these patients.

Researchers conducted a study that included brain imaging in patients with tuberous sclerosis who were treated with everolimus, an FDA-approved medication used to treat features of this disease, including seizures. The researchers found that everolimus treatment improved white matter structural integrity in the brain. The changes were sustained over time and were greater with longer treatment and in younger patients. The results suggest that everolimus treatment in children with tuberous sclerosis may improve abnormal white matter development and the associated outcomes.

U01NS092595; U54NS092090; U01NS082320; U54HD090255; R01NS079788

<https://www.ncbi.nlm.nih.gov/pubmed/30424962>

[NINDS, NICHD]

Development of Memory Networks in Children and Adolescents with Intractable Epilepsy

With advanced technologies, scientists can now precisely record both the timing of and tiny changes in activity in the developing brain. Researchers analyzed patterns of brain activity in 17 patients ages 6 to 19 that predicted better performance on a memory test. The patients had had electrodes implanted on the surface of the brain to manage epileptic seizures. Data from recordings of the patients' brain activity were "cleaned" to ensure that only activity occurring when the patients were not having seizures was analyzed. The researchers looked at activity in the prefrontal cortex, a large component at the front of the brain best known for its role in controlling the ability to plan, make decisions, and solve problems. They showed that in the developing brain, the prefrontal cortex also supports memory formation and that split-second changes in the flow of activity between brain subregions can predict whether a memory is formed.

R01MH107512; R01NS064033

<https://www.ncbi.nlm.nih.gov/pubmed/30585286>

[NIMH, NINDS]

Gene Therapy Approved for Spinal Muscular Atrophy

Researchers have developed the first gene therapy for spinal muscular atrophy, a rare disorder that begins in infancy or childhood and leads to the degeneration of spinal motor neurons, the neurons that control skeletal muscles. The therapy (Zolgensma, or onasemnogene abeparvovec-xioi) was approved by the Food and Drug Administration (FDA) in May 2019. Preclinical development and natural history data on the progression of untreated spinal muscular atrophy aided clinical assessment and allowed approval of the therapy.

R01NS038650; R21NS064328; P01NS057228; P30NS045758; RC2NS069476; RC2NS069476

<https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease>

[NINDS]

Early Diagnosis of Prader-Willi Syndrome Using Newborn Screening Techniques

Prader-Willi syndrome (PWS) is a genetic disease that can cause low muscle tone, intellectual disability, obesity, growth problems, and other health issues. Because PWS symptoms are not always obvious in babies, early diagnosis and treatment can be difficult without genetic testing. Researchers showed that they could correctly identify PWS in blood samples taken from newborn screening filter paper cards. They were also able to identify the specific DNA changes in each person that resulted in PWS. The researchers concluded that diagnosing PWS during routine newborn screening is possible and, after confirmation, advocated for consideration of PWS testing in the Recommended Uniform Screening Panel. Earlier diagnosis would help doctors develop effective early intervention plans to improve the health and quality of life for people with PWS.

P30HD02528; U54HD061222; UL1TR001414

<https://www.ncbi.nlm.nih.gov/pubmed/30556641>

[NICHD, NCATS]

Early Detection of Cerebral Palsy in Preterm Infants

Cerebral palsy is the most common physical disability in children. Extremely preterm infants are at greater risk for cerebral palsy than infants born at term are. Although cerebral palsy originates before or soon after birth, most cases are diagnosed at 2 years of age or older. Researchers used brain imaging to study structural connectivity in white matter pathways, or tracts, in the brains of extremely low birthweight infants to determine whether differences in microstructural features over time could predict which infants would develop cerebral palsy. They found that injury or immaturity in one or more tracts in the brain preceded cerebral palsy and that a combination of markers achieved 95 percent accuracy in classifying subsequent diagnoses. Earlier diagnosis could enable treatment interventions during the critical periods in early brain development.

R01NS094200; UL1TR003167; R01NS096037; UL1RR024148; UL1TR000371

<https://www.ncbi.nlm.nih.gov/pubmed/31201071>
[NINDS, NCATS]

Hydroxyurea Causes Mild Improvement of Brain Function in Mice with Down Syndrome

Down syndrome, the most common genetic cause of intellectual disability, is characterized by distinct changes in the brain and brain activity. Down syndrome mice models have problems with memory and other challenges as the mice develop. Researchers tested whether a Food and Drug Administration (FDA)–approved substance called hydroxyurea, which can prevent or slow down cell damage, could improve learning and memory in this mouse model. They found that treating these mice with hydroxyurea slightly improved memory retention. Hydroxyurea also boosted brain function in control mice. These findings suggest that hydroxyurea has the potential to improve cognition in individuals with Down syndrome.

R01HD038384; RF1AG055974
<https://www.ncbi.nlm.nih.gov/pubmed/31139073>
[NICHD, NIA]

Monitoring Health Behaviors in Youth with Spina Bifida

Youth with disabilities are at higher risk for obesity, disordered eating, and poor body image, but they are often excluded from research on these topics. In addition, adolescents and young adults with spina bifida are often advised to lose weight without being provided clear guidance. Researchers assessed health behaviors, body mass index (BMI), and disordered eating behaviors in young adults with spina bifida who were between 15 and 24 years old. The participants ranged from underweight to severely obese. Most did not eat healthy foods or exercise as much as recommended by the Centers for Disease Control and Prevention. Both male and female respondents were more likely to report purging and restricting food compared with established norms. Some participants reported these behaviors even if they were not overweight. The results suggest that young people with spina bifida, including those with a lower BMI, be watched for disordered eating behaviors.

R01HD048629; R01NR016235
<https://www.ncbi.nlm.nih.gov/pubmed/30978107>
[NICHD, NINR]

Defining Brain Activity in Children Unable to Feel Pleasure

Using data from the first release of the Adolescent Brain Cognitive Development (ABCD) Study, researchers identified changes in brain connectivity and activity during rest and reward anticipation in children with anhedonia, the loss of motivation and lack of pleasure. Researchers used data from functional magnetic resonance imaging to compare brain connectivity in this disorder with other types of brain disorders. This project sheds light on brain function associated with anhedonia and helps differentiate anhedonia from other related mental or behavioral disorders.

Intramural Research, ZIAMH002957; U01DA041022; U01DA041025; U01DA041028; U01DA041048; U01DA041089; U01DA041093; U01DA041106; U01DA041117; U01DA041120; U01DA041134; U01DA041148; U01DA041156; U01DA041174; U24DA041123; U24DA041147
<https://www.ncbi.nlm.nih.gov/pubmed/30865236>
[NIMH, NIAAA, NCI, NHLBI, NICHD, NIDA, NIMHD, NINDS, OBSSR, ORWH]

Evaluating Abnormal Attachment and Depression in Children and Adolescents Over Time

Children with insecure attachment, whose emotional needs are not being met by the caregiver, are more likely to be or become depressed. Researchers monitored this association over time in children and adolescents, finding that higher reported levels of anxiety and avoidance were correlated with higher levels of symptoms of depression over time. This link between insecure attachment and depressive symptoms during childhood and adolescence suggests that depression in children may be addressed by

improving relationships with their caregivers and that doing so early may help reduce depressive symptoms as children grow.

R01MH077195; R01MH077178; R01MH109662; R01MH105501; R21MH102210

<https://www.ncbi.nlm.nih.gov/pubmed/31144587>

[NIMH]

Traffic-Related Air Pollution Exposure, Childhood Anxiety, and Changes in the Brain

Researchers used brain imaging techniques to study a proposed link between children's exposure to traffic-related air pollution and an increase in anxiety. Imaging measured specific brain metabolites in otherwise healthy children. Researchers reviewed the data against calculated pollution exposure. They found that children exposed to higher levels of recent traffic-related air pollution had higher levels of myo-inositol, a brain metabolite linked to inflammation in the brain, than children with lower exposure. The observed increases in myo-inositol also appeared to be associated with generalized symptoms of anxiety.

R01ES027224; R01ES019890; P30ES006096; R01ES011170; R00ES024116; UL1TR001425

<https://www.ncbi.nlm.nih.gov/pubmed/31103795>

[NIEHS, NCATS]

Using Social Media Platforms to Reach People Who May Have Eating Disorders

Many individuals suffer from eating disorders. These conditions often emerge during adolescence. Scientists are seeking to understand the level of risk among people networking on Twitter and other online platforms about their own eating disorder risk behaviors. The researchers are studying how these messages flow through Twitter networks and individuals' openness to suggestions for treatment and prevention messages via social media. Studies are considering the use of digital language processing to find those people who may be at risk based on their posts. This pilot project represents the beginning of a line of research that will work toward using social media to deliver body-positive and eating disorder recovery messages and to identify and connect at-risk individuals with the treatment help that they need. This study may help overcome common treatment barriers (e.g., the belief that one's problems are not serious enough) and facilitate timely access to care so that the best possible outcomes can be achieved among the greatest number of individuals.

R21MH112331; K08MH120341

<https://www.ncbi.nlm.nih.gov/pubmed/29300696>

<https://www.ncbi.nlm.nih.gov/pubmed/29414146>

<https://www.ncbi.nlm.nih.gov/pubmed/31381168>

<https://www.ncbi.nlm.nih.gov/pubmed/31679144>

[NIMH]

Childhood Injuries, Maltreatment, and Violence

A Chemical Link Between Childhood Abuse and Adult Cognitive Challenges

People who experienced childhood abuse had high adult levels of IL-6, an immune system protein involved in the swelling or inflammation produced in response to an injury. People who were mistreated as children are at higher risk for cognitive decline, depression, and other health problems. Researchers found that people who experienced early abuse, who had high adult levels of IL-6 and depressive symptoms, were more likely to have lower cognitive performance scores than other participants who had experienced abuse. The researchers theorize that exposure to childhood abuse may lead to elevated IL-6 levels and higher chances of depression, contributing to less cognitive ability later in life. Interventions to lower IL-6 levels and reduce depression may help improve cognitive function in this group.

R01HD086085; R01HD079520; R01AG026006

<https://www.ncbi.nlm.nih.gov/pubmed/29562248>

[NICHD]

Caregiver Characteristics and Child Physical Abuse

Researchers performed a study comparing the characteristics of caregivers and caregiving arrangements of young children who were taken to the emergency department for medical care. The children were evaluated to assess whether they experienced physical abuse or accidental injuries. In this study, 24 percent of the children were found to be physically abused. Child abuse was much more likely when a male caregiver was present, and the resulting injuries were more likely to be severe or fatal. Caregiving arrangements that differed from a routine arrangement, and caregiver relationships of less than 1 year, were also associated with increased risk of child abuse. Although these findings are not absolute predictors of child abuse, this research can help tailor efforts to prevent child abuse based on caregiver characteristics.

R01HD060997

<https://www.ncbi.nlm.nih.gov/pubmed/31255388>

[NICHD]

Video Data Reveals Teens' Risky Behaviors While Behind the Wheel

Motor vehicle crashes are the leading cause of death and disability among drivers between the ages of 15 and 20, according to the National Highway Traffic Safety Administration. Researchers used real-time driving data to learn about distractions that caused teens' eyes to shift away from the road, increasing the risk of a crash. Using 6-second videos of driver behavior prior to a crash, researchers found that for every second that a teen's eyes were off the road, the risk of a crash rose by 28 percent. Handling a cell phone doubled the drivers' odds of crashing. Reaching for things while driving increased the risk of a crash nearly sevenfold. This study confirms the need for technologies or other ways to encourage young drivers to keep their eyes on the road at all times.

Intramural Research, ZIAHD001707

<https://www.ncbi.nlm.nih.gov/pubmed/30799162>

[NICHD]

Trends in Family Firearm Ownership and Firearm-Related Fatalities Among Young Children

Firearm-related fatalities are the third leading cause of injury-related death among children under 18 years old in the United States. Although the percentage of households owning guns has declined in recent decades, the firearm-related mortality rate among children 1 to 4 years old almost doubled between 2006 and 2016. Researchers analyzed changes in firearm ownership among families with young children from 1976 to 2016. They found that, although firearm ownership has generally declined over the past 4 decades among both White and African American families with young children, the types of guns that families own have changed. Specifically, the proportion of White families with young children who reported having pistols or handguns in the home increased by close to one third. Among African American families with young children, the proportion who owned handguns declined over the study period. For White families, handgun ownership was more strongly associated with firearm-related fatalities among 1- to 5-year-olds than overall firearm ownership. The results suggest that changes in the types of firearms in family homes may partially explain the rising firearm-related mortality rate among young White children.

F32HD086994

<https://www.ncbi.nlm.nih.gov/pubmed/30835244>

[NICHD]

Substance Use and Misuse

Disparities in Secondhand Smoke Exposure Persist in U.S. Children

Tobacco smoke exposure is a common health hazard for children. Scientists used National Health and Nutrition Examination Survey data to learn that the percentage of children exposed to secondhand tobacco smoke went down overall, from 65 percent to 38 percent between 1999 and 2014. However, African American or Black children were nearly twice as likely to be exposed to tobacco smoke as White children were. Hispanic Mexican children had a lower risk of exposure. The study also showed that exposure to smoke increased with higher levels of family poverty. Children who lived in rented homes were twice as likely to have secondhand smoke exposure compared with children who lived in owned homes. Targeted tobacco control efforts are needed to help reduce exposure to secondhand smoke, especially for African American or Black children and children who live in poverty and in rented homes. K01DA044313; R01HD083354; R01ES027815; ZIAMD000006
<https://www.ncbi.nlm.nih.gov/pubmed/30902698>
[NIMHD, NICHD, NIDA, NIEHS]

E-Cigarettes Disrupt Lung Function, Raise Risk of Infection

In 2018, more than 3 million high school–age adolescents in the United States reported using e-cigarettes. However, few studies have looked at the long-term effects of breathing in vaporized chemicals (glycerin and propylene glycol) that are often added to vaping fluids. In a study done in mice, scientists showed that long-term exposure to vapors from e-cigarettes disrupted normal lung function, even when the vaping fluid did not contain nicotine. Cells in the mice’s lungs showed abnormal buildup of fats called phospholipids, impairing the cells’ role in gas exchange. The vapors also reduced the ability of immune cells (macrophages) to respond to infection by the influenza virus. These discoveries may help explain how using e-cigarettes can lead to a severe type of pneumonia in humans. R01ES029442; R01AI135803
<https://www.ncbi.nlm.nih.gov/pubmed/31483291>
[NIEHS, NCI, NIAID, NCATS]

Survey Shows Dramatic Increases in Nicotine E-Cigarette Use Among Students

Rates of nicotine vaping among 8th, 10th, and 12th graders doubled between 2018 and 2019—a single year. The 2019 Monitoring the Future study showed that more than 1 in 4 students in 12th grade, more than 1 in 5 in 10th grade, and more than 1 in 11 in 8th grade reported vaping nicotine during the past month. Some of the most common reasons that high school seniors gave for vaping were to “experiment,” “because it tastes good,” “to have a good time with my friends,” and “to relax or relieve tension.” The doubling of the number of 12th graders who said they vape because they are “hooked” is of particular concern. Rates of vaping during the prior month exceeded any other kind of substance use, including alcohol and marijuana, for all three grades. The Monitoring the Future study provides information about trends in substance use among American adolescents, college students, and young and middle-age adults. P50DA039838; R01DA001411; R01DA037902
<https://www.ncbi.nlm.nih.gov/pubmed/29273302>
<https://www.ncbi.nlm.nih.gov/pubmed/31532955>
[NIDA]

Tobacco-Cessation Drug and Adolescent Smokers

Cigarette smoking is the leading cause of preventable death and disease in the United States and worldwide. Most tobacco users begin smoking while they are teens. Scientists wanted to find out whether varenicline, a drug that can help adults quit smoking, would help adolescents who are trying to stop smoking. For this 12-week study, participants took either the drug or a placebo. Both groups received counseling about how to quit smoking. Urine tests for nicotine at the end of the study showed no difference between the two groups, a sign that the varenicline drug did not help with quitting smoking. The drug seemed to be safe for teens, and the participants reported that it helped them take weeklong breaks from smoking during the treatment period. K01DA036739; K23AA025399; K12DA031794; K12HD055885; U01DA031779

<https://www.ncbi.nlm.nih.gov/pubmed/31609433>
[NIDA, NIAAA, NICHD]

Teen Tobacco Use Linked to Strength of Retail Laws and Enforcement

Federal laws prohibit the sale of tobacco to minors and require annual checks to make sure that stores comply. However, whether these compliance checks occur can depend on whether there is funding from city or town ordinances. To study the effect of these retail licensing regulations on teen tobacco use, scientists surveyed 1,553 teens in areas of Southern California where such ordinances were either weak or strong. The researchers judged ordinance strength based on enforcement and whether the licensing fees cover the cost of compliance checks. Researchers found that youths were one-third to one-half less likely to report using tobacco products in the areas with stronger ordinances than areas with weaker regulations. These findings suggest that stronger enforcement might help to reduce the use of tobacco products among youths.

P30ES007048; P50CA180905; R21HD084812
<https://www.ncbi.nlm.nih.gov/pubmed/30617237>
[NICHD, NIEHS, NCI]

Exposure to Cannabis Can Change How Certain Brain Cells Develop

The prefrontal cortex is the part of the brain that deals with higher cognitive functions, like decision making, behavior, and controlling emotions. In psychiatric disorders, connections between cells in the prefrontal cortex are disrupted. Since previous research has suggested that cannabis use in youth can increase the risk for psychiatric disorders later in life, scientists set out to study cannabis effects on cells of the prefrontal cortex. By exposing rats to tetrahydrocannabinol (THC)—the active chemical in cannabis—researchers found that rat brain cells did not develop in a normal way. Researchers also found differences in the structure of the brain cells that resembled patterns seen in people who have addiction or schizophrenia. This research suggests that young people could become more susceptible to psychiatric disorders if exposed to THC while their brains are still developing.

R01DA030359; R01DA033660; F30DA038954; R01AG050986; R01MH109677; T32GM007280
<https://www.ncbi.nlm.nih.gov/pubmed/30283037>
[NIDA, NIA, NIMH, NIGMS]

Healthcare Use Over 3 Years After Adolescent Screening, Intervention, and Treatment Referral

Screening, brief intervention, and referral to treatment (SBIRT) is a public health approach to alcohol and substance use prevention and early intervention. Using electronic health data, researchers found that adolescent patients with access to SBIRT for 1 year in pediatric primary care were less likely to have a chronic disease or condition than patients with usual care were. Over 3 years, those patients also had fewer substance use diagnoses and fewer health clinic visits, as well as fewer psychiatry visits after 1 or 3 years, than patients with usual care did. These findings suggest that providing SBIRT in pediatric primary care may improve healthcare use, as well as improving the health, mental health, and substance use recovery of adolescent patients.

R01AA016204
<https://www.ncbi.nlm.nih.gov/pubmed/31018988>
[NIAAA]

Medication-Assisted Treatment for Youths with Opioid Use Disorder

Studies have shown that medications, including buprenorphine, naltrexone, and methadone, can help treat opioid use disorder in adolescents and young adults. Researchers looked at the treatment and retention of more than 4,800 youths ages 13 to 22 who had been diagnosed with opioid use disorder. Among these youths, about three-quarters (76 percent) received any treatment within 3 months of their opioid use disorder diagnosis. Just over one-half (52 percent) received only behavioral health services, and only

about one-quarter (24 percent) received medication. Youth who received timely medication-assisted treatment were more likely to continue treatment than those who received behavioral treatment alone. K24HD081057; K23DA045085; L40DA042434; K23DA044324; R25DA013582; K23DA042168
<https://www.ncbi.nlm.nih.gov/pubmed/30208470>
[NIDA, NICHD]

Reporting Prenatal Substance Exposure to Child Protective Services

Infants exposed to drugs or alcohol in utero are at risk for serious health and developmental harm. Fewer than half of the states in the United States require that physicians report infants born with prenatal substance exposure to child protective services (CPS). There are limited data on how often hospitals report these births and how child protective service agencies respond to the reports. When studying the frequency of immediate removals by CPS related to prenatal substance exposure and maternal race, researchers found that opioid exposure was the most common prenatal substance exposure among newborns. Less than half (42 percent) of those cases were reported to CPS within the first month after birth, and only 13 percent of these infants were removed from their home by CPS. The majority of infants with prenatal substance exposure are not removed by CPS within the neonatal period. The likelihood of removal was different for different substances: Newborns exposed to cocaine or amphetamines were most likely to be reported and removed, while removal was less likely for those exposed to alcohol, opioids, or marijuana. Racial bias may play a role in the reporting of prenatal substance exposure. P2CHD042828; TL1 TR002318
<https://www.ncbi.nlm.nih.gov/pubmed/30445334>
[NICHD, NCATS]

Pediatric Critical Care and Emergency Care

Air Pollution Linked to Rise in Newborn Intensive Care Admissions

Having a newborn who needs to go to the neonatal intensive care unit (NICU) is traumatizing for families and can be very expensive. Air pollution is known to raise the risk of premature birth and other pregnancy complications that often lead to NICU admission. Researchers looked further into the effects of air pollution on NICU admission by connecting birth data from hospitals across the country with air quality data in those areas. The study found that high levels of certain air pollutants during the week before, the day before, and the day of delivery all raised the risk of NICU admission. These pollutants typically come from traffic emissions. Intramural Research, ZIAHD008794; ZIAHD008923
<https://www.ncbi.nlm.nih.gov/pubmed/31445753>
[NICHD]

Better Ways to Predict Seizures in Newborns

Critically ill newborns are at high risk of seizures. Diagnosing these seizures in newborns requires continuous monitoring with a video camera and an electroencephalogram (cvEEG) to record brain activity. But this technique is expensive and requires expertise and resources that can be limited in hospitals. Predicting which newborns are most likely to have seizures—and when—can help doctors use cvEEG monitoring on the right newborns at the right times. Scientists looked at data from newborns who underwent cvEEG to learn more about how to predict seizures. From this, they created a model that could predict seizures by looking at traditional EEG results and factors such as the newborn's sex, age, and disorder. R01HD076258; R01EB017337; U54HD090255; R21HD083956; R01NS066929
<https://www.ncbi.nlm.nih.gov/pubmed/30882530>
[NICHD, NIBIB, NINDS]

Reducing Risky Intubations of Premature Newborns

Premature newborns often need help breathing right after birth. But traditional ventilation with an intubation tube can damage their fragile lungs and lead to serious lung disease. A less risky option is to use continuous positive airway pressure (CPAP), which uses a face mask instead of intubation, in the delivery room. Researchers at a large public hospital reviewed newborn records to understand why doctors did not try CPAP or why it failed to work, leading to intubation. The researchers came up with a series of changes to address these reasons, such as having doctors use round CPAP masks that better fit newborns' faces. After these measures were put in place, intubation of premature newborns in the delivery room dropped by more than 20 percent. This was linked to a drop in the number of lung diseases and deaths at the hospital, suggesting that the measures may be able to improve newborn health at other hospitals.

K23HD083511

<https://www.ncbi.nlm.nih.gov/pubmed/30602545>

[NICHD]

Researchers Develop a New Method for Measuring Stress in Preterm Infants

Infants in the neonatal intensive care units experience many stressful events, from normal infant care (e.g., diaper changes) to blood draws and intubation. To measure how infants respond to these stressful events, researchers tested a new way to study stress responses. They used a piece of tape to remove shed skin cells, then measured the cells' level of cortisol, a hormone closely associated with stress. The researchers found that infants born before and after 28 weeks' gestation had different cortisol responses to stress. Infants born after 28 weeks produced higher levels of cortisol in response to stressful events. Infants born before 28 weeks did not show that pattern, probably because their system for stress response had not yet developed. This novel skin test could be useful as a noninvasive and less disruptive method for assessing stress in vulnerable infants.

R21NR013094

<https://www.ncbi.nlm.nih.gov/pubmed/30583244>

[NINR]

Quality of Life in Children Who Survive Sepsis

Sepsis is a systemic infection of blood and tissue that can be life-threatening. An increasing number of children are surviving sepsis, both because the number of cases of sepsis in children is increasing and because the rate of death from sepsis is falling. However, scientists know little about sepsis survivors' health after they leave the hospital. To learn more, researchers used data from 790 children who had survived sepsis to assess their health-related quality of life after hospital discharge. The researchers compared information collected before the children became ill, when they were admitted to the hospital for sepsis, and 2 to 12 weeks after hospital discharge. Most patients fully recovered, but 23.8 percent did not. Factors that appear to contribute to a failure to recover include having a severe form of sepsis called septic shock, older age, a compromised immune system, and a longer hospital stay.

R01HD073362; T32HD057822

<https://www.ncbi.nlm.nih.gov/pubmed/30720672>

[NICHD]

Extracorporeal Membrane Oxygenation (ECMO) Treatment Can Affect Action of Antibiotic Drug in Critically Ill Children

A complex technological intervention known as ECMO can keep critically ill patients with failing heart and lung function alive to permit life-saving treatment to take effect. An ECMO system drains the patient's blood from the body and pumps it across a membrane that oxygenates the blood and eliminates carbon dioxide before returning the blood to the body. However, ECMO alters drug pharmacokinetics—that is, how a drug is distributed and eliminated from the body. Because of the extra blood and fluid needed to fill the ECMO circuit outside of the body, the drugs are distributed through a larger volume of

blood. Also, ECMO often reduces clearance—that is, elimination of the drug from a patient’s body. Scientists observed the effects of ECMO on the pharmacokinetics properties of cefepime, an antibiotic commonly used for the seriously ill, in a small group of very young pediatric patients (age 30 days to less than 2 years old) on ECMO. The scientists found that cefepime clearance was reduced in ECMO patients and that only about three-fourths (74 percent) of the drug doses reached the minimum level needed to treat serious infections. Study results suggest that pediatric patients on ECMO might benefit from additional monitoring to ensure appropriate dosing.

U10HD063108; UG1HD050096; UG1HD049983; U10HD050096; UG1HD083170; UG1HD083166; U10HD049983; U10HD050012; UG1HD083171; UG1HD063108; U10HD063114; K99HD096123; U01HD049934; R01HL112745

<https://www.ncbi.nlm.nih.gov/pubmed/30431557>

[NICHD, NHLBI]

Racial and Ethnic Variation in Emergency Department Care for Children with Asthma

Asthma is a common diagnosis in the United States, affecting close to 10 percent of children. Past studies have found that children of different racial and/or ethnic groups are given different treatments.

Researchers in Minnesota studied the differences in asthma treatment for pediatric patients ages 2 to 18 in six emergency departments in the Upper Midwest. The current guidelines for treating asthma recommend administering inhaled steroids for all emergency department visits and ordering radiology tests, such as chest X-rays, only in some cases. After adjusting for demographics, insurance type, and triage score, the researchers found that African American and Hispanic patients were more likely to receive steroids than White patients were. They also found less radiological testing among African American and American Indian children compared with Whites.

U54MD008164

<https://www.ncbi.nlm.nih.gov/pubmed/28926508>

[NIMHD]

Clinical Care, Outreach, and Services

Verifying Whether Children Fasted Before Medical Testing

To test children for type 2 diabetes, doctors measure their levels of blood sugar, or glucose. Patients must fast overnight before the test. To check whether children had fasted, researchers paired the blood glucose test with another blood test that measures free fatty acids. They compared the free fatty acid test results of children who were inpatients—and whose food intakes were controlled by hospital staff—against those of children who were outpatients. The researchers found that about 10 percent of outpatients had low free fatty acid levels, indicating that they probably did not fast, compared with fewer than 2 percent of inpatients. The results suggest that doctors should not assume that children have fasted enough and that testing for free fatty acids may help doctors interpret glucose test results in children.

Intramural Research, ZIAHD000641

<https://www.ncbi.nlm.nih.gov/pubmed/31053621>

[NICHD]

Physicians May Overprescribe Antibiotics to Children During Telemedicine Visits

Many companies allow patients to connect with physicians through audio or video conferencing, called telemedicine. Researchers use billing data to compare antibiotic prescribing practices for telemedicine, urgent care, and primary care visits by children with respiratory infections. The researchers found that children who had telemedicine visits were more likely to receive prescriptions for antibiotics and that their treatment with antibiotics was less likely to follow clinical guidelines that are intended to prevent inappropriate use of antibiotics, which can increase bacterial resistance. The researchers theorize that physicians providing telemedicine visits may overprescribe antibiotics because they cannot closely

examine patients or perform tests, potentially limiting their ability to distinguish between bacterial and viral infections.

K23HD088642

<https://www.ncbi.nlm.nih.gov/pubmed/30962253>

[NICHD]

Parental Disengagement Tied to Higher Risk of Adolescent Male Gun Carrying

Adolescent gun violence is a serious public health problem in the United States, and gun carrying is a likely lead-in to gun violence. To identify important factors in gun carrying, researchers followed 503 urban public school boys from first grade to age 20. The researchers interviewed the boys, their parents, and their teachers and found that boys who experienced parental disengagement—indicated by parent-reported poor communication and other factors—were more likely to report carrying a gun. The findings suggest that interventions designed to improve parental engagement may help prevent gun carrying by youths.

R01HD086761; R01MH050778

<https://www.ncbi.nlm.nih.gov/pubmed/30833298>

[NICHD]

Safe Infant Sleep Practices Need Improvement

Approximately 3,500 infants die annually in the United States from unexpected sleep-related causes. Safe sleep practices, such as placing infants to sleep on their backs, can reduce the risk of these deaths.

Researchers used survey data to study mothers' safe sleep practices. They found that 78 percent of mothers put infants to sleep on their backs, but fewer followed other recommended practices, such as putting infants to sleep in their parents' room but not in their parents' bed. Mothers were more likely to follow safe sleep practices if doctors or other healthcare providers had advised them to do so. More than 90 percent of mothers had received provider advice on back sleeping, but fewer had received advice on other safe sleep practices. The researchers suggest that provider advice could help improve safe sleep practices.

Intramural Research

<https://www.ncbi.nlm.nih.gov/pubmed/31636142>

[NICHD]

Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) and Preterm Birth

Preterm birth is a leading cause of infant death and long-term childhood disability. By one estimate, the annual societal economic cost of preterm birth in the United States is \$26.2 billion. Pregnant women who lack adequate nutrition and prenatal care are more likely to give birth preterm. Researchers evaluated the cost-effectiveness of pregnant women's participation in WIC, which provides food assistance, education, and referrals for prenatal care to low-income women. The researchers applied economic modeling methods to a hypothetical group of 500,000 California women. They found that prenatal WIC participation prevented 7,575 preterm births and would produce cost savings of about \$349 million over the lives of infants born to those women. The researchers suggest that enrolling all eligible women in WIC would reduce preterm births and result in cost savings.

R01HD072296

<https://www.ncbi.nlm.nih.gov/pubmed/30998955>

[NICHD]

Pediatric Pharmacology

General Anesthesia's Effect on Infant Brain Development

The results of research into the effects of general anesthesia on infant brain development have been mixed. To help understand whether general anesthesia has a negative effect on infants' brains, researchers in seven countries studied more than 700 infants having surgery for to repair a hernia. Half of the infants received regional anesthesia, and the other half were given general anesthesia. Comparing test results of the children's thinking, behavior, language, and judgment at age 5, the researchers found no significant difference between the groups. The results may reassure some doctors and parents who are considering delaying a procedure requiring general anesthesia until an infant is older.

R01HD061336; R01HD084566; U54HD090255

<https://www.ncbi.nlm.nih.gov/pubmed/30782342>

[NICHD]

Optimizing Antibiotic Treatment in Premature Infants

The antibiotic ticarcillin-clavulanate is commonly used to treat infection in premature infants in neonatal intensive care units. However, figuring out the right dose can be difficult because the infants' immature physical development affects how quickly their bodies can process the drug. A small study of premature infants now provides guidance for these decisions. Based on measurements from 15 infants born before 30 weeks of gestation, the researchers built a computer program to model antibiotic levels in 1,000 infants over time. The model incorporated a range of antibiotic doses and infant characteristics, including age and weight. The researchers found that it took longer for the infants who were less than 2 weeks old to break down the medicine and process it, suggesting that older infants have more mature kidney function. The researchers calculated recommended doses based on age to account for this difference. They also determined that treating highly drug-resistant organisms effectively requires more frequent dosing or extended infusion of the antibiotic.

K23HD075891

<https://www.ncbi.nlm.nih.gov/pubmed/30710387>

[NICHD]

Methotrexate Dosing in Infants with Acute Lymphoblastic Leukemia

Despite improvements, treatments for acute lymphoblastic leukemia (ALL), the most common form of pediatric cancer, are not as effective in infants as they are in older children. One factor may be how efficiently infants' kidneys process and get rid of methotrexate, an anti-cancer drug. Using a new statistical model, scientists were able to detect a high degree of variation in how quickly individual infants cleared methotrexate from their body each treatment cycle. The researchers suggested that monitoring individual patients closely and adjusting the amount of methotrexate they receive in each treatment cycle could improve therapy for infants with ALL.

U10CA098413; T32GM086330; K23HD083465

<https://www.ncbi.nlm.nih.gov/pubmed/30810947>

[NICHD, NCI, NIGMS]

Technology and Tools

Improving the Diagnosis of Appendicitis in Children

Researchers developed a new calculator that can more accurately gauge children's risk of appendicitis. Analyzing data from children's electronic health records, the researchers used an initial test group of 2,423 children, 40 percent of whom had appendicitis, to create the tool. To verify its accuracy, the researchers then tested it on an additional 1,426 children. The researchers found that their new calculator was more accurate than the current most widely used risk assessment tool. Up to 40 percent of children who would otherwise have been considered high risk for appendicitis had low scores. Using the new tool to calculate children's risk of appendicitis could reduce the need for additional testing.

R01HD079463

<https://www.ncbi.nlm.nih.gov/pubmed/29535251>
[NICHD]

Improving MRIs for Pediatric Patients

When a patient moves during magnetic resonance imaging (MRI), the movements must be removed with rapid imaging and image processing techniques. To avoid this difficult and time-consuming task, providers often give children a sedative or anesthesia before an imaging procedure. This study applied a deep learning method to correct for motion during a scan. Scans were about 60 percent shorter, on average, than current scans for pediatric patients. In addition to offering faster scan times, this new approach could reduce the need for anesthesia during MRI scans for children.

R01EB009690; R01HL127039

<https://www.ncbi.nlm.nih.gov/pubmed/31322799>

[NIBIB, NHLBI]

Diagnosing Congenital Heart Disease Before Birth

Congenital heart disease happens when the heart or nearby blood vessels do not develop normally before birth. To diagnose congenital heart disease before birth, doctors study images of the fetus's heart. But image quality varies with the skill of those who take the images. A new method called FINE (fetal intelligent navigation echocardiography) automatically shows standard views of the heart. The researchers used FINE images from fetuses with congenital heart disease diagnoses or normal hearts and tested whether users could identify the cases of congenital heart disease. The researchers compared diagnoses of fetuses made with FINE and diagnoses of infants after birth. In most cases, the diagnoses either matched or were very close. The researchers believe that FINE could be a way to diagnose congenital heart disease before birth.

Intramural Research, ZIAHD002401

<https://www.ncbi.nlm.nih.gov/pubmed/29603310>

[NICHD]

Global Pediatric Health

Feeding Gut Microbes to Help Malnourished Children

Malnourished children lack important nutrients and can have loss of muscle and fat tissue and low height for their age. Complementary foods provide nutrients that malnourished children lack. Studies show that microbes in the gut play a role in malnutrition. Researchers designed a complementary food based on boosting healthy microbes in the guts of severely malnourished Bangladeshi children. The researchers studied proteins from blood and fecal samples from children treated with previously available complementary foods and matched the proteins with the children's muscle, bone, and fat tissue growth. The researchers put microbes from a recovering child into mice and piglets' guts. The researchers fed the animals ingredients associated with the children's gut microbes and improved growth. After identifying a formula that drove growth in the animals, the researchers used it in a new complementary food. Children who ate the complementary food showed signs of improved growth, bone formation, nervous system development, and immune function. These signs were more like those seen in healthy children.

P30CA91842; UL1TR002345; T32GM007200; P30DK052574; P30DK020579; P30DK056341; P30AR057235

<https://www.ncbi.nlm.nih.gov/pubmed/31296738>

[NIDDK, NIAMS, NIGMS, NCI]

Inexpensive Supplement to Boost Newborn Size

In places without many resources, a new daily nutritional supplement taken before pregnancy or in early pregnancy may boost growth of the fetus. The supplement, made from dried skim milk and soybean and

peanut extracts, has the vitamins, minerals, protein, and fatty acids that women's diets often lack. Researchers gave the supplement to women in rural areas of the Democratic Republic of the Congo, Guatemala, India, and Pakistan. The women either began taking the supplement 3 months before they got pregnant or during early pregnancy or did not take the supplement. Compared with women who received no supplements, women who took supplements were 31 percent less likely to have infants with shorter length at birth and 22 percent less likely to have infants who were small for gestational age.

P30DK048520; U24HD092094; U10HD078438; UG1HD076465; U10HD076474

<https://www.ncbi.nlm.nih.gov/pubmed/30721941>

[NICHD, NIDDK]

Pregnancy Results in Low- and Middle-Income Countries

Cesarean birth involves surgery to deliver a baby when a vaginal delivery would put the baby or mother in danger. Fetuses that are in a breech position (feet or buttocks first) are often delivered by cesarean births. But in low- and middle-income countries, women may not have access to cesarean birth, or it may pose more danger than it does in high-income countries. Researchers examined cesarean birth of fetuses in breech position in India, Pakistan, Guatemala, Zambia, Kenya, and the Democratic Republic of the Congo, as well as the results for newborns of 400,000 mothers between 2010 and 2016. Across all countries, rates of stillbirth and newborn death were higher among breech babies. Compared with cesarean birth, vaginal birth of these babies was related to greater chance of harm for the mother, especially heavy bleeding after delivery.

U24HD092094; U10HD078438; UG1HD078439; U10HD076461; U10HD07646

<https://www.ncbi.nlm.nih.gov/pubmed/30414270>

[NICHD]

Diagnosing Pulmonary Tuberculosis (TB) in Children in Resource-Limited Settings

Pulmonary TB occurs when bacteria that cause TB mostly attack the lungs. For doctors, recognizing pulmonary TB as different from other diseases is hard. Exams, X-rays, and other images are usually used to diagnose childhood pulmonary TB, but these methods do not always give enough information and may expose children to radiation. The preferred magnetic resonance imaging (MRI) or computed tomography (CT) scans are sometimes unavailable. Researchers found that chest ultrasound, which involves no radiation exposure, may be a viable alternative. The researchers conducted chest ultrasounds in South African children with diagnosed pulmonary TB, unconfirmed pulmonary TB, and other lower respiratory tract infections, then compared the findings from the different groups of children. The scientists found that technicians reading chest ultrasounds detected lung features associated with pulmonary TB. The researchers suggested chest ultrasound as the first imaging tool for children with suspected TB, especially in settings that lack other imaging technology.

R01HD058971

<https://www.ncbi.nlm.nih.gov/pubmed/30632712>

[NICHD]

Preventing Malaria in Children

Malaria can cause serious health problems, especially in young children. Regular treatment with a drug called dihydroartemisinin-piperazine (DHA/PPQ) can help prevent malaria. Scientists wanted to know what dose of DHA/PPQ is best for young children and whether they are protected against malaria after they stop taking the drug. For 2 years, the researchers treated young children in groups that got DHA/PPQ every 4 weeks or every 12 weeks, comparing how many children in each group had malaria. Children who received treatment every 4 weeks had far fewer cases of malaria during treatment and for a year after treatment. The two dosing plans were equally safe. The researchers concluded that treating children with DHA/PPQ every 4 weeks is very effective at preventing malaria.

P01HD059454; K23AI100949; K24AI113002; UM1AI069496; R01AI093615

<https://www.ncbi.nlm.nih.gov/pubmed/31307883>

[NICHD, NIAID]

Promising transmission-blocking malaria vaccine now being tested in children

Results from a recent first-in-human trial demonstrated that Pfs230-EPA vaccination reduces transmission in a significant proportion of vaccinees, is lasting, well-tolerated, and safe in adults. Recent natural history data also clearly indicate that children play a disproportionate role in malaria transmission. An age de-escalation trial is now being conducted to ensure that the vaccine is safe to administer to children and then will conduct a community clinical trial to assess efficacy in family groups.

<https://clinicaltrials.gov/ct2/show/NCT03917654>

[NIAID]

SELECTED NEW AND EXPANDED RESEARCH EFFORTS FOR FY 2019 IN PEDIATRICS

Selected New Pediatric Research Efforts

NIH institutes, centers, and offices (ICOs) launched a range of new and expanded research programs and efforts related to pediatrics in fiscal year (FY) 2019. Selected highlights of new initiatives and funding opportunity announcements (FOAs) are listed below. Several programs are focused on understanding risk factors for complex conditions in children, including vulnerable populations in research, gauging environmental and social factors, and examining pain. Overall, many programs are concerned with developing and delivering evidence-based interventions.

The HEALSM Healthy Brain and Child Development Study

This trans-NIH longitudinal study is supported by the NIH HEALSM (Helping to End Addiction Long-term) Initiative. The study will follow a large population of children from the prenatal period to age 10 to examine how early exposure to opioids, other substances, and social stressors affect brain development in children. The study is expected to enroll women during their second trimester of pregnancy or after the birth of their baby. The study will gather data on potentially important factors about their environment, including drug and alcohol use, and will follow the women and their children over the subsequent decade. The study is currently in Phase I, an 18-month planning phase, which will help ensure a robust study design for the Phase II study, which is expected to launch in 2021.

<https://heal.nih.gov/research/infants-and-children/healthy-brain>

[NIDA, NIAAA, NICHD, NIEHS, NIMH, NIMHD, NINDS, ECHO (NIH OD Environmental influences on Child Health Outcomes program), OBSSR, ORWH]

Study of Pregnancy and Neonatal Health (SPAN)

Researchers are exploring the developmental origins of health and disease hypothesis, which indicates that early life exposures can “program” a person’s health, including their risk of chronic diseases, through cellular adaptations in biological processes. Specifically, scientists will examine prenatal exposures and genetic factors, including paternal contributions (e.g., father’s cardiovascular disease risk factors and semen epigenetic differences); placental factors; and timing of delivery in relation to fetal and neonatal health and development, especially regarding deliveries complicated by gestational diabetes. This project will develop a cohort study of about 7,770 pregnant women (55 percent Black or African American), their newborns, and about 3,825 male partners, with a randomized control trial conducted in women with gestational diabetes across several study sites.

https://projectreporter.nih.gov/project_info_description.cfm?aid=10017468&icde=49402904

[NICHD]

NIH Baby Toolbox

The NIH Infant and Toddler Toolbox (a.k.a. the NIH Baby Toolbox, or NBT) is a comprehensive developmental assessment tool for infants and toddlers ages 1 month to 42 months. With this tool, researchers and clinicians will be able to evaluate brain development in infants and toddlers, using a computer tablet to assess their thinking (cognition), social functioning, spoken and understood language, ability to understand numbers (numeracy), self-regulation, and ability to accomplish a task (executive function). Children will be able to provide most of the responses themselves, and parents or legal guardians may give answers for them as needed. Current developmental assessment tools are time-intensive and expensive; require highly trained personnel for administration, scoring, and interpreting; and often rely on outdated norms. The NBT is an innovative solution that will be easy to administer, score, and interpret within a relatively brief time frame and will be able to capture multiple areas of neurodevelopment across this age range.

https://projectreporter.nih.gov/project_info_description.cfm?aid=10045604&icde=49505791
[NICHD]

Basic Neurodevelopmental Biology of Circuits and Behavior

This program supports research projects focused on the dynamic and mechanistic links between the maturation of brain circuits and behaviors across development in rodents and nonhuman primates. This research aims to enhance understanding of neural circuit development in humans. Specifically, researchers are encouraged to investigate mechanisms associated with altered neurodevelopmental trajectories and/or behaviors relevant to mental health.

<https://grants.nih.gov/grants/guide/pa-files/par-19-027.html>
[NIMH]

Biological Underpinnings of First Menstrual Cycles

To chart the normal developmental path of the beginning of menstruation, researchers will conduct a large, comprehensive study of the biological underpinnings of a girl's first few menstrual cycles. The goal of the study is to develop a way to differentiate between girls who will go on to establish regular cycles and those who may be at high risk for infertility and other issues. The American Academy of Pediatrics has designated a girl's menstrual cycle length as a vital sign of overall health. The study is enrolling 75 girls ages 10 to 14, who will be followed for 2 years.

<https://joinastudy.niehs.nih.gov/studies/first-period/index.htm>
https://projectreporter.nih.gov/project_info_description.cfm?aid=10016010&icde=49574281
[NIEHS]

Linking Psychosocial Determinants, DNA Methylation, and Early Developmental Health Disparities

Despite improvements in access and quality of healthcare in the United States, children from socioeconomically disadvantaged families and racial and ethnic minority communities have an elevated risk for impaired cognitive and social-emotional development, particularly if they live in poverty. This research project will determine the association between the maternal psychosocial experience and the change in infant DNA methylation (DNAm, a genetic process) during the first year of life. The study will also characterize the association between a mother's psychosocial experiences in her infant's first year of life and infant DNAm and will determine the impact of DNAm at two time points during the child's first 18 months. This research will be conducted within a large, regional home visiting program.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9984525&icde=49505984
[NIMHD]

Midlife Reversibility of Early-Life Biobehavioral Risk Factors

Epidemiological evidence links exposure to early-life adversities, such as childhood maltreatment, with impaired health and well-being in adulthood. Since these long-term risk factors are usually unrecognized or unaddressed in childhood, preventive and remediating interventions in adults are needed. Experts from

NIH and the United Kingdom established a research agenda on adult interventions that is informed by emerging findings on critical periods of sensitivity to adversity in fetal and child development, improved understanding of risk mechanisms that may persist across the lifespan, and new insights on enhancing adult neuroplasticity—that is, the adaptive capacities of brain cells.

<https://www.ncbi.nlm.nih.gov/pubmed/31368762>

[NIA, NICHD]

Collateral Consequences of Parents' Incarcerations for Adolescent Children

More than 2.3 million people are incarcerated in the United States. One in 9 African American or Black children and 1 in 28 Hispanic or Latino children have a parent in prison, compared with 1 in 56 White children. Research shows that children whose parents are incarcerated are at a higher risk for emotional, physical, and economic hardship and are six times more likely to become incarcerated themselves. This prospective longitudinal study focuses on the effects of parents' incarceration on their children's psychosocial outcomes and will identify characteristics that are likely to ameliorate the consequences of parents' incarceration. Findings will provide vital information for designing effective programs and services to address the psychosocial outcomes of children of incarcerated parents.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9949787&icde=49508084

[NIMHD]

Reducing Sugared Drink Consumption by Alaska Native Children

Yup'ik children in Alaska consume an average of 50 teaspoons of sugar each day, 16 times the American Heart Association's recommended maximum, and experience tooth decay rates that are 16 times the average rate for the U.S. population. A behavioral trial in three small, isolated Alaska Native communities is testing whether community health worker-led health education and confidence training for caregivers, together with introduction and access to sugar-free water enhancers, will reduce unhealthy sugar consumption.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9697537&icde=47691936

[NIDCR]

Clarifying Risk and Protective Factors for Neurocognitive Complications of Pediatric Type 1 Diabetes

Planning grants are expected to set the stage for a national, multisite, observational cohort study to prospectively examine the risk and protective factors for neurocognitive complications of pediatric type 1 diabetes and a comparison sample. The cohort study, in turn, is expected to inform the timing and approach for future research to reduce adverse neurodevelopmental outcomes and long-term neuropsychological consequences of type 1 diabetes.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-18-007.html>

[NIDDK]

Acute Flaccid Myelitis Natural History Study

This international multisite study will help fill knowledge gaps about the rare neurological disorder acute flaccid myelitis (AFM) by developing data on its incidence (the proportion of the population that is affected) and distribution (the pattern of its occurrence). The study will gradually enroll children with symptoms of AFM and follow them for 1 year. Household contacts of children with suspected AFM will also be enrolled and followed, for purposes of comparison with affected children.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9915700&icde=49508497

[NIAID]

Clinical Trial on Malaria Vector and Parasite Control

Malaria-carrying mosquitos' resistance to insecticides and the growing resistance of the malaria parasite to approved drugs are increasing problems in the fight against malaria. A new clinical trial uses a novel strategy to integrate programs targeting both the mosquito vector and the malaria parasite to control the

spread of the disease. In this trial, children will be given ivermectin, an antiparasitic drug that is thought to be able to target both the vector and the parasite.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9565317&icde=41973426&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

[NIAID]

Impact of Initial Influenza Exposure on Immunity in Infants

This program supports research to establish and follow cohorts of infants to determine how initial and repeated natural influenza infections and/or vaccinations shape infant and childhood immunity to future influenza exposures. One program-supported study will follow more than 2,000 infants and their mothers from sites in Cincinnati and Mexico City for at least 3 years; during weekly clinical visits, researchers will gather data about changes in participants' immune systems. A second study will establish and collect data from a cohort of more than 3,000 children at sites in Nicaragua, New Zealand, and California.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-18-010.html>

[NIAID]

Examining Antibiotics in Juvenile Idiopathic Arthritis Development and Treatment Response

Antibiotic overprescription is a significant public health risk, especially for pediatric populations. Antibiotic exposure in early childhood can lead to long-term changes in population of microorganisms (microbiota) in the gut that play a key role in immune system development. Such changes have been implicated in the development of juvenile idiopathic arthritis (JIA), and drugs commonly used to treat JIA can be metabolized by the gut microbial populations. In adult patients, differences in the gut microbial populations have been associated with varying treatment effectiveness. Researchers will examine whether antibiotic exposure contributes to development of JIA or impairs the ability of JIA patients to respond to standard treatments. Results could inform the development of new efforts to reduce antibiotic overprescription and help identify interventions to promote healthy gut microbial populations (e.g., through diet or probiotics), possibly improving treatment of or preventing JIA altogether.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9818326&icde=47910827&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

[NIAMS]

Improving Predictions of Food Allergy in Children and Young Adults with Atopic Dermatitis

Atopic dermatitis, also called eczema, results in dry, red, and itchy skin and can be predictive of a food allergy. Measurements of levels of a food-specific antibody called immunoglobulin E (IgE) are common but often produce inaccurate results. Investigators launched a clinical trial for individuals 3 to 21 years old who have atopic dermatitis. The goal is to establish a threshold of IgE antibody reactivity to milk and peanuts that predicts an allergic response and could help guide clinicians in their treatment of atopic dermatitis.

<https://clinicaltrials.gov/ct2/show/NCT03835767>

[NIAID]

Childhood Cancer Data Initiative

This initiative, launched in 2019, will focus on enhancing and integrating data collection and ensuring the accessibility of data on childhood cancers. Tissue samples from pediatric cancer patients are a valuable resource but are critically limited. Data generated from these samples are often fragmented and not broadly available to researchers. The Childhood Cancer Data Initiative (CCDI) aims to build a connected data infrastructure that would enable the sharing of childhood cancer data from various sources. By integrating different types of data from different sources, including biospecimen repositories, clinical trials, basic research, preclinical models, real-world patient data, and population studies, CCDI aims to increase data use and sharing among the pediatric cancer research community to improve understanding of childhood cancers and advance research to develop new and better treatments. The CCDI complements

other NCI initiatives working to advance the study of childhood cancer, including efforts aligned with the implementation of the Childhood Cancer STAR Act (see STAR Act below).
<https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative>
[NCI]

Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act: Examples of Implementation Efforts

In 2019, efforts to support pediatric survivorship research and biospecimen collection and enhancement aligned with provisions of the 2018 Childhood Cancer STAR Act. Ongoing research in childhood cancer survivorship includes using results from the Childhood Cancer Survivor Study (CCSS) to help design treatment protocols and interventions to increase survival while minimizing harmful late effects and to develop and expand programs for early detection and prevention of late effects in children and adolescent cancer survivors. A 2019 funding opportunity announcement expanded support with three new research projects, and more new projects are anticipated in 2020. Supported projects include the following:

- Evaluating the Symptom Monitoring & Systematic Assessment and Reporting System in Young Survivors (SyMon-SAYS) to determine the system's effects on patient symptom burden, identify parent-perceived barriers in patient symptom management, increase parent/patient self-efficacy, and increase patient quality of life.
- Evaluating a physical activity intervention (wearable activity monitor, individualized goal-setting, electronic account for virtual peer support) to address childhood cancer survivors' tendency toward sedentary behavior.
- Determining whether oral memantine for children receiving cranial radiotherapy for brain tumors is associated with reduction in decline of cognitive function. The drug has been used with adult dementia patients and has been shown to reduce changes in thinking and memory that occur after whole brain radiotherapy in adults with brain metastasis.

An additional 2019 award will support specimen collection and other activities to enhance the Children's Oncology Group Biospecimen Core Resource. Further, through the Childhood Cancer Data Initiative (CCDI), the NCI plans to enhance data collection and integration with other existing NCI-funded repositories and ensure data accessibility for childhood cancers, to complement STAR Act research activities. Although these two efforts began independently, they are moving forward together. The CCDI hopes to develop a federated data framework that connects multiple existing and new data repositories and offers tools for sharing and analyzing data—including data generated through STAR Act efforts.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-033.html>

https://projectreporter.nih.gov/project_info_description.cfm?aid=9893629&icde=46897427

https://projectreporter.nih.gov/project_info_description.cfm?aid=9895223&icde=46897607

https://projectreporter.nih.gov/project_info_description.cfm?aid=9892593&icde=46897678

[NCI]

Pediatric Musculoskeletal and Rheumatology Innovation Core Center

This initiative at a children's hospital medical center seeks to develop evidence-based medical care models tailored to the unique needs of children with pediatric rheumatic and noninflammatory musculoskeletal diseases (PMSKD). The initiative's cross-disciplinary team will develop integrated models of patient care, incorporating advanced data-science techniques, diagnostic testing and imaging services, and patient-reported outcome assessments, to improve shared medical decision-making. The initiative aims to improve disease control and health-related quality of life of children with PMSKD, reduce disease damage, and reduce long-term disability and societal cost.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9851085&icde=47892071

[NIAMS]

Great Beginnings for Healthy Native Smiles

Early childhood caries (ECC) is the most common chronic disease among children, and American Indian/Alaska Native (AI/AN) children are four times more likely to have untreated dental decay than White children are. This randomized controlled study will evaluate the impact on ECC of combining several individually effective best practices together into one intervention of “bundled” best practices for pediatric oral health. The intervention bundle will be delivered by community health workers, and its effects will be compared with the effects of a standard prenatal/postnatal healthy lifestyle intervention. https://projectreporter.nih.gov/project_info_history.cfm?aid=9697534&icde=47691694
[NIDCR]

Improving Oral Health and Reducing Disparities in Adolescents

An initiative to stimulate research to improve the oral health of adolescents in the United States aims to reduce disparate and inequitable oral health outcomes observed in certain populations. Research proposed in response is expected to help to elucidate key common risk and protective factors that contribute to oral and overall disease development in adolescents. Proposed research is also expected to evaluate strategies for oral health promotion and disease prevention in youth. <https://grants.nih.gov/grants/guide/pa-files/par-20-058.html>
[NIDCR]

Reducing Oral Health Disparities in Children: Assessing the Multilevel Impact of a Standardized Preventive Dental Care System

With a goal of reducing oral health disparities in children, this study will leverage sophisticated dental informatics to assess the impact of an evidence-based approach to delivery of pediatric dental care. The study will mine big data to examine the incidence of childhood caries (tooth decay) over time in the context of real-world clinical care. Study findings will elucidate evidence-based strategies to reduce pediatric oral health disparities so as to establish the foundation of a sustainable, scalable road map to inform dental policy. https://projectreporter.nih.gov/project_info_description.cfm?aid=9883043&icde=49508651
[NIMHD]

Adalimumab in Juvenile Idiopathic Arthritis–Associated Uveitis Stopping Trial

Adalimumab, an immunosuppressive drug, has shown efficacy in treating juvenile idiopathic arthritis (JIA)–associated uveitis, a sight-threatening complication that is caused by eye inflammation and associated with childhood arthritic disease. However, the drug is associated with potentially serious adverse events and imposes a substantial financial burden. Many patients with JIA-associated uveitis who have reached disease control on adalimumab are interested in stopping the drug, but there are only minimal data on whether uveitis recurs after the drug is discontinued. This multicenter, double-masked, randomized clinical trial of patients with JIA-associated uveitis will compare rate of recurrence and time to recurrence of eye inflammation in patients randomized to discontinue adalimumab, compared with patients who continue treatment. https://projectreporter.nih.gov/project_info_details.cfm?aid=9633759&icde=47882207
[NEI]

Newborn Screening Translational Research Network (NBSTRN) Core Common Data Elements

The NIH Common Data Elements (CDE) Repository provides access to structured human data definitions—which can be processed by computers—of types of information (data elements) that NIH institutes, centers, and offices (ICOs) and other organizations recommend or require to be used in research and for other purposes. The use of such “common” definitions adds value to research data by, for example, facilitating analysis of data from multiple studies. In 2019, 151 core common data elements, developed by the NBSTRN, were added to this repository. The new elements include genetic information, whether a child’s development was typical or atypical for the child’s age, and whether there was maternal treatment during pregnancy that was intended to treat the fetus.

<https://www.nbstrn.org/>
[NLM, NICHD]

Primary Immunodeficiency Disorders/Inborn Errors of Immunity

The aim of this initiative is to stimulate research to characterize genetic mutations that result in dysfunction of the immune system or primary immunodeficiency diseases (PIDs). The goal is to understand the immunological mechanisms of the disorders, which interfere with the normal functioning of the body's defenses against infection, in infancy, childhood, or adulthood.

<https://www.niaid.nih.gov/clinical-trials/primary-immune-deficiency-clinic>

<https://grants.nih.gov/grants/guide/pa-files/par-19-078.html>

<https://grants.nih.gov/grants/guide/pa-files/par-19-079.html>

[NIAID]

Blood and Immune Deficiency Cellular Therapy Program (BID-CTP)

This new collaboration brings immunologists, transplant specialists, geneticists, and hematologists from across NIH together to deliver state-of-the-art and experimental care for conditions associated with blood disorders or immune deficiencies, many of which are diagnosed in childhood. A unified approach is applied to assessing, treating, and monitoring patients and the centralized tracking of treatment outcomes.

<https://www.nih.gov/news-events/news-releases/new-nih-program-provides-comprehensive-treatment-inherited-blood-immune-diseases>

[NIAID, NCI, NHLBI, NHGRI]

Pediatric Autoinflammatory Conditions

This translational autoinflammatory research program is focused on clinical and translational studies in children with early-onset autoinflammatory diseases. Efforts are aimed at integrating insights gained from disease pathogenesis in order to find novel treatments.

<https://clinicaltrials.gov/ct2/show/NCT02974595>

[NIAID]

Interventions to Sustain ADHD Treatment Effects Across Settings and Developmental Transitions

The aim of this program is to encourage pilot studies to assess the preliminary effectiveness of augmented or modified interventions for attention deficit hyperactivity disorder (ADHD), a neurodevelopmental disorder with deleterious consequences that affects at least 11 percent of American children. Specifically, the research is on interventions that are designed to promote enhanced and sustained improvement in ADHD symptoms and reduction of functional impairments across settings and transitions in children, adolescents, and young adults.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-20-100.html>

[NIMH]

Mindfulness-Based ADHD Treatment for Children

Gold-standard pharmacological interventions for attention deficit hyperactivity disorder (ADHD) can be efficacious but may have adverse side effects, and current nonpharmacologic interventions are generally less efficacious. This project aims to determine the feasibility of a novel, neuroscience-informed, mindfulness-based ADHD intervention for children that may be as efficacious as pharmacotherapy but without harmful side effects. This research is intended to be the first in a series of mechanism-focused efficacy, effectiveness, and dissemination studies of a treatment that may ultimately alter standard treatment of children with ADHD.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9746277&icde=47966372

[NCCIH]

A Dried Blood Spot Companion Diagnostic to Measure Neuroendocrine Changes in ADHD

Stimulant medications can treat attention deficit hyperactivity disorder (ADHD) symptoms, but some patients' ADHD does not respond to such treatment, or the medication may cause adverse side effects, so finding a helpful ADHD treatment can involve trial and error. Currently there are no widely used laboratory tests that can predict treatment success and symptom remission. To complement existing ADHD symptom evaluation questionnaires, which can only indirectly measure treatment outcome, this project will develop a clinical test for selected neuroendocrine molecules. Using blood samples from children with ADHD, researchers will evaluate and confirm dysregulation in the interaction of the nervous and endocrine systems as a possible marker of ADHD. The study will provide proof-of-concept for a fully validated test for baseline (no treatment) levels of the selected molecules. Such proof will pave the way for a Phase II, comprehensive clinical study of neuroendocrine changes in response to stimulant medication, nonstimulant intervention, and nutritional supplements used to treat ADHD.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9846068&icde=47966673

[NCCIH]

Early Screening for Autism Spectrum Disorder

In 2019, NIH awarded support for seven research projects aimed at developing and validating screening tools for autism spectrum disorder (ASD) that could be used in the first year of an infant's life. Although the age of ASD onset is variable, there is evidence that subtle signs of the disorder, including brain volume changes and behavioral changes in social, visual, and vocal engagement, emerge in the first year of life. To date, however, reliably detecting ASD in young children is difficult, and the average age of diagnosis for ASD remains at approximately 4 years of age, which may delay interventions that can be effective at earlier ages. The projects were proposed in response to funding opportunity announcements (FOAs) seeking research to translate evidence of early signs of ASD into practical screening tools that could be implemented in the general population, within community settings. One project aims to validate the effectiveness of a new automated online screening tool to assess communication delay and autism at well-child visits between the ages of 9 and 24 months. The use of innovative technology, user-friendly tools and web applications, and implementation science methodology enhances the potential for sustainability and scalability of screening for ASD.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-19-120.html>

https://projectreporter.nih.gov/project_info_description.cfm?aid=9863072&icde=47773161

[NIMH, NICHD, NINDS, NIDCD, NIEHS]

Musical Rhythm Sensitivity to Support Social Engagement in Autism Spectrum Disorder

The primary goals of the current project are to examine musical rhythm entrainment as a mechanism of healthy social development, as well as disruptions thereof in children with autism spectrum disorder (ASD). Building on prior findings demonstrating that infant eye-looking responds interactively ("entrains") to the rhythmic social cueing of a caregiver during musical interactions, this collaborative project uses singing directed at an infant to examine predictability as a driver of social rhythmic entrainment. The researchers proposed that the use of music and rhythm enhance the predictability of delivery of social information provided during naturalistic, developmental, behavioral interventions for ASD. This collaborative research has the potential to inform understanding of basic mechanistic processes of social entrainment in ASD and may support the development of evidence-based music interventions for social communication in ASD.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9883577&icde=47966517&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

[NCCIH, NIMH]

Clinical Trial Readiness for Rare Neurological and Neuromuscular Diseases

This program supports research to fill gaps in the design of upcoming clinical trials in rare neurological or neuromuscular diseases, including pediatric disorders. Through the support of trial readiness studies, such as efforts to validate clinical outcome measures or biomarkers or characterize patient cohorts, the NINDS

expects to accelerate the initiation of clinical trials for rare diseases and increase the likelihood of success in those trials. In 2019, new projects supported through this initiative included studies on juvenile neuronal ceroid lipofuscinosis and Aicardi-Goutières syndrome, both rare neurological diseases with onset in infancy through adolescence.

<https://grants.nih.gov/grants/guide/pa-files/PA-18-534.html>

https://projectreporter.nih.gov/project_info_description.cfm?aid=9649560&icde=48002801

https://projectreporter.nih.gov/project_info_description.cfm?aid=9648621&icde=48002801
[NINDS]

Understanding Genetic Contributions to Cerebral Palsy

Cerebral palsy (CP) is a neurodevelopmental disorder that alters brain development and impairs motor function. Known causes and risk factors include preterm birth and early insults to the brain, but little is known about the role of genetic factors. A new project will look for genetic variants and gene pathways linked to CP by analyzing the genomes of 500 parent–child trios.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9661124&icde=47968688
[NINDS]

Endoscopic Versus Shunt Treatment of Hydrocephalus in Infants

In hydrocephalus, excess cerebrospinal fluid (CSF) accumulates in the brain’s ventricles (a linked network of spaces within the brain), leading to harmful pressure on surrounding brain tissue. The most common treatment is surgical placement of a shunt to remove excess brain fluid, but shunts often fail, requiring surgical revision and leading to increased risk for infection. A surgical procedure called endoscopic third ventriculostomy with choroid plexus cauterization (ETV+CPC) may present an alternative to shunts, but this treatment’s impact on cognitive outcomes in infants is not known. A new clinical trial will compare cognitive outcomes and measures of brain structure in infants with hydrocephalus treated with either shunts or ETV+CPC.

https://projectreporter.nih.gov/project_info_description.cfm?icde=0&aid=9739214

<https://clinicaltrials.gov/ct2/show/NCT04177914>
[NINDS]

Research on Prenatal and Pediatric Hydrocephalus

New funding opportunity announcements sought to stimulate research on the molecular, cellular, and developmental mechanisms involved in prenatal and/or pediatric hydrocephalus and to develop new and improved research tools to advance such research as well as to develop new therapies. New projects supported through these initiatives include a study to understand how hydrocephalus develops after a type of bleeding (germinal matrix hemorrhage) into the fluid-filled spaces (ventricles) of the brain—an important risk factor for hydrocephalus in preterm infants.

<https://grants.nih.gov/grants/guide/pa-files/PA-18-622.html>

<https://grants.nih.gov/grants/guide/pa-files/PA-18-623.html>

https://projectreporter.nih.gov/project_info_description.cfm?aid=9714090&icde=47885947
[NINDS]

Using Social Media to Identify and Help Teens with Eating Disorders

Eating disorders (EDs) often emerge in adolescence, and most teens with EDs do not receive treatment. A pilot project is using social media to reach teens who are already networking about ED behaviors. The researchers are testing a mobile app specifically developed for teens to help reduce ED symptoms and improve their quality of life. To inform a future version of the app, the pilot aims to obtain teen perspectives on acceptable approaches to include parents in this intervention. Effect size and attrition estimates from this project will aid in planning a larger randomized clinical trial of an expanded app-based intervention (e.g., adding automated coaching, augmenting with parental involvement) to test

the app on a larger scale and improve its potential to reduce the extraordinary burden of EDs among teens.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9719997&icde=47559430
[NIMH]

Neural Mechanisms of Meditation Training in Healthy and Depressed Adolescents

Meditation training shows promise for improving adolescents' emotional health and facilitating treatment of their depression. There is a fundamental gap, however, in understanding the neural reorganization that results from meditation training, and this gap needs to be filled so that more effective interventions can be designed. This study of adolescents undergoing meditation training uses magnetic resonance imaging (MRI) to map changes in integrated connections in the putamen, a region of the brain associated with meditation practice and lessened shrinkage in Zen meditators. The putamen is also associated with a range of positive feelings, including increasing intensity of happiness. In two cohorts, one of adolescents with depression and one of adolescents without depression, researchers will use MRI to assess structural connectivity within the putamen as the adolescents undergo a 12-week meditation training. Effects in each cohort will be compared with images from cohorts of adolescents who are wait-listed for the training.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9648872&icde=47967056
[NCCIH]

Benefits of Preventing Mental Health Disorders

To enhance use of existing data sets to improve mental health outcomes, a funding opportunity announcement encouraged research to integrate/harmonize existing data sets from trials of preventive intervention trials implemented early in life. The goals are to examine risk and protective factors relevant to later mental health outcomes in childhood, adolescence, and young adulthood and determine whether preventive interventions delivered earlier in life have long-term and/or crossover effects (e.g., unanticipated beneficial effects) on important mental health outcomes, including serious mental illness (e.g., depression, anxiety, psychosis) and suicide ideation and behaviors.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-20-110.html>
[NIMH, NCCIH, ORWH]

Trauma-Informed Mental Health in Education

To provide middle school students and their teachers with an effective approach to relieving stress and anxiety, which can interfere with children's well-being and academic success, this project will adapt an existing mindfulness curriculum for this age group. Mindfulness-based interventions are increasingly used in schools, but most such interventions have not undergone rigorous empirical study and lack a trauma-sensitive approach to delivery. In addition, most such interventions target elementary and high school students, even though the average onset of pediatric mental health diagnoses is during middle school. Researchers will adapt the TimeIn (Trauma-Informed Mental Health in Education) curriculum for the middle school setting and develop related professional learning communities for middle school teachers. Expanding access to empirically based mental health services in rural communities, where such services are now lacking, is an important goal for the project. The project includes evaluation of the efficacy, feasibility, and user satisfaction of the adapted TimeIn curriculum and teacher resources in a randomized controlled trial.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9776178&icde=47967123
[NCCIH, NIMH, NICHD]

Improving Clinical Guideline Adherence in Pediatric Traumatic Brain Injury

Traumatic brain injury (TBI) is a leading cause of death in children worldwide. Evidence-based guidelines are available for the clinical care of pediatric TBI, but adherence to these guidelines is low, with implications for patient outcomes. Through a new multisite study called Pediatric Guideline

Adherence and Outcomes, researchers in the United States and Argentina aim to understand and address barriers to guideline adherence for pediatric TBI and to develop real-world best practices that may improve guideline use and outcomes.

https://projectreporter.nih.gov/project_info_description.cfm?icde=0&aid=9678497

[NINDS]

Reducing Racial and Ethnic School Violence Disparities

One prevalent form of discrimination in schools is overly harsh discipline for racial and ethnic minority students, and children exposed to such adverse childhood experiences (ACEs) are at high risk for school violence. In partnership with six school districts, researchers will conduct a randomized controlled trial of a culturally responsive support system, Link for Equity, for ACE-exposed children. The project will adapt, implement, and evaluate the effect of the program school violence disparities; evaluate the program's effect in reducing teacher-to-student racial and ethnic discrimination and determine whether the program effect on school violence is mediated through discrimination; and explore how the program's effects on school violence are mediated through stress and connectedness mechanisms. The trial will enroll about 1,200 students from backgrounds that would have exposed them to four or more ACEs or who have screened positive for post-traumatic stress.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9703209&icde=47867162

[NIMHD]

Screening and Brief Intervention Tools for Adolescent Substance Use Disorders

Spring 2019 saw the launch of two brief online validated substance use screening tools for adolescents seen in clinical settings. The tools, the Brief Screener for Tobacco, Alcohol, and other Drugs (BSTAD) and the Screening to Brief Intervention (S2BI), had each been validated in adolescent samples. Validation demonstrated the tools' accuracy in identifying adolescents with and without substance use disorders who were seen in pediatric primary care settings.

<https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/screening-tools-for-adolescent-substance-use>

[NIDA]

Mind and Body Approaches to Pain Reduction in Youth with Migraine

Migraine affects more than 6 million children and adolescents in the United States and leads to significant pain and disability. Cognitive behavioral therapy (CBT), which reduces the number of headache days in pediatric patients, combines mind-body approaches such as deep breathing and progressive muscle relaxation with "cognitive reappraisal training" (learning to reduce the impact of a stressful situation by rethinking how one perceives it). To find out how different components of CBT techniques affect the nervous system, a clinical trial will compare the effects of relaxation training against cognitive reappraisal training in young people (ages 10 to 17) with migraine. Before and after the interventions, objective data on the two techniques' effects will be collected with functional magnetic resonance imaging and quantitative sensory testing (a method of assessing possible impacts on small and large nerve endings). This study will lead to greater understanding of the brain and the body's sensing mechanisms involved with mind-body approaches to pain reduction in youth with migraine.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9637619&icde=47966781

[NCCIH]

Intensive Infant Rehabilitation after Perinatal Arterial Stroke

Perinatal arterial stroke (PAS) occurs in an estimated 1 in 1,150 infants. There is no evidence-based standard of care for PAS rehabilitation, and most affected infants develop lasting motor (movement) and other disabilities. A new randomized controlled clinical trial will determine whether intense rehabilitation incorporating constraint-induced movement therapy (CIMT) improves upper extremity motor function in babies who have had a perinatal stroke. CIMT combines restraint of a limb unaffected by stroke with

intensive use of the affected limb. The trial will also assess the intervention's effects on gross motor development and cognition. This I-ACQUIRE (Infant Abatacept Comparison of sub[QU]cutaneous versus intravenous in Inadequate Responders to methotrexatE) trial is the first pediatric stroke study conducted through StrokeNet, a clinical trials network dedicated to advancing stroke prevention, treatment, and recovery.

https://projectreporter.nih.gov/project_info_description.cfm?icde=0&aid=9662340

<https://clinicaltrials.gov/ct2/show/nct03910075>

[NINDS]

Scalable Evidence-Based Prevention Interventions in Primary Care Settings

In November 2019, a new funding opportunity announcement (FOA) encouraged research to test the effectiveness of developmentally focused, theory-based prevention interventions that may affect children's mental health outcomes, including suicide behaviors and serious mental illness. Research is expected to test prevention approaches that are both scalable (capable of being used widely) and sustainable for implementation in pediatric-serving primary care settings, with an emphasis on populations experiencing mental health disparities. This FOA also seeks to support clinical trials to establish the effectiveness of scalable prevention interventions that are implemented using available resources within the pediatric care settings.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-20-505.html>

[NIMH]

Clinical Decision Support Use and Clinical Outcomes

Clinical decision support (CDS) is a process for enhancing health-related decisions and actions with pertinent, organized clinical knowledge and patient information to facilitate adherence to evidence-based practices. This program's long-term objective is to empower organizations to incorporate scientific knowledge efficiently into high-value clinical care through incremental, data-driven improvements of CDS. Such improvements are informed by understanding of the relationships between use of CDS, process measures, and patient outcomes. In the near term, the project will establish the technical feasibility of associating CDS use patterns with process and outcome metrics using electronic health record log data through a proof-of-concept demonstration using inpatient data from children's hospitals on pediatric migraine. The resulting architecture will generalize across clinical use cases.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9907877&icde=46648535

[NLM]

Bridging the Epilepsy Treatment Gap in Africa

An estimated 67 percent to 90 percent of children with epilepsy in low- and middle-income countries (LMICs) do not receive treatment. A new randomized clinical trial in three Nigerian cities will assess the efficacy, implementation, and cost-effectiveness of a novel intervention that shifts childhood epilepsy care to epilepsy-trained community health workers, an approach to addressing the treatment gap in areas with few or no highly trained clinicians. This research will inform efforts to expand epilepsy treatment for children in LMICs and other locations where access to medical care is limited.

https://projectreporter.nih.gov/project_info_description.cfm?icde=0&aid=9819826

[NINDS, FIC]

Selected Expanded Pediatric Research Efforts

In addition to launching new research programs, NIH institutes, centers, and offices (ICOs) build on successful programs to expand research efforts related to pediatrics. Selected highlights of expanded research efforts are given below. As with the new programs, many of these expanded initiatives are concerned with developing and delivering evidence-based interventions.

Human Health Exposure Analysis Resource

This resource (formerly the Children’s Health Exposure Analysis Resource) provides the NIH-funded research community with access to laboratory and statistical analyses that will allow for the addition or expansion of environmental exposures as part of ongoing epidemiological and clinical research. Such additions will create a public resource of population exposures, including those of children, across the country. Exposures measured encompass the breadth of the exposome, which is the totality of biological, psychosocial, chemical, and physical factors to which humans are exposed. To date, the program has supplemented the work of 32 projects through analysis of more than 50,000 samples.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-ES-15-011.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-ES-15-009.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-ES-15-010.html>

[NIEHS, NCI]

Nonalcoholic Steatohepatitis (NASH) Clinical Research Network (CRN)

The NASH CRN is composed of multiple clinical sites across the United States that have conducted several clinical trials to test potential treatments for forms of nonalcoholic fatty liver disease. These forms of the disease include NASH in children and adults. The trials are made possible through public–private partnerships. The overriding objective of this research program is to pursue clinical research on adult and pediatric NASH, with a secondary objective to encourage reverse translational research to understand disease origins. Such understanding will provide the basis for understanding the natural history of disease and developing means for its diagnosis, treatment, and clinical management. In fiscal year (FY) 2019, the initiative to continue this network included a new study on the use of losartan in the treatment of children with nonalcoholic fatty liver disease.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-18-505.html>

<https://jhuccs1.us/nash/>

[NIDDK]

Childhood Liver Disease Research Network

The overarching mission of this pediatric research network is to improve understanding of and treatment options for cholestatic and rare pediatric liver diseases, such as biliary atresia, Alagille syndrome, alpha-1 antitrypsin deficiency, progressive familial intrahepatic cholestasis syndromes, bile acid synthesis defects, mitochondrial hepatopathies, idiopathic neonatal hepatitis, and cystic fibrosis liver disease. The network has conducted several clinical studies to date. The fiscal year (FY) 2019 initiative to continue support for this network also expanded its scope to include another disorder, primary sclerosing cholangitis.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-18-501.html>

<https://childrennetwork.org/>

[NIDDK]

Adolescent Medicine Trials Network for HIV/AIDS Interventions

This project is the only national multicenter research network devoted to the health and well-being of HIV-infected and at-risk adolescents and young adults. The network’s primary mission is to conduct both independent and collaborative research that explores promising behavioral, microbicidal, prophylactic (preventive), therapeutic, and vaccine modalities in HIV-infected youth and at-risk adolescents ages 12 to 24, and its researchers have extensive experience in recruiting and retaining understudied youth populations in the United States. Research from this program informed U.S. Food and Drug Administration approval of tenofovir (Truvada), a drug combination used in pre-exposure prophylaxis (PrEP) for HIV, for use in at-risk adolescents.

<https://www.NICHD.nih.gov/research/supported/atn>

<https://www.NICHD.nih.gov/newsroom/news/051618-PrEP>

[NICHD, NIDA, NIMH, NIMHD, NIAID, OD]

Pediatric HIV/AIDS Cohort Study

This long-term study addresses the long-term safety of fetal and infant exposure to antiretroviral therapy and the effects on adolescents of perinatally acquired HIV infection. The study's overall goals are to understand how HIV and its treatment affect growth and development, sexual maturation, organ function, and socialization of perinatally HIV-infected preadolescents, adolescents, and young adults; acquire more definitive information on the long-term safety of antiretroviral therapy when used during pregnancy and in newborns; ensure that a mechanism is in place to estimate the upper bounds of risk for children who were exposed to this therapy during maternal treatment to prevent perinatal HIV transmission; and continue the follow-up study of these populations.

<https://www.NICHD.nih.gov/research/supported/Pages/phacs.aspx>

[NICHD, NIAAA, NIAID, NIDCD, NIDCR, NIDA, NIMH, NINDS]

International Maternal Pediatric Adolescent AIDS Clinical Trials Network

This international project supports studies on prevention and treatment of HIV and its complications and co-infections, such as tuberculosis (TB), a major cause of death for HIV-infected infants, children, adolescents, and pregnant/postpartum women worldwide. The project's clinical trials are assessing treatments to prevent people at high risk of multidrug-resistant TB from contracting it and include studies that will evaluate the safety and efficacy of delamanid, a new TB drug, in children with and without HIV infection.

<https://impaactnetwork.org/>

[NIAID, NICHD]

Cooperative Centers on Human Immunology

This program supports studies to understand the human immune responses to infection, vaccination and adjuvants (substances that enhance the body's immune response), and mechanisms leading to immune-mediated diseases. Several new awards include studies involving children, with projects to study vaccine-induced immunity to dengue fever, dengue hemorrhagic fever and influenza. Other new projects include a study of antibody response in human recurrent tonsillitis, a common pediatric disease, and an investigation of the lungs' immune responses to viral infection in samples of airway-derived cells from asthmatic and healthy children.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-ai-17-040.html>

[NIAID]

Clinical Trials Program for Children with Cancer

This program supports nationwide clinical trials through multiple multisite infrastructures, including the Children's Oncology Group (COG), the Pediatric Early Phase Clinical Trials Network (previously the COG Phase I/Pilot Consortium), and the Pediatric Brain Tumor Consortium (PBTC). Additional clinical trials are conducted by intramural researchers at the National Institutes of Health (NIH) Clinical Center and are also supported internationally. During fiscal year (FY) 2019, clinical trials that were initiated or expanded in scope to evaluate novel treatments and new approaches to various pediatric cancers included the following:

- *NCI Pediatric MATCH (Molecular Analysis for Therapy Choice)*: This trial, enrolling children and adolescents ages 1 to 21 with advanced solid tumors that have progressed or recurred on standard therapy, uses genetic sequencing to identify eligible participants whose tumors (including central nervous system tumors and non-Hodgkin lymphomas) have a genetic abnormality for which an approved or investigational targeted therapy exists. The trial encompasses 10 different treatment arms, with three additional arms expected to be activated and one closed because it has met its target accrual. Through September 2019, 721 children and adolescents have been enrolled into the screening protocol.

<https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/pediatric-match>

<https://clinicaltrials.gov/ct2/show/NCT03155620>

- Additional clinical trials activated by COG and PBTC in FY 2019 include a trial of the anticancer agents dinutuximab and sargramostim and combination chemotherapy in treating patients with newly diagnosed neuroblastoma (a solid cancer of nerve tissue) who underwent a stem cell transplant; a PBTC Phase I/II and surgical study of the agent CX-4945 for patients with recurrent sonic hedgehog (SHH) medulloblastoma (a subgroup of tumors of the central nervous system); a Phase I trial in children and young adults of multitargeted immunotherapy, with chimeric antigen receptor (CAR) T cells, to prevent relapse and resistance to therapy targets for hematologic (blood) cancers; a Phase II trial in adolescent girls to evaluate one dose versus two doses of the vaccine for HPV (human papillomavirus, which can cause cervical cancer), with a concurrent epidemiologic survey for HPV status among unvaccinated young women, who are offered HPV vaccination at enrollment and at subsequent visits (supported by the NCI and the Bill & Melinda Gates Foundation); and a pilot feasibility study of the Pediatric Cancer Resource Equity (PediCARE) intervention to determine whether researchers can give this support program to pediatric cancer families. The program offers an online grocery delivery service and transportation to and from the hospital to these families. The pilot seeks to understand whether most pediatric cancer families are interested in participating in a support program study and whether they use the support program during the study. The findings will provide information on the role of the PediCARE support program in reducing financial stress for families of children undergoing cancer therapy.

<https://clinicaltrials.gov/ct2/show/NCT03786783>

<https://clinicaltrials.gov/ct2/show/NCT03904862>

<https://ccr.cancer.gov/news/article/phase-I-clinical-trial-will-test-multi-targeted-immunotherapy-in-common-childhood-cancer>

<https://clinicaltrials.gov/ct2/show/NCT03448393>

<https://dceg.cancer.gov/news-events/news/2019/controlling-cervical-cancer>

<https://clinicaltrials.gov/ct2/show/NCT03638453>

[NCI]

Cancer Moonshot

The broad mission of this initiative is to accelerate cancer research to make more therapies available to more patients while also improving prevention of cancer and its detection at an early stage. The Moonshot's blue ribbon panel identified two high-priority pediatric cancer research opportunities as poised for acceleration, prompting the establishment of two major pediatric projects, both expanded in 2019. One project focuses on fusion oncoproteins, which are distinctive proteins that are unique to childhood cancers and drive cancer growth. The Fusion Oncoproteins in Childhood Cancers Consortium is a collaborative network of multidisciplinary investigators who focus on uncovering the mechanisms that govern how the proteins drive childhood cancers. The Pediatric Immunotherapy Discovery and Development Network focuses on pediatric immunotherapy translational science. This is a priority because many effective immunotherapies for cancer in adults have not been applicable to childhood cancers. Additional childhood cancer Moonshot activities include developing a pediatric tumor cell atlas, improving management of pediatric patients who develop an adverse response (graft-versus-host disease) to stem cell transplantation therapy, and developing effective, feasible, and scalable interventions for adverse physical and psychosocial effects of pediatric and/or adolescent/young adult cancers in these early-life malignancies. The Moonshot Pediatric, Adolescent, and Adult Rare Tumors Network (MyPART) is focused on research on a range of pediatric, adolescent, and young adult solid rare tumors, specifically teaming with advocacy groups to raise awareness about rare tumors among researchers and increase access to biospecimens for research. In fiscal year (FY) 2019, a natural history pediatric trial began enrolling children with rare solid tumors. The goal of the study is to better understand how these tumors develop. The findings may also lead to improved screening, preventive guidelines, and treatments. https://projectreporter.nih.gov/project_info_details.cfm?aid=9834606

https://projectreporter.nih.gov/project_info_description.cfm?aid=9833682
https://projectreporter.nih.gov/project_info_description.cfm?aid=9834547
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https://projectreporter.nih.gov/project_info_description.cfm?aid=9895223
https://projectreporter.nih.gov/project_info_description.cfm?aid=9892593
https://projectreporter.nih.gov/project_info_description.cfm?aid=9893629
[NCI]

FaceBase: Comprehensive Craniofacial Data and Resources

The FaceBase consortium aims to advance craniofacial and developmental research by building a knowledge base of integrated, comprehensive (-omic) molecular and phenotypic (whole-organism) human and model system data on typical and atypical craniofacial (skull and face) development. Additional consortium activities include developing tools for using these data and disseminating the sets of data and tools to the research community. In fall 2019, the consortium restructured around a data management and integration “hub,” which will curate and integrate the data on craniofacial development and the developmental disorders that lead to birth defects and facial malformations and will also open the knowledge base to the entire research community to help enhance the data offerings.

<https://www.facebase.org>

[NIDCR]

SELECTED MAJOR ONGOING NIH PROGRAMS IN PEDIATRIC RESEARCH

NIH supports a large number of ongoing programs in pediatric research. Many—but not all—pediatric research programs focus exclusively on child health. For example, the NICHD’s Collaborative Pediatric Critical Care Research Network links pediatric intensive care units at hospitals across the country to conduct clinical studies to improve research practice in pediatric critical care. The center/network programs supporting pediatric research at NIH include some that are targeted to a specific disease or condition, such as the Autism Centers of Excellence. Others, such as the pediatric component of the Clinical and Translational Science Awards Program, are not specific to any one condition. Other pediatric research programs are funded using non-center research mechanisms, such as R01 research grants. This report highlights selected key ongoing NIH programs in pediatric research, funded through a variety of research grant and contract mechanisms.

Pregnancy and Newborn Health

Department of Health and Human Services (HHS) Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

Assessing differences in biological processes or the effects of different exposures during pregnancy and lactation is crucial, yet research to test the safety and effectiveness of medications typically does not include pregnant and lactating women. Mandated by the 21st Century Cures Act (P.L. 114-255), the Task Force reported in September 2018 to the HHS Secretary and Congress on the state of the science and research gaps that need to be filled to inform the use of medications (pharmaceuticals and dietary supplements) by pregnant and lactating women. In addition to reporting extensive research gaps involving safety, efficacy, and dosing of medications that are widely used for clinical management of both pregnancy-related and other disorders in pregnant and lactating women, the Task Force found a lack of safety, efficacy, and dosing data specifically for the unique physiology and other characteristics of these populations. The Task Force recommendations included more, better, and more timely research.

<https://www.nichd.nih.gov/about/advisory/PRGLAC>

[NICHD, NIMH, NIDDK, NIAID, NCATS, NHLBI, ORWH]

PregSource[®]

This citizen science research project aims to improve understanding of pregnancy by gathering information directly from pregnant women via confidential online questionnaires. Getting information directly from women about what they feel, think, do, and experience during pregnancy and after giving birth can provide more insights into pregnancy and how to improve care.

<https://pregsource.nih.gov/>

[NICHD, NCCIH, NHLBI, NIEHS, NINR, NIMHD, OBSSR, ORWH]

Human Placenta Project

Designed to provide information about placental health noninvasively and in real time, the Human Placenta Project is yielding new insights to help researchers further their efforts to improve maternal health and pregnancy outcomes. For example, several research studies have now assessed technologies that image the placenta in real time during pregnancy, obtaining data on placental blood flow, oxygen levels, and/or metabolism. The Placental Atlas Tool, launched in 2018, is a curated data set that serves as a resource for placental research. Current funding opportunity announcements emphasize novel approaches to safe, noninvasive, real-time assessment of human placenta development and function across pregnancy.

<https://www.nichd.nih.gov/research/supported/HPP/default>

<https://pat.nichd.nih.gov/>

<https://grants.nih.gov/grants/guide/pa-files/PAR-18-884.html>

[NICHD]

Maternal-Fetal Medicine Units (MFMU) Network

The NICHD's MFMU Network is designed to conduct rigorous clinical trials in maternal-fetal medicine and obstetrics, particularly with respect to the continuing problem of preterm birth. The aims of the network are to reduce maternal, fetal, and infant morbidity related to preterm birth, fetal growth abnormalities, and maternal complications and to provide the rationale for evidence-based, cost-effective obstetric practice. Current projects include randomized controlled trials of preventing obstetrical hemorrhage after cesarean delivery, preventing effects from cytomegalovirus infection, and treating sleep apnea in pregnancy. Completed projects include randomized controlled trials on fetal heart rate monitoring, preventing preterm birth, and preventing preeclampsia.

<https://www.nichd.nih.gov/research/supported/mfmu>

[NICHD]

Neonatal Research Network (NRN)

The NRN is a collaborative network of neonatal intensive care units across the United States that is composed of 18 clinical centers and a data coordinating center. Focused on newborns, particularly extremely low-birth-weight infants, the network conducts clinical trials and clinical studies in such areas as sepsis and other infections, bronchopulmonary dysplasia and other lung conditions, and necrotizing enterocolitis, a condition in which the intestines lack oxygen or blood flow.

<https://www.nichd.nih.gov/research/supported/nrn>

[NICHD]

NICHD Fetal Growth Studies

Normal fetal growth is a critical component for a healthy pregnancy and for ensuring the health and well-being of infants throughout childhood and adolescence. Pivotal to understanding the dynamics of human fetal growth and defining normal and abnormal fetal growth is the development of standards for fetal anthropometric (body measurement) parameters, measured longitudinally throughout gestation. The

NICHHD Fetal Growth Studies followed a diverse cohort of women, including an obese cohort and a twin cohort, where study participants underwent five ultrasounds during pregnancy at different gestational ages, along with nutritional assessments, body measurements, and analysis of blood samples. This intramural research found that, because of racial and ethnic differences in normal growth patterns, the current standards used in obstetric care may lead to misclassification of up to 15 percent of fetuses of minority mothers as being too small. The inaccurate standards may lead to unnecessary tests and stress for these minority women, when their pregnancies are actually on track. Another project found that maternal stress levels, measured via survey, in low-risk pregnant women did not affect newborn growth.

<https://www.nichd.nih.gov/about/org/diphr/officebranch/eb/fetal-growth-stud>

[NICHD]

Prenatal Exposure to Metals and Risk for Autism Spectrum Disorder

Researchers are engaged in the first prospective longitudinal study to examine the contribution of prenatal exposure to lead, cadmium, mercury, selenium, and manganese on the risk of autism. The study is using data from 456 mother–child pairs from the two largest enriched-risk, prospective pregnancy autism cohorts in the United States: the Early Autism Risk Longitudinal Investigation (EARLI) and Markers of Autism Risk in Babies–Learning the Early Signs (MARBLES).

https://projectreporter.nih.gov/project_info_description.cfm?aid=9552837&map=y

[NIEHS]

Study to Explore Early Development

This study at the Maryland Centers for Autism and Developmental Disabilities Research and Epidemiology aims to shed light on prenatal and early-life risk factors for autism spectrum disorder and help articulate the differences and similarities in preschoolers with autism in terms of their symptoms, behavior, functional ability, health, sleep, genetics, and autoimmunity. The project is also exploring participant families' sociodemographics, healthcare access, lifestyle, and reproductive history. The project is key to understanding the rise in prevalence of this disorder, modifying risk factors, and improving children's outcomes.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9516712&map=y

[NIEHS]

Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs

Epilepsy is one of the most common neurological disorders affecting women of childbearing age. The Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs study follows more than 400 women with epilepsy recruited during pregnancy to determine the effects of common epilepsy drugs (alone or in combination) on long-term neurodevelopment in children, as well as on maternal outcomes. The project was renewed in fiscal year 2018, with new aims to determine the effects of breastfeeding while taking antiepileptic drugs. Results from prior funding periods are already informing clinical practice for managing epilepsy in women of childbearing age to optimize outcomes for both mother and child.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9697870&icde=42395026

[NINDS, NICHD]

Joint Committee on Infant Hearing (JCIH) Position Statement on Newborn Hearing Screening and Intervention

Two to three out of 1,000 children in the United States are born deaf or hearing impaired or develop hearing loss during childhood. The Health Resources and Services Administration (HRSA), the Centers for Disease Control and Prevention (CDC), and the National Institute on Deafness and Other Communication Disorders (NIDCD) collectively work to ensure that identification and intervention for deaf and hearing-impaired infants occurs early to support improved outcomes for these children. Supported research has identified effective methods to screen for hearing loss in newborns and shows that early intervention for hearing loss can help children meet age-appropriate language, social, and other

communication development milestones. In 2019, the JCIH published an updated position statement on newborn hearing screening and intervention. The JCIH is composed of experts in audiology, otolaryngology, pediatrics, and child language, and is supported by the NIDCD and other federal agencies. The updated position statement advocates for research to improve detection of hearing loss and best practices for interventions. It also highlights the importance of risk factors for infant and childhood hearing loss, such as certain prenatal infections, premature birth, and genetics.

<https://digitalcommons.usu.edu/cgi/viewcontent.cgi?article=1104&context=jehdi>

[NIDCD, CDC, Maternal and Child Health Bureau, Boys Town National Research Hospital, other advocacy groups]

Newborn Screening Coding and Terminology Guide

This online guide uses nationally accepted vocabulary and electronic messaging standards to enable laboratories, clinicians, public health officials, and researchers to exchange and aggregate newborn screening results from all of the states as a key big data resource.

<https://lhncbc.nlm.nih.gov/newbornscreeningcodes/>

[NLM]

Hunter Kelly Newborn Screening Research Program

This program funds an array of research related to newborn screening that focuses on developing systematic methods to identify additional conditions appropriate for newborn screening, developing and testing innovative interventions and treatments to improve outcomes, educating the provider workforce, developing and implementing appropriate information and communication systems for parents and providers, and sponsoring ongoing programs of research and research training in newborn screening.

<https://www.nichd.nih.gov/health/topics/newborn>

[NICHD]

Newborn Screening Translational Research Network (NBSTRN)

The NBSTRN seeks to improve the health outcomes of newborns with genetic or congenital disorders through an infrastructure that provides the research community with access to resources for newborn screening. The NBSTRN has developed three tools to facilitate newborn screening research:

- *Virtual Repository of Dried Blood Spots (VRDBS)*: a web-based tool that enables state program personnel to control and manage access to specimens for newborn screening–related research.
- *Longitudinal Pediatric Data Resource (LPDR)*: a secure informatics system designed to enable enhanced data collection, sharing, management, and analysis for conditions identified as part of newborn screening or for conditions that may benefit from newborn screening.
- *Laboratory Performance Database (RAS)*: a web-based application for the collection and reporting of analytical results that has been developed and widely adopted into the routine practice of newborn screening laboratories worldwide.

<https://www.nichd.nih.gov/research/supported/nbstrn>

<https://www.nbstrn.org/>

[NICHD]

Child Development

Adolescent Brain Cognitive Development (ABCD) Study

The ABCD study is the largest long-term study of brain development and child health in the United States, enrolling 11,878 children ages 9 to 10. Researchers will track participants' biological and behavioral development for 10 years, through adolescence and into young adulthood. ABCD sites began the 3-year follow-up assessments in fall 2019, having retained 99 percent of participants in the study. The comprehensive baseline data set, released to the scientific community early in 2019, includes measures of physical and mental health, substance use, culture and environment, neurocognition, structural and

functional magnetic resonance imaging (MRI), pubertal hormone levels, genotypic data, and residential history–derived data (e.g., crime, pollution, area deprivation).

<https://abcdstudy.org/>

[NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OBSSR, ORWH]

Add Health Study

The Add Health study, formerly the National Longitudinal Study of Adolescent Health and also known as the National Longitudinal Study of Adolescent to Adult Health, is the largest longitudinal sampling of adolescents ever undertaken. Science advances from the Add Health study have helped identify trends and differences between groups in adolescent risk behavior.

<https://www.cpc.unc.edu/projects/addhealth>

[NICHD, NIA, NCI, NIMHD, NIAID, NIDCD, NIGMS, NIMH, NINR, NIAAA, NIDA, OAR, OBSSR, ORWH, OD]

Upstate New York Infant Development Screening Program (KIDS) Study and Follow-Up Study

The Upstate KIDS study was designed to determine whether fecundity and various infertility treatments adversely affect the growth and motor and social development of children from birth through age 3. Researchers tracked infants who resided in the 57 counties of upstate New York (exclusive of the five boroughs of New York City), using the “infertility checkbox” on the birth certificate for cohort selection. Parents and their infants were recruited at ages 4 to 8 months, with 1,297 infants born after reported infertility treatment and more than 3,692 “unexposed” infants whose parents did not report infertility treatment. Recent studies have drawn attention to the concern that children conceived by infertility treatment may have higher cardio-metabolic risk than spontaneously conceived children do. Through a follow-up study, the cohort will be followed to age 8, focusing on childhood cardio-metabolic outcomes (i.e., obesity, high blood pressure, and metabolism) and assessing epigenetic differences as measured by DNA methylation, using biospecimens collected from approximately 900 children.

<https://www.nichd.nih.gov/about/org/diph/eb/research/pages/infant-development.aspx>

[NICHD]

Novel Computational Tools for Investigating Cortical Brain Development in Infants

The increasing availability of large-scale longitudinal multimodal infant brain magnetic resonance imaging (MRI) data sets provides an unprecedented opportunity to precisely chart the dynamic trajectories of early brain development, information that is essential for understanding normative growth and neurodevelopmental disorders. A major barrier is the critical lack of computational tools, atlases, and parcellations for cortical surface–based analysis of the challenging infant MRI, which typically exhibits low tissue contrast and regionally heterogeneous, dynamic changes of cortical properties. To address these issues, researchers are creating and disseminating novel computational tools based on developmental patterns of multiple brain properties from multimodal magnetic resonance images. These tools will enable investigators to better explore inter-individual variability and early brain development.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9743237&icde=47801788

[NIMH]

Typical and Atypical Patterns of Language and Literacy in Dual Language Learners

About one of every five people age 5 and older in the United States speaks a language other than English in the home. Children and adolescents who are learning English in addition to a language spoken or signed at home are known as dual language learners. Dual language learners account for more than 9 percent of enrollment in grades K to 12 in schools throughout the United States. NIH will support research to improve understanding of the typical and atypical patterns of language and literacy development of dual language learners in the United States.

<https://grants.nih.gov/grants/guide/pa-files/PA-18-316.html>

<https://grants.nih.gov/grants/guide/pa-files/PA-18-328.html>

[NICHD, NIDCD]

Molecular Transducers of Physical Activity in Humans

The Molecular Transducers of Physical Activity in Humans program includes a clinical research study designed to extensively catalogue the biological molecules affected by physical activity in people, identify some of the key molecules that underlie the systemic effects of physical activity, and characterize the function of these molecules. One of the clinical sites is focusing on the molecular changes that occur when children and adolescents exercise. This portion of the study began recruitment in late November 2019 and is looking to enroll more than 320 participants through 2024. When combined with data from the six clinical sites actively recruiting adults, the research will show whether the molecular transducers of health benefits from exercise differ in children and adults and during different stages of development.

<https://commonfund.nih.gov/MolecularTransducers>

[OD/Common Fund]

Center for Pediatric Research (Center of Biomedical Research Excellence)

Many pediatric diseases have their origins in altered developmental programming related to the processes of cell proliferation, morphogenesis, migration, differentiation, and programmed death. These developmental processes are at the root of many pediatric disease and are disrupted through genetic disorders, aberrant fetal programming, altered growth and development, and environmental pressures. One Center of Biomedical Research Excellence applies genetic, biochemical, cell, and molecular approaches across several model organisms to characterize alterations during development as they pertain to pediatric diseases and disorders.

<https://research.sanfordhealth.org/fields-of-research/pediatrics-and-rare-diseases/cobre-grant>

[NIGMS]

Social and Environmental Influences

Environmental influences on Child Health Outcomes (ECHO) Including Clinical Sites for the Institutional Development Award (IDeA) States Pediatric Clinical Trials Network

To enhance the health of children for generations to come, the ECHO program aims to study the impacts of a broad range of early environmental exposures on child health and development by aggregating existing and new study populations of pregnant women and their offspring into a large longitudinal database—the ECHO-wide Cohort—while taking advantage of evolving scientific technologies. The ECHO-wide Cohort Data Collection Protocol standardizes data collection and management across all ECHO program participants. The cohort will serve as a nationwide resource for solution-oriented analyses of geographic, physical, chemical, social, behavioral, and biological exposure data with child development and health outcomes. Additionally, NIH has announced renewal funding opportunities for the IDeA States Pediatric Clinical Trials Network, which aims to enhance pediatric research infrastructure and capacity at institutions in IDeA states with historically low levels of funding from NIH. These opportunities will increase the participation of rural and/or underserved children in clinical trials and answer critical questions to help improve the health of these populations and bridge important gaps in pediatric care and research.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-19-025.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-19-026.html>

[OD/ECHO, OBSSR]

Clinical Sites for the Institutional Development Award (IDeA) States Pediatric Clinical Trials Network

The IDeA States Pediatric Clinical Trials Network provides medically underserved and rural populations with access to state-of-the-art clinical trials, applies findings from relevant pediatric cohort studies to children in IDeA states, and builds pediatric research capacity at a national level.²

<https://grants.nih.gov/grants/guide/rfa-files/rfa-od-16-001.html>

[OD]

Responsive Evaluation and Assessment of Chemical Toxicity (REACT)

Per- and polyfluorinated alkyl substances (PFAS) are industrial chemicals used for a variety of products, including nonstick cookware, stain-resistant fabrics, food packaging, and firefighting foams. Public health concerns regarding pollution caused by these industrial chemicals are growing. The REACT approach will use chemical-specific studies to evaluate a number of endpoints relevant to children's exposures to PFAS, including developmental toxicity and neurotoxicity, effects on the placenta and inhibition of milk protein production, and changes to human embryonic stem cells.

<https://www.niehs.nih.gov/health/topics/agents/pfc/index.cfm>

[NIEHS]

WHO–NIEHS Network of Collaborating Centres for Children's Environmental Health

Children have a special vulnerability to physical, chemical, and biological environmental threats.

According to the World Health Organization (WHO), environmental factors account for one-third of the global disease burden in children. The Network of WHO Collaborating Centres for Children's Environmental Health, which consists of 14 research institutes around the world, receives support so that each institute serves as a hub to strengthen national or regional capacity to advance children's environmental health.

<https://www.niehs.nih.gov/research/programs/geh/partnerships/network/index.cfm>

[NIEHS]

Early-Life Risk and Protective Factors for Later-Life Cognitive Health

NIA-supported investigators are using longitudinal data to identify potential early-life risk and protective factors for later-life cognitive impairment, including Alzheimer's disease and related dementias. For example, a new study explores whether social and educational disparities by race and/or ethnicity in adolescence shape disparities in cognitive impairment at midlife, whether biological and social factors moderate the effects of education on cognitive functioning and impairment, and which social and economic pathways those effects operate through over the life course. Another newly funded study will use a diverse cohort to analyze educational quality and occupational complexity associated with reduced risk of Alzheimer's disease and related dementias in White populations. A third study will link fetal immune system disruptions with sex differences in adult depression, early Alzheimer's disease pathology, and neurovascular dysfunction 60 years later, integrating associations between mood, memory, and biological sex. These and other ongoing studies will provide important information that will help us identify at-risk individuals across the life course and develop potential interventions to mitigate risk.

https://projectreporter.nih.gov/project_info_description.cfm?projectnumber=1R01AG058719-01A1

https://projectreporter.nih.gov/project_info_description.cfm?projectnumber=1R01AG066132-01

https://projectreporter.nih.gov/project_info_description.cfm?projectnumber=1R01AG067019-01

[NIA]

Nutrition and Obesity

Addressing Childhood Obesity Through Traditional Foods in Alaska

² This network partially meets the requirement in Section 409D(d) of the Public Health Service Act for a National Pediatric Research Network as part of the Pediatrics Research Initiative.

Back to Basics is an intervention to address childhood obesity in Alaska Native children up to 5 years old by reducing their consumption of sugar-sweetened beverages and increasing their consumption of nutrient-dense traditional and nontraditional foods. In 12 predominantly Alaska Native communities, scientists are working with community groups, including Head Start, Early Head Start, the Rural Community Action Group, and Parents as Teachers, to support a home education and Head Start center-based meal service program. The program's goal is to increase consumption of Alaska Native traditional foods by the children and their families. Childhood obesity is a serious health problem for Alaska Native children—41 percent of Alaska Native children ages 2 to 5 were overweight or obese in 2009—often leading to chronic health conditions such as glucose intolerance, hypertension, diabetes, and cancer in adulthood.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9752666&icde=49483101
[NINR]

The Impact of Obesity on Pubertal Development in Girls

Over the past decade, there has been an alarming trend toward earlier breast development in girls. There have been some recent reports that overweight girls are developing breast tissue earlier than normal-weight girls. However, questions remain about the validity of reports of early puberty among overweight girls, due to the difficulty in distinguishing fatty tissue from breast tissue in this population. This study is using breast ultrasound to better determine whether overweight girls have breast tissue, in order to understand whether overweight girls are truly entering puberty before normal-weight girls.

<https://www.niehs.nih.gov/research/clinical/studies/bwps/index.cfm>
[NIEHS]

Diabetes

The Environmental Determinants of Diabetes in the Young (TEDDY)

Insights about strategies to prevent type 1 diabetes could be identified through the ongoing TEDDY study, which is following more than 6,000 children at high genetic risk of developing type 1 diabetes to identify environmental factors that trigger or protect against disease development. Researchers aim to characterize type 1 diabetes progression through -omics studies to identify how genes, proteins, metabolic markers, and the microbiome change over time in those at high risk of developing the disease.

<https://teddy.epi.usf.edu>
[NIDDK, NIAID]

TrialNet

Type 1 Diabetes TrialNet is an international clinical trials network that screens up to 15,000 individuals annually and conducts trials of agents to prevent clinical diagnosis of type 1 diabetes in people with early-stage disease and to slow disease progression in the newly diagnosed. Blood tests can accurately identify relatives of people with type 1 diabetes who are at early stages of the disease (at high or moderate risk of developing clinical symptoms within 5 years), enabling TrialNet to initiate clinical trials of promising prevention strategies.

<https://www.trialnet.org>
[NIDDK, NIAID]

Childhood Diseases

International Study Group of Pediatric Pancreatitis: In Search for a Cure (INSPPIRE) to Study Pediatric Chronic Pancreatitis

INSPPIRE, a multinational study group, was established to investigate risk factors for and outcomes of pediatric pancreatitis. It is currently part of the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer and has enrolled the largest cohort of pediatric pancreatitis patients to

date, collecting genetic, demographic, and clinical data from children with acute, recurrent, or chronic forms of pancreatitis. The goal of this program is to develop improved diagnostic, disease prognostic, and treatment approaches for pancreatitis in children.

<https://medicine.uiowa.edu/pediatrics/research/pediatric-centers-and-programs/insppire-pediatric-pancreatitis-research-project>

[NIDDK, NCI]

Cure Glomerulopathy Network

This multisite, prospective observational research network is longitudinally following 2,400 children and adults with glomerular diseases (minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, and immunoglobulin A nephropathy) to better understand the causes, responses to therapy, and progression of these diseases. The network includes ancillary studies that will help inform new diagnostic and treatment strategies.

<https://curegn.org/default.aspx>

[NIDDK]

Chronic Kidney Disease in Children

This prospective cohort study of kidney disease in children and adolescents seeks to identify risk factors for progression of disease, as well as the impact of chronic kidney disease on neurocognitive development, cardiovascular disease, and growth. The study has identified several risk factors for pediatric kidney disease, as well as early manifestations of disease. An ancillary study has been funded to investigate genetic factors associated with progression of kidney disease in the study population.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-12-507.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-17-034.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-17-502.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-17-503.html>

https://projectreporter.nih.gov/project_info_description.cfm?aid=9785638&icde=49518328&ddparam=&ddvalue=&ddsub=&cr=4&csb=default&cs=ASC&pball=

[NIDDK, NICHD, NHLBI]

Nephrotic Syndrome Study Network

This longitudinal, observational study focuses on three glomerular diseases associated with nephrotic syndrome: minimal change disease, focal segmental glomerulosclerosis, and membranous nephropathy. Participants are enrolled before their first clinically indicated biopsy; when the biopsy is performed, a research core is obtained for genomic analysis. Using systems biology, scientists are analyzing tissue, serum, urine, and phenotypic and genomic data in approximately 500 children and adults.

<https://www.neptune-study.org/>

<https://clinicaltrials.gov/ct2/show/NCT01209000>

[NIDDK, NCATS, ORDR]

Gabriella Miller Kids First Pediatric Research Program (Kids First)

Kids First is developing a large-scale data resource for the pediatric research community, providing access to vast amounts of genetic and clinical data from patients with childhood cancer and structural birth defects and their families. The data resource will allow researchers to examine these conditions together to uncover shared pathways between them that might not have been uncovered had they been examined independently. From 2015 to 2019, the Kids First program selected 39 childhood cancer and structural birth defects patient cohorts for whole genome sequencing, representing 37,000 genomes and 154,000 patients. The program will select additional cohorts in 2020–2022, pending available funding. Clinical and genetic data from 10 of the Kids First projects are publicly available through the Gabriella Miller Kids First Data Resource Portal. Small grants to analyze data from the Gabriella Miller Kids First Pediatric Data Resource are supported in a collaborative effort by several institutes.

<https://commonfund.nih.gov/KidsFirst>
<https://commonfund.nih.gov/kidsfirst/x01projects>
<https://kidsfirstdrc.org/portal/portal-features/>
<https://grants.nih.gov/grants/guide/pa-files/PAR-19-375.html>
[OD/Common Fund, NICHD, NHLBI, NIDCR, NCI, NIAAA]

Prone and Oscillation Pediatric Clinical Trial

Severe pediatric acute respiratory distress syndrome (ARDS) continues to be associated with 20 percent to 30 percent mortality, and the roles of prone positioning and high-frequency oscillatory ventilation have not been assessed in a randomized controlled trial. An ongoing study plans to enroll 1,000 children with severe pediatric ARDS to examine the impact of prone positioning and use of high-frequency oscillatory ventilation on ventilator-free days and outcomes. This 7-year clinical trial is now in Year 2 and is actively enrolling subjects.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9723514&icde=48006632
[NHLBI]

Neuroprotective Intervention in Infants Born with Hypoxic-Ischemic Encephalopathy

Erythropoietin is a cytokine with neuroprotective effects demonstrated in animal models of neonatal brain injury. It is commercially available, relatively inexpensive, and safe in newborns. A clinical trial is assessing erythropoietin for preventing death or neurodevelopmental disability in infants. The trial will determine whether erythropoietin therapy combined with therapeutic hypothermia will reduce death and neurodevelopmental impairment in infants at or after 36 weeks of gestational age who have moderate/severe hypoxic-ischemic encephalopathy.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9743886&icde=0
[NINDS]

Vascular Effects of Infection in Pediatric Stroke

Each year, approximately 2,000 children in the United States experience an ischemic stroke. Through an international network of 37 sites, scientists have found that minor infections like the common cold act as a trigger for ischemic stroke in children, routine childhood vaccinations are protective, and the risk for stroke recurrence is high. In a continuation of this study, researchers aim to identify infectious pathogens and inflammatory factors involved in childhood stroke and stroke recurrence, to inform the development of targeted prevention strategies.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9733354&icde=47987684
[NINDS]

Pediatric Heart Network

The Pediatric Heart Network was established in 2001 to help doctors and nurses design and conduct clinical research so that children with heart disease can receive high-quality, evidence-based care. This network has launched the Do It! study to investigate whether pitavastatin can help improve cardiovascular outcomes in obese children and teens ages 10 to 17 who have a particular type of abnormal cholesterol because of their obesity.

<http://www.pediatricheartnetwork.org/>
[NHLBI]

Pediatric Cardiac Genomics Consortium

After successfully uncovering the genetic architecture of congenital heart disease for the past 10 years, in the new funding cycle, the Consortium will seek to translate those findings into clinical applications that have meaningful impact for patients.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-16-004.html>
<https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-15-012.html>

[NHLBI, NICHD]

Genomic Centers for Infectious Diseases

This program provides insights into the biology of microbes, their role in pathogenesis, and their interactions with the host, including the microbiome. Ongoing efforts relevant to pediatric disease include a study on surveillance of viral gastroenteritis, active surveillance for acute respiratory illness among pediatric patients, and a global enteric multisite study focused on bacterial infections caused by *Aeromonas*, *Escherichia coli*, and *Shigella*.

<https://www.niaid.nih.gov/research/genomic-centers-infectious-diseases>

[NIAID]

Immunity and Allergies

Respiratory Syncytial Virus (RSV) Vaccine Trials

In a collaborative effort, RSV vaccines for pediatric populations are being developed. Several ongoing clinical trials compare multiple promising vaccine candidates for intranasal administration in infants and young children. The candidates are different versions of attenuated, or weakened, live virus and are designed to elicit a strong immune response. One recent study of an investigational vaccine elicited an immune response to both human parainfluenza virus type 1 and RSV, potentially protecting children from the two leading causes of respiratory tract infections. The trial showed that the vaccine was safe and well tolerated.

<https://www.niaid.nih.gov/research/vaccine-treatment-evaluation-units>

<https://clinicaltrials.gov/ct2/show/NCT03422237>

<https://clinicaltrials.gov/ct2/show/NCT03227029>

<https://clinicaltrials.gov/ct2/show/NCT03916185>

<https://clinicaltrials.gov/ct2/show/NCT03473002>

[NIAID]

An Influenza Vaccine for Pediatric Stem Cell Transplant Subjects

The safety and immunogenicity of a high-dose influenza vaccine (HD Fluzone) in pediatric stem cell transplant patients is being tested in a clinical trial. Because immunosuppression is required to prevent rejection of the transplant, the standard flu vaccine does not elicit a robust response in these individuals. Researchers are testing whether HD Fluzone, which provides three times the dose that the standard flu vaccine does, can provide better protection against influenza for this population.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9527735&icde=48035423&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

[NIAID]

Primary Immune Deficiency (PID) Clinic

The NIAID PID clinic is the focal point for studies of the genetics, pathophysiology, and treatment of PID diseases, which are rare and often very severe disorders of the immune system that frequently appear during infancy or childhood. Joint clinical trials are looking at ways to continuously improve bone marrow transplantation and gene therapy for the treatment of PID diseases. In addition to activities in the PID clinic, investigators publish important findings to further our understanding of basic mechanisms and improve clinical practice.

<https://www.niaid.nih.gov/clinical-trials/primary-immune-deficiency-clinic>

[NIAID, NCI, CC]

Immune Mechanisms at the Maternal–Fetal Interface

The focus of this program is to characterize the roles and interactions of immune cells at the maternal–fetal interface that protect or affect the fetus and influence fetal immune system development throughout

pregnancy. Eleven studies under this program in fiscal year 2019 include projects focusing on placental antiviral/antibacterial defenses, immune cell characterization and regulation, metabolic processes, and hormone-induced immune system changes during pregnancy.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-18-023.html>

[NIAID, NICHD]

Improving Medication Adherence in Children Who Had a Liver Transplant

This multisite study being conducted at leading pediatric liver transplant centers in the United States and Canada is testing a tailored telemetric intervention to reduce transplant rejection rates by improving adherence to immunosuppressant medication. Nonadherence to such medication is the leading cause of organ rejection in adolescent transplant recipients.

<https://imalt.org/>

<https://clinicaltrials.gov/ct2/show/NCT03691220>

[NIDDK]

Clinical Trials in Organ Transplantation in Children

The goal of this program is to reduce immune-mediated morbidity and mortality in vulnerable pediatric transplant recipients. Ongoing studies focus on learning more about the immune response to Epstein-Barr virus in pediatric transplant recipients.

<https://www.niaid.nih.gov/research/clinical-trials-organ-transplantation-children>

[NIAID]

Immune Tolerance Network

The Immune Tolerance Network develops treatment and prevention strategies for food allergies, autoimmune diseases, and organ transplantation in adult and pediatric populations by inducing tolerance. Capitalizing on previous research in the network, scientists are investigating whether the low rate of peanut allergy in children who began eating peanut-containing foods early in life persists until age 12. Another trial is being developed to assess whether early consumption of eggs and milk will prevent allergies to these foods in young infants. Additionally, researchers recently enrolled 81 children in a clinical study that will test whether a therapy called tocilizumab can extend the ability to naturally produce insulin in individuals recently diagnosed with type 1 diabetes.

<https://www.immunetolerance.org/>

[NIAID]

Consortium for Food Allergy Research

The Consortium for Food Allergy Research develops and conducts cutting-edge clinical trials and studies to advance prevention and management strategies and improve knowledge on the origins and the pathophysiology of food allergies. One trial currently underway investigates treating food allergies with the medication omalizumab alone or in combination with oral immunotherapy in children and adults.

<https://www.niaid.nih.gov/research/consortium-food-allergy-research>

<https://clinicaltrials.gov/ct2/show/NCT03881696>

[NIAID]

Rare Pediatric Diseases

Rare Diseases Clinical Research Network (RDCRN)

The RDCRN conducts collaborative clinical research in rare diseases, including longitudinal studies of individuals with rare diseases, clinical studies, and clinical trials. The RDCRN is composed of 21 distinctive research consortia and a central Data Management and Coordinating Center that are working in concert to improve availability of rare disease information, treatment, clinical studies, training of new scientists, and general awareness for both patients and the medical community. The RDCRN also aims to

provide up-to-date information for patients and to assist in connecting patients with advocacy groups, expert doctors, and clinical research opportunities. One-half to two-thirds of rare diseases manifest in children, so many of the rare diseases studied by this network occur primarily or frequently in children. Current consortia that study such disorders cover primary immune deficiency diseases; urea cycle disorders; mitochondrial diseases; lysosomal diseases; rare lung, bone, kidney, and metabolic disorders; and neurodevelopmental and degenerative disorders, such as Rett syndrome.

<https://ncats.nih.gov/news/releases/2019/rdcm-funding>

<https://ncats.nih.gov/rdcm>

[NCATS, NCI, NEI, NHLBI, NIAID, NIAMS, NICHD, NIDCR, NIDDK, NINDS, ODS]

Undiagnosed Diseases Network (UDN)

The UDN is a research study designed to improve and accelerate diagnosis of rare and undiagnosed conditions. By bringing a nationwide network of top clinicians and laboratory researchers together, the UDN is able to come up with diagnoses for some of the most complex medical cases. Also, by promoting research into the biological mechanisms of these rare conditions, the likelihood of designing treatments and, it is hoped, cures for these diseases will be increased. Approximately 58 percent of the participants enrolled in the UDN are children. Examples of new developmental disorders recently discovered by the network include methenyltetrahydrofolate synthetase (MTHFS)–associated disorder and *TBX2*-related disorder.

<https://commonfund.nih.gov/diseases>

<https://www.ncbi.nlm.nih.gov/pubmed/30031689>

<https://www.ncbi.nlm.nih.gov/pubmed/29726930>

[OD/Common Fund]

Pediatric Cancer

Specialized Programs of Research Excellence (SPOREs) in Pediatric Oncology

The SPOREs support efforts to promote collaborative, interdisciplinary translational cancer research. SPORE grants involve both basic and clinical/applied scientists working together and support projects that will result in new and diverse approaches to the prevention, early detection, diagnosis, and treatment of human cancers. Each SPORE focuses on a specific organ site; currently, 19 organ sites, systems, or pathway-specific themes are represented in the SPORE portfolio. SPOREs focused on pediatric cancers are looking at pediatric astrocytoma, pediatric glioma, and pediatric melanoma. In particular, the Developmental and Hyperactive Ras Tumor SPORE focuses on developing better treatment for cancers and premalignant conditions associated with neurofibromatosis 1 (NF1) mutations, including plexiform neurofibroma (pNF), malignant peripheral nerve sheath tumors (MPNST), juvenile myelomonocytic leukemia (JMML), and subsequent malignant neoplasms (SMNs) in NF1 patients receiving radiation and chemotherapy for primary tumors.

<https://trp.cancer.gov/spores/bylocation.htm>

https://trp.cancer.gov/spores/abstracts/indiana_hyperactive.htm

[NCI]

Pediatric Brain Tumor Consortium, Pediatric Preclinical Testing Consortium (PPTC), and Clinical Studies of Familial Cancer Syndromes

- The Pediatric Brain Tumor Consortium is a multidisciplinary cooperative research organization devoted to identifying superior treatment strategies for children with primary brain tumors.
<https://www.pbtc.org/>
- The PPTC identifies new, more effective agents for treating childhood cancers.
<https://www.ncipptc.org/>

- In addition, NCI’s Comprehensive Program of Clinical Studies of Familial Cancer Syndromes studies a range of inherited syndromes that may predispose individuals and their families to cancer. Several of these studies include children.
<https://dceg.cancer.gov/research/what-we-study/hereditary-cancer-syndromes>

[NCI]

Pediatric Oncology Branch

The Pediatric Oncology Branch conducts high-risk, high-impact basic, translational, and clinical studies. Within the branch, the NCI recently launched the Psychosocial Support and Research Program, which carries out research to learn how best to help patients and their families prepare for, adjust to, and cope with the effects of cancer and other related medical conditions while enrolled in research protocols in several NCI branches and NIH institutes, centers, and offices.

<https://ccr.cancer.gov/pediatric-oncology-branch>

[NCI]

Therapeutically Applicable Research to Generate Effective Treatments (TARGET)

The TARGET Initiative is a comprehensive genomic approach to determine molecular changes that drive childhood cancers and further stratify patients to improve therapeutic outcomes. TARGET project teams study primarily high-risk, often relapsed/refractory leukemias and solid tumors of the kidney, osteosarcoma, and neuroblastoma. Results from this large-scale characterization and sequencing initiative are made broadly available to the research community through the NCI Genomic Data Commons to promote discovery. The current data available for analysis is from more than 12,000 tumor and normal samples representing nearly 5,000 unique pediatric cancer cases.

<https://ocg.cancer.gov/programs/target>

[NCI]

Children’s Oncology Group

The Children’s Oncology Group develops and coordinates pediatric cancer clinical trials that are available at more than 200 member institutions, including cancer centers throughout the United States and Canada. Many of these clinical trials study high-priority novel agents, including targeted therapies and immunotherapies. The types of cancers addressed include relapsed/refractory solid tumors and lymphomas, newly diagnosed high-risk Hodgkin lymphomas, certain relapsed leukemias, osteosarcoma, Ewing sarcoma, and certain pediatric brain tumors.

<https://www.childrensoncologygroup.org/>

[NCI]

Pediatric Early Phase Clinical Trials Network (PEP-CTN)

The PEP-CTN, which builds upon the success of the Children’s Oncology Group Phase 1 and Pilot Consortium, conducts “first-in-children” early-phase clinical trials of new agents that are relevant to one or more childhood cancers. In addition, the PEP-CTN conducts pilot studies of novel agents/regimens to determine their tolerability so that promising regimens can proceed to definitive testing in Phase III clinical trials. The PEP-CTN includes 21 core member institutions, representing many of the leading childhood cancer centers in the United States.

<https://ctep.cancer.gov/initiativesprograms/pep-ctn.htm>

[NCI]

Pediatric Cancer Immunotherapy Trials Network

The Pediatric Cancer Immunotherapy Trials Network conducts clinical trials of immunotherapy agents of specific relevance to children and adolescents with cancer. Examples of the types of novel treatments to be investigated include cellular therapies (e.g., chimeric antigen receptor [CAR] T cells targeting pediatric cancer antigens) and antibody-based therapies, such as antibody–drug conjugates, that target surface

antigens preferentially expressed in childhood cancers.

https://ctep.cancer.gov/MajorInitiatives/cancer_immunotherapy_trials_network.htm

[NCI]

New Approaches to Neuroblastoma Therapy (NANT) Consortium

The NANT consortium consists of a multidisciplinary team of laboratory and clinical scientists focused on improving outcomes for patients with high-risk neuroblastoma by discovering mechanisms of resistance to therapies, finding targetable vulnerabilities driving resistance, and translating these insights into clinical trials. NANT works closely with the Children's Oncology Group (COG) to translate their experimental therapy findings into Phase III clinical trials for the COG. The consortium's findings regarding the tumor microenvironment, tumor response to therapy, and application of cellular therapies to solid tumors have implications beyond neuroblastoma.

<http://www.nant.org/>

[NCI]

NCI Experimental Therapeutics (NExT) Program

The NExT Program has prioritized the development of new treatments for pediatric cancer. This program focuses on advancing breakthrough discoveries in basic and clinical research into new therapies. Each agent accepted into the NExT Program is considered for its relevance to pediatric cancers.

<https://next.cancer.gov/>

[NCI]

Li-Fraumeni Syndrome (LFS) Study

LFS is a rare, inherited disorder that leads to a higher risk of developing certain cancers. These cancers tend to occur at younger ages in patients with LFS than in the general population. The types of tumors most frequently seen in LFS include bone and soft tissue cancers (sarcomas), breast cancer, brain tumors, and cancer of the adrenal gland. The diagnosis of LFS is based on an individual's personal and family history of cancer. Heritable disease-causing change in a gene called *TP53* is currently the only known cause of LFS and is identified in about 70 percent of families with a clinical diagnosis of LFS.

<https://lfs.cancer.gov/>

[NCI]

Inherited Bone Marrow Failure Syndrome Study

The inherited bone marrow failure syndromes are a group of rare genetic blood disorders in which there is usually some form of aplastic anemia (failure of the bone marrow to produce blood), associated with a family history of the same disorder. Some of these conditions have typical changes in physical appearance or in laboratory findings, suggesting a specific diagnosis. Patients with these syndromes have a very high risk of developing cancer (either leukemia or certain solid tumors). An ongoing clinical study seeks to better understand how cancers develop in people with these disorders, with the aim of improving the care that can be offered.

<https://marrowfailure.cancer.gov/index.html>

[NCI]

Pleuropulmonary Blastoma (PPB) DICER1 Syndrome Study

PPB is a rare tumor of the lung. Research has shown that PPB may be part of an inherited cancer predisposition syndrome caused by changes in a gene known as *DICER1*. The PPB Cancer Study is an observational study of children with PPB and their families.

<https://ppb.cancer.gov/>

[NCI]

Retinoblastoma (Rb) Survivors Follow-Up Study

Rb is a cancer that forms in the tissues of the retina (the light-sensitive layers of nerve tissue at the back of the eye). Rb usually occurs in children under age 5 years and may be either hereditary or nonhereditary. Despite excellent survival rates among children treated for Rb, survivors with a germline mutation in their *Rb1* gene (hereditary Rb) are prone to subsequent cancers, including sarcomas, melanoma, and cancers of the brain and nasal cavity. An ongoing study monitors cancer incidence and mortality in the largest cohort of Rb survivors diagnosed from 1914 through 2007 in the United States. <https://dceg.cancer.gov/research/cancer-types/retinoblastoma>

[NCI]

Childhood Cancer Survivor Study (CCSS)

The CCSS examines the long-term adverse effects of cancer and cancer therapy on approximately 35,000 survivors of childhood cancer who were diagnosed between 1970 and 1999. The study was created to gain new knowledge about the long-term effects of cancer and its treatment and to educate survivors and the medical community about the potential impacts of a cancer diagnosis and treatment. The results obtained from the CCSS are used to help design treatment protocols and interventions that will result in an increase in survival while minimizing harmful late effects. This research is also used to develop and expand programs for early detection and prevention of late effects in child and adolescent cancer survivors.

<https://www.cancer.gov/types/childhood-cancers/ccss>

[NCI]

International Data on Parental Occupational Exposure to Pesticides, Animals, and Organic Dust

Using pooled data from birth cohorts in five countries in an international consortium, researchers are assessing risk for acute lymphoblastic leukemia, acute myeloid leukemia, and childhood brain tumors in relation to maternal and paternal exposures to pesticides, organic dust, and animals on the job during pregnancy.

<https://www.ncbi.nlm.nih.gov/pubmed/30466188>

[NCI]

Proximity to Agricultural Pesticides and Childhood Cancer in the Danish National Birth Cohort

Investigators are conducting analyses of agricultural pesticides applied near homes of childhood cancer cases and a 10 percent sample of non-cases in the Danish National Birth Cohort, one of the cohorts participating in the International Childhood Cancer Cohort Consortium. Investigators are using national pesticide use data to estimate pesticide use near homes during the pregnancy and will be evaluating the associated risk of childhood leukemia and childhood brain tumors.

<https://www.ncbi.nlm.nih.gov/pubmed/30466188>

[NCI]

Childhood Cancer Survivor Study (CCSS)/NCI Collaborative Studies

In 2011, a collaboration with the CCSS began to conduct a genome-wide association study aimed at identifying genetic variants associated with development of second cancers (either independent of treatment exposures or jointly with specific treatments), development of childhood cancer, and development of nonmalignant late adverse effects of treatment (e.g., cardiomyopathy, obesity, ototoxicity). The investigators are currently conducting whole exome sequencing of the cohort to identify other types of genetic variants (e.g., rare variants, multi-allelic substitutions, insertions, deletions) that may be related to the development of childhood cancer and late effects following childhood cancer diagnosis. In addition, the investigators are collaborating on a case-control study of breast cancer occurring after childhood cancer.

<https://dceg.cancer.gov/research/who-we-study/cohorts/childhood-cancer-survivors>

[NCI]

The Human Papillomavirus (HPV) Serology Standards Laboratory (HPV-SSL)

The HPV-SSL was established in January 2017 and is part of an international initiative to standardize and harmonize serological assays for HPV antibody testing in the context of vaccine trials. Serology standardization is particularly important, as new HPV prophylactic vaccine trials are proposing to use serology data as endpoints for licensure of new vaccine indications or new vaccines. The main goals of the HPV-SSL include the development of qualified secondary assay standards, critical reagents (HPV virus-like particles), and assays that will be made available to the scientific community. Overall, this initiative will enable comparisons of data across different vaccines and different studies, facilitating vaccine development and implementation of new vaccine indications and new vaccine candidates. <https://frederick.cancer.gov/news/new-hpv-serology-laboratory-aims-standardize-assays-and-contribute-vaccine-implementation-and> [NCI]

Bone and Muscle Health

Clinical Trial of Sodium Thiosulfate to Treat Calcinosis Associated with Juvenile Dermatomyositis

Calcinosis is a debilitating complication of dermatomyositis in up to 40 percent of patients, resulting in increased disability, frequent infections, and impaired quality of life. No known therapy exists to treat calcinosis after it occurs. Based on anecdotal experiences suggesting significant improvement in the calcifications of dermatomyositis with sodium thiosulfate treatment, a Phase I/II pilot study began looking at the efficacy of using sodium thiosulfate in juvenile and adult dermatomyositis with moderate to severe calcinosis. Sodium thiosulfate is Food and Drug Administration (FDA)–approved for the treatment of cyanide poisoning, but it also acts as a calcium chelator, an antioxidant, and a vasodilator. The study also aims to assess the safety of longer-term use of sodium thiosulfate in children and adults and to evaluate the impacts of treatment on quantitative changes in calcium lesions by imaging, quality of life, functional disability, muscle strength, laboratory values (including biomarkers of inflammation and endothelial activation), and overall myositis disease activity and damage. The study expanded enrollment this year to include children of at least 7 years of age. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821280/> [NIEHS]

Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers

The six Wellstone Muscular Dystrophy Cooperative Research Centers promote collaborative basic, translational, and clinical research on muscular dystrophies, including those affecting children. The centers also provide resources including outstanding training environments, community outreach, and shared core facilities. The Wellstone Centers are designed to foster the translation of new scientific findings and technological developments into novel treatments for muscular dystrophies and to provide important resources that can be used by the national muscle biology and neuromuscular research communities. The centers also engage patients and patient advocates in educational programs. Centers include one or more scientific research resource cores that support specific projects and serve as a resource for the international research community. <https://www.wellstonemdccenters.nih.gov/> <https://www.nichd.nih.gov/research/supported/Pages/mdcrc.aspx> [NINDS, NIAMS, NICHD, NHLBI]

Oral Health, Speech, Hearing, and Vision

Myopia Progression and Soft Multifocal Contact Lens Myopia Control

Myopia, or nearsightedness, affects approximately one-third of people in the United States, approximately 60 percent (60 million) of whom become nearsighted during childhood. This study aims to continue collecting information on the progression of myopia in children by measuring specific noninvasive

biomarkers and exposure to outdoor light. The results of this study have the potential to affect the standard of care for young nearsighted children and lead to important information regarding features of the eye and factors in the environment that may affect myopia progression.

https://projectreporter.nih.gov/project_info_description.cfm?aid=10015988&icde=47881658&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pbll=

[NEI, CC]

Intellectual and Developmental Disabilities, Neurological Disorders, and Mental Health

Learning Disabilities Research Centers (LDRC) Consortium

The LDRC Consortium develops knowledge on the causes, origins, and developmental course of learning disabilities. The LDRC Consortium addresses learning disabilities that affect reading and writing, including basic reading skills, reading fluency, reading comprehension, and written expression.

Complementing the LDRC Consortium, the Learning Disabilities Innovation Hubs focus on understudied research topics and projects that study people diagnosed with and at risk for learning disabilities. Projects also include mentorship of researchers who are in the early stages of their careers, with a particular focus on enhancing involvement of underrepresented groups in scientific careers.

<https://www.nichd.nih.gov/research/supported/Pages/lsrc.aspx>

<https://www.nichd.nih.gov/research/supported/Pages/ldhubs.aspx>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-17-006.html>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-17-003.html>

[NICHD]

INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome)

The INCLUDE project was launched in June 2018 in support of a congressional directive in the fiscal year (FY) 2018 Omnibus Appropriations. The directive calls for a new trans-NIH research initiative on critical health and quality-of-life needs for individuals with Down syndrome. INCLUDE will investigate conditions that affect individuals with Down syndrome and the general population, including Alzheimer's disease/dementia, autism, cataracts, celiac disease, congenital heart disease, and diabetes. Applying the expertise and resources from multiple NIH institutes, centers, and offices, INCLUDE will conduct targeted, high-risk, high-reward basic science studies on chromosome 21; assemble a large study population of individuals with Down syndrome; and include individuals with Down syndrome in new and existing clinical trials.

<https://www.nih.gov/include-project>

[NICHD, NCI, NEI, NHLBI, NHGRI, NIA, NIAID, NIAMS, NIAMS, NIDCD, NIDCR, NIDDK, NIEHS, NIGMS, NIMH, NIMHD, NINDS, NINR, NCATS, NCCIH]

Down Syndrome (DS) Consortium

Since 2011, this public-private collaboration has fostered communication and idea sharing among NIH, individuals with DS and their families, national organizations interested in DS, and pediatric and other organizations. The consortium also supports and publicizes DS-Connect[®] and works toward implementing the updated 2014 NIH Research Plan on Down Syndrome.

<https://downsyndrome.nih.gov/>

[NICHD, NCI, NHLBI, NHGRI, NIA, NIAID, NIDCD, NIDCR, NIDDK, NIMH, NIMHD, NINDS, NCATS]

DS-Connect[®]

DS-Connect[®] is a web-based health registry that serves as a national health resource for individuals with Down syndrome and their families, researchers, and healthcare providers. The registry facilitates communication and online resource sharing through a secure, confidential database. With more than

4,200 registrants to date, DS-Connect® has allowed 35 researchers to successfully complete recruitment for their studies.

<https://dsconnect.nih.gov>

[NICHD, NCI, NHLBI, NHGRI, NIA, NIAID, NIDCD, NIDCR, NIDDK, NIMH, NIMHD, NINDS, NCATS]

Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Centers (IDDRCs)

The IDDRCs employ advanced technologies to support a broad range of research projects related to intellectual and developmental disabilities (IDDs). The centers have cores to provide infrastructure support and must support new research component projects that use the Center cores, focusing on comprehensive -omic approaches to IDDs, outcome measures for interventions or treatments, multimodal treatment approaches, shared resources across IDDRCs for treatment or assessment, and/or public health approaches. Examples of disabilities that the IDDRCs study include chromosomal conditions that cause IDDs, such as Prader–Willi, Angelman, Williams, and Down syndromes; X chromosome disorders, such as Rett and Fragile X syndromes; and disorders that involve biochemical processes and metabolic issues related to brain functioning, such as hypoxia and phenylketonuria.

<https://www.nichd.nih.gov/research/supported/eksiddrc>

[NICHD]

Centers for Collaborative Research in Fragile X

This program supports research to improve the diagnosis and treatment of Fragile X syndrome and its related conditions. The centers are geared toward stimulating multidisciplinary, multi-institutional research with the common goal of facilitating the translation of basic research findings from bench to bedside and bedside to community.

<https://www.nichd.nih.gov/research/supported/Pages/ccrfx.aspx>

[NICHD, NINDS, NIMH]

Autism Centers of Excellence (ACE)

Since 2007, this trans-NIH initiative has supported large-scale multidisciplinary studies on autism spectrum disorders, with the goal of determining the disorders' causes and best treatments. Research efforts are coordinated across NIH by the Autism Coordinating Committee. Through the ACE program, NIH supports large research projects aimed at understanding autism spectrum disorder and developing interventions. These awards seek to build upon prior knowledge by supporting the most innovative, multidisciplinary science. ACE projects are focused on studying the earliest brain and behavioral markers of autism spectrum disorder, identifying its subtypes, understanding the differences between males and females with this disorder, evaluating screening practices, and developing innovative treatments.

<https://www.nichd.nih.gov/research/supported/ace>

[NICHD, NIDCD, NIEHS, NIMH, NINDS]

Language Learning in Children with Fragile X Syndrome

Preclinical evidence suggests that blockers of the metabotropic glutamate receptor (mGluR) could be an effective therapy in treating Fragile X syndrome. The FX-Learn trial will test whether a blocker of mGluR5 (AFQ056, developed by Novartis) can boost language learning in very young children with Fragile X who undergo an intensive language intervention in combination with the drug. The study will also identify biomarkers correlated with developmental outcome measures and assess whether the intervention alters the developmental trajectory of children with Fragile X syndrome, including whether they develop autism. This study is significant because it will address factors that may have contributed to negative results in previous clinical trials and will provide a definitive test of the mGluR theory in humans.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9712968&icde=32552846

[NINDS, NICHD, NIDCD]

Preventing Epilepsy in Infants with Tuberous Sclerosis Complex

Recent NIH-supported research showed that electroencephalography (EEG) biomarkers can predict seizure activity before onset in infants with tuberous sclerosis complex (TSC). This trial will use this marker to test whether presymptomatic treatment with the anti-seizure medication vigabatrin prevents the development of epilepsy in infants with TSC and whether treatment improves cognitive and behavioral outcomes or reduces the risk of developing autism spectrum disorder.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9693335&icde=42391735

[NINDS]

Channelopathy-Associated Epilepsy Research Center

As part of the Centers Without Walls for Collaborative Research in the Epilepsies, this research program includes investigators at five academic medical centers and three freestanding research hospitals, as well as two industry partners. The research focuses on understanding the genetic basis of epilepsy and specifically on the role of sodium and potassium channel genes, which are among the most common genetic causes of severe pediatric epilepsy. This research will help to improve the accuracy of epilepsy diagnoses and inform optimal drug therapy selection and development for specific mutations.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9792292&icde=42392803

<https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-18-001.html>

<https://news.feinberg.northwestern.edu/2018/09/northwestern-receives-12-million-grant-to-advance-epilepsy-research/>

[NINDS]

Childhood Injuries, Maltreatment, and Violence

National Center for Medical Rehabilitation Research (NCMRR)

Through basic, translational, and clinical research, the NCMRR aims to foster development of scientific knowledge needed to enhance the health, productivity, independence, and quality of life of people with physical disabilities. The NCMRR supports research on pathophysiology and management of chronically injured nervous and musculoskeletal systems (including stroke, traumatic brain injury, spinal cord injury, and orthopedic conditions); repair and recovery of motor and cognitive function; functional plasticity, adaptation, and windows of opportunity for rehabilitative interventions; rehabilitative strategies involving pharmaceutical, stimulation, and neuroengineering approaches; exercise, motor training, and behavioral modifications; pediatric rehabilitation; secondary conditions associated with chronic disabilities; improved diagnosis, assessment, and outcome measures; and development of orthotics, prosthetics, and other assistive technologies and devices. The NCMRR also supports research on therapies and rehabilitative approaches for cerebral palsy.

<https://www.nichd.nih.gov/about/org/ncmrr/Pages/overview.aspx>

[NICHD]

Medical Rehabilitation Research Resource Network

This network builds research infrastructure in medical rehabilitation by providing researchers with access to expertise, courses and workshops, technologies, and collaborative opportunities from allied disciplines, such as neuroscience, engineering, applied behavior, and the social sciences.

<https://www.nichd.nih.gov/research/supported/Pages/mrrin.aspx>

[NICHD, NINDS, NIBIB]

CAPSTONE Centers for Multidisciplinary Research in Child Abuse and Neglect

These centers address child maltreatment as a significant public health concern. This program will allow researchers to assess the efficacy and effectiveness trials of child abuse and neglect interventions, examine the long-term impact of specific and understudied types of maltreatment, study the neurobiology

of abuse and neglect and implications for health outcomes, and develop screening tools and assessment measures for early identification and treatment of specific types of abuse and neglect.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-hd-18-012.html>

[NICHD]

Substance Misuse

National Institutes of Health (NIH) Helping to End Addiction Long-termSM (HEAL) Initiative: Preventing Opioid Use Disorder

As part of its HEAL Initiative to speed development and implementation of scientific solutions to the national public health opioid crisis, NIH is supporting research grants and a coordinating center to establish a stronger evidence base for interventions and strategies to prevent initiation of opioid misuse and development of opioid use disorder in at-risk older adolescents and young adults.

<https://grants.nih.gov/grants/guide/rfa-files/rfa-da-19-035.html>

<https://grants.nih.gov/grants/guide/rfa-files/rfa-da-19-034.html>

[NIDA, NIAAA, NIMH, NCCIH, NICHD, NIDCR, OBSSR]

Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW)

The ACT NOW initiative aims to inform clinical care for newborns with neonatal opioid withdrawal syndrome (NOWS). The study is a collaborative effort with sites in rural and medically underserved communities. Together, the sites are assessing the prevalence of newborns with opioid withdrawal syndrome across the country, gathering information on the range of ways cases currently are being managed, and developing common protocols for comparative effectiveness studies to inform practice. The goal of these trials is to find innovative ways to identify and treat newborns exposed to opioids, thus improving their cognitive and health outcomes.

<https://heal.nih.gov/research/infants-and-children/act-now>

[NICHD, OD]

Population Assessment of Tobacco and Health (PATH) Study

The PATH Study is a national longitudinal study of approximately 49,000 people age 12 and older that examines the relationship between use of tobacco products, including electronic nicotine delivery systems, and health. Conducted in collaboration with the Food and Drug Administration (FDA), the PATH Study yields insight into how and why people use tobacco products, which products they use, how and why they quit, changing attitudes toward tobacco products, and other important areas of inquiry.

<https://pathstudyinfo.nih.gov/UI/HomeMobile.aspx>

[NIDA, FDA]

Information Tool Available to Teens to Quit Smoking and Vaping

Despite significant progress in reducing the prevalence of smoking in the United States, smoking continues to represent a major threat to public health for certain populations, including teenagers. Part of Smokefree.gov, Smokefree Teen is a teen-oriented smoking and vaping cessation program that provides evidence-informed resources to teens who smoke and/or vape. The initiative comprises four core components: Teen.Smokefree.gov; SmokefreeTXT, a text message-based intervention; quitSTART, an interactive quit-tracking application that features games to play during cravings; and Smokefree Teen-branded social media pages on Twitter, Facebook, and Tumblr. Many of these components use mobile technology, given teens' unique usage patterns of emerging mobile technologies, social media, and text messaging. The use of text messaging to deliver cessation treatment is seen as a core feature of the teen site. As a result of significant gains in web and social media referrals and better search engine optimization, the Smokefree Teen website experienced a 143 percent increase in users and a 147 percent increase in sessions in fiscal year (FY) 2019 compared with the same time period in FY 2018.

<https://teen.smokefree.gov/>

[NCI]

Tobacco Regulatory Science Program

NIH coordinates several programs and activities to increase collaboration, coordination, and communication of tobacco and nicotine research among its institutes, centers, and offices (ICOs) and with partnering U.S. Department of Health and Human Services agencies. The Tobacco Regulatory Science Program is a trans-NIH partnership with the Food and Drug Administration (FDA) Center for Tobacco Products that supports a wide array of research to inform the FDA's tobacco regulatory priorities, including e-cigarettes. The centerpiece of the program, the Tobacco Centers of Regulatory Science funds research to better understand tobacco product usage patterns, how labeling and advertising affect tobacco use, and the impact of these products on health. The NIH ICOs also participate in several funding opportunity announcements (FOAs) that solicit research on tobacco products, including e-cigarettes, and support research project grants and career development and career transition awards that examine a breadth of topics relevant to e-cigarettes and youth, including basic science (e.g., chemistry and toxicity of vaping aerosols, flavorants, engineering of devices), behavioral and addiction science, and science to understand industry marketing, public health communications, and the potential impact of FDA regulatory actions.

<https://prevention.nih.gov/tobacco-regulatory-research>

<https://prevention.nih.gov/tobacco-regulatory-research/funded-research/funded-research-tobacco-centers-regulatory-science>

<https://prevention.nih.gov/funding/funding-opportunity-announcements#!/tool?terms=tobacco-regulatory-science>

[ODP, other ICOs]

Research on Fetal Alcohol Spectrum Disorders (FASD)

Research to improve the prevention, diagnosis, and treatment of FASD is a highly supported effort. For example, the Collaborative Initiative on Fetal Alcohol Spectrum Disorders is a research consortium established to address prevention of FASD, diagnosis of the full range of birth defects associated with prenatal alcohol exposure, and ameliorative interventions for affected individuals. Some supported studies examine how prenatal alcohol exposure may contribute to the etiology of chronic diseases and health conditions later in life, including the development of diseases not typically associated with FASD.

<https://cifasd.org/>

<https://grants.nih.gov/grants/guide/pa-files/PA-18-507.html>

[NIAAA]

College Alcohol Intervention Matrix (CollegeAIM)

CollegeAIM was developed to help college and university officials address alcohol misuse on their campuses. This user-friendly guide and website rates more than 60 evidence-based alcohol interventions in terms of effectiveness, costs, and other factors. *CollegeAIM* was revised in 2019 to reflect new research findings. Several additional interventions were added, and some interventions received updated ratings of effectiveness.

<https://www.collegedrinkingprevention.gov/CollegeAIM/>

[NIAAA]

Monitoring the Future (MTF)

Since 1975, the MTF survey has measured drug and alcohol use and related attitudes among adolescent students nationwide. Survey participants report their drug use behaviors across several time periods, including lifetime, past-year, past-month, and, for some substances, daily use. Overall, 42,531 students from 396 public and private schools participated in this year's MTF survey.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9979208&icde=46798750

[NIDA, University of Michigan]

Rural Families Affected by Opioid Use

Researchers are adapting and testing both the efficacy and the effectiveness of an online telehealth intervention—the Family Check-Up Online (FCU-Online) program—to improve parenting skills and subsequent early childhood behavior in a high-risk sample of opioid-using mothers. The FCU-Online program will be adapted to include content focused on early childhood parenting skills and family health routines for high-risk mothers and will be delivered to a study population of 300 children ages 2 to 5 and their opioid-using mothers in rural Oregon in a hybrid efficacy–effectiveness design. The study will significantly contribute to our understanding of effective parenting interventions during early childhood with high-risk, opioid-using mothers, to enhance long-term reductions in child problem behavior and ultimately reduce adult substance abuse.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9793742&icde=48156877
[NIDA]

Prevention of Opioid Use Disorder

Evidence suggests that homeless youth have the highest rates of opioid use among youth subgroups in the country. Resolving youth homelessness through housing and prevention services, often called “Housing First,” has great potential to reduce the likelihood for the development of an opioid use disorder, as well as other problem behaviors associated with living on the streets. However, only 20 percent to 30 percent of homeless youth sampled report having ever stayed at a crisis shelter, 9 percent report having ever accessed mental health services, and 15 percent report having ever received treatment for substance use disorder, indicating a need to reach and engage youth in services that are feasible and acceptable. The results of this study will provide essential information for researchers and providers on the efficacy of housing plus opioid and related risk prevention services in a randomized controlled trial on opioid use, how moderators affect response, and mechanisms underlying change.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9888864&icde=48156928
[NIDA]

Substance Use Disorder (SUD) Treatment for Youth in the Juvenile Justice System

Fewer than one-half of the youth in the juvenile justice system who meet the criteria for SUD have ever received treatment, and fewer than one-third of those youth received treatment while under community or correctional supervision. SUD during adolescence can lead to significantly longer periods of substance use, more severe offenses, and penetration in the justice system. Researchers will develop and test implementation strategies and associated measures to improve the continuum of substance abuse and HIV prevention and treatment services delivered to youth under juvenile justice supervision.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9923816&icde=48142314
[NIDA]

Risk for Opioid Abuse and Misuse in Adolescents Prescribed Opioids for Pain

Adolescents who are exposed to opioid medications through legitimate prescriptions are at higher risk for misuse after high school. However, there is a substantial gap in our knowledge of what factors might contribute to the development of misuse and related poor outcomes in these high-risk youth. This study will follow adolescents ages 14 to 18 who are exposed to opioids through medical prescriptions, to identify factors that convey risk for increasing opioid use and problematic use, inform adolescent models of opioid abuse, and inform the development of preventive interventions to modify risk in the medical setting.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9665719&icde=48142119
[NIDA]

Pediatric Critical Care and Emergency Care

Collaborative Pediatric Critical Care Research Network (CPCCRN)

Focusing on critically ill infants and children, this national resource aims to reduce morbidity and mortality from pediatric critical illness and injury by enhancing knowledge of the scientific bases of pediatric critical care practice. The CPCCRN conducts a wide range of research activities, reaching across traditional disciplinary lines and transcending customary thinking and organizational structures to achieve innovative research in the care of critically ill and injured children. Research topic areas include bereavement and grief, functional outcomes, intensive care clinical processes and protocols, and infection and sepsis.

<https://www.nichd.nih.gov/research/supported/cpcrm>

[NICHD]

End-of-Life and Palliative Needs of Adolescents and Young Adults with Serious Illnesses

The purpose of this funding opportunity announcement is to foster research on the unique perspectives, needs, wishes, and decision-making processes of adolescents and young adults with serious, advanced illnesses and research focused on specific end-of-life/palliative care models that support the physical, psychological, spiritual, and social needs of adolescents and young adults with serious illness and their families and caregivers.

<https://grants.nih.gov/grants/guide/pa-files/PA-19-136.html>

<https://grants.nih.gov/grants/guide/pa-files/PA-19-153.html>

[NCI]

Clinical Care, Outreach, and Services

Patient–Provider Collaboration in Symptom Self-Management and Clinical Care

The long-term goal of this proposed research is to empower patients and providers to leverage the unprecedented potential of self-tracking data in moving from population-level understanding to personalized insights in self-management and clinical care. The project develops a suite of open tools for end-to-end support of self-tracked health data, informed by and evaluated in participatory research with patients and providers in three symptom management contexts: irritable bowel syndrome, chronic headaches, and juvenile idiopathic arthritis. The project advances the mission of personal health libraries by developing self-tracking solutions that empower patients who want personalized insights from their data, developing design patterns for self-experimentation and patient–provider collaboration with self-tracking data, and developing open tools for extending these approaches to rapid innovation and research in additional self-tracking contexts.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9776614&icde=44771362

[NLM]

Linking the Provider Recommendation to Adolescent Human Papillomavirus (HPV) Vaccine Uptake

This funding opportunity announcement encourages research on how the healthcare delivery system enhances or inhibits the effectiveness of a provider’s recommendation of the adolescent HPV vaccine. Characteristics of the provider, parent/patient, and clinical setting can all affect whether a provider makes a recommendation and whether that recommendation results in uptake of the HPV vaccine. This research requires expertise in cancer prevention, adult and childhood behavior, immunization promotion, and healthcare delivery.

<https://grants.nih.gov/grants/guide/pa-files/PA-19-358.html>

<https://grants.nih.gov/grants/guide/pa-files/PA-19-359.html>

<https://grants.nih.gov/grants/guide/pa-files/PA-19-360.html>

[NCI]

Personal Health Record for Youth Emancipating from Foster Care

There are 427,000 children in the custody of child protective services (i.e., foster care) in the United States, and approximately 5,000 youths emancipate from foster care annually. Their healthcare outcomes

are generally poor, in part because of a lack of access to medical history. The proposed research will create and distribute a personal health record for foster youth, to be distributed at age 18 to improve their healthcare knowledge and utilization.

https://projectreporter.nih.gov/project_info_description.cfm?projectnumber=5R01LM012816-03

[NLM]

Pediatric Pharmacology

Obstetric-Fetal Pharmacology Research Centers (OPRC) Network

Many factors influence pharmacology during both normal and abnormal pregnancies. However, very little is known about the effects of these variables on drugs that are necessary for the health and well-being of pregnant women and their fetuses. The OPRC Network provides the expert infrastructure needed to test therapeutic drugs during pregnancy, allowing researchers to conduct safe, technically sophisticated, and complex studies that will help clinicians protect women's health, improve birth outcomes, and reduce infant mortality.

https://www.nichd.nih.gov/research/supported/opru_network

[NICHD]

Neuroscience and Novel Therapeutics Unit

The mission of the Neuroscience and Novel Therapeutics Unit is to leverage neuroscience and therapeutics to develop and test novel interventions. One area of research covered by the unit is irritability. Irritability is among the most common reasons why children and adolescents present for mental healthcare, and developing mechanism-based interventions for irritability is essential. Researchers are leveraging existing knowledge about the overlapping neural circuitry between irritability and motor inhibition to create a smartphone app that aims to probe motor inhibition and has the potential to extend understanding of irritability. This app will also collect real-time clinical and behavioral data in naturalistic settings, possibly eventually augmenting clinical assessment and care.

https://projectreporter.nih.gov/project_info_description.cfm?aid=10011380&icde=47941784&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=

<https://www.ncbi.nlm.nih.gov/pubmed/31373756>

<https://www.ncbi.nlm.nih.gov/pubmed/28482689>

<https://www.ncbi.nlm.nih.gov/pubmed/?term=29625429>

[NIMH]

Technology and Tools

Center for Translational Pediatric Research (CTPR)

The CTPR is a Center of Biomedical Research Excellence (COBRE) in Phase I supported by the Institutional Development Award (IDeA) Program. This COBRE is located at the Research Institute of Arkansas Children's Hospital, the state's only pediatric hospital, which provides a unique environment and clinical population in which to study pediatric diseases. By applying a systems biology approach to the study of pediatric diseases, the CTPR hopes to expand existing knowledge of pediatric disease development and contribute to new therapeutic targets. The center's long-term goal is to build an innovative, multidisciplinary pediatric research center that utilizes cutting-edge systems biology technologies and state-of-the-art translational research to study pediatric diseases.

<https://www.archildrens.org/research/research-programs-and-centers/translational-pediatric-research/translational-pediatric-research>

https://projectreporter.nih.gov/Reporter_Viewsh.cfm?sl=15E1CD084E8FC4D37598B8961CAA4A01A2FFCEB861BF

[NIGMS]

Supporting Pediatric Research on Outcomes and Utilization of Telehealth (SPROUT)–Clinical and Translational Science Awards (CTSA) Collaborative Telehealth Research Network

The SPROUT Collaborative was established in 2016, in collaboration with the American Academy of Pediatrics, to rigorously evaluate pediatric telehealth services through the development of multicenter research on telehealth implementation and practice and has grown rapidly to include 104 healthcare institutions across the country. The SPROUT–CTSA Collaborative Telehealth Research Network, awarded in April 2019, will enhance the existing infrastructure and expertise of SPROUT with the established research resources of the national CTSA consortium to develop, iteratively test and enhance, and disseminate an innovative model for clinical and translational telehealth research. Although there is a lot of anecdotal or small-scale evidence for the benefits of telehealth, including cost reduction, improved quality of care in some patient populations, and improved access to care for some rural and underserved populations, barriers to fully demonstrating the gains made via telehealth care delivery persist.

<https://mhealthintelligence.com/news/musc-to-create-a-national-pediatric-telehealth-research-network>

<https://web.musc.edu/about/leadership/institutional-offices/communications/pamr/news-releases/2019/prove-it-national-telehealth-research-network-greenlighted>

[NCATS]

Pediatric Genomic Data Inventory (PGDI)

Pediatric cancer is a genetic disease that can differ significantly from similar malignancies in an adult population. To fuel new discoveries and treatments specific to pediatric cancers, the NCI has developed a dynamic resource known as the PGDI to allow investigators to more easily locate genomic datasets. This resource lists known ongoing and completed sequencing projects of pediatric cancer cohorts from the United States and other countries, along with some basic details and reference metadata. This inventory is an evolving list that will be updated continually as new information is deposited by the research community.

<https://ocg.cancer.gov/programs/target/pgdi/overview>

[NCI]

Global Pediatric Health

Domestic and International Pediatric and Maternal HIV Clinical Studies Network

Currently composed of 15 domestic sites in 11 states and territories and 14 international sites in Argentina, Brazil, Kenya, Tanzania, and Thailand, plus a data coordinating center, this network conducts trials related to preventing and treating HIV infection and its complications in newborns, infants, children, adolescents, and pregnant women. Recently, network researchers have broadened their focus to include tuberculosis, malaria, hepatitis, and investigation of vaccines that might prevent HIV-related or other high-priority infectious diseases in children, adolescents, and pregnant women, in addition to treatment of HIV infection. This network has collaborated closely with the International Pediatric Maternal Adolescent AIDS Clinical Trials (IMPAACT) Network, which has made it possible to conduct an expanded clinical trial portfolio advancing pediatric HIV/AIDS clinical research.

<https://www.nichd.nih.gov/research/supported/Pages/pphsn.aspx>

[NICHD]

Global Network for Women’s and Children’s Health Research

The Global Network supports and conducts clinical trials in resource-limited countries by pairing international and U.S. researchers, with the goal of evaluating low-cost, sustainable interventions to improve maternal and child health while building local research capacity and infrastructure. Today the Global Network focuses on community-based common protocols, conducted at three or more sites, that address major maternal and newborn health challenges, with the goal of evaluating low-cost, sustainable interventions to improve maternal and child health. This unique position allows scientists to identify gaps between science and practice and disseminate the research findings to inform local and national health

policy. Each study examines either a novel evidence-based treatment or an innovative use of a proven treatment to improve the health, well-being, and survival of pregnant women and infants.

<https://www.nichd.nih.gov/research/supported/Pages/globalnetwork.aspx>

[NICHD]

Pediatric Research at the NIH Clinical Center

The NIH Clinical Center provides patient care, services, training, and the environment in which NIH clinician-scientists creatively translate emerging knowledge into better understanding, detection, treatment, and prevention of human diseases. In fiscal year (FY) 2019, 3,157 children on 335 research protocols were treated at the Clinical Center. This included 313 patients having a combined 4,436 inpatient hospital days, an increase of 12 percent in inpatient days. Overall, 13 percent of Clinical Center patients were under age 18. Natural history studies, often in patients with rare diseases, make up about half of the pediatric clinical research conducted at the Clinical Center. Understanding the basis for rare diseases often leads to new approaches to common problems. Most of the other clinical research studies are the early Phase I and II trials that are the first studies of new treatments and therapies.

<https://www.cc.nih.gov/ccc/pedweb/pedsinfec.html>

[CC]

Other Cross-Cutting Areas

Pediatric Pharmacology and the Best Pharmaceuticals for Children Act (BPCA)

Testing the safety and efficacy of drugs in children presents significant scientific, clinical, ethical, technical, and logistical challenges. Over the years, several practical challenges have discouraged the testing of drugs in pediatric populations. These challenges include lack of incentives for companies to study drugs in neonates, infants, and children; lack of technology to monitor patients and assay very small amounts of blood; and lack of a suitable infrastructure for conducting pediatric pharmacology drug trials. As a result, most drugs used in children today are not approved for use in children and are therefore used without adequate understanding of appropriate dose, safety, or efficacy. The BPCA established a process for NIH, the Food and Drug Administration (FDA), and pediatric experts to identify drugs that are used in pediatric care and for which studies would have public health benefit. If industry does not fund studies on drugs prioritized under the BPCA, NIH institutes, centers, and offices (ICOs) support research to address the need.

<https://bpca.nichd.nih.gov/>

[NICHD, other NIH ICOs]

Specialized Centers in Research in Pediatric Developmental Pharmacology (RPDP)

The RPDP's overall goals are to investigate the fundamental mechanisms of changes in drug disposition and response over the course of human development from birth through adolescence, provide an arena for multidisciplinary interactions between basic and clinical scientists who are interested in establishing high-quality translational research programs in pediatric pharmacology, serve as national resource for training and career development of new scientists electing to pursue careers in translational research in high-priority areas of pediatric developmental pharmacology, and facilitate important community outreach and education efforts to increase awareness and convey the importance and implications of the research activities to the general public. This program is designed to establish predictive nonclinical models, including animal studies; cell-, tissue-, and organ-based systems; computational and systems modeling; and integration of signals and information from multiple systems to evaluate response- and age-specific toxicity, particularly neurologic and behavioral effects. The RPDP performs nonclinical and clinical research to understand mechanisms of age- and development-related changes in metabolism and response to medicinal products, and it develops outcome and assessment measures that are age appropriate to determine response or toxicity. The Food and Drug Administration (FDA) is working closely with NIH to maximize the success of this important program.

<https://www.nichd.nih.gov/research/supported/scrpdp>
[NICHD]

Clinical and Translational Science Awards (CTSA)

The CTSA Program supports an innovative national network of medical research institutions that work together to improve the quality and efficiency of all phases of translational research, including clinical trials, and to foster innovation in research training, new methodologies, and research participant engagement. Based on the recommendations of the Institute of Medicine, the CTSA Program incorporated the strategic goal of promoting the integration of special and underserved populations in translational research across the lifespan, from conception to mature adulthood. This recommendation has been operationalized as the CTSA Consortium Lifespan Domain Task Force, which includes subject matter experts from nearly all CTSA Program hubs, a significant number of whom are pediatric or child health clinical scientists. Currently, at least eight CTSA Program hubs are led by scientists or co-principal investigators who are also pediatricians, and more than 50 of the hubs include children's hospitals conducting pediatric research as partners in their proposals. CTSA Program hubs fund pilot awards that involve many pediatric studies, including scientific areas and conditions such as peanut allergy, Niemann-Pick type C1 disease, Fragile X syndrome, rare muscle diseases, cystic fibrosis, and Charcot-Marie-Tooth disease.

<https://ncats.nih.gov/ctsa>
[NCATS]

Research, Training, Career Development, and Loan Repayment Programs

Research Career Development Support for Child Neurologists

The Child Neurologist Career Development Program (CNCDDP) supports child neurologists who have made a commitment to independent research careers. This single national program is currently based at the Hugo W. Moser Research Institute, Kennedy Krieger Institute, and the Johns Hopkins University School of Medicine. The CNCDDP provides up to 3 years of support to successful applicants to the program to provide them with the knowledge, tools, and research experience that will enable them to develop a research project for which they can obtain subsequent funding.

<https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-16-003.html>
[NINDS]

Training the Science of Child Mental Health Treatment

This unique training program aims to train researchers in translational intervention science for child mental disorders and prepare the trainees to become independent transdisciplinary researchers. Trainees will identify specific areas of mental illness and choose research strategies that advance such research at a variety of levels—treatment mechanisms, biomarkers of outcomes, efficacy study methodology, and implementation science.

https://projectreporter.nih.gov/project_info_description.cfm?aid=9280686
[NIMH]

Maternal-Fetal Medicine Fellowship Training Program

The goal of the fellowship is to train individuals to provide specialized patient care in maternal-fetal medicine, as well as to prepare candidates for a career in academic medicine as physician scientists. It is a 3-year training program, as required by the American Board of Obstetrics and Gynecology. The clinical rotations include maternal-fetal medicine service, obstetrical ultrasound, reproductive genetics, fetal echocardiography, anesthesia/intensive care unit, and elective rotations. The program includes 18 months dedicated to laboratory and clinical research. The fellowship emphasizes a multidisciplinary approach to complications of pregnancy. There is a strong emphasis on the prenatal diagnosis of congenital anomalies

with ultrasound and on the performance of invasive procedures such as amniocentesis, chorionic villus sampling, and intravascular transfusion.

<https://www.nichd.nih.gov/about/org/dir/osd/tp/mfmftp>

[NICHD]

Pediatric Endocrinology Inter-Institute Training Program

The Fellowship in Pediatric Endocrinology is a 3-year, Accreditation Council for Graduate Medical Education–accredited program. Applicants must have completed a residency in pediatrics or medicine/pediatrics and be eligible to sit for the American Board of Pediatrics certification examination. Three fellows are accepted per year. The fellowship is designed to provide clinical and research exposure that permits the development of academic pediatric endocrinologists with experience in both clinical and bench research.

<https://science.nichd.nih.gov/confluence/display/pe>

[NICHD]

Fellowship in Pediatric Hematology/Oncology

The Pediatric Hematology/Oncology Fellowship is a joint program of the NIH Pediatric Oncology Branch and the Johns Hopkins University. Fellows receive combined clinical training during their first year at both the Johns Hopkins Hospital and the NIH Clinical Center, with exposure to clinical issues in pediatric hematology/oncology. The variety of patients across institutions gives trainees unique exposure to a wide range of diagnoses and management strategies. Fellows also have access to a variety of basic and translational research opportunities at both campuses during subsequent years of the program.

<https://ccr.cancer.gov/Pediatric-Oncology-Branch/training-fellowship>

[NCI, CC]

Pediatric Scientist Development Program (PSDP)

The PSDP provides scientific research experience (particularly in basic science areas) for pediatricians wishing to pursue careers in academic medicine. This program has provided research training for more than 175 scholars across the country. Many PSDP scholars have gone on to strong research careers and have received subsequent NIH funding in pediatric research.

<https://amspdc-psdp.org/>

[NICHD]

Child Health Research Career Development Award Program

This program was created to fill the gap in training for junior faculty who intend to devote their careers to academic pediatrics. The program provides funding for sustained mentoring and laboratory-based training and offers the vital foundation to compete for grant funding.

<https://www.nichd.nih.gov/research/supported/Pages/chrcda.aspx>

<https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-18-011.html>

[NICHD]

Pediatric Loan Repayment Program

The NIH's Loan Repayment Program is designed to further recruitment and retention of highly qualified health professionals in careers in scientific research. Within the overall NIH Loan Repayment Program, there is a special program to promote pediatric research. Under the program, NIH repays a portion of the educational loan debt incurred to pay for the researcher's undergraduate, graduate, and/or health professional school educational expenses.

<https://www.lrp.nih.gov/eligibility-programs>

[All NIH ICOs]

ADDITIONAL PEDIATRIC COLLABORATIONS

Pediatric research at NIH involves various collaborations between NIH institutes, centers, and offices (ICOs) and other Department of Health and Human Services (HHS) and federal agencies. During fiscal year (FY) 2019, NIH spearheaded and participated in a broad array of workshops, committees, working groups, and task forces encompassing many aspects of pediatric health. For example, the Trans-NIH Fragile X Coordinating Committee (including representatives from the NICHD, NCATS, NIA, NIDDK, NIGMS, NIMH, NINDS, NIH OD, CDC, HRSA, and Department of Defense [DOD], as well as academic subject matter experts) worked with external stakeholders to develop the new [NIH Strategic Plan for Research on *FMRI*-Associated Conditions](#) to improve the health of individuals with *FMRI*-associated conditions, which are linked to intellectual and developmental disabilities. A selection of additional NIH-supported collaborative efforts for pediatric populations follows.

Several NIH collaborations are also devoted to understanding *genetic and developmental disorders*. For example, the NICHD, NCI, NEI, NHLBI, NHGRI, NIA, NIAID, NIAMS, NIDCD, NIDCR, NIEHS, NIGMS, NIMH, NIMHD, NINDS, NINR, NCATS, and NCCIH all participate in the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome) Initiative, which was launched in 2018 to expand research on Down syndrome and associated conditions like autism and diabetes. The Federal Interagency Workgroup on Autism Spectrum Disorders (FIWA) is composed of representatives from the NIMH, NICHD, ACF, AHRQ, CDC, CMS, HRSA, IHS, and SAMHSA to coordinate research, services, and support activities related to autism spectrum disorder.

There are numerous trans-NIH collaborations that enhance our understanding of other *diseases and conditions* that affect pediatric populations. NIH ICOs (the FIC, NIAID, NICHD, NIMH, and OAR), the OGAC, the CDC, and the USAID are members of the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA), which facilitates collaboration and communication to address implementation challenges related to prevention, screening and treatment of HIV in adolescents. The NHGRI, NINDS, NCATS, NHLBI, NIGMS, OD, NICHD, NIAID, NIDDK, NINR, NCI, NIMH, and the NIH Common Fund collaborate to manage the Undiagnosed Diseases Network (UDN), a research study funded by the Common Fund and the NHGRI to improve and accelerate the diagnosis of rare and undiagnosed conditions. The Common Fund also supports the Gabriella Miller Kids First Pediatric Research Program (Working Group members include the NICHD, NCI, NINDS, NIEHS, NIDA, NIDDK, NIDCR, NIAMS, (NIAAA), NHGRI, NHLBI, NEI, (ORIP and CDC) to foster collaborative research to uncover the causes of childhood cancers and structural birth defects and support data sharing within the pediatric research community.

Development, assessment, and optimization of pediatric *drugs and devices* are the subjects of many collaborative activities at NIH. The NICHD, NHLBI, and NCI collaborate with the FDA for the Best Pharmaceuticals for Children Act (BPCA) Working Group, which provides safety oversight for the development and testing of pediatric medications. The NICHD and FDA work with the American Academy of Pediatrics (AAP) Committee on Drugs to review all aspects of pediatric pharmacology. The NICHD and FDA also participate in the Pediatric Device Consortia Program to facilitate the development, production, and distribution of pediatric medical devices through funding of nonprofit consortia.

NIH engages in additional collaborations that affect *children's health*. The NIH Pediatric Research Consortium (N-PerC) is a trans-NIH initiative that was established in 2018 to harmonize pediatric research, resources, and training opportunities across all 27 NIH ICOs. The NICHD collaborates with the CDC, HRSA, IHS, and ACF on a range of activities for the Federal Sudden Unexpected/Unexplained Infant Death (SUID)/Sudden Infant Death Syndrome (SIDS) Workgroup to reduce and eliminate SIDS and SUID, including the elimination of racial, ethnic, and socioeconomic disparities. The NICHD, CDC,

HRSA, SAMHSA, and DOD serve on the Collaborative on Healthy Parenting in Primary Care, which supports the integration of effective programs that promote healthy parenting into primary care settings in order to achieve optimal health for children.

NIH collaborations also address multiple aspects of *obesity* among children and adolescents, as well as broader areas of *nutrition* for pregnant women and children. The NIDDK, NCI, NICHD, and NHLBI collaborate with the USDA, CDC, HRSA, FDA, and HHS OS on the Pregnancy and Birth to 24 Months project, which conducts dietary reviews, makes dietary recommendations, and examines topics of public health importance for pregnant women, infants, and toddlers less than 2 years old. The Joint Agency Nutrition Working Group supports dietary supplementation and nutritional research for pregnant women and children (current collaborators are the NICHD, NIDDK, ODS, and FDA). The NIH Childhood Obesity Working Group (consisting of the NICHD, NHLBI, NIDDK, and NIEHS) brings scientists together to coordinate research and consider cross-cutting initiatives on childhood obesity. The National Collaborative on Childhood Obesity Research (NCCOR), a collaboration between the CDC, the USDA, NIH ICOs (the NCI, NHLBI, NICHD, NIDDK, OBSSR, and ODP), and private foundations, speeds progress in reducing childhood obesity through surveillance, policies, research, and interventions.

Environmental factors and conditions are the subject of several NIH collaborations. The OD, NICHD, and NIEHS collaborate on the trans-NIH group within the Environmental influences on Child Health Outcomes (ECHO) program, whose goal is to understand the effects of a broad range of early environmental influences on child health and development. The President's Task Force on Environmental Health and Safety Risks to Children coordinates the federal government's effort to explore, understand, and improve children's environmental health. Its Federal Action Plan to Reduce Childhood Lead Exposure helps federal agencies work strategically and collaboratively to reduce exposure to lead (the NIEHS, NHLBI, ODP, NICHD, CDC, ACF, FDA, HRSA, Office of the Assistant Secretary for Health [OASH], Consumer Product Safety Commission [CPSC], Council of Economic Advisers [CEA], Council on Environmental Quality [CEQ], USDA, Department of Commerce [DOC], Department of Education [DoED], Department of Energy [DOE], Department of Homeland Security [DHS], Department of Housing and Urban Development [HUD], Department of Justice [DOJ], Department of Labor [DOL], Department of Transportation [DOT], Environmental Protection Agency [EPA], National Economic Council [NEC], Office of Management and Budget [OMB], and Office of Science and Technology Policy [OSTP] all participate). The Children's HHS Interagency Leadership on Disasters (CHILD) Working Group identifies and integrates activities related to the needs of children across governmental disaster planning and determines how best to deliver care to children affected by disasters. The CHILD Working Group involves the efforts of NIH ICOs (the NIAID, NICHD, NIDA, NIMH, and NIEHS), the ACF, the CDC, the HRSA, the SAMHSA, and the Assistant Secretary for Preparedness and Response.

NIH also works with other federal agencies to address multiple forms of childhood *violence and injury*. The Federal Interagency Workgroup on Child Abuse and Neglect brings together numerous federal entities to provide a forum for discussion of ideas and funding for child maltreatment-related activities (members include the NIAAA, NICHD, NIDA, NIMH, OBSSR, ACF, USDA, DOD, DoED, HUD, DOI, DOJ, Department of State [DOS], USAID, and U.S. Interagency Council on Homelessness [USICH]). The Federal Partners in Bullying Prevention includes the NIAAA, NICHD, NIDA, OBSSR, ACF, CDC, HRSA, IHS, SAMHSA, DOD, Department of the Interior (DOI), DOJ, DoED, Federal Trade Commission (FTC), USDA, and White House Initiative on Asian Americans and Pacific Islanders (WHIAAPI) to provide information on identifying, preventing, and responding to bullying and cyberbullying. Members from the NICHD, ACF, HRSA, and IHS serve on the American Academy of Pediatrics Council on Injury, Violence, and Poison Prevention, which aims to address all facets of injury prevention policy, programs, advocacy, and education of general pediatricians, pediatric subspecialists, and families.

APPENDIX

- Table 1: All National Institutes of Health (NIH) Pediatric Research, Fiscal Year (FY) 2019
- Table 2: National Institutes of Health (NIH) Funding Opportunity Announcements That Solicited Applications for Pediatric Research, Released in Fiscal Year (FY) 2019
- Table 3: Acronyms for NIH Institutes, Centers, and Offices and Other Federal Agencies Referred to in This Report

Table 1: All NIH Pediatric Research, FY 2019

The totals below were derived from the NIH Research, Condition, and Disease Categorization (RCDC) system, which uses sophisticated text data mining (categorizing and clustering using individual words and multiword phrases) in conjunction with NIH-wide definitions for matching extramural and intramural research grants and projects to categories. The RCDC use of data mining is designed to improve consistency and eliminate wide variability in defining the research categories reported. The reported levels represent NIH’s best estimates based on the category definitions. NIH does not expressly budget by category. The annual estimates reflect amounts that change as a result of science, actual research projects funded, and the NIH budget. A list of FY 2019 NIH-funded grants and projects in pediatric research is available at

https://report.nih.gov/categorical_spending_project_listing.aspx?FY=2019&ARRA=N&DCat=Pediatric.

The term “Common Fund” refers to research funded through the Office of Strategic Coordination, Office of the Director (OD), NIH, to address key scientific issues that no one institute, center, or office (ICO) is positioned to address alone.

| NIH ICO | Fiscal Year 2019 |
|--------------------|-------------------------|
| Common Fund | \$40,249,749 |
| FIC | \$8,515,872 |
| NCATS | \$68,006,147 |
| NCCIH | \$6,857,524 |
| NCI | \$519,343,181 |
| NEI | \$81,492,102 |
| NHGRI | \$70,777,562 |
| NHLBI | \$439,431,168 |
| NIA | \$42,920,439 |
| NIAAA | \$121,344,534 |
| NIAID | \$476,618,880 |
| NIAMS | \$82,542,388 |
| NIBIB | \$21,505,782 |
| NICHD | \$865,604,135 |
| NIDA | \$230,933,490 |
| NIDCD | \$88,616,603 |
| NIDCR | \$115,597,607 |
| NIDDK | \$286,395,824 |
| NIEHS | \$134,010,429 |
| NIGMS | \$137,689,576 |
| NIMH | \$442,958,607 |
| NIMHD | \$66,081,017 |
| NINDS | \$267,338,290 |
| NINR | \$32,723,760 |
| NLM | \$4,238,772 |
| OD | \$223,866,982 |
| Type 1 Diabetes | \$46,520,405 |
| Grand Total | \$4,922,180,825 |

Table 2: NIH Funding Opportunity Announcements That Solicited Applications for Pediatric Research, Published in FY 2019

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| PA-19-200 | NCCIH | R01 | Mechanisms Underlying the Contribution of Sleep Disturbances to Pain (R01 Clinical Trial Optional) |
| PA-19-201 | NCCIH | R21 | Mechanisms Underlying the Contribution of Sleep Disturbances to Pain (R21 Clinical Trial Optional) |
| PAR-18-950 | NICHD | X02 | Pre-application: Opportunities for Collaborative Research at the NIH Clinical Center (X02 Clinical Trial Optional) |
| PAR-18-951 | NICHD | U01 | Opportunities for Collaborative Research at the NIH Clinical Center (U01 Clinical Trial Optional) |
| PAR-19-039 | NINDS | U01 | Countermeasures Against Chemical Threats (CounterACT): Identification of Therapeutic Lead Compounds (U01 Clinical Trial Not Allowed) |
| PAR-19-040 | NINDS | U01 | Countermeasures Against Chemical Threats (CounterACT): Optimization of Therapeutic Lead Compounds (U01 Clinical Trial Optional) |
| PAR-19-064 | NIDA | R21 | Mechanism for Time-Sensitive Drug Abuse Research (R21 Clinical Trial Optional) |
| PAR-19-069 | NICHD | R03 | Small Research Grants for Analyses of Data for the Gabriella Miller Kids First Data Resource (R03 - Clinical Trial Not Allowed) |
| PAR-19-104 | Common Fund | X01 | Discovery of the Genetic Basis of Childhood Cancers and of Structural Birth Defects: Gabriella Miller Kids First Pediatric Research Program (X01 Clinical Trial Not Allowed) |
| PAR-19-136 | NINR | R01 | End-of-Life and Palliative Needs of Adolescents and Young Adults (AYA) with Serious Illnesses (R01 Clinical Trial Optional) |
| PAR-19-153 | NINR | R21 | End-of-Life and Palliative Needs of Adolescents and Young Adults (AYA) with Serious Illnesses (R21 Clinical Trial Optional) |
| PAR-19-162 | NIDA | R01 | Accelerating the Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R01-Clinical Trial Not Allowed) |
| PAR-19-163 | NIDA | R21 | Accelerating the Pace of Child Health Research Using Existing Data from the Adolescent Brain Cognitive Development (ABCD) Study (R21-Clinical Trial Not Allowed) |
| PAR-19-209 | NIAID | R01 | Next Generation Multipurpose Prevention Technologies (NGM) (R01 Clinical Trial Optional) |
| PAR-19-235 | NIMH | R34 | Reducing the Duration of Untreated Psychosis in the United States (R34 Clinical Trial Required) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| PAR-19-236 | NIMH | R01 | Reducing the Duration of Untreated Psychosis in the United States (R01 Clinical Trial Required) |
| PAR-19-267 | ORIP | K01 | HIV/AIDS Scholars Using Nonhuman Primate (NHP) Models Program (K01 Independent Clinical Trial Not Allowed) |
| PAR-19-274 | NCI | R01 | Dissemination and Implementation Research in Health (R01 Clinical Trial Optional) |
| PAR-19-276 | NCI | R03 | Dissemination and Implementation Research in Health (R03 Clinical Trial Not Allowed) |
| PAR-19-307 | NIAID | R01 | Mechanisms of Mycobacterial-Induced Immunity in HIV-Infected and/or Uninfected Individuals to Inform Innovative Tuberculosis Vaccine Design (R01 Clinical Trial Not Allowed) |
| PAR-19-315 | NINDS | R61/R33 | Discovery of Biomarkers and Biomarker Signatures for Neurological and Neuromuscular Disorders (R61/R33 Clinical Trial Optional) |
| PAR-19-326 | FIC | R21 | Reducing Stigma to Improve HIV/AIDS Prevention, Treatment and Care in Low- and Middle-Income Countries (R21 Clinical Trial Optional) |
| PAR-19-346 | NIAID | R21 | Investigations on Primary Immunodeficiency Diseases/Inborn Errors of Immunity (R21 Clinical Trial Not Allowed) |
| PAR-19-347 | NIAID | R03 | Investigations on Primary Immunodeficiency Diseases/Inborn Errors of Immunity (R03 Clinical Trial Not Allowed) |
| PAR-19-358 | NCI | R21 | Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (R21 Clinical Trial Optional) |
| PAR-19-359 | NCI | R03 | Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (R03 Clinical Trial Optional) |
| PAR-19-360 | NCI | R01 | Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (R01 Clinical Trial Optional) |
| PAR-19-373 | OPPNET | R01 | Research on biopsychosocial factors of social connectedness and isolation on health, wellbeing, illness, and recovery (R01 Clinical Trials Not Allowed) |
| PAR-19-375 | NICHD | R03 | Small Research Grants for Analyses of Gabriella Miller Kids First Pediatric Research Data (R03 Clinical Trial Not Allowed) |
| PAR-19-376 | FIC | R21/R33 | Mobile Health: Technology and Outcomes in Low and Middle Income Countries (R21/R33 - Clinical Trial Optional) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|---|
| PAR-19-378 | NIDDK | F31 | Bioinformatics Interdisciplinary Predoctoral Fellowship in Diabetes, Endocrinology and Metabolic Diseases (F31) |
| PAR-19-379 | NIDDK | F31 | Bioinformatics Interdisciplinary Postdoctoral Fellowship in Diabetes, Endocrinology and Metabolic Diseases (F32) |
| PAR-19-384 | OPPNET | R01 | Research on biopsychosocial factors of social connectedness and isolation on health, wellbeing, illness, and recovery (R01 Basic Experimental Studies with Humans Required) |
| PAR-19-385 | NIEHS | R21 | Environmental Risks for Psychiatric Disorders: Biological Basis of Pathophysiology (R21 Clinical Trial Not Allowed) |
| PAR-19-386 | NIEHS | R01 | Environmental Risks for Psychiatric Disorders: Biological Basis of Pathophysiology (R01 Clinical Trial Not Allowed) |
| RFA-AA-19-001 | NIAAA | U10 | Collaborative Study on the Genetics of Alcoholism (COGA) (Clinical Trial Not Allowed U10) |
| RFA-AA-20-003 | NIAAA | U01 | Consortium on the Neurobiology of Adolescent Drinking in Adulthood (NADIA) Research Projects (Collaborative U01 - Clinical Trial Not Allowed) |
| RFA-AA-20-004 | NIAAA | U24 | Consortium on the Neurobiology of Adolescent Drinking in Adulthood (NADIA) Administrative Resource (Collaborative U24 - Clinical Trial Not Allowed) |
| RFA-AA-20-005 | NIAAA | U24 | Consortium on the Neurobiology of Adolescent Drinking in Adulthood (NADIA) Research Resource (Collaborative U24 - Clinical Trial Not Allowed) |
| RFA-AI-18-057 | NIAID | R61/R33 | Long-acting Drug Delivery Systems for ART Optimization in HIV-1 Infected Children (R61/R33 Clinical Trial Not Allowed) |
| RFA-AI-19-003 | NIAID | UM1 | HIV/AIDS Adult Therapeutics Clinical Trials Network Leadership and Operations Center (UM1 Clinical Trial Required) |
| RFA-AI-19-004 | NIAID | UM1 | HIV/AIDS Maternal, Adolescent and Pediatric Therapeutics Clinical Trials Network Leadership and Operations Center (UM1 Clinical Trial Required) |
| RFA-AI-19-005 | NIAID | UM1 | HIV Prevention Clinical Trials Network Leadership and Operations Center (UM1 Clinical Trial Required) |
| RFA-AI-19-006 | NIAID | UM1 | HIV Vaccines Clinical Trials Network Leadership and Operations Center (UM1 Clinical Trial Required) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|---|
| RFA-AI-19-014 | NIAID | UM1 | Atopic Dermatitis Research Network Leadership Center (UM1) Clinical Trial Required |
| RFA-AI-19-015 | NIAID | U01 | Atopic Dermatitis Research Network -Clinical Research Centers (U01 Clinical Trial Optional) |
| RFA-AI-19-017 | NIAID | U24 | Development of Sample Sparing Assays for Monitoring Immune Responses (U24 Clinical Trial Not Allowed) |
| RFA-AI-19-022 | NIAID | R01 | U.S.-South Africa Program for Collaborative Biomedical Research - Phase 2 (HIV/AIDS) (R01 Clinical Trial Optional) |
| RFA-AI-19-023 | NIAID | U01 | U.S.-South Africa Program for Collaborative Biomedical Research - Phase 2 (HIV/AIDS) (U01 Clinical Trial Optional) |
| RFA-AI-19-024 | NIAID | R01 | U.S.-South Africa Program for Collaborative Biomedical Research - Phase 2 (Infectious Diseases) (R01 Clinical Trial Optional) |
| RFA-AI-19-025 | NIAID | U01 | U.S.-South Africa Program for Collaborative Biomedical Research - Phase 2 (Infectious Diseases) (U01 Clinical Trial Optional) |
| RFA-AI-19-030 | NIAID | U01 | Feasibility of Novel Diagnostics for TB in Endemic Countries (FEND for TB) (U01 Clinical Trial Not Allowed) |
| RFA-AI-19-036 | NIAID | R01 | Advancing Biomarker Discovery and Novel Point-of-Care Diagnostics for Active TB Disease Detection in HIV-1 Infected and Exposed Children (R01 Clinical Trial Optional) |
| RFA-AI-19-045 | NIAID | UM1 | HIV/AIDS Clinical Trials Units (UM1 Clinical Trial Required) |
| RFA-AR-19-026 | NIAMS | U19 | HEAL Initiative: Back Pain Consortium (BACPAC) Research Program: Mechanistic Research Centers (U19 Clinical Trial Optional) |
| RFA-AR-19-027 | NIAMS | U24 | HEAL Initiative: Back Pain Consortium (BACPAC) Research Program Data Integration, Algorithm Development and Operations Management Center (U24 Clinical Trial Not Allowed) |
| RFA-AR-19-028 | NIAMS | UH2/UH3 | HEAL Initiative: Back Pain Consortium (BACPAC) Research Program Technology Research Sites (UH2/UH3 Clinical Trial Optional) |
| RFA-AR-19-029 | NIAMS | UG3/UH3 | HEAL Initiative: Back Pain Consortium (BACPAC) Research Program: Phase 2 Clinical Trials (UG3/UH3 Clinical Trial Required) |
| RFA-AT-19-004 | NCCIH | UG3/UH3 | HEAL Initiative: Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM) (UG3/UH3, Clinical Trials Optional) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|---|
| RFA-AT-19-006 | NCCIH | R61/R33 | HEAL Initiative: Behavioral Research to Improve MAT: Behavioral and Social Interventions to Improve Adherence to Medication Assisted Treatment for Opioid Use Disorders (R61/R33 Clinical Trial Optional) |
| RFA-CA-19-033 | NCI | U01 | Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors (U01 Clinical Trial Required) |
| RFA-CA-19-035 | NCI | R01 | Optimizing the Management and Outcomes for Cancer Survivors Transitioning to Follow-up Care (R01 Clinical Trial Required) |
| RFA-CA-19-045 | NCI | U2C | Participant Engagement and Cancer Genome Sequencing (PE-CGS): Research Centers (U2C Clinical Trial Optional) |
| RFA-CA-19-056 | NCI | UM1 | Limited Competition: AIDS Malignancy Consortium (AMC) (UM1 Clinical Trials Required) |
| RFA-CA-19-059 | NCI | UM1 | Limited Competition: Pediatric Brain Tumor Consortium (UM1 Clinical Trials Required) |
| RFA-DA-19-019 | NIDA | R43/R44 | HEAL Initiative: Americas Startups and Small Businesses Build Technologies to Stop the Opioid Epidemic (R43/R44 - Clinical Trial Optional) |
| RFA-DA-19-020 | NIDA | R41/R42 | HEAL Initiative: Americas Startups and Small Businesses Build Technologies to Stop the Opioid Epidemic (R41/R42 - Clinical Trial Optional) |
| RFA-DA-19-025 | NIDA | UG1 | HEAL Initiative: Justice Community Opioid Innovation Network (JCOIN) Clinical Research Centers (UG1 Clinical Trial Optional) |
| RFA-DA-19-029 | NIDA | R34 | HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (Collaborative R34 Clinical Trial Not Allowed) |
| RFA-DA-19-034 | NIDA | U24 | HEAL Initiative: Coordinating Center to Support NIDA Preventing Opioid Use Disorder in Older Adolescents and Young Adults (ages 16–30) Initiative (U24 Clinical Trial Not Allowed) |
| RFA-DA-19-035 | NIDA | UG3/UH3 | HEAL Initiative: Preventing Opioid Use Disorder in Older Adolescents and Young Adults (ages 16–30) (UG3/UH3 Clinical Trial Required) |
| RFA-DA-19-036 | NIDA | R34 | HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (R34-Clinical Trial Not Allowed) |
| RFA-DA-20-001 | NIDA | R25 | Workshops on the Use of Adolescent Brain Cognitive Development (ABCD) Data (R25 Clinical Trial Not Allowed) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|---|
| RFA-DA-20-002 | NIDA | U01 | Limited Competition for Adolescent Brain Cognitive Development (ABCD) Study - Linked Research Project Sites (Collaborative U01 Clinical Trial Not Allowed) |
| RFA-DA-20-003 | NIDA | U24 | Limited Competition for Adolescent Brain Cognitive Development (ABCD) Study - Data Analysis, Informatics and Resource Center (U24 Clinical Trial Not Allowed) |
| RFA-DA-20-004 | NIDA | U24 | Limited Competition for Adolescent Brain Cognitive Development (ABCD) Study - Coordinating Center (U24 Clinical Trial Not Allowed) |
| RFA-DA-20-016 | NIDA | U01 | National Drug Early Warning System Coordinating Center (U01 Clinical Trial Optional) |
| RFA-DA-20-024 | NIDA | UG1 | The National Drug Abuse Treatment Clinical Trials Network (UG1 Clinical Trial Required) |
| RFA-DK-18-007 | NIDDK | U34 | Establishing a Cohort to Clarify Risk and Protective Factors for Neurocognitive Complications of Pediatric Type 1 Diabetes (T1D) - Planning Cooperative Agreements (U34 Clinical Trial Not Allowed) |
| RFA-DK-18-008 | NIDDK | U01 | Type 1 Diabetes TrialNet Clinical Network Hub (U01 Clinical Trial Not Allowed) |
| RFA-DK-18-018 | NIDDK | U01 | Understanding the Glycemic Profile of Pregnancy - Clinical Centers (U01 Clinical Trial Not Allowed) |
| RFA-DK-18-019 | NIDDK | U01 | Understanding the Glycemic Profile of Pregnancy - Biostatistics Research Center (U01 Clinical Trial Not Allowed) |
| RFA-DK-18-509 | NIDDK | U01 | Limited Competition for the Continuation of the Coordinating Center for Type 1 Diabetes TrialNet (U01 Clinical Trial Required) |
| RFA-DK-18-512 | NIDDK | U01 | Limited Competition: Follow-up on Subjects, Integrative Data Analysis and Measurement of Viral Antibodies in The Environmental Determinants of Diabetes in The Young Study (TEDDY) (U01 Clinical Trial Not Allowed) |
| RFA-DK-19-004 | NIDDK | P30 | Silvio O. Conte Digestive Diseases Research Core Centers (P30 Clinical Trial Optional) |
| RFA-DK-19-009 | NIDDK | U01 | Continuation of the Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer Clinical Centers (CPDPC-CCs) (U01 Clinical Trial Optional) |
| RFA-DK-19-014 | NIDDK | DP1 | Catalyst Award In Diabetes, Endocrinology and Metabolic Diseases (DP1 Clinical Trial Not Allowed) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| RFA-DK-19-015 | NIDDK | U01 | Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium Clinical Research Centers (U01 Clinical Trial Optional) |
| RFA-DK-19-016 | NIDDK | U24 | Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium Scientific and Data Coordinating Center (U24 Clinical Trial Optional) |
| RFA-DK-19-504 | NIDDK | U01 | Limited Competition: Continuation of the Consortium for the Study of Chronic Pancreatitis, Diabetes and Pancreatic Cancer Coordination and Data Management Center (CPDPC-CDMC) (U01 Clinical Trial Optional) |
| RFA-HD-19-025 | NICHD | PL1 | HEAL Initiative: Antenatal Opioid Exposure Longitudinal Study Consortium (PL1 Clinical Trials Not Allowed) |
| RFA-HD-20-004 | NICHD | P2C | Medical Rehabilitation Research Resource (P2C Clinical Trial Optional) |
| RFA-HD-20-005 | NICHD | R01 | Research Project Grants in Pediatric Rehabilitation (R01 Clinical Trial Optional) |
| RFA-HD-20-006 | NICHD | R01 | US Children with Perinatal HIV who were Born Internationally (R01 Clinical Trial Optional) |
| RFA-HD-20-008 | NICHD | R61/R33 | Innovative Epidemiologic Approaches for Understanding Long-term Health Outcomes of HIV-exposed Uninfected (HEU) Populations (R61/R33 Clinical Trial Not Allowed) |
| RFA-HD-20-010 | NICHD | R43/R44 | Technologies to Advance Precision Medicine Diagnosis and Treatment of Infertility, Reproductive Tract and Gynecologic Disorders Affecting Fertility (R43/R44 Clinical Trial Optional) |
| RFA-HD-20-012 | NICHD | R13 | Pediatric Critical Care Conferences Initiative (R13 Clinical Trial Not Allowed) |
| RFA-HD-20-019 | NICHD | R43/R44 | Non-invasive Diagnostics to Improve Gynecologic Health (R43/R44 Clinical Trial Optional) |
| RFA-HD-20-020 | NICHD | R21 | Using Archived Data and Specimen Collections to Advance Maternal and Pediatric HIV/AIDS Research (R21 Clinical Trial Not Allowed) |
| RFA-HD-20-021 | NICHD | R21 | Fertility and Fertility Preservation for Patients with Diseases that Previously Precluded Reproduction (R21 Clinical Trial Optional) |
| RFA-HG-19-013 | NHGRI | U01 | The Electronic Medical Records and Genomics (eMERGE): Genomic Risk Assessment and Management Network – Clinical Sites (U01 Clinical Trial Required) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| RFA-HG-19-014 | NHGRI | U01 | The Electronic Medical Records and Genomics (eMERGE): Genomic Risk Assessment and Management Network – Enhanced Diversity Clinical Sites (U01 Clinical Trial Required) |
| RFA-HG-19-015 | NHGRI | U01 | The Electronic Medical Records and Genomics (eMERGE): Genomic Risk Assessment and Management Network – Coordinating Center (U01 Clinical Trial Required) |
| RFA-HL-20-014 | NHLBI | UG3/UH3 | Rare Disease Cohorts in Heart, Lung, Blood and Sleep Disorders (UG3/UH3 Clinical Trial Not Allowed) |
| RFA-HL-20-015 | NHLBI | U01 | Pediatric Cardiac Genomics Consortium (U01 - Clinical Trial Not Allowed) |
| RFA-HL-20-017 | NHLBI | U01 | Cardiovascular Developmental Biology Data Resource Center (U01 - Clinical Trial Not Allowed) |
| RFA-HL-21-002 | NHLBI | U01 | Bench to Bassinet Program Administrative Coordinating Center (U01 - Clinical Trial Not Allowed) |
| RFA-MD-20-001 | NIMHD | P50 | Limited Competition: Specialized Centers of Excellence on Environmental Health Disparities Research (P50) |
| RFA-MH-19-120 | NIMH | R01 | Early Screening for Autism Spectrum Disorder (R01 Clinical Trial Not Allowed) |
| RFA-MH-19-121 | NIMH | R21 | Early Screening for Autism Spectrum Disorder (R21 Clinical Trial Not Allowed) |
| RFA-MH-19-210 | NIMH | R21 | Dysregulation and Proximal Risk for Suicide (R21 Clinical Trial Optional) |
| RFA-MH-19-211 | NIMH | R01 | Dysregulation and Proximal Risk for Suicide FOA (R01 Clinical Trial Optional) |
| RFA-MH-19-225 | NIMH | U19 | A Practice-Based Research Network to Transform Mental Health Care: Science, Service Delivery and Sustainability (U19 Clinical Trial Required) |
| RFA-MH-19-410 | NIMH | R34 | Promoting Reductions in Intersectional StigMa (PRISM) to Improve the HIV Prevention Continuum (R34 Clinical Trial Required) |
| RFA-MH-19-411 | NIMH | R21 | Promoting Reductions in Intersectional StigMa (PRISM) to Improve the HIV Prevention Continuum (R21 Clinical Trial Optional) |
| RFA-MH-19-412 | NIMH | R01 | Promoting Reductions in Intersectional StigMa (PRISM) to Improve the HIV Prevention Continuum (R01 Clinical Trial Optional) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| RFA-MH-19-525 | NIMH | U01 | HEAL Initiative: Effectiveness Trials to Optimize, Implement, Scale, and Sustain the Collaborative Care Model for Individuals with Opioid Use Disorders and Mental Health Conditions (U01 Clinical Trial Required) |
| RFA-MH-20-100 | NIMH | R34 | Refinement and Testing of Interventions to Sustain ADHD Treatment Effects Across Settings and Developmental Transitions (R34 Clinical Trial Required) |
| RFA-MH-20-110 | NIMH | R01 | Secondary Data Analysis to Examine Long-Term and/or Potential Cross-Over Effects of Prevention Interventions: What are the Benefits for Preventing Mental Health Disorders? (R01 Clinical Trial Not Allowed) |
| RFA-NS-19-010 | NINDS | UG3/UH3 | Optimization of Non-addictive Therapies [Small Molecules and Biologics] to Treat Pain (UG3/UH3 Clinical Trial Not Allowed) |
| RFA-NS-19-020 | NINDS | U44 | HEAL Initiative: Optimization of Non-addictive Therapies [Small Molecules and Biologics] to Treat Pain - (U44 Clinical Trial Not Allowed) |
| RFA-NS-19-021 | NINDS | UG3/UH3 | HEAL Initiative: Pain Management Effectiveness Research Network: Clinical Trial Planning and Implementation Cooperative Agreement (UG3/UH3 Clinical Trial Required) |
| RFA-NS-19-022 | NINDS | U54 | Biological Measures for Prognosing and Monitoring of Persistent Concussive Symptoms in Early and Middle Adolescents: Center Without Walls (PCS-EMA CWOW) (U54 Clinical Trial Not Allowed) |
| RFA-NS-19-031 | NINDS | P50 | Senator Paul D. Wellstone Muscular Dystrophy Specialized Research Centers (MDSRC) (P50) |
| RFA-NS-19-040 | NINDS | K12 | NINDS Child Neurologist Career Development Program (CNCDP) (K12 Clinical Trial Not Allowed) |
| RFA-OD-19-011 | NIH | T32 | Predocutorial Training in Advanced Data Analytics for Behavioral and Social Sciences Research (BSSR) - Institutional Research Training Program [T32] |
| RFA-OD-19-012 | OBSSR | R25 | Short Courses on Innovative Methodologies and Approaches in the Behavioral and Social Sciences (R25 Clinical Trial Not Allowed) |
| RFA-OD-19-013 | ORWH | U54 | Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional) |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|------------------------------|---|
| RFA-OD-19-015 | NIH | R21 | INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE) Clinical Trial Readiness (R21 Clinical Trial Not Allowed) |
| RFA-OD-19-016 | NIH | R01 | Transformative Research Award for the INCLUDE (Investigation of Co-occurring Conditions across the Lifespan to Understand Down syndrome) Project (R01 Clinical Trial Not Allowed) |
| RFA-OD-19-018 | NIH | R61/R33 | Clinical Trials Development for Co-Occurring Conditions in Individuals with Down syndrome: Phased Awards for INCLUDE (R61/R33 Clinical Trials Required) |
| RFA-OD-19-019 | ODP | R01 | Tobacco Regulatory Science (R01 Clinical Trial Optional) |
| RFA-OD-19-022 | ODP | R21 | Secondary Analyses of Existing Datasets of Tobacco Use and Health (R21 Clinical Trial Not Allowed) |
| RFA-OD-19-025 | NIH | U24 | Data Coordinating and Operations Center for the ECHO IDeA States Pediatric Clinical Trials Network - 2 (U24 - Clinical Trial Required - Infrastructure) |
| RFA-OD-19-026 | NIH | UG1 | Clinical Sites for the ECHO IDeA States Pediatric Clinical Trials Network - 2 (UG1 Clinical Trial Required) |
| RFA-OD-19-028 | ODP | R01 | Tobacco Regulatory Science (R01 Clinical Trial Optional) |
| RFA-OD-19-029 | ORWH | R01 | The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional) |
| RFA-TR-19-014 | NCATS | UG3/UH3 | Clinical Trials” on a Chip: Tissue Chips to Inform Clinical Trial Design and Implementation in Precision Medicine (UG3/UH3 - Clinical Trial Not Allowed)” |
| NOT-DA-19-037 | NIDA | R01, R03, R21 | Notice of Special Interest (NOSI): Health Services and Economic Research on the Treatment of Drug, Alcohol, and Tobacco Use Disorders (R01, R21, R03) |
| NOT-DA-19-038 | NIDA | R01, R21 | Notice of Special Interest (NOSI): Gene-Environment Interplay in Substance Use Disorders (R01, R21) |
| NOT-DC-19-007 | NIDCD | U01, R01, R21, R24, P50, UG1 | Notice of Special Interest (NOSI) of NIDCD and NEI in Supporting Research on Usher Syndrome |
| NOT-DK-19-007 | NIDDK | R01 | Notice of Special Interest in Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development |

| Announcement Number | Issuing Organization | Activity Code | Title |
|----------------------------|-----------------------------|----------------------|--|
| NOT-HD-19-019 | NICHD | R01, R21, R03 | Notice of Special Interest: Research to Improve Pre-Pregnancy Care and Enhance Healthy Birth Intervals |
| NOT-HD-19-020 | NICHD | R01, R21 | Notice of Special Interest: Mechanisms Underlying the Contribution of Sleep Disturbances to Pain |
| NOT-HD-19-021 | NICHD | R01, R21 | Notice of Special Interest: Advancing the Understanding, Prevention, and Management of Infections Transmitted from Women to their Infants |
| NOT-HD-19-023 | NICHD | R01, R21 | Notice of Special Interest: Research to Advance the Understanding and Management of the Multiple Organ Dysfunction Syndrome in Children (R01, R21) |
| NOT-HL-19-695 | NHLBI | R01 | Notice of Special Interest (NOSI): Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development |
| NOT-HL-19-705 | NHLBI | R01 | Notice of Special Interest (NOSI): Leveraging existing HIV observational cohorts to study HIV-associated HLBS disorders |
| NOT-MD-19-001 | NIMHD | | Notice of Special Interest in Research on the Health of Sexual and Gender Minority (SGM) Populations |
| NOT-MH-19-039 | NIMH | R01, R21, P50 | Notice of Special Interest in High Priority Research Areas for Sex and Gender Influences on the Adolescent Brain and the Mental Health of Girls and Young Women (Ages 12-24) |
| NOT-OD-19-071 | NIH | R01, R03, R21, U01 | Notice of Availability of Competitive Supplements/Revisions for the INCLUDE (Investigation of Co-occurring Conditions across the Lifespan to Understand Down syndrome) Project (Competitive Supplement/Revision Clinical Trial Optional) |
| NOT-OD-19-087 | NIH | Admin Supp | Notice of Availability of Administrative Supplements for the INCLUDE (Investigation of Co-occurring Conditions across the Lifespan to Understand Down syndrome) Project (Administrative Supplement/ Clinical Trial Optional) |
| NOT-OD-19-102 | NIH | Admin Supp | Notice of Special Interest for Administrative Supplements for Research on Sexual and Gender Minority (SGM) Populations (Admin Supp Clinical Trial Optional) |

Table 3: Acronyms for NIH Institutes, Centers, and Offices and Other U.S. Federal Agencies Referred to in This Report

| Acronym | Organization |
|----------------|--|
| ACF | Administration for Children and Families |
| AHRQ | Agency for Healthcare Research and Quality |
| CC | Clinical Center |
| CDC | Centers for Disease Control and Prevention |
| CMS | Centers for Medicare & Medicaid Services |
| CPSC | Consumer Product Safety Commissions |
| DHS | Department of Homeland Security |
| DOC | Department of Commerce |
| DOD | Department of Defense |
| DoED | Department of Education |
| DOE | Department of Energy |
| DOI | Department of the Interior |
| DOJ | Department of Justice |
| DOL | Department of Labor |
| DOS | Department of State |
| DOT | Department of Transportation |
| DPCPSI | Division of Program Coordination, Planning, and Strategic Initiatives, OD |
| EPA | Environmental Protection Agency |
| FDA | Food and Drug Administration |
| FIC | John E. Fogarty International Center |
| FTC | Federal Trade Commission |
| HHS | Department of Health and Human Services |
| HRSA | Health Resources and Services Administration |
| HUD | Department of Housing and Urban Development |
| ICOs | NIH institutes, centers, and offices |
| IHS | Indian Health Service |
| NCATS | National Center for Advancing Translational Sciences |
| NCCIH | National Center for Complementary and Integrative Health |
| NCI | National Cancer Institute |
| NCMRR | National Center for Medical Rehabilitation Research |
| NEC | National Economic Council |
| NEI | National Eye Institute |
| NHLBI | National Heart, Lung, and Blood Institute |
| NHGRI | National Human Genome Research Institute |
| NIA | National Institute on Aging |
| NIAAA | National Institute on Alcohol Abuse and Alcoholism |
| NIAID | National Institute of Allergy and Infectious Diseases |
| NIAMS | National Institute of Arthritis and Musculoskeletal and Skin Diseases |
| NIBIB | National Institute of Biomedical Imaging and Bioengineering |
| NICHD | <i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development |
| NIDA | National Institute on Drug Abuse |
| NIDCD | National Institute on Deafness and Other Communication Disorders |
| NIDCR | National Institute of Dental and Craniofacial Research |
| NIDDK | National Institute of Diabetes and Digestive and Kidney Diseases |
| NIEHS | National Institute of Environmental Health Sciences |

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|--------|--|
| NIGMS | National Institute of General Medical Sciences |
| NIH | National Institutes of Health |
| NIMH | National Institute of Mental Health |
| NIMHD | National Institute on Minority Health and Health Disparities |
| NINDS | National Institute of Neurological Disorders and Stroke |
| NINR | National Institute of Nursing Research |
| NLM | National Library of Medicine |
| OAR | Office of AIDS Research, DPCPSI |
| OASH | Office of the Assistant Secretary for Health |
| OD | Office of the Director, NIH |
| OBSSR | Office of Behavioral and Social Sciences Research, DPCPSI |
| ODP | Office of Disease Prevention, DPCPSI |
| ODS | Office of Dietary Supplements, ODP |
| OMB | Office of Management and Budget |
| ORDR | Office of Rare Diseases Research |
| ORIP | Office of Research Infrastructure Programs, DPCPSI |
| ORWH | Office of Research on Women's Health, DPCPSI, OD |
| OSTP | Office of Science and Technology Policy |
| SAMHSA | Substance Abuse and Mental Health Services Administration |
| USAID | U.S. Agency for International Development |
| USDA | U.S. Department of Agriculture |