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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. In 1960, 26 of every 1,000 babies born in the United States died before their first birthday. By 2016, that rate had fallen to under 6 per 1,000 babies, thanks in part to NIH research on reducing preterm birth, neonatal mortality, and other complications. Phenylketonuria (PKU), once a leading cause of intellectual disabilities, has been nearly eliminated as a factor in cognitive development, following NIH-funded research on newborn screening and dietary therapy. NIH-funded research established that daily eye-patching or the use of atropine eye drops can improve vision in those suffering from amblyopia, a common vision disorder in children where the brain does not process images from one eye. NIH research informed the implementation of HIV testing and preventive measures that have led to a more than 90 percent decrease in the number of children perinatally infected with HIV in the United States. Scientists’ understanding of how children grow and develop has improved 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) 2018, NIH funded research projects directed specifically at pediatric research for a total of $4,498,638,876, 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 of the ICOs support various aspects of pediatric research, such that the 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.

In FY 2018, several drugs, initially supported by NIH funding, were approved by the Food and Drug Administration (FDA). For example, based on studies in NICHD's Adolescent Trials Network, a drug combination in Pre-Exposure Prophylaxis (PrEP) for preventing HIV was approved for use in adolescents. There were two FDA label changes in FY 2018, based on studies conducted by the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network: Raltegravir (Isentress) and Etravirine (Intelence). A new precision medicine drug that specifically targets genes that have been fused together, resulting in a cancer-causing mechanism, received accelerated approval for adult and pediatric patients, regardless of tumor type or organ site. The FDA also approved a gene therapy to treat patients with an inherited retinal disease. New technologies supported by NIH included the ability to track development cell by cell, a rapid diagnostic device for identifying nutrient deficiency, a blood test to monitor recurrence of blood cancer, and a risk calculator for predicting long-term course of pediatric bipolar disorder. In April 2018, NIH launched the HEAL (Helping to End Addiction Long-termSM) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. The HEAL Initiative includes research projects to enhance outcomes for infants and children exposed to opioids, including Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW), which aims to inform clinical care of infants who are exposed to opioids in the womb. Pediatric research at NIH improves health and saves lives.
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 Office of the Director (OD) of NIH. 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 request, NIH has prepared the following report for FY 2018. 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). It should be noted that the PRI reporting provides an incomplete picture of NIH’s total investments in pediatric research. 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 provides funding amounts for NIH’s total investment in pediatric research by ICO in FY 2018.

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 PRI at NIH and coordinate preparation of the Pediatric Research Report.

Additionally, the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act of 2018 (Public Law No: 115-180) directs NIH to ensure that 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.

**Child Development**

**Limiting screen time and encouraging healthy sleep associated with better cognition in children**

Using data from over 4,500 children ages 8 to 11 years old in the first wave of the Adolescent Brain Cognitive Development (ABCD) study, researchers determined that only half of the children met the sleep recommendation (9-11 hours per day), 37 percent met the screen time recommendation (less than 2 hours), and only 18 percent met the physical activity recommendation (1 hour). Global cognition was positively associated with each additional recommendation met. Children who met all 3 recommendations, children who met the screen time and sleep recommendations, and children who met only the screen time recommendation had higher cognitive scores than children who met none of the recommendations.

Supported by NICHD, NIDA, NCI, NIMHD, NIAAA, NIMH, NINDS, OBSSR


**Characterization of stages of infant microbiome development**

Researchers in The Environmental Determinants of Diabetes in the Young (TEDDY) study analyzed stool samples from hundreds of participating children and identified three distinct phases of gut microbiome development: a developmental phase (3-14 months of age), a transitional phase (15-30 months of age) where the microbiome diversifies, and a stable phase (31-46 months of age) where the microbiome’s composition is largely established. Researchers found that breastfeeding (even partially) can play a crucial role in an infant’s gut microbiome development, and bacteria that produce short-chain fatty acid molecules may have protective effects on the risk for type 1 diabetes.

Supported by NIDDK, NIAID, NICHD, NIEHS, NCATS


**A safety promotion intervention for toddlers of low-income families**

Unintentional injuries are the leading cause of death among children, and US children in low-income families tend to have a higher injury rate. To try to reduce injury rates, researchers provided a safety promotion intervention to mothers with toddlers. Health educators covered fire prevention, fall prevention, poison control, and car seat usage during an 8-session intervention. Educators also taught about setting safety goals, conducted group activities to promote safe behaviors, and followed up with mothers by telephone. The research team found that households had numerous safety issues in their homes. Mothers that went through safety promotion training had significantly fewer home safety problems at 12 months after the intervention compared to mothers that did not. This work suggests that educating low-income mothers about safety and goal-setting and providing them with information about affordable safety equipment can improve home safety for toddlers.

Supported by NICHD

**Environmental and Social Influences**

**Early childhood lead exposure and the risk of ADHD in boys**
Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurobehavioral disorders in children. To examine the relationship between early childhood lead exposure and the development of ADHD, researchers analyzed electronic record data on blood lead levels from 1,479 mother-infant pairs (299 with ADHD in the children and 1,180 with children who were not affected with ADHD). This population was predominantly urban, low income, and minority. The study results showed that about 9 percent of the children had elevated lead levels, and lead exposure was associated with an increased risk of ADHD. There was a strong association between elevated lead levels and ADHD in boys, but there wasn’t a significant association among girls. However, the risk of ADHD in boys was reduced by more than one-half if the mother had high maternal high-density lipoprotein levels or low stress during pregnancy.

Supported by NICHD, NIAID, NIEHS

**Phthalate exposure model shows impacts on developing brain**
A rat model of human prenatal exposure to phthalates found effects on brain structure, including reduced numbers of neurons and synapses, reduced size of the medial prefrontal cortex (mPFC), and a deficit in cognitive function. The mPFC is involved in executive function and associated with development of many neuropsychiatric disorders.

Supported by NIEHS

**Infants’ gut microbiome and arsenic exposure**
Scientists explored the relationship between arsenic exposure and gut microbiome in 204 infants. The researchers analyzed infant urine and stool samples. After stratification by sex and feeding method, the researchers found associations between arsenic exposure and the microbiome among formula-fed males, but not in other groups. These findings suggest that even moderate arsenic exposure may have meaningful, sex-specific effects on the gut microbiome during a critical window of infant development.

Supported by NIEHS, NIGMS, NLM

**Arsenic exposure and risk of nonalcoholic fatty liver disease (NAFLD) among U.S. adolescents**
The prevalence of nonalcoholic fatty liver disease (NAFLD) has been rising in adolescents. Researchers examined urinary biomarkers of liver function in adolescents and adults. The scientists found positive association between arsenic exposure and risk of NAFLD among U.S. adolescents and adults. The risk was highest among Mexican Americans and among obese adolescents, regardless of race and/or ethnicity.

Supported by NIEHS, NIMHD

**Effects of air pollution exposure on glucose metabolism**
In 429 overweight and obese African American and Latino urban youth, researchers assessed cumulative residential air pollution exposure (e.g., nitrogen dioxide, ozone, particulate matter (PM2.5), and nitric oxides) from the prior 12 months. They used data on fasting glucose, insulin sensitivity, insulin secretion, and adiposity to define diabetes risk. Results showed that elevated air pollution exposure was associated with a metabolic profile that is characteristic of increased risk for type 2 diabetes.

Supported by NIEHS, NIMHD
**Exposure to media violence and aggressive behavior in adolescents**

Using survey data from 1,990 adolescents and analysis of the content of U.S. top-grossing films and popular TV shows, researchers evaluated the relationships among media violence exposure, family conflict, adolescent characteristics such as impulsiveness, and parental monitoring and involvement in their children’s activities. The scientists found that exposure to media violence was one of the strongest predictors of aggression, after impulsivity and family conflict. Parental monitoring remained a significant protective factor against aggressive behavior, even when accounting for all risk factors.

Supported by NICHD


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**Exposure to gun violence, but not exposure to non-gun violence, influences gun carrying**

Firearms-related violence is a major cause of death and injury among young people, and disproportionately affects young men. Researchers followed a group of over 1,100 male juvenile offenders over time to determine if these young men’s gun carrying behavior increased after exposure to violence, or whether other factors led to gun carrying regardless of whether the young men experienced or witnessed violence themselves. The scientists found that these adolescents were significantly more likely to carry a gun within 6 months after they witnessed or were a victim of gun-related violence. However, if the young men witnessed or were a victim of violence that did not involve a gun, there was no subsequent increase in gun carrying behavior. The results suggest that further study is needed on the effects of exposure to gun violence on the behavior of witnesses.

Supported by NICHD


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**Coal and oil power plant retirements in California associated with reduced preterm birth**

Scientists examined preterm birth rates before and after eight power plants in California closed between 2001 and 2011. They assessed the probability of preterm birth before and after power plant retirement among mothers residing within 0-5 km and 5-10 km of the 8 power plants, controlling for demographic and other trends among the population living within 20 km. The researchers determined that the shutting down of these coal- and oil-fired power plants lowered the rate of preterm births in neighboring communities. The reduction in risk seemed strongest among non-Hispanic black and Asian mothers compared with White non-Hispanic mothers.

Supported by NIEHS


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**Air pollution exposure, maternal asthma, and neonatal respiratory outcomes**

Using data from over 220,000 electronic health records, NICHD intramural researchers assessed the possible role for prenatal air pollution exposure and/or maternal asthma in the risk of neonatal respiratory complications. The scientists found significant associations between neonatal respiratory complications and prenatal exposure to common air pollutants including particulate matter, carbon monoxide, and nitrogen oxides. While maternal asthma also increased risk, the researchers found the relation with air pollution was separate from maternal asthma as an independent factor in the newborns’ illnesses.

Supported by NICHD

**Pregnancy and Health of the Newborn**

*Altered maternal immune networks, alcohol use during pregnancy, and child neurodevelopment*

Consumption of alcohol during pregnancy can lead to changes in a woman’s immune system, including elevated levels of specific cytokines (substances secreted by certain cells within the immune system). Disruption in cytokine balances can alter the course of typical brain development in the fetus, perhaps increasing the risk for neurodevelopmental disorders. Scientists identified distinct clusters of cytokine alterations that were associated with alcohol-related neurodevelopmental delay. These findings may help inform the development of biomarkers for early identification of children prenatally exposed to alcohol. Supported by NIAAA, NICHD

Articles:  

*Immune activation products can help predict pregnancy complications in women with lupus*

Adverse pregnancy outcomes -- including stillbirth, complications resulting in preterm birth, or growth restriction -- occur in over 20 percent of women with lupus or with anti-phospholipid antibodies (aPL). Researchers analyzed complement activation products in blood samples from participants at their monthly visits during pregnancy. The scientists found that about 20 percent of participants with lupus or aPL developed adverse pregnancy outcomes. The levels of complement activation products were elevated sooner in pregnancy, and remained higher for longer, in women who experienced adverse pregnancy outcomes compared with women who did not. These findings may help researchers and clinicians identify a subset of at-risk patients for future intervention trials to improve outcomes for children born of mothers with lupus. Supported by NIAMS

Articles:  

*Methadone versus buprenorphine for opioid use dependence and risk of neonatal abstinence syndrome*

The misuse of opioids has risen alarmingly in the United States, including among pregnant women. Use of opioids during pregnancy can affect the health and well-being of women and lead to withdrawal symptoms in newborns. Reported cases of neonatal abstinence syndrome (NAS), also known as neonatal opioid withdrawal syndrome (NOWS), have been rising rapidly at hospitals across the nation. Newborns with the syndrome have been exposed to maternal drugs (usually opioids) in utero and experience drug withdrawal symptoms after birth. To lessen these adverse effects, pregnant women with opioid use dependence may be treated with methadone or buprenorphine as opioid maintenance therapy. Research has consistently shown maternal buprenorphine treatment to be associated with lower risk of NAS/NOWS and shorter duration of its treatment in an affected infant, compared with methadone; there has been concern, however, that the favorable profile of buprenorphine might be biased by a methodological issue in the research. Specifically, the large databases that researchers generally rely on typically do not include information on the severity of maternal addiction, which varies, and could therefore skew findings. Now, newly reported research supports the earlier favorable conclusions about buprenorphine. These researchers, also working with a large data set (electronic pharmacy records) that lacked severity data, conducted a separate “validation” study of medical records of subsets of women in their large study cohort. This approach enabled them to conclude that their finding of lesser NAS/NOWS risk with buprenorphine than methadone was subject only to “minimal bias” from not having addiction severity data for every woman in their cohort. Supported by NICHD

Article:  

*Outpatient pharmacotherapy for neonatal abstinence syndrome*

Scientists analyzed health records data from the Tennessee Medicaid program in 2009-2011 to assess treatment patterns for infants with neonatal abstinence syndrome (NAS), a withdrawal syndrome that can
affect infants whose mothers used opioids during pregnancy. Almost three quarters of the 736 infants with NAS in the study were treated with medication. Almost half of these infants were discharged from the hospital on outpatient medications, commonly phenobarbital, which has been associated with poor neurologic outcomes. The NAS infants on outpatient medications had a shorter length of stay in the hospital; however, the median length of treatment was longer (60 days for outpatients versus 19 days for inpatients) and repeat visits to the emergency room were more frequent for the outpatient-treated infants. Supported by NIDA
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29754866

**Newborns treated for opioid withdrawal at greater risk for developmental delay at age 2**

Use of opioids during pregnancy can affect the health and well-being of women and lead to withdrawal symptoms in newborns. Symptoms often include tremors, excessive crying, sleep deprivation and swallowing difficulties. NICHD-supported researchers assessed whether newborns treated for neonatal opioid withdrawal syndrome (NOWS) were at greater risk for developmental delay years later. They followed up with a group of 87 two-year-old participants who had been treated for NOWS as newborns. The scientists found that the toddlers who had been treated for NOWS scored lower, compared with the general population, on measures of cognitive, language, and motor development. The children who had been treated for NOWS were also more likely to have strabismus, or misalignment of the eyes. Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29515225

**Inflammation in pregnant mothers linked to children's brain development**

Researchers measured blood levels of an inflammatory messenger chemical, IL-6 (interleukin-6), in 84 pregnant mothers – and followed-up with neuroimaging and behavioral assessments of their children. High levels of IL-6 during pregnancy were linked to reduced brain circuit communications and altered long-distance brain wiring at birth, poorer cognitive function at one year – and to reduced impulse control and working memory at two years. Supported by NIMH, OD, NIGMS, NCATS, NICHD, NLM
Articles:  

**Genetic variations linked to severity of Zika-related birth defects**

Zika infection during pregnancy is associated with severe congenital anomalies in surviving infants, but outcomes for Zika-exposed infants vary widely. Researchers found that, of 52 women who had given birth after testing positive for Zika virus infection, 28 gave birth to children with reduced head size and other Zika-related birth defects. Infants born to the remaining 24 women did not appear to have any Zika-related effects. After sequencing genes from the women, the researchers found that mothers of severely affected infants were more likely to have variations in two genes essential for making adenylate cyclase, which is required to make cyclic adenosine monophosphate (cAMP), a protein that contributes to placental development and immune response to infection. The researchers noted that, because of the relatively small number of women studied, additional research is needed to confirm these results. However, future research on drugs that influence cAMP production might yield potential therapies to protect against Zika exposure during pregnancy. Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30222212
Zika infection during pregnancy may disrupt fetal oxygen supply

Zika virus infection among pregnant women can lead to developmental problems in fetuses and newborns. Scientists used non-invasive imaging to evaluate how persistent Zika infection affects pregnancy in five rhesus macaques. The team found that the virus induces high levels of inflammation in the blood vessels of the uterus and damages placental villi, the branch-like growths that help transfer oxygen and nutrients from maternal blood to the fetus. The researchers suggest that this damage may disrupt oxygen transport to the fetus, which can restrict its growth and lead to stillbirth, among other conditions. The team observed evidence of fetal brain abnormalities in two of the five animals, but the researchers did not see any obvious signs of microcephaly. This finding, they reason, is consistent with previous studies that establish microcephaly as only one of a spectrum of Zika-induced complications. Supported by NICHD, OD, NIAAA
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29343712

Anti-HIV drug combination does not increase preterm birth risk

Following research studies that had found combination therapies containing the drug tenofovir disoproxil fumarate (TDF) to be safe for women with HIV to use during pregnancy, the World Health Organization recommended that all adults with HIV, including pregnant women, receive a combination therapy that includes TDF. However, another research study found different results, indicating that combination therapy that included TDF may raise the risk of preterm birth. To assess this discrepancy in research findings, scientists assessed the risk of preterm birth and other adverse birth outcomes by reviewing records from two studies of U.S. women. These studies had compared three anti-HIV drug combinations, two of which included TDF. The analysis found no significant differences in the risk of preterm birth or low birthweight between women receiving combination therapy with TDF and those receiving combination therapy without TDF. Further, there were no significant differences in severe birth outcomes, including very low birth weight, very preterm birth, or infant death in the first 14 days after birth. Comparing women treated with a second combination with TDF and the combination without TDF, researchers found that the TDF group had a 10 percent lower chance of preterm birth, low birth weight, and infant death. Supported by NICHD, NIAID
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29694825

HIV infants are at high risk for acquiring congenital CMV infection

Infection with cytomegalovirus (CMV) is common and rarely causes problems for healthy people. However, if a woman experiences CMV infection during pregnancy, she can transmit the virus to her infant. An estimated 10 percent to 15 percent of infants infected at birth with CMV show symptoms, and the infection can lead to severe neurodevelopmental delays and hearing loss. Approximately 5 percent to 17 percent of asymptomatic infants with CMV may also develop symptoms later, as the disease progresses. HIV-infected infants are more likely to have symptomatic CMV and CMV co-infection may accelerate the progression of HIV disease. To expand understanding of HIV/CMV co-infection, researchers focused on a subset of infants enrolled in a clinical trial that compared three antiretroviral drug regimens to prevent maternal HIV transmission to the developing fetus or perinatally. These were infants whose mothers’ HIV infection was not treated during pregnancy because it was not detected until they received clinical care at the time of labor and delivery. Compared with infants whose exposure to maternal HIV did not result in HIV infection, exposed infants with HIV had a fourfold higher risk of CMV co-infection, which rose to a six-fold higher risk if the HIV infection occurred in utero. The researchers concluded that CMV screening was an important part of comprehensive evaluation of HIV-exposed infants, especially those whose mothers’ HIV was not treated with antiretrovirals during pregnancy. Supported by NICHD, NIAID
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30216294
Antiviral drug did not help reduce mother-to-child transmission of hepatitis B when added to existing preventatives

Hepatitis B can cause serious, long-term health problems, such as liver disease and cancer, and can spread from mother-to-child during delivery. Countries in Asia have a high burden of hepatitis B. There is no cure, and antiviral drugs used to treat the infection usually need to be taken for life. To prevent infection, the World Health Organization recommends that all newborns receive their first dose of hepatitis B vaccine within 24 hours of delivery. Infants born to hepatitis B-infected mothers are also given protective antibodies called hepatitis B immune globulin. However, mother-to-child transmission can still occur in women with high levels of virus in their blood, as well as those with mutated versions of the virus. In Thailand, a country with high rates of hepatitis B, researchers tested whether adding Tenofovir disoproxil fumarate (TDF), an antiviral drug commonly prescribed to treat hepatitis B, to the standard prevention measures could reduce mother-to-child transmission rates. The researchers observed no significant reduction in infection rates in the group given TDF. The rate of infection was low in both the group given TDF and the group given the standard regimen.

Supported by NICHD
Article: https://www.ncbi.nlm.nih.gov/pubmed/29514030

Racial and ethnic disparities in infant outcomes in New York City hospitals

Although rates of newborn infant deaths have decreased over the last decade, there are still differences in infant mortality among racial and ethnic groups. Non-Hispanic black newborns have a death rate that is more than twice the rate of non-Hispanic white newborns; Puerto Rican newborns also have a higher risk of death. To better understand these patterns, researchers studied outcomes for a diverse group of 7,177 infants born between 24 and 31 weeks in 39 NYC hospitals between 2010 and 2014. The study results showed that the overall rates of morbidity and mortality were higher among black and Hispanic infants compared with non-Hispanic white infants. These rates varied widely among the 39 NYC hospitals in the study. Black (43.4%) and Hispanic (34.4%) very preterm infants were more likely than white (22.9%) very preterm infants to be born in hospitals with the highest morbidity and mortality risk rates. These differences in hospital of birth explained 39.9 percent of the black-white disparity and 29.5 percent of the Hispanic-white disparity, indicating that the hospital of birth is an important factor in explaining patterns of infant mortality. Other factors that need to be evaluated include the distance from home to the hospital, insurance status, and patterns of referrals and transfers.

Supported by NICHD
Article: https://www.ncbi.nlm.nih.gov/pubmed/29297054

Early antibiotic use among premature infants

Preterm infants, especially those born with very low birth weight, are at risk for potentially serious or fatal infections in the early days of life. Frequently, physicians give infants in the neonatal intensive care unit (NICU) antibiotics even if they do not have an infection. However, although these medications are given to protect premature newborns, previous research indicates that the medications have potential risks as well as benefits. Early and prolonged use of antibiotics in newborns without infection has been linked to subsequent infections and complications of prematurity, as well as contributing to antibiotic resistance. To describe the use of antibiotics in newborns, researchers analyzed data from a large administrative database that included over 40,000 preterm infants from about 300 hospitals across the United States. The results showed that over 87 percent of preterm, low birth weight infants received antibiotics. The use of antibiotics varied substantially across hospitals.

Supported by NICHD
Article: https://www.ncbi.nlm.nih.gov/pubmed/30646054
Extremely premature infants with enlarged fluid spaces in the brain are more likely to experience neurodevelopmental impairment

The brain contains a clear protective liquid called cerebrospinal fluid (CSF), which fills spaces called ventricles. In the brain of a healthy fetus, the ventricles are about 10mm wide. However, excess fluid (either CSF or blood) cause the ventricles to grow larger. This condition, called “ventriculomegaly,” can be seen using a prenatal ultrasound. The term “nonhemorrhagic ventriculomegaly” denotes enlarged ventricles that are not caused by blood vessels rupturing. The effects of nonhemorrhagic ventriculomegaly have not been well characterized in extremely preterm neonates younger than 27 weeks’ gestational age. Using data from over 3,000 infants born prior to 27 weeks’ gestational age, researchers measured cognitive development, cerebral palsy, vision impairment, and hearing impairment of infants with nonhemorrhagic ventriculomegaly versus those with normal ultrasound images. Nonhemorrhagic ventriculomegaly was associated with lower gestational age, being male, and several conditions affecting the lungs, brain, bloodstream, intestines, and eyes. Overall, the researchers found that, among extremely preterm neonates, nonhemorrhagic ventriculomegaly is associated with increased odds of neurodevelopmental impairment, poor cognitive outcomes, moderate to severe cerebral palsy, and either death or neurodevelopmental impairment at 1-2 years of age.

Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29181530

Potential genetic risk factor for sudden infant death syndrome (SIDS)

Genetic mutations that impair the muscles that control breathing may put infants at risk for sudden infant death syndrome, or SIDS. SIDS is the leading cause of death among infants between 1 month and 1 year of age. Researchers explored whether mutations in SCN4A—a gene important to breathing function—can contribute to SIDS risk. Examining genetic samples from 278 SIDS cases from the United States and the United Kingdom, the researchers found that for a few infants with SIDS, a type of SCN4A mutation associated with breathing problems was present. In a “control group” of 729 adults, none had these types of genetic mutations. Further, the researchers suggested that the genetic defects they detected in the SIDS cases may be especially important during a period when an infant’s respiratory muscles are particularly dependent on the processes controlled by this gene. Identifying factors that contribute to SIDS could potentially help parents and health care providers reduce the risk.

Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29605429

Nutrition and Obesity in Pregnancy and Childhood

High blood sugar during pregnancy increases risk of mother’s type 2 diabetes, child’s obesity

The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) looked at 23,316 mother-infant pairs and found that maternal blood sugar levels below those diagnostic of overt diabetes were associated with a newborn’s birth weight and body fat. Based on these results many, but not all, organizations adopted a new definition of gestational diabetes (GDM). The HAPO Follow-Up Study (HAPO-FUS) followed a subset of the cohort and has reported that maternal blood sugar levels that would meet this new GDM definition—but were not treated at the time of pregnancy—are strongly associated with adverse effects a decade later, including increased risk for type 2 diabetes in mothers and obesity in their offspring. These results reinforce the importance of trying to prevent GDM in women at high risk, and of advancing research studies that can lead to improved GDM screening approaches and inform the timing and approach for future clinical trials to decrease adverse short- and long-term outcomes from abnormal blood sugar levels during pregnancy for both mothers and offspring.

Supported by NIDDK, NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30208453
**Health risks following obesity during pregnancy**

Overweight or obesity affects almost two thirds of all pregnant women in the United States. Obesity during pregnancy is associated with increased risk for pregnancy complications, and increased risk for the offspring to develop obesity, diabetes, and cardiovascular disease later in life. Researchers have developed a new mouse model of maternal obesity, which provides insights on maternal diet and metabolism, pregnancy outcomes, and the development of metabolic and cardiovascular disease in the adult offspring. Using this model, researchers discovered that low levels of the hormone adiponectin in mothers with obesity may be the underlying cause of subsequent health risks. Furthermore, normalizing levels of adiponectin in the pregnant animal with obesity prevented pregnancy complications and reduced later risk to the offspring. This model suggests that measures to stimulate maternal adiponectin signaling may present a novel approach to prevent pregnancy complications and poor health in the children of mothers with obesity.

Supported by ORIP, NIDDK, NICHD

Article: https://www.ncbi.nlm.nih.gov/pubmed/30346829

**Human milk consumption improves health in very low birthweight infants**

Previous research has shown that very low birthweight infants who receive human milk while in the neonatal intensive care unit (NICU) have lower infection rates and better health outcomes. However, fewer studies have been done to follow these infants after hospital discharge. Researchers followed a group of very low birth weight infants for two years after they left the NICU. They found that consuming human milk in the first 14 days of life was associated with fewer hospitalizations in the first year of life, and fewer specialized pediatric therapies used at 2 years of life.

Supported by NINR

Article: https://www.ncbi.nlm.nih.gov/pubmed/30341399

**Probiotics not helpful for children with gastroenteritis**

Probiotics are often recommended for children with acute gastroenteritis. However, in a large study at 10 children’s emergency rooms across the U.S., researchers found that a probiotic treatment did not show any benefit for young children brought to the hospital with acute gastroenteritis. For every outcome, in every subgroup of patients, the probiotic made no difference.

Supported by NICHD, NIDDK

Article: https://www.ncbi.nlm.nih.gov/pubmed/30462938

**Home visiting parenting program helps reduce child obesity**

Although more than half of overweight or obese children are already overweight before the age of 2, most obesity prevention interventions have focused on school-aged children and adolescents. Researchers studied a home visiting program (called Minding the Baby, or MTB) that focused on first-time mothers and their babies. MTB consisted of weekly home visits from a social worker and pediatric nurse from the first trimester of pregnancy until the child’s first birthday, and then bi-weekly until the second birthday. The MTB program was not primarily an obesity prevention program, but focused more broadly on mother-child attachment, health, mental health, and positive parenting behaviors. Researchers randomly divided the 158 mother-child pairs into two groups -- a control group that received standard prenatal and primary care at community health clinics, and an intervention group that participated in the MTB program. The study results clearly showed that more children in the MTB intervention group had a healthy BMI at 2 years compared with the control group. The rate of obesity at age 2 was significantly higher in the control group (19.7%) compared with the MTB group (3.3%). These findings suggest that home visiting programs that focus on the whole child and on the early mother-child relationship can be beneficial for helping prevent childhood obesity.

Supported by NICHD, NCATS, NINR

Article: https://www.ncbi.nlm.nih.gov/pubmed/29339565
Short physical activity interruptions improve glucose metabolism in overweight children
Sedentary children have greater risk of obesity, and also may experience abnormalities in how they process glucose (sugar), even before they develop diabetes or pre-diabetes. NICHD-supported researchers found that interrupting sedentary behavior (sitting) with very short periods of walking improved glucose metabolism, without affecting food intake, in children who had overweight or obesity. Children 7 to 11 years of age with overweight or obesity underwent two experiments in random order: (1) prolonged sitting (3 hours of continuous sitting) and (2) interrupted sitting (every 30 minutes, sitting was interrupted by 3 min of moderate-intensity walking, over a total time of 3 hours). The researchers measured biomarkers for how the children metabolized glucose, as well as the children's food intake at a buffet meal after each session. Interrupting sedentary behavior, even with short moderate-intensity walking sessions, may be a promising intervention strategy for reducing health risks in overweight children.
Supported by NICHD, NIDDK
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30082324

Diabetes

Hydrolyzed formula does not reduce incidence of type 1 diabetes in high-risk infants
Because early exposure to complex foreign proteins may increase the risk of type 1 diabetes in genetically susceptible children, researchers tested whether hydrolyzed infant formula, which lacks intact proteins, could decrease the risk of type 1 diabetes. In a large international trial, researchers found that weaning to hydrolyzed formula, compared to conventional formula, failed to reduce overall incidence of type 1 diabetes. Thus, there was no evidence to support revising dietary guidelines for at-risk infants.
Supported by NICHD, NIDDK
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29297078

Picky eaters improved diet quality in a study in youth with type 1 diabetes
Youth with type 1 diabetes typically receive nutrition education about healthy eating. However, many young people with type 1 diabetes continue to have poor diet patterns. Scientists tested whether the effect of a behavioral nutritional intervention in youth with type 1 diabetes differed between picky and non-picky eaters. The study participants were youth (8 and 16.9 years) diagnosed with type 1 diabetes for 1 or more years. At the beginning of the study, the diet quality was lower in picky eaters than in non-picky eaters. Among picky eaters, diet quality for those receiving the behavior intervention significantly improved, whereas diet quality for those not receiving the intervention remained low.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29389510

Treatment of pediatric type 2 diabetes and differences from adult form of the disease
Recent results show that in severely obese teens with T2D, bariatric surgery led to better outcomes than medical intervention. In a related study, neither insulin nor metformin, the two medications approved for treating type 2 diabetes in children, could prevent or delay rapid progression of the dysglycemia; the study also found that young people with T2D produce much more of their own insulin while being significantly more insulin resistant than people who develop T2D later in life.
Supported by NIDDK, NCATS
Articles:  https://www.ncbi.nlm.nih.gov/pubmed/29532078
**Childhood Disease, Allergies, and Immunity**

**New biomarker to diagnose life-threatening liver disease in children**
Researchers have identified a protein present at high levels in blood from infants with biliary atresia that may enable early and accurate detection of this potentially deadly disease. NIDDK-supported scientists analyzed samples from infants to identify a clinically useful biomarker for diagnosing biliary atresia, called matrix metalloproteinase-7 (MMP-7). MMP-7 is not only a promising candidate as a much-needed biomarker for improving early diagnosis of biliary atresia, but also likely plays a role in disease development and may be a therapeutic target.

Supported by NIDDK  

**Estimating disease progression risk in children with chronic kidney disease**
A combination of three factors provide best predictors for estimating the progression of chronic kidney disease (CKD) in children: glomerular filtration rate, proteinuria, and whether CKD is glomerular-based or nonglomerular-based. Data obtained from 1,232 children with CKD led to the identification of 6 progression models leading to kidney failure. This tool will aid in determining when a child with CKD will likely progress to need for transplant or dialysis.

Supported by NIDDK, NICHD, NHLBI  

**Improving treatment for children with multidrug-resistant tuberculosis**
The powerful antibiotic amikacin is currently recommended for treating multidrug-resistant tuberculosis, because conventional drugs are ineffective. Amikacin treatment, however, requires four to eight months of injections that often involve pain and other side effects. Scientists conducted a clinical trial in South Africa to test a new way to make this treatment easier for children with multidrug resistant tuberculosis. The researchers showed that administering amikacin together with the pain medicine lidocaine immediately reduced the pain associated with the antibiotic injection, without altering two important measures of the antibiotic’s efficacy. The results indicate that co-administration of lidocaine may help children with multidrug-resistant tuberculosis better tolerate the difficult treatment they need to get well.

Supported by NICHD, NIAID  

**Metabolic effects of initiating anti-HIV regimens among young children**
Exposure over time to the anti-HIV drugs known as protease inhibitors increases the risks of certain metabolic and cardiovascular disorders in adult and child patients. Newer protease inhibitors (e.g. atazanavir, darunavir) have safer metabolic profiles, but the only protease drug regimen commonly used for initial treatment in HIV-infected children under age three is a combination of older protease inhibitors, lopinavir/ritonavir (LPV/r). The approval reflects clinical trial evidence that treatment failure is less likely to occur with LPV/r than with another class of drug called nevirapine (NVP). Following up on their earlier LPV/r vs NVP trial, researchers recently assessed the metabolic status of children whose HIV treatment had started with one of the two drug regimens in the trial, seven years earlier. They found that, compared with NVP, LPV/r was associated with higher cholesterol in the children, although the treatment was not a strong predictor of various other metabolic warning signs, including biomarkers of inflammation or immune activation. Children on long-term LPV/r regimens should, in the view of the researchers, have their cholesterol monitored regularly.

Supported by NICHD, NIAID  
**Drug combination reduces risk of HIV infection among teen males**
Researchers from the NICHD’s Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) reported that an HIV prevention therapy commonly prescribed for adults also is safe and can be effective for teenagers when taken appropriately. Truvada, a single pill containing the drugs tenofovir and emtricitabine, had originally been FDA-approved for daily use in adults. The drug combination (Truvada) is the cornerstone of pre-exposure prophylaxis (PrEP), a strategy in which individuals at risk for HIV infection take a combination of two or more anti-HIV drugs to reduce this risk. While several studies have shown that daily PrEP is safe and effective, the studies were limited to adults. The ATN study provides crucial data for this population and shows that PrEP can safely reduce HIV risk among teens ages 15 to 18 years who take it as prescribed. The study was also instrumental in supporting FDA approval for using PrEP to treat adolescents with HIV.

Supported by NICHD, NIMHD, NIMH, NIAID

**Association of dental caries with HIV exposure and infection in Nigerian children**
Based on previous reports of increased caries experience in HIV-infected children and adults, NIDCR-supported researchers evaluated caries incidence in children in Nigeria. Children with HIV infection were at significantly increased risk of caries compared to uninfected children with and without exposure to HIV. This finding supports a need to develop integrated oral health management strategies for HIV infected children on antiretroviral therapy.

Supported by NIDCR, Fogarty AIDS International Training and Research Program

**Youth perinatally infected with HIV may have severe lung disease complications**
Previous research indicated that youth who were exposed to and infected with HIV in the womb have an increased risk for asthma, compared with youth who were exposed to HIV in the womb but uninfected. NICHD-supported researchers reviewed medical records and reports for 218 HIV-infected youth with asthma, and 152 young people with asthma who had been exposed to HIV before birth but were uninfected. The researchers administered pulmonary function tests to these youths to classify the types of lung disease. To distinguish asthma from other causes of obstructive lung disease, a reversibility test is used to measure the flow of air into the lungs before and after treatment. In asthma, treatment can usually reverse the obstruction of airflow. In this study, the prevalence of obstructive lung disease did not differ by HIV status, but obstruction of airflow was less likely to be reversible in HIV-infected youth, compared to uninfected youth. HIV-infected youth also had lower levels of allergen-associated antibodies and lower ratios of different white blood cells, which indicate an immune imbalance. These findings indicate that HIV-infected youth may be more prone to a complex combination of asthma and chronic obstructive pulmonary disease and should be further observed to determine lung disease outcomes in adulthood.

Supported by NICHD, NIAID

**RSV vaccines are highly attenuated and immunogenic**
Respiratory syncytial virus, or RSV, is a respiratory virus that infects the lungs and breathing passages and can cause severe health implications in infants and the elderly. Researchers recently completed Phase 1 testing of two of RSV live attenuated vaccines in children. The first, RSV cold-passage/stabilized 2 (RSVcps2), was well tolerated and moderately immunogenic. Another RSV vaccine candidate, LIDΔM2-2, which contains a deletion of the RSV protein M2-2, had excellent infectivity and immunogenicity, encouraging further study of vaccine candidates containing the M2-2 deletion.

Supported by NIAID, NICHD
[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5894092](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5894092)
Explaining sex differences in the risk for bronchopulmonary dysplasia

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that affects newborns (mostly premature) and infants. Male infants are at greater risk for developing BPD, but the reasons why are largely unknown. Scientists used a mouse model to explore the hypothesis that a specific type of microRNA, which tends to be differentially expressed in males and females, may play a role in determining the risk for BPD. The researchers found greater levels of this microRNA in female mice recovering from exposure to hyperoxia compared to male mice. These findings indicate that there may be sex-specific molecular mechanisms underlying the risk for BPD.

Supported by NHLBI, OD

Bacteria therapy for eczema shows promise

A NIAID clinical trial is testing a novel therapy for the treatment of eczema (atopic dermatitis) in children. Topical treatment with live *Roseomonas mucosa*—a bacterium naturally present on the skin—was safe for a small cohort of adults and children with eczema and was associated with reduced disease severity. Results from the ongoing study will provide the foundation for larger trials to evaluate the efficacy of this novel investigational therapy, as well as to better understand the role of *R. mucosa* in eczema.

Supported by NIAID

Gene complex governs skin-intrinsic immunity

Human papilloma virus type-β (β-HPV) infection usually does not cause symptoms for most people. However, individuals with the primary immunodeficiency disorder epidermodysplasia verruciformis (EV) typically experience β-HPV warts in childhood, and the condition often progresses to squamous cell carcinoma. Defects in two genes -- *EVER1* and *EVER2* -- are known to increase susceptibility to β-HPV infection and EV. Scientists identified mutations in another gene -- *CIB1* -- as another component of the genetic risk for EV. Their research suggests that the *CIB1-EVER1-EVER2* complex is integral to skin-intrinsic immunity in humans.

Supported by NIAID, NCI, NCATS

Therapeutic biomarker in systemic juvenile idiopathic arthritis

Systemic juvenile idiopathic arthritis (sJIA) is a severe form of childhood arthritis that is marked by inflammatory episodes with recurrent fever, together with chronic arthritis, a characteristic skin rash, and enlargement of the lymph nodes, liver and spleen. About half children with sJIA will develop lifelong, chronic arthritis. The goal of sJIA treatment is to quickly halt systemic inflammation to avoid development of this chronic arthritis. An international team of researchers evaluated previously reported genomic regions associated with sJIA to determine if any conferred sJIA risk. Researchers found that only one region, IL1RN, was associated with sJIA risk, and disease risk correlated with the level of IL1RN gene expression. In addition, IL1RN expression was also linked to the patient’s likelihood to respond to anakinra treatment.

Supported by NIAMS, NHGRI

Bone marrow transplantation in children with severe combined immunodeficiency

Severe combined immunodeficiency (SCID) is a group of rare disorders caused by mutations in different genes involved in the development and function of infection-fighting immune cells. Researchers analyzed
one of the largest and most detailed cohorts of children with SCID. The scientists confirmed higher survival after hematopoietic cell transplantation from matched sibling donors versus non-matched, and they determined that SCID genotype strongly influenced survival and immune reconstitution. These findings emphasize the need for patient-tailored treatment strategies depending upon the underlying SCID genotype.
Supported by NIAID, ORDR, NCATS, NHLBI, NCI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30154114

**Bone and Muscle Health**

**Rare disease suggests potential targets for developing future osteoporosis treatments**
Timothy syndrome is a rare genetic disorder characterized by life-threatening problems with irregular heart rhythm, webbed fingers and toes, and dental and bone abnormalities. Using genetically engineered mouse models, researchers found a link between bone formation and a mutation in the calcium channel that causes Timothy syndrome. Increasing activity in this calcium channel increased bone formation in a mouse model of Timothy syndrome and prevented bone loss in a model of osteoporosis. Identifying how this calcium channel mutation relates to bone health provides insights on potential targets for treating bone loss.
Supported by NICHD, NIAMS, NHLBI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29202453

**FDA approves first therapy for rare inherited form of rickets, XLH**
In April 2018, the FDA approved the monoclonal antibody Crysvita (burosumab-twza) for adults and children ages 1 year and older who have x-linked hypophosphatemia (XLH). XLH is a rare, inherited form of rickets that leads to impaired bone growth and development in children and adolescents and problems with bone mineralization throughout a patient’s life. The drug’s development stems from NIH-funded grants that led to the discovery of the causative genetic defect and characterized the disease’s underlying mechanism.
Supported by NIAMS
News Release:  https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm604810.htm

**Exercise and antidepressants affect bone health in adolescent girls with anorexia nervosa**
Anorexia nervosa, often referred to as “anorexia,” is an eating disorder characterized by depression, altered body image, and abnormal self-imposed caloric restriction, leading to malnutrition. Globally, as of 2015, anorexia is estimated to affect 2.9 million people, affecting about 0.4 percent of women each year. To assess how malnutrition and lifestyle affect bone health in this eating disorder, researchers compared 70 adolescent females with anorexia and 132 controls. The scientists found that for adolescents with anorexia, antidepressants may negatively affect bone mineral density, whereas exercise can positively influence bone mineral density. Although exercise had benefits on bone growth in adolescent females with anorexia, they still had evidence of weaker bones and increased fracture risk.
Supported by NICHD, NIAMS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/27939877

**Young patients with certain autoantibodies experience more severe muscle disease**
A new study of children with the autoimmune muscle disease juvenile myositis (inflammation) showed more than a quarter of them (compared to only 12% of healthy children) had a certain autoantibody. These children had greater pulmonary symptoms, more hospitalizations, and needed more medications.
Supported by NIEHS, NIAMS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29363513
**Structural Congenital Anomalies and Newborn Screening**

**A novel gene network identified in cleft lip/cleft palate**
The gene Crispld2 has previously been shown to be associated with cleft lip/palate. NIDCR-funded researchers combined RNA profiling data and in silico gene regulatory network analysis to identify cleft lip/palate risk genes following knockdown of Crispld2 in zebrafish. Of the 249 genes exhibiting differential expression, three were identified as novel risk genes based on validated differential expression in zebrafish and genotyping in families with this disorder. Further analysis revealed a novel underlying gene network including these three novel genes and over 20 previously reported ones.

Supported by NIDCR

**Identifying crucial genes for craniofacial development**
Two groups of NIDCR-supported researchers independently studied cleft palate in Pax9-deficient mice. Using these mice that do not produce functional Pax9 protein and have abnormal craniofacial, tooth, and limb development, the groups discovered that during development the tissues that form the palate of the mouth have increased amounts of a protein called Dkk1. Blocking the Dkk1 protein with small molecules or deleting one Dkk1 allele led to more complete palate development and reversed the mutant phenotype in some embryonic mice, demonstrating that Pax9 and Dkk1 are critically important for craniofacial development.

Supported by NIDCR

**Research gaps complicate efforts to address disorder characterized by lack of amniotic fluid**
Anhydramnios is the complete, or nearly complete, lack of amniotic fluid surrounding the developing fetus in the uterus. Lack of amniotic fluid can cause devastating complications for the fetus, including severe skeletal structural abnormalities or stillbirth, as well as incomplete lung development that can prove fatal in a newborn. Thus far, no standardized approaches exist to manage such cases, especially if anhydramnios is secondary to absence of fetal kidneys or abnormalities of the urinary tract in the fetus.

Recently, some medical centers are offering medical and surgical interventions for anhydramnios that include infusing normal saline to restore the amniotic fluid volume, in an attempt to support development of the fetal lungs. Researchers and clinical experts were invited to a conference where they reviewed the current knowledge and gaps in scientific understanding of anhydramnios in the context of fetal kidney abnormalities. They assessed the benefits and risks of currently used clinical interventions, post-natal and long-term outcomes in children with kidney abnormalities identified before birth, and ethical aspects of decisions about maternal-fetal interventions for the condition and its complications. Published workshop findings suggested priority areas for research, including research to better understand how amniotic fluid is produced and cleared, as well as to develop markers for assessing fetal kidney function.

Supported by NICHD, NIDDK

**Fever from cold or flu during pregnancy and the risk for noncardiac birth defects.**
Approximately six to eight percent of pregnant women experience fever early in their pregnancies. NICHD-supported researchers found that maternal cold or flu with fever early in pregnancy was significantly associated with eight birth defects (anecephaly, spina bifida, encephalocele, cleft lip with or without cleft palate, colonic atresia/stenosis, bilateral renal agenesis/hypoplasia, limb reduction defects, and gastrochisis). However, early-pregnancy cold or flu without a fever was not associated with any of the birth defects studied.

Supported by NICHD
The drug nifedipine increases survival of placental cells exposed to alcohol
During pregnancy, alcohol can pass through the placenta and umbilical cord into the developing fetus. The toxic effects of alcohol on the developing fetus can then lead to poor growth as well as later problems in behavior, attention, and learning. These conditions, known collectively as fetal alcohol spectrum disorders (FASD), are the most common preventable cause of intellectual disability. In early pregnancy, cells called trophoblasts eventually develop into the placenta. These cells regulate how maternal and fetal cells interact; therefore, problems in the trophoblasts can lead to problems in the pregnancy. Previous studies have suggested that alcohol increases the level of calcium in trophoblasts, which can lead to cell death. Nifedipine is a common calcium channel blocker that may block the calcium levels from increasing in the trophoblast cells, thus preventing cell death, and has been used safely during pregnancy.

Researchers studied placental cells acquired using chorionic villus sampling, a procedure routinely used to test for birth defects in the first trimester. The scientists divided these cells into three groups: one group was exposed to alcohol, another group was pretreated with nifedipine before being exposed to alcohol, and a third group was not exposed to either alcohol or nifedipine. Cells exposed to only alcohol died, as expected. In the group pretreated with nifedipine, nifedipine appeared to prevent the cells from dying after alcohol exposure. Clinical studies are needed to confirm these results, but they raise the possibility that calcium channel blockers could help protect placental cells from some toxic effects of alcohol.

Supported by NICHD, NHLBI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29048755

Copy number variation and congenital diaphragmatic hernia
Congenital diaphragmatic hernia (CDH) is one of the most common and severe congenital anomalies. In CDH, the large muscle (diaphragm) that separates the chest and abdominal cavities fails to develop normally in the fetus, allowing the contents of the abdomen move up into the chest. Almost always, CDH causes incomplete lung development and high blood pressure in lung arteries. Up to 80 percent of infants with CDH can survive, with expert surgical and medical care, but long-term illness is common in survivors. Analyses of CDH patients’ genetic makeup have identified more than 70 genes that may be related to disorder, but assessing exactly how genetic differences can lead to CDH has been challenging. Recently, researchers tried a different approach: analyzing sections of the human genome that are repeated and vary in the number of repeats between individuals, known as Copy Number Variation (CNV). The researchers searched for CNVs in both research participants with CDH and healthy “control” participants without the disorder. They were able to identify six CNVs that were either unique to, or overrepresented in, individuals with CDH. The researchers suggested that prioritizing these CNVs for further study could yield insight into the causes of CDH.

Supported by NICHD, NIGMS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29712845

Sleep-disordered breathing among newborns with myelomeningocele
Myelomeningocele, one of the most severe forms of spina bifida, can now be repaired with surgery, often performed before the child is born (known as intrauterine surgery). The procedure closes the external exposure of the spinal cord and its surrounding membranes (meninges). Despite early repair of myelomeningocele, many surviving children remain at risk for long-term neuromotor and intellectual disabilities. These include suffering from disordered breathing during sleep, such as sleep apnea (total cessation of breathing for brief periods during sleep) and hypopnea (abnormally slow and/or shallow breathing). In adults with myelomeningocele, sleep-disordered breathing increases the risk for heart diseases, and, on rare occasions, sudden death. In an NICHD-supported study of newborns with myelomeningocele that had been repaired either before or after the child was born, researchers found significantly greater sleep disturbances during the neonatal period, even after the surgical repair, compared to a matched group of newborn infants with no congenital anomalies being cared for in the neonatal intensive care units. The researchers suggest that infants with myelomeningocele be assessed for...
sleep disordered breathing as early as the first week of life, to ensure they are monitored and get treatment if needed.  
Supported by NICHD  
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29221695

Sleep disturbances in adolescents with spina bifida
Sleep disturbances are associated with pervasive impairments in adolescents’ cognitive, emotional, and physical functioning. Research has shown high rates of sleep deficiency in multiple pediatric illnesses, but such problems have received little attention in spina bifida research. In this relatively common congenital anomaly, a portion of the neural tube in which the spinal cord and brain develop and one or more vertebrae surrounding the spinal cord fail to close during fetal development. Using multiple methods to assess sleep in adolescents with spina bifida and typically-developing peers, researchers found that the young people with spina bifida were significantly more likely to experience shorter duration of nighttime sleep, more difficulty staying asleep, and higher levels of daytime fatigue. Girls with spina bifida were especially at risk for sleep problems. The researchers suggested that sleep problems may be underdiagnosed and undertreated in young people with spina bifida.  
Supported by NICHD, NINR  
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29272431

Vision, Hearing, and Speech

Blurry vision in babies may guide brain development
At birth, the shape of the eye does not allow images to be seen in sharp focus. As babies grow, their eyes change shape, improving visual focus. At the same time, areas of their brains that process visual images develop, forming connections and networks that help the infants recognize objects. Children who never experience this initial phase of out of focus imagery can later have difficulty with complex visual tasks. NEI-supported researchers observed that older children treated for bilateral congenital cataracts beyond a critical period of development rescued sharp vision (acuity) but were impaired in face-discrimination performance. They developed a computer simulation that compared the effects of training with high-resolution or blurred images on development of high-order receptive fields in the brain. The results showed that blurred images forced development of larger receptive fields that integrated information across a larger image area, improving performance and generalization across a range of resolutions. Blurred vision in babies may be a “feature” not a “bug” that actually drives formation of larger receptive fields in the brain required for recognizing faces.  
Supported by NEI  
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30322940

New mutation-independent gene therapy for childhood blindness
Patients with autosomal dominant retinitis pigmentosa (adRP) have a mutant form of rhodopsin that is toxic, killing rod photoreceptors. Over 150 mutations can cause adRP. Unlike most gene therapies that replace missing copies of normal genes, an approach developed by NEI-supported researchers involved a short-hairpin RNA interference-based gene therapy, which knocked down 98% of the rod's ability to produce rhodopsin in a dog model. Because rods need rhodopsin to function, the researchers also added a hardened shRNA-resistant rhodopsin gene to the same AAV vector.  
Supported by NEI  
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30127005
Learning Disabilities

Differences in brain development in preschoolers with ADHD
Attention deficit hyperactivity disorder (ADHD) is a condition marked by a pattern of inattention, hyperactivity and impulsive behavior. Using high-resolution brain scans, NICHD-supported researchers found that children as young as four years old with ADHD symptoms may have significant differences in brain structure, compared to children without symptoms. The study included 90 young children: 38 typically developing preschoolers and 52 preschoolers with symptoms of ADHD. The children’s scans revealed that those with ADHD symptoms had multiple areas with less brain matter volume than their typical peers, and these differences were consistent with parent reports of hyperactive and impulsive behaviors. The scientists will continue to follow the children, monitoring brain changes or differences as they grow older.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29576028

Individuals with ADHD show higher risk of early and persistent smoking
Children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for smoking cigarettes. To assess characteristics associated with long-term smoking outcomes into adulthood, scientists followed 469 children with ADHD from ages 7-10 into early adulthood, along with a matched control sample of 240 children without ADHD. In adulthood, the ADHD group had higher rates of daily cigarette smoking, one or more quit attempts, shorter time to first cigarette of the day, and more severe withdrawal than the control group. The ADHD group also reported younger daily smoking onset and moving more quickly from smoking initiation to daily smoking. Severity of ADHD symptom in later adolescence and adulthood was associated with higher risk for daily smoking. This study shows that ADHD-related smoking risk begins at a young age, progresses rapidly, and becomes resistant to quitting by adulthood.
Supported by NIDA, NIMH
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29538764

Intellectual and Developmental Disabilities, Neurological Disorders, and Mental Health

New prevalence estimates of fetal alcohol syndrome disorders (FASDs)
Using a comprehensive approach consisting of school-based assessments, a common methodology and classification system, and expert in-person evaluations, NIAAA’s Collaboration on FASD Prevalence recently found FASD rates ranging from one to five percent among more than 6,000 first-grade students across four U.S. communities. The research findings suggest that children with FASD often go undiagnosed or misdiagnosed, and that strategies to expand FASD screening, diagnosis, prevention, and treatment are needed.
Supported by NIAAA
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29411031

Existing salivary diagnostics products problematic for detecting BDNF in children.
Previous research suggests that altered expression of brain-derived neurotrophic factor (BDNF), a protein that plays an important role in the survival, growth and regulation of nerve cells, may explain some of the symptoms of Rett syndrome (RTT), a rare neurological disorder. Recently, researchers tested the ability of two commercially available saliva tests to measure BDNF levels in samples from 16 RTT patients. One of the tests did not detect BDNF levels in the saliva of any of these patients. A second saliva test was performed in 10 of these patients who had additional saliva samples available; all but one had BDNF
levels that were outside the range that could be accurately measured by the assay. The researchers concluded that commercially available assays cannot yet reliably detect BDNF levels in saliva, and suggest caution in using salivary BDNF to measure the impact of interventions for people with RTT.
Supported by NICHD, NCATS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29373156

Breathing disturbances in individuals with Rett syndrome
Rett syndrome is a genetic neurodevelopmental disorder that begins early in childhood and predominantly affects females. Children with Rett syndrome often regress in their skills, or alternate between being able and unable to perform certain tasks. Most girls with Rett syndrome experience breathing disturbances during their waking hours. For example, they may experience hyperventilation (shallow, fast and/or forceful breathing) or breath-holding. How these breathing disturbances affect an individual’s health over time is not understood but it has been suggested that cardiorespiratory dysfunction could cause a quarter to almost a half of the sudden, unexpected deaths in individuals with Rett syndrome. NICHD’s large, ten-year natural history study of a cohort of over 1,000 individuals with Rett syndrome has provided a clearer picture of awake breathing problems in the major subtypes of this disorder. The researchers found that almost all girls with “classic” Rett and a majority of those with “atypical” Rett develop breathing disturbances. These breathing disturbances have a negative impact on the quality of life of those with Rett and their caretakers, although severe breathing dysfunction is relatively uncommon. Both breath-holding and hyperventilation occur in a majority of individuals with Rett by age five. Severe breathing disturbances peak at ages six to 11, and then wane in adolescence. The researchers suggested that clinicians consider the possibility of Rett syndrome in individuals, particularly girls, with developmental delay and prominent hyperventilation or breath-holding while awake.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29657083

Racial differences in the age of first autism diagnosis may be related to how parents report concerns
Children with autism spectrum disorder (ASD) tend to have better outcomes if they are diagnosed early and receive early intervention services. However, black children are typically diagnosed with ASD later than children of other races. The reason behind this difference is unclear. Researchers set out to assess whether race was a factor in parents’ reports of concerns about their child’s development and ASD symptoms with health care providers. The research team asked parents of 18- to 40-month-old toddlers about concerns they had regarding their child’s development before these children were eventually diagnosed with ASD. They categorized these concerns as involving ASD issues (like repetitive behaviors) or non-ASD issues (like motor difficulties and disruptive behaviors). Black parents were less likely to express concerns about ASD issues than white parents. Black parents were specifically less likely to express concerns about deficits in social interaction and repetitive or restricted behaviors, even if their children’s symptoms related to social feelings and moods were significantly more severe than the children of white parents. Both black and white parents were most concerned about their child’s communication and speech. There were no differences in parental reporting of non-ASD issues.
Supported by NICHD, NIMH
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29100475

Using baby teeth to predict autism
Scientists in a recent study were able to predict ASD diagnosis using baby teeth to measure fluctuations in the essential nutrients zinc and copper during early development. Children that were diagnosed with ASD had both shorter and less organized zinc-copper cycles, which suggests that the regulation of metal absorption may be a factor in risk for ASD.
Supported by NIEHS, NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29854952
**Exposure to DDT and increased risk of autism**
Despite DDT’s being banned in most developed countries for several decades, a primary metabolite of the insecticide is stored for long periods in fatty tissues of the body, with measurable levels present in most women of child-bearing age. A recent NIEHS-supported study found that children of mothers with the highest prenatal levels of this metabolite were at increased risk of autism diagnosis, and that this increased risk was greater for autism with other types of intellectual disability.
Supported by NIEHS

**Children with autism spectrum disorders, gastrointestinal symptoms, and immune system imbalance**
Children with autism spectrum disorders (ASD) are more likely to have gastrointestinal (GI) symptoms than typically developing children. Researchers analyzed blood and stool samples from four groups of children: (1) children with ASD and GI symptoms; (2) children with ASD but without GI symptoms; (3) children with GI symptoms but not ASD; and (4) children with neither ASD nor GI symptoms. The scientists found that children with ASD who also experience GI symptoms may have an imbalance in their immune system responses. The researchers also suggested that imbalance in the intestinal microorganisms that help with digestion may play a role in these problems.
Supported by NICHD, NIEHS, NIDDK, NCATS, NIMH

**Imaging in infants with fragile X syndrome**
Fragile X Syndrome (FXS) is a genetic disorder that affects a person’s development, behavior, and ability to learn. FXS results from a mutation in a specific gene on the X chromosome that codes for a critical brain protein called FMRP. People with FXS do not make enough FMRP; however, the ways in which having too little FMRP lead to changes in brain structure and function are not fully understood. In this study, researchers used brain imaging to study infants with and without FXS. They looked at the development of white matter tracts, which connect different areas of the brain and play key roles in communication and coordination between brain regions. They found that 12 of 19 major white matter tracts were underdeveloped in infants with FXS, compared with typically-developing peers. They also found that these changes were established by six months of age, far younger than the average age at which FXS is diagnosed, though the changes did not worsen over time.
Supported by NICHD, NIBIB, NIMH

**Epigenetic editing reactivates FXS gene**
FXS results from a mutation in a specific gene on the X chromosome. This mutation silences the *FMRI* gene. The silencing occurs because specific sites upstream of the *FMRI* gene are hypermethylated, a type of epigenetic modification that suppresses gene expression. Researchers used a CRISPR/Cas9-derived tool to block DNA methylation specifically at these sites in induced pluripotent stem cells from individuals with FXS, thereby restoring *FMRI* expression. This finding demonstrates that epigenetic editing may be a promising therapeutic approach for disorders caused by the silencing of specific genes.
Supported by NINDS, NIGMS, NIMH

**The role of microglia in epilepsy associated with tuberous sclerosis complex**
Tuberous sclerosis complex (TSC) is a rare genetic condition that is characterized by epilepsy, intellectual disability, and autism. It is caused by abnormalities in the *TSC1* or *TSC2* gene in humans, or the *Tsc1* gene in mouse models. In brain tissue samples from individuals with TSC, researchers detected abnormalities in microglia, a type of cell that functions as a form of immune defense in the nervous system. Scientists have not known whether problems in the microglia contribute to epilepsy in people with TSC, whether the microglia defects are secondary effects of epileptic seizures, or whether the
Microglia defects are not related to seizures at all. Scientists used experimental mouse models of TSC to explore the possibility that inactivating the \textit{Tsc1} gene in microglia would be enough to cause epilepsy in the mice. The researchers found that microglia abnormalities may be related to epilepsy in mouse models of TSC, but that selective inactivation of the \textit{Tsc1} gene in microglia may not, by itself, be enough to cause epilepsy.

**Common data elements for cerebral palsy research**

NINDS and the American Academy of Cerebral Palsy and Developmental Medicine collaborated to develop the first comprehensive set of Common Data Elements (CDEs) for cerebral palsy research, to increase the efficiency and effectiveness of clinical research studies. Based on a review of existing NINDS CDEs and tools used in studies of children and young people with CP, the CDEs were compiled, subjected to internal review, and posted online for external public comment in September 2016. The resulting CDEs are publicly available on the NINDS CDE website and are categorized into six domains: (1) participant characteristics; (2) health, growth, and genetics; (3) neuroimaging; (4) neuromotor skills and functional assessments; (5) neurocognitive, social, and emotional assessments; and (6) engagement and quality of life. The use of these CDEs for CP will help to standardize data collection, improve data quality, and facilitate comparisons across studies.

**Measuring pain interference in children with cerebral palsy**

The wide range of cognitive and physical abilities in children with cerebral palsy has made it challenging for physicians and researchers to assess pain for these children. Other individuals ("proxies") often need to report pain on behalf of individuals who cannot report for themselves. NICHD-supported researchers evaluated the consistency and accuracy of a 12-item pain questionnaire that was modified for use in children with cerebral palsy, with or without cognitive impairment. The questionnaire collected information from proxies (in this case, children’s caregivers) about the children’s experiences of "pain interference" – that is, the degree to which pain interfered with their activities of daily living such as school and communication. The resulting pain interference scores had strong internal consistency for reporting of children’s pain, making this questionnaire a potentially useful tool for researchers and clinicians.

**Executive function in school-aged children with cerebral palsy**

For about 40 percent of children with cerebral palsy, the predominant injury is of the brain tissue known as white matter. White matter plays a key role in developing executive functioning (EF) skills—higher-order cognitive abilities that guide and manage an individual’s functioning and behaviors. Studies of adolescents and school-age children with cerebral palsy have found that they have difficulties with self-control, working memory, flexibility, paying attention, planning, and other EF skills. Little is known, however, about possible relationships between EF skills and the speech and language problems that many children with cerebral palsy also experience. Scientists found that, as expected, children with cerebral palsy were more likely to have EF difficulties compared with typically developing children. The proportion of children with cerebral palsy that had EF difficulties was far greater than the researchers expected, however. They also found that that EF deficits weren’t necessarily restricted to one type of deficit, and that children with cerebral palsy but without speech and language problems still struggled with EF skills, suggesting that these deficits are not directly associated with a child’s speech or language abilities. The researchers concluded that the potential for EF vulnerabilities should be considered for all
children with cerebral palsy, and that even those without speech and language problems may need interventions for possible EF problems.
Supported by NICHD, NIDCD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29853333

**Resistance training on treadmill improves movement function in children with cerebral palsy**
Cerebral palsy is the most common childhood-onset physical disability. Up to 90 percent of children diagnosed with cerebral palsy have difficulty walking. Treadmill training may improve the ability of children to walk, either through resistance training (forcing the leg to move against a load) or assistance training (facilitating leg movement while walking). NICHD-supported researchers studied 23 children with spastic cerebral palsy between 6- and 14-years-old who exhibited limitations in movement. The children trained for three times a week for six weeks, with approximately half the participants receiving controlled resistance training, and the other half receiving controlled assistance training. The resistive or assistive forces were applied to the legs during swing by a custom-built exoskeleton robot. After the 18 sessions, the children who underwent resistance training showed improvements in walking speed and distance walked within six minutes. Most importantly, improvements in walking distance persisted eight weeks after the training ended. The children who underwent assistance training showed no significant changes in walking speed or distance. These findings indicate that resistance treadmill training may be more effective than assistance training in improving movement function in children with cerebral palsy.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/28576629

**Undescended testicles in boys with cerebral palsy**
Among the anomalies associated with cerebral palsy is cryptorchidism or “undescended testicles”, a condition in which one or both testes fail during fetal development to move down from the abdomen into the scrotum. Untreated cryptorchidism can cause infertility. Analyzing electronic health records for 839 boys followed at least until age seven at a large pediatric cerebral palsy clinic, researchers found that this condition was far less common than previously reported. About 24 percent of the boys had completely “undescended” testes and 5 percent had a less severe, “retractile” condition of variable testes position. Cryptorchidism was most strongly associated with cerebral palsy spasticity in both arms and legs of the young patients and was more likely to occur when cerebral palsy was associated with other congenital anomalies and poor fetal growth.
Supported by NICHD, NIGMS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29713311

**Gene therapy approach to LAMA2 muscular dystrophy in a mouse model**
Muscular dystrophies (MD) are a group of hereditary diseases characterized by progressive weakening and wasting of muscles. Limb girdle muscular dystrophy type 1A, also named LAMA2-related muscular dystrophy (LAMA2 MD), is caused by mutations in the LAMA2 gene. There is no treatment approved for LAMA2 MD. It has been challenging to develop a gene-replacement therapy for LAMA2 MD, but recently researchers developed a novel viral vector, designed to carry a functional substitute for the mutated laminin α2 subunit of the gene to the host cell genome (full component of genes). An early version of this vector, tested in a mouse model of LAMA2 MD, showed significant effect in skeletal muscle. More recently, the researchers tested a second version of the vector, which has been shown to have a wider distribution in the host animal. The results demonstrated that this newer vector not only had more widespread transduction – that is, the capacity stably to introduce a foreign gene to host cell genome – but also extended the lifespan of the experimental mice and improved muscle pathology and motor function. In addition, this study demonstrated improved neurological function by reducing peripheral nerve pathology and improving cognitive function in the LAMA2 mice.
Supported by NICHD, NINDS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29766020
**Alternative steroid in an animal model as treatment for limb girdle muscular dystrophy**

In limb girdle muscular dystrophy type 2B (LGMD2B), limb muscles closest to the trunk are most affected, that is, shoulders, upper arms, pelvic area, and thighs. This disorder is caused by a mutation in the dysferlin gene, which leads to reduced levels or a lack of the dysferlin protein. This protein is necessary for normal repair of muscle fibers; its absence results in inadequate repair, chronic muscle inflammation, and progressive muscle degeneration. Recent drug research utilizing a mouse model of LGMD2B compared two synthetic steroids: vamorolone and prednisone. Vamorolone, was associated with stabilization of dysferlin-deficient muscle cell membrane and repair of injured myofibers (heterogeneous muscle fibers). Prednisone did not have these effects and instead increased muscle weakness and myofiber atrophy, a finding consistent with reports that prednisone worsened symptoms in patients with LGMD2B.

Supported by NICHD, NINDS, OD

**Gene editing restores expression of a key protein in an animal model of Duchenne muscular dystrophy**

Mutations in the gene encoding dystrophin, a protein that maintains muscle integrity and function, cause Duchenne muscular dystrophy (DMD). Using an animal model, researchers tested whether delivering gene editing components to animals’ muscles could restore the dystrophin protein. After the genetic material was delivered into skeletal muscle, dystrophin expression increased. The results of these experiments support the idea that, with further development, gene editing approaches may prove useful for the treatment of DMD.

Supported by NICHD, NIAMS, NHLBI

**Zebrafish model of muscular dystrophy shows negative impact of infection**

Duchenne muscular dystrophy (DMD) is the most common congenital muscle disease. Influenza A and B viruses are frequently associated with muscle complications, especially in children, and drugs that suppress the immune system can reduce DMD symptoms. Taken together, these data suggest that the immune system may contribute to muscle pathology. NICHD researchers studied both (a) healthy zebrafish and (b) a special group of zebrafish that genetically mimic DMD after all the zebrafish were infected with the influenza A virus. The scientists found that all the infected zebrafish displayed muscle degeneration. However, the zebrafish that modeled DMD displayed more severe muscle damage than would be expected, even from adding together the negative effects of DMD and influenza A infection. This suggests that DMD and influenza A infection might combine to have a stronger negative effect on muscles. These data demonstrate the importance of preventing influenza infections in individuals with genetic muscle diseases.

Supported by NICHD

**Risk calculator for predicting long-term course of pediatric bipolar disorder**

Childhood onset bipolar disorder is associated with elevated risk for suicide, substance use disorders, and psychosocial impairment. However, little is known about how bipolar disorder progresses across development and which individuals will have persistent or worsening symptoms, versus which individuals will remain stable or improve. In order to address this knowledge gap, NIMH-supported researchers studied 140 youth, ages 6-17, who were assessed on average every seven months for a median of 11.5 years. The researchers developed a risk calculator which was able to discriminate individuals who converted from a subclinical diagnosis to bipolar I or II. This tool could potentially inform individualized interventions for optimal treatment.

Supported by NIMH
Mental health of transgender and gender nonconforming youth
To better understand the magnitude of mental health problems experienced by transgender and/or gender non-conforming (TGNC) children (3-9 years) and adolescents (10-17 years), NICHD-supported researchers examined electronic medical records of 588 transfeminine (assigned male at birth but identified as female) and 745 transmasculine (assigned female at birth but identified as male) children and adolescents. Each study participant was matched to ten male and ten female cisgender (identify with the gender assigned to them at birth) participants with similar demographic characteristics. For all diagnostic categories, TGNC participants were more likely to experience mental health concerns than cisgender participants. Of special concern, both self-inflicted injury and suicidal thoughts were significantly higher in TGNC participants compared with the cisgender participants.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29661941

Brain mechanisms of attention orienting following frustration
Researchers in the NIMH Intramural Research Programs (IRP) used functional magnetic resonance imaging (fMRI) to examine associations between irritability and neural activation across age in youths. Following a frustrating task, levels of irritability correlated with activity in neural systems mediating attention orienting, regulation of emotions, and movement. Although most associations were independent of age, dysfunction in some regions was more pronounced in young children with irritability.
Supported by NIMH
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30336704

Developing therapies for pediatric anxiety
Anxiety disorders are one of the most common mental health issues affecting children. NIMH intramural researchers are developing and refining novel computer-based cognitive training therapies for pediatric anxiety. Researchers found that attention bias modification therapy (ABMT) is complementary to cognitive-behavioral therapy (CBT), as each of the two treatments appear to target different behaviors and parts of the brain. Youth who received the combination of the two therapies (ABMT + CBT) exhibited less severe anxiety after treatment, than those who received CBT and placebo. Accumulating results suggest that these therapies could significantly enhance the available treatments for anxiety disorders.
Supported by NIMH
Article:  https://www.ncbi.nlm.nih.gov/pubmed/28407726
https://www.ncbi.nlm.nih.gov/pubmed/30426323

Pediatric Pharmacology
Diuretic therapy for extremely preterm infants
Diuretic medicines are commonly given to preterm infants to help drain fluid from the lungs, but there is little research evidence to support the practice. Researchers analyzed data collected on 835 preterm infants at 13 U.S. neonatal intensive care units to understand respiratory difficulties in extremely premature infants during the first year of life. Surprisingly, infants in the study who received diuretic therapy were more likely to require additional respiratory support in the days following diuretic therapy, compared to extremely preterm infants with similar respiratory problems who did not receive the therapy. In addition, the different hospitals varied widely in their use of diuretic therapy. The results call into question whether diuretic therapy is helpful for preterm infants.
Supported by NICHD, NHLBI, NIAID
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29599068
Understanding how newborns process acetaminophen
The availability of an intravenous form of acetaminophen has significantly increased its use in neonatal intensive care units (NICUs) to treat pain in medically fragile newborns. Marketed as Tylenol and under other brand names, acetaminophen is known to have variable effects in adults because of genetic variability in the enzymes involved in the body’s processing of the drug. This variability could lead to possible adverse effects from overdosing, such as poisoning the liver. Very young infants are undergoing developmental changes in the drug-metabolizing enzymes that process acetaminophen. A new research model recently developed and tested in a group of 33 NICU patients has found that those with a specific genetic variant have a 42 percent reduced elimination (“clearance”) of acetaminophen through one of several metabolic pathways. This reported effect may not be clinically significant, because that specific pathway accounts for a small fraction of overall acetaminophen clearance from the newborn body. Still, the research model provides a better description of variability of acetaminophen’s effects in newborns and highlights the importance of further research on the genetics of drug treatments in the youngest patients. Supported by NICHD, NCATS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29654492

Acetaminophen may decrease risk of kidney injury in pediatric heart surgery
Acute kidney injury (AKI) occurs in approximately 25 percent of children admitted to intensive care units. Among children who have cardiac surgery, rates of AKI are even higher, and AKI is associated with increased health problems and even death. Acetaminophen (marketed under the brand name Tylenol) is a well-established drug used to reduce pain and fever. Prior research has suggested that acetaminophen might help prevent AKI. Analyzing data from children who underwent surgery in 2008 to 2016, NICHD-supported researchers found that children who were given acetaminophen in the first 48 hours immediately following surgery may have a lower rate of AKI. Supported by NICHD, NHLBI, NCATS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29799947

Children with obesity require lower doses of medication for gastroesophageal reflux disease
Children with obesity are six times more likely than normal-weight children to experience GERD, an uncomfortable and potentially dangerous condition in which the esophagus is chronically exposed to stomach acid. Proton pump inhibitor (PPI) drugs are a primary therapy for GERD, and weight-based determinations of PPI dosing amounts are standard treatment for GERD in adults and children. However, results of a recent clinical study of a PPI, (pantoprazole, brand name Protonix) in children and adolescents with obesity and GERD suggest that simply increasing PPI dosing on the basis of total body weight is not appropriate. Studying the drug’s pharmacokinetics showed higher exposures and slower clearance (elimination from the body) in these young study participants. Thus, reducing, not increasing the drug dose may be warranted for young patients with obesity and GERD. Study results also suggested that observed differences in two participant age groups (children age 6-11 years and adolescents age 12-17 years) may not be simply a matter of body size, but also effects of obesity on certain drug-metabolizing enzymes, which were analyzed as part of the research. This study highlights the need for more dosing-based research in the pediatric population for various conditions and therapeutics. Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29389444

Duration of pediatric clinical trials submitted to the US Food and Drug Administration
As chronic disease becomes more prevalent in children, there are questions about the safety of long-term pharmacologic therapies for such conditions and the implications of such therapies for children’s growth and development. NICHD-supported researchers recently assessed the length of pediatric clinical drug trials yielding data submitted to the U.S. Food and Drug Administration (FDA), between late 2007 and the end of 2014, for “pediatric labeling” --- that is, FDA-approved, evidence-based information on pediatric drug safety, indications, dosing, and other concerns. Of 306 trials submitted in support of 86
drugs intended for long-term use in children, those most commonly studied were for treating common pediatric conditions, such as neurologic conditions (e.g., ADHD) at 29 percent, pulmonary conditions (e.g., asthma) at 19 percent, and infections at 16 percent of the drugs studied. The median maximum duration trial of a drug was 44 weeks and for nearly two-thirds of the drugs (61 percent), the longest duration of a trial was less than 52 weeks. The authors concluded that because of the potential extended use of drugs for chronic conditions in children, the clinical community should consider the possible need of new approaches to understanding the long-term safety of drugs for chronic diseases in children.

Supported by NICHD

**Rare Pediatric Diseases**

**Drug is not effective in children with Angelman syndrome**
Occurring in 1 in 12,000 to 20,000 people, Angelman syndrome (AS) is a genetic neurodevelopmental disorder that causes global developmental delay, intellectual disability, epilepsy, and other symptoms. Research in mouse models has indicated that levodopa, a drug used to treat Parkinson disease, could target the underlying pathological process of AS. Because levodopa is being prescribed “off label” for children with AS by an increasing number of clinicians without science-based FDA approval for this use, NICHD-supported researchers conducted a randomized, controlled clinical trial of levodopa to assess its effects in 4- to 12-year-old children with AS. At the dosage used in the year-long trial, there were no clinically or statistically significant improvements in neurodevelopmental, cognitive, or behavioral outcomes in children treated with levodopa versus those receiving a placebo.

Supported by NICHD

**Treatment of rare autoinflammatory diseases**
Interferon-mediated autoinflammatory diseases, or interferonopathies, are rare immune deficiencies that present in infancy with systemic inflammation, inflammatory organ damage, and high mortality. Scientists demonstrated that treatment with the interferon-blocking drug, baricitinib, may improve symptoms in patients with rare autoinflammatory diseases, suggesting that this class of drug is a promising therapeutic strategy for interferonopathies.

Supported by NIAID, NIAMS

**Potential treatment for disorders involving excess red blood cells**
Chuvash polycythemia is an inherited life-threatening disorder characterized by overproduction of red blood cells and similar to mountain sickness, a blood complication experienced in high-altitude settings with low oxygen levels. Using a mouse model of Chuvash polycythemia, NICHD researchers found that feeding the mice a diet containing an experimental drug (Tempol) for three to six months decreased the animals' red blood cell levels and disease symptoms (reddish, swollen paws and snouts) went away. Next, to mimic mountain sickness, normal mice were placed in low-oxygen housing for 23 days and developed polycythemia; all five of the mice that were fed a Tempol-supplemented diet survived, whereas two of five mice with a regular diet died. These findings offer hope that Tempol, or a similar drug, may treat similar disorders that affect human beings, such as mountain sickness.

Supported by NICHD

**Advancing potential gene editing treatment into clinical trials**
Funded by the Rare Diseases Clinical Research Network, the Lysosomal Disease Network (LDN) supports clinical studies of children and adults with a lysosomal disease, including natural history studies
to reveal how these diseases progress over time. LDN scientists found that a gene editing technique could prevent or reverse Hurler syndrome in some tissues in mice with the disease. When the researchers evaluated the technique’s effects in a learning behavior test, the results in treated mice suggested that the therapy reached the brain, along with similarly promising findings in mice with Hunter syndrome. Scientists made the first attempt to edit a gene inside the human body in a patient with Hunter syndrome and continue to work on this potential treatment.

Supported by NCATS, NINDS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29517765

**Feline model accelerates clinical translation of experimental therapy for Niemann-Pick Disease, Type C1**

Niemann-Pick disease type C1 (NPC1) is a lipid storage disease that damages the nervous system and typically results in death between age 5 and 15. A new NPC1 feline model has accelerated the clinical translation of a promising experimental therapy initially developed in the NPC1 mouse model by providing critical information on route of delivery, scaling of dose, adverse events, and surrogate biomarkers that would not have been feasible using the mouse model. Notably, this work led to the development of a phase 1/2a trial of 2-hydroxypropyl-beta-cyclodextrin that has yielded promising efficacy data and supported the initiation of a multinational phase 2b/3 clinical efficacy trial that has been approved by both the Food and Drug Administration and the European Medicines Agency.

Supported by ORIP, NICHD, NINDS, NCI
Article:   https://www.ncbi.nlm.nih.gov/pubmed/25717099

**Localized aggressive periodontitis (LAP) disease progression in children**

Localized aggressive periodontitis (LAP) is a rare and severe form of periodontal disease that is more common in African American children and adolescents. Because LAP is rare, dentists often do not recognize early signs of disease, hindering timely diagnosis and treatment. To address this problem, NIDCR-supported scientists studied primary teeth of children with LAP and charted the course of disease progression, which begins with bone loss around the first molars. This new knowledge may allow dentists to identify and treat LAP earlier in children and help prevent loss of adult teeth.

Supported by NIDCR
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29087795

**Mitochondrial function in glycogen storage disease type Ia**

Mitochondria are a type of subcompartment in cells where sugars, fats, and proteins are converted into energy that is essential for healthy body functioning. A rare inherited metabolic disorder, known as glycogen storage disease type Ia (GSD-Ia), results from liver malfunctioning that makes the body unable to maintain normal blood sugar levels between meals. Consequently, individuals with GSD-Ia must eat extremely frequently, including through the night, so as to prevent crises in low blood sugar levels that can cause seizures. One of the most severe long-term complications in GSD-Ia is benign and malignant liver tumors. NICHD-supported scientists determined that GSD-Ia is caused by a deficiency in a specific enzyme called glucose-6-phosphatase-α (G6Pase-α). Recent studies have shown that G6Pase-α deficiency in the mouse liver leads to mitochondrial dysfunction that can contribute to tumor development in GSD-Ia. However, normalizing the defective enzyme expression has the effect of restoring mitochondrial function. The research also provides important new insights into basic processes that cause the mitochondrial dysfunction.

Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29740774
**Effect of treatments in animal models of mitochondrial complex I disease**

Mitochondria are organelles within cells that are responsible for generating more than 90 percent of the energy needed by the body to sustain life and support organ function. Mutations that affect mitochondrial function can lead to decreased energy production, which can result in cell injury and/or death. Because many different genetic mutations can affect the mitochondria, and the effects of mitochondrial damage vary widely across individuals, mitochondrial disorders are challenging to diagnose and treat. For one type of mitochondrial disorder, called mitochondrial complex I disease, a key contributing factor is oxidative stress—an imbalance between two types of molecules (free radicals and antioxidants) in the body. Researchers tested potential treatments, including vitamins, in several animal models of mitochondrial complex I disease to see if they could reduce oxidative stress, improve mitochondrial function, and extend the animals’ lifespan. The scientists found that most of these treatments had physiological benefits, and that vitamin E and another compound also extended lifespan in the animal models.

Supported by NICHD, NIGMS, NIDDK


**Pediatric Cancer**

**Developmental origins of fusion oncoprotein-negative rhabdomyosarcoma**

Rhabdomyosarcoma (RMS) is a pediatric soft tissue cancer that was thought to originate from skeletal muscle progenitor cells. RMS can occur throughout the body, including sites that lack skeletal muscle tissue. It can be classified as fusion oncoprotein positive or fusion-negative based on the presence or absence of specific gene fusions. Researchers showed that endothelial progenitor cells, which should develop into blood vessel cells, can give rise to fusion-negative RMS through aberrant activation of the Hedgehog signaling pathway in non-myogenic cells.

Supported by NCI


**Selected gene enhancer elements are potential therapeutic targets for metastatic osteosarcoma**

Osteosarcoma is the most common type of bone cancer in children and adolescents. Lung metastases occur in approximately half of osteosarcoma patients, but effective therapies to treat these metastases are lacking. This study identified gene enhancer elements that are specific to metastatic osteosarcoma cells compared with non-metastatic osteosarcoma cells in a model of lung metastasis. These enhancer elements control the expression of genes necessary for osteosarcoma metastatic colonization and may be ideal targets for therapeutic intervention.

Supported by NCI, NIGMS


**Identifying a specific genetic locus that is associated with survival in osteosarcoma patients**

Over the past three decades, there has been little improvement in survival rates for patients with metastatic osteosarcoma at diagnosis. Researchers conducted a multi-institutional genome-wide association study to identify germline genetic variants associated with overall survival in 632 patients with osteosarcoma. The strongest single association was localized to the GLDC gene, adjacent to the IL33 gene, on chromosome 9p24.1. Using publicly available data, the risk allele was associated with lower expression of IL33. In an independent set of osteosarcoma patients, low expression of IL33 was associated with poorer overall survival.

Supported by NCI

**BRCA1 protein plays a role in treatment response of Ewing sarcoma cells**

Ewing sarcoma forms in the bones or the soft tissue around bones. Eighty-five percent of this cancer, which occurs primarily in children and young adults, is driven by a fusion oncoprotein (EWS-FLI1). Recent findings revealed that EWS-FLI1 increases gene expression and DNA damage, while simultaneously reducing a cell’s ability to repair damaged DNA through a process called homologous recombination. Researchers identified the protein BRCA1 as playing a key role in the impairment of this type of DNA repair mechanism. These findings enhance our understanding of the molecular mechanisms by which fusion oncoproteins drive pediatric cancers and explain why Ewing sarcoma cells are sensitive to certain chemotherapies.

Supported by NCI, NIEHS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29513652

**Genome-wide DNA methylation patterns are predictive of outcome in juvenile myelomonocytic leukemia**

Juvenile myelomonocytic leukemia (JMML) is a rare blood cancer of childhood caused by mutations in the RAS oncogene pathway. Outcomes in JMML vary markedly from spontaneous resolution to rapid relapse after hematopoietic stem cell transplantation. Scientists found that methylation patterns in the DNA of blood cells of JMML patients are predictive of outcome and can identify patients most likely to experience spontaneous resolution.

Supported by NCI, NHLBI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29259179

**Preventive antibiotic treatment reduced risk of bacteremia in children with acute leukemia**

The presence of bacteria in the blood, called bacteremia, can cause serious illness among children with acute leukemia and those undergoing hematopoietic stem cell transplantation (HSCT). NCI-supported researchers showed that prophylactic administration of the drug levofloxacin significantly reduced the risk of bacteremia in children with acute leukemia receiving intensive chemotherapy. However, it did not have a similar effect in those undergoing HSCT.

Supported by NCI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30208456

**DPP8/DPP9 inhibitors are potential treatment agents for acute myeloid leukemia**

Researchers identified a potential new therapeutic strategy for the treatment of acute myeloid leukemia (AML), a type of leukemia that affects both children and adults. The scientists found that small-molecule inhibitors of the serine dipeptidases DPP8 and DPP9 induce a type of cell death known as pyroptosis in the majority of AML cell lines and primary AML samples tested. The inhibitors also hindered AML progression in mouse models.

Supported by NCI, NIAID, NIGMS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29967349

**Advances in understanding the genomics of childhood solid tumors and leukemias**

In the past year, three NCI-supported publications have advanced understanding of the genomics of childhood cancers. The first provided a pan-cancer genome and transcriptome analyses for 1,699 pediatric leukemias and solid tumors, presenting a comprehensive genomic architecture for pediatric cancers and emphasizing the need for pediatric cancer-specific development of precision therapies. A second publication focused on the molecular landscape of pediatric acute myeloid leukemia (AML) and characterized nearly 1,000 participants in AML trials. The results highlighted the need for age-tailored targeted therapies for the treatment of pediatric AML. A third publication defined the genetic landscape of Wilms tumor by comprehensive analysis of 117 Wilms tumors followed by targeted sequencing of 651 tumors. Integrated analyses showed that two major classes of genetic changes involving microRNA
biogenesis and transcriptional elongation interrupted developmental pathways resulting in Wilms tumor oncogenesis.

Supported by NCI

Article: https://www.ncbi.nlm.nih.gov/pubmed/29489755

**FDA approved use of the drug iobenguane I-131 (Azedra) for adrenal gland tumors**

Adrenal gland tumors occur in approximately 200 to 500 people in the U.S. annually. In 2018, the FDA approved iobenguane I-131 (Azedra) for the treatment of adults and adolescents age 12 and older with tumors of the adrenal gland. The company that developed iobenguane I-131, Molecular Insight, received funding from NCI’s SBIR program in 2005 to develop the agent and was acquired by Progenics Pharmaceuticals in 2013.

Supported by NCI

FDA: https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm615155.htm

**A new source of therapeutic targets in MYCN-amplified neuroblastoma**

High-risk neuroblastomas with amplification of the MYCN oncogene are difficult to treat effectively. Researchers used genome editing and high-throughput genome sequencing to detect genes involved in tumor cell growth and survival of MYCN-amplified neuroblastoma cell lines. The findings demonstrated that a small number of essential transcription regulatory factors function as a circuit to maintain the cancer-cell state in MYCN-amplified neuroblastoma and identify 147 candidate gene dependencies selective for MYCN-amplified neuroblastoma. The dependency genes were found to contribute to the initiation, maintenance, and survival of MYCN-amplified neuroblastoma and provide a source of additional 'druggable' targets for this cancer.

Supported by NCI, NIGMS, NINDS

Article: https://www.ncbi.nlm.nih.gov/pubmed/30127528

**Potential new drug combinations for childhood cancers**

A team of researchers are using matrix combination screening capabilities to advance research on several difficult-to-treat childhood cancers. The team uses this screening technique to rapidly test the effects of thousands of different drug combinations on key disease processes. Scientists can examine the most effective combinations, find the best doses of each drug and learn more about their effects on cells. In Rhabdomyosarcoma, the scientists have discovered different combinations for the two major subtypes of this devastating disease based upon each variant unique oncogenic signaling pathway. In Ewing Sarcoma, a novel drug combination emerged which attacks a key DNA repair pathway that the cancer cells require. In diffuse intrinsic pontine glioma, the screening datasets revealed a combination of drugs which rewire the cell in a way that collapses the metabolic systems that they need to survive.

Supported by NCATS, NCI

Website: https://ncats.nih.gov/pubs/features/childhood-cancer

**Novel drug is effective in TRK fusion-positive cancers in children and adults**

Fusions involving tropomyosin receptor kinase genes (TRK) occur in a number of cancers in children and adults. One TRK inhibitor, larotrectinib, demonstrated marked and durable antitumor activity in patients with TRK fusion-positive cancers, regardless of the patient’s age or tumor type. In 2018, the FDA issued larotrectinib an orphan drug status and Priority Review, and, in November 2018, the FDA granted accelerated approval to larotrectinib. This is the second tissue-agnostic FDA approval for a precision cancer therapy.

Supported by NCI, NCATS

Article: https://www.ncbi.nlm.nih.gov/pubmed/29466156
Anticancer drug continues to show promise in children with neurofibromatosis type 1 (NF1)
Selumetinib is an anticancer drug that has been shown to shrink tumors in children and young adults with a genetic syndrome called neurofibromatosis type 1 (NF1). Selumetinib may improve symptoms, such as pain and reduced mobility, that result from tumors called plexiform neurofibromas, which develop in many people with NF1. Preliminary results from a phase II trial confirm the results of a smaller trial in 2016 that demonstrated for the first time this drug could also shrink large tumors and appeared to help improve other health problems associated with tumors. After a year of treatment, most patients in the trial (or their parents) reported improved pain scores, strength, and range of motion.
Supported by NCI
Article: https://ascopubs.org/doi/abs/10.1200/JCO.2018.36.15_suppl.10503

Over half of childhood survivors of tumors in the central nervous system (CNS) do not achieve complete independence as adults
Beyond survival, achieving independence is a primary goal for adult survivors of pediatric CNS tumors. NCI-supported scientists assessed indicators of functional and social independence in 306 survivors of childhood CNS tumors. Sixty percent of the survivors assessed did not achieve complete independence as adults. Reductions in the intensity of primary therapies and interventions that target physical performance and adaptive deficits may help survivors to achieve greater independence.
Supported by NCI
Article: https://www.ncbi.nlm.nih.gov/pubmed/30091946

Childhood Injuries and Maltreatment

Neonatal erythropoietin mitigates deficits in a rat model of prenatal brain injury
In rat model of prenatal brain injury, researchers investigated whether functional deficits and brain imaging abnormalities could be reversed by postnatal treatment with erythropoietin (EPO). The results showed that postnatal EPO treatment mitigated impairments in behavior and gait as well as microstructural brain imaging abnormalities. These findings suggest that functional deficits resulting from perinatal brain injury may be reversible.
Supported by NINDS, NICHD, NIGMS
Article: https://www.ncbi.nlm.nih.gov/pubmed/29288070

Treating major depression following traumatic brain injury
More than half of people that have a traumatic brain injury (TBI) will develop major depressive disorder within the first year after their injury. Many providers prescribe antidepressants, particularly a type of antidepressants called selective serotonin reuptake inhibitors, to treat depression after a brain injury. NICHD-supported researchers studied one of these drugs, called sertraline, in patients who were depressed after TBI. Half of the participants received the sertraline, and the other half received a placebo pill, and which patients received which pill was kept secret. After 12 weeks, depression in both groups had improved, with the sertraline patients doing no better than the patients who received the placebo.
Supported by NICHD
Article: https://www.ncbi.nlm.nih.gov/pubmed/28520672

Persistent postconcussion symptoms after injury
Postconcussion symptoms occur in about 30 percent of the children with mild traumatic brain injury (mTBI) seen in emergency departments. Although the symptoms may resolve within a week or month in
some children, they may persist, affecting children’s functioning at home and at school. NICHD-supported scientists found that nearly a third of children who had been admitted for concussion to emergency departments in Texas and Utah had post-concussive symptoms, including headache, irritability, and fatigue, for up to a year after their injury. Girls tended to have more symptoms and to experience them longer, compared to boys. Adolescents were more likely to experience more symptoms than younger children but tended to recover from them more rapidly. Children who had mood problems before a concussion, those from lower income families, and those from troubled families had elevated symptoms and symptoms of longer duration than other children. Children from families that had more social connections to their community tended to experience milder symptoms than those who were less socially connected.

Supported by NICHD

**Negative and unrealistic descriptions of infant attributes and child maltreatment**

To assess ways to predict the risk for child maltreatment, researchers studied a group of infants found to have bruising or skin injury on the initial physical exam. NICHD-supported scientists asked infants’ parents to describe their child’s personality. Separate teams of medical professionals, including child abuse pediatricians, emergency medicine physicians and injury experts, characterized the parents’ descriptors as positive, neutral or negative/unrealistic, and characterized each infants’ bruises as accidental or abusive. Bruising in a large majority of the 185 infants (79 percent) was considered accidental, with the remaining 21 percent abusive. Parents that used at least one negative or unrealistic descriptor of their children were more likely to have children with bruising identified as abusive. The researchers suggested that their pilot study could inform future efforts to develop a child abuse screening tool for medical providers, using parents’ descriptions of their children, along with other predictive factors, to help identify infants at high risk for physical child abuse.

Supported by NICHD

**Substance Misuse**

*Alterations in adolescent brain development after initiating drinking*

Using magnetic resonance imaging (MRI), NIAAA-supported researchers showed that relative to adolescents who initiated no or low alcohol consumption, those who initiated heavy drinking exhibited accelerated declines in gray matter volume and slower expansion of white matter at later time points. These results reveal disruptions in the characteristic pattern of brain maturation among adolescents who reported heavy alcohol use. In another study, researchers found that connectivity of the executive control network continued to strengthen in adolescents with no/low alcohol exposure, but not in adolescents with greater alcohol exposure. Further, among the adolescents with a history of alcohol consumption that exceeded no/low exposure, weakened connectivity of the emotion network was observed.

Supported by NIAAA

**Opioid prescriptions to children decreased dramatically by early 2017**

Opioid use early in life is associated with several health risks, and also is related to a higher likelihood of opioid misuse in the future. Using data from a large national insurance company, NICHD-supported researchers evaluated trends in opioid prescriptions dispensed to individuals 18 years or younger between 2004 and 2017. In 2004, an average of 3.3 of every 1000 children under 18 received an outpatient opioid prescription in a given month. This increased by 24 percent—to 4.1 of every 1000 children—in the period
between 2009 and 2012, and then dropped even more dramatically, to 2.1 per 1000 children at the beginning of 2017. A similar trend was observed for long-term opioid use.
Supported by NICHD

**Communities That Care program shows success in reducing substance use and behavioral issues in adolescents**

A study of the Communities That Care (CTC) system showed success in preventing youth substance use and antisocial behaviors years after exposure to prevention efforts. The CTC is a prevention planning and implementation system that trains community coalitions to assess their communities’ needs, then select and use evidence-based programs and policies to reduce risk factors and enhance protective factors.
Researchers conducted a community-randomized trial involving over 4,400 youth followed from grade 5 through age 21 years and found that CTC participation in adolescence resulted in longer periods of abstinence from alcohol, tobacco, or marijuana use and less antisocial behavior as compared to individuals in a control group. Findings suggest that using the CTC system strengthened norms against substance use and antisocial behavior, which resulted in fewer youths and young adults initiating these behaviors. The study findings also suggested that once youth were engaged in the behaviors, the CTC system did not affect the outcome.
Supported by NIDA, NIAAA, NCI

**Pain and Pain Management**

**Preventing long-term pain after injury**

Long-term pain and inflammation after nerve injury is triggered by a specific protein known as dual leucine zipper kinase (DLK). Intramural researchers sought to identify the role of DLK to develop insights on new ways to treat long-term pain without opioids. The research team developed mice that lack DLK and compared how these animals and normal mice recovered from nerve injury. They found that mice missing DLK did not develop long-term pain after injury, nor did their spinal cords develop a hallmark of nerve inflammation called microgliosis.
Supported by NICHD, NCCIH

**Pain education programs, delivered electronically, reduced health care expenditures**

Using data from a multicenter randomized controlled trial, researchers evaluated the longitudinal effects of internet-delivered cognitive behavioral therapy (i-CBT) among adolescents with chronic pain in the United States. The scientists also examined subsequent healthcare costs among youth who had received adjunctive internet-delivered cognitive behavior therapy, compared to adjunctive internet-based pain education program without CBT. Both interventions were associated with subsequent reductions in healthcare expenditures; contrary to researchers’ hypotheses, there were no significant differences in rates of change in subsequent healthcare costs between the two intervention groups.
Supported by NICHD, NINDS
Pediatric Critical Care and Emergency Care

Determining optimal blood pressure levels during CPR for infants and children
Traditionally, when children suffer cardiac arrest, rescuers focus on chest compressions during CPR, trying to jumpstart the heart. Because laboratory studies have established that maintaining adequate blood pressure during CPR is important to successful resuscitation, rescuers are taught to “Push Hard and Push Fast” to save lives. However, more than 95% of the U.S. children who require CPR each year are in the intensive care unit of a hospital. These children are already connected to monitors tracking their “beat-to-beat” vital signs, such as arterial blood pressure and heart rate. While rescuers are trained to focus on the depth of compressions, researchers from NICHD’s Collaborative Pediatric Critical Care Research Network hypothesized that a more objective measure may lie on the hospital monitor—specifically arterial blood pressure levels. Researchers analyzed hospital monitors and charts of 164 children during CPR treatments at 11 U.S. hospitals from 2013 to 2016. They found that for infants, the optimal diastolic blood pressure should be maintained at greater than 25 mmHg during CPR. In children ages 1 and older, the optimal diastolic blood pressure should be greater than 30 mmHg. When these blood pressure rates were maintained throughout the course of CPR, infants and children had a 70% greater likelihood of surviving and being discharged from the hospital and a 60% higher likelihood of surviving with favorable neurological outcomes. When the diastolic blood pressure values were lower than these levels, survival rates dropped markedly. These data provide a foundation to guide practitioners in administering effective CPR to infants and children.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29279413

Hyperoxia and hypocapnia during pediatric extracorporeal membrane oxygenation
Patients with severe, life-threatening conditions that significantly impair cardiac and lung function may be temporarily helped by extracorporeal membrane oxygenation (ECMO). These complex machines, used in such critical disorders as cardiac arrest and life-threatening breathing problems, direct blood out of the body, infuse the blood with oxygen and eliminate carbon dioxide as the blood circulates through the machine, and then channel the oxygen-rich blood back into the patient’s body for distribution to tissues. While ECMO is potentially lifesaving, because it is so effective at adding oxygen and eliminating carbon dioxide, certain physiological complications can occur in patients on ECMO support. These include hyperoxia (excessive blood oxygen levels) and hypocapnia (decreased carbon dioxide in the bloodstream). NICHD-supported scientists assessed data from a prospective study of 514 pediatric and neonatal ECMO patients. Hyperoxia occurred in 68.4 percent of the children and was associated with higher mortality, compared to patients without hyperoxia (50.5 percent vs 31.4 percent). There was no difference in functional status among survivors. Hypocapnia occurred in 20.2 percent of patients; these patients were more likely to experience a neurological event (such as a seizure or brain hemorrhage) or hepatic (liver) dysfunction than those without hypocapnia. There was no difference in survival between those with hypocapnia and those without. Among survivors of hypocapnia, there was no difference in functional status. These findings also suggested that if the oxygen availability is too low (presumably before ECMO) or too high while on ECMO, patients may have worse outcomes. These findings will help inform the timeliness and optimization of ECMO therapy.
Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29319634

National survey of medication safety practices in neonatal intensive care units
Medication errors in infant patients can be dangerous, and preterm infants’ immature physiology and other characteristics make them more likely than older patients to be harmed by such errors. Because of their health concerns, preterm infants are also more likely to receive more medications that potentially carry higher risk. In a NICHD-funded survey of NICU safety practices, researchers found that more than 85 percent of NICUs adhered to certain safety practices, including use of electronic health records,
computerized physician order entry, and clinical decision support. However, fewer NICUs reported adopting barcoding to match medication to patient and patient record, formal safety surveys, formal training in fostering a culture of safety, and other proven approaches to enhancing patient safety. Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29906795

Clinical Care, Outreach, and Services

Genome sequencing in NICU babies accelerates diagnosis, decreases infant morbidity, and decreases cost of hospitalization
Genetic diseases are one of the leading causes of mortality in newborns. Recent studies have shown that sequencing the genomes of NICU babies accelerates the time to diagnosis, thereby allowing doctors to intervene more quickly than would otherwise be possible. Appropriate intervention has led to decreases in infant morbidity as well as cost savings due to avoidance of inappropriate treatment and rehospitalization. Supported by NHGRI, NICHD

Six-year follow-up of infant cardiac surgery trial
In 2010, NHLBI’s Pediatric Heart Network completed the Single Ventricle Reconstruction (SVR) Trial, which compared two surgical strategies for newborns with single ventricle physiology. The trial was positive, with improved one-year transplant-free survival with the novel procedure compared to the conventional surgery. Six years later, the results from the two groups are comparable, and the previously favored surgical procedure is associated with higher rates of catheter-based interventions. Supported by NHLBI
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29437119

Medication adherence in adolescent kidney transplant recipients
Researchers reported that electronic monitoring, reminders, and personal coaching lead to significantly improved adherence to critical immunosuppressive medications in teenage recipients of kidney transplants. This finding could inform strategies to reduce kidney graft failure rates in this high-risk age group. Supported by NIDDK
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29602631

Injuries and post-injury care in AI/AN and rural patients
Researchers found that a significantly higher percentage of AI/ANs were hospitalized for intentional and unintentional injuries compared to non-Hispanic Whites. AI/AN patients were most likely to be discharged to their own homes without home health services. AI/AN patients were also more likely to use physical therapy or occupational therapy (PT/OT) services, but less likely to use speech therapy or mental health services than their urban peers. Total health care costs were higher for rural children, due mainly to the higher costs of PT/OT. Supported by NICHD, NCATS, NINDS

Reproductive health care use of young adults insured on their parent’s policy
Since the Affordable Care Act of 2010, young adults have been able to continue on their parent’s health insurance policy until they reach 26 years of age. Because many insurance companies send
documentation about recently used health services to the policy holder, young adults on their parent’s policy may have their reproductive health services revealed to their parents against their wishes. This has raised concern that young adults may forgo reproductive health care because of lack of confidentiality. NICHD-supported researchers compared reproductive health care use of young adults who used their parent’s policy and young adults who had their own health insurance policy. They used nationally representative data of 18- to 25-year-old young adults, who were either insured through their parent’s policy, private policyholders, or insured by Medicaid. The researchers examined the use of four reproductive health services that young adults may want to keep private: HIV testing, obstetrician/gynecologist visits, hormonal contraceptive use, and Pap tests. After taking sociodemographic variables into consideration, there was no significant difference in use of reproductive health services between individuals insured through their parent’s policy and private policyholders. Improved insurance billing processes to ensure confidentiality are still recommended.

Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29415821

**Contraceptive use and the decline in rates of pregnancy and birth among U.S. adolescents**
Using data from young women age 15 – 19 years old who participated in the National Survey of Family Growth, researchers assessed changes in teen sexual activity, use of contraception, and birth rates from 2007 to 2014. They found that while rates of young women’s sexual activity had not changed over time, there was a significant increase in the use of contraception and a corresponding drop in adolescent pregnancy and birth rates. The researchers noted, however, that three of every four adolescent pregnancies are still reported as unintended, which suggested that further efforts to understand contraceptive use by adolescents are warranted.

Supported by NICHD
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30149926

**Web-based program improves communication between parents and adolescents about sexual activity**
In a randomized controlled trial, a web-based intervention to improve communication between parents and adolescents about sexual activity was found to improve discussions about peer pressure, sexual prevention, protection, and risk over time in a community in San Juan, Puerto Rico.

Supported by NINR, NIDA
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30431467

**Parent education intervention improved childhood weight outcomes at 3 years of age**
Rapid growth in early childhood can increase the risk for obesity later in life. In a randomized clinical trial, researchers found that a responsive parenting intervention initiated early in infancy compared to a control intervention resulted in a modest improvement in BMI at 3 years of age.

Supported by NIDDK, NCATS
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30088009

**Interventions improve custodial grandmother’s parenting skills for their grandchildren**
NINR-supported researchers conducted a randomized controlled trial with over 300 custodial grandmothers with the goal of improving parenting skills, limiting custodial grandparents’ psychological distress, and improving the psychological well-being of the custodial grandchildren. The trial tested a behavioral parent training (BPT) intervention and a cognitive-behavioral training (CBT) intervention, comparing both to a control group receiving information only. The study found that both BPT and CBT had positive effects as measured by an improvement in parenting practices and reduced psychological distress in the custodial grandmothers and improved psychological well-being in their grandchildren.

Supported by NINR
Article:  https://www.ncbi.nlm.nih.gov/pubmed/30188171
**Improving maternal knowledge of oral health**
The NIDCR-funded Center for Native Oral Health Research focused on reducing early childhood caries (ECC) in young American Indian children living on reservations. In one study, researchers tested the effectiveness of a specific counseling approach to improve maternal oral health behaviors and reduce ECC. The intervention improved maternal knowledge of oral health but did not show an effect on oral health behaviors or caries development in children. This finding suggests an approach that more fully addresses community and family factors may be needed to address oral health behaviors in high-risk communities.

Supported by NIDCR

**State fluoride varnish programs improve the oral health of children**
Children from low-income families are disproportionately affected by early childhood dental caries. State Medicaid programs support application of fluoride varnish (FV), a coating material that prevents caries, to children’s teeth by primary care doctors. NIDCR-supported researchers examined the national impact of these policies on children’s oral health using data from the National Survey of Children’s Health. Because FV policies were adopted by individual states over 20 years, researchers were able to examine the association between the years since a state implemented a FV policy and teeth quality, as well as compare publicly insured children in states with FV policies to those in states without FV policies. Fluoride varnish policies were associated with better oral health, and children in states that had FV policies for ≥4 years had significantly greater odds of having very good or excellent teeth compared to those in states without FV policies.

Supported by NIDCR

**Health messages and maternal decisions about infant sleep position**
In the U.S., sudden infant death syndrome (SIDS) and other sleep-related deaths (such as accidental suffocation and strangulation in bed, and ill-defined deaths) account for approximately 4,000 infant deaths annually. In a randomized controlled study, NIMHD-supported scientists assessed the impact of a health education program targeting African Americans. Over the first six months after the education program, more mothers placed their infants in the recommended supine sleep position. However, an enhanced version of the education intervention did not improve the proportion of infants placed as recommended compared with the standard education intervention.

Supported by NIMHD

**Prevention of underage drinking in an at-risk population**
NIAAA-supported researchers developed and evaluated the effects of a combined individual- and community-level intervention to reduce underage drinking among American Indian youth living on rural California reservations. Individual-level strategies included motivational interviewing and education, whereas community-level strategies focused on outreach and reducing access and sales of alcohol to minors. The combined intervention reduced measures of drinking among underage youth in this at-risk population.

Supported by NIAAA
**Technology and Tools**

**Tracking genetic activity as a single cell develops into an entire body**

A single fertilized egg develops into many different cell types, tissues, and organs that fit together to create a body. Researchers used a combination of sensitive nucleic acid sequencing and labeling technologies, together with innovative computational tools, to construct a detailed picture of this process at the level of individual cells. By taking multiple snapshots of the genetic activity within single cells of developing zebrafish and frog embryos, they were able to show how each early cell differentiates into a specific cell type. Researchers also injected some of the fish embryos with tiny pieces of unique DNA, which were incorporated into the embryos’ DNA as the cells multiplied. Analyzing the patterns of these DNA pieces and the RNA in each cell, the researchers could trace how the cells changed over time, seeing how a fertilized egg develops into a variety of specialized cells, such as heart, nerves, and skin. In another study, researchers sampled cells every 45 minutes over 9 hours, using a computational method to compare the gene activity of different cell types between time points. They traced cells with the most similar gene activity from 25 cell types back to the fertilized single-celled egg cell. From these detailed molecular descriptions, researchers can determine which genes affect different processes within cells throughout development.

Supported by NICHD, NIMH, NHGRI, NIGMS, NCI

Articles:  

**Testing blood using sound waves**

NICHD-supported intramural researchers reported a new method that uses sound waves to isolate exosomes from blood. Exosomes are bubble-like particles excreted by cells, and they contain information that may be useful for monitoring or detecting various health conditions. However, the use of exosomes as biomarkers is limited by the ability to separate them from body fluid samples, such as blood, saliva, urine, and breast milk. According to the study team, the new "acoustofluidic" platform offers a simple, quick, and potentially cost-effective strategy to isolate exosomes.

Supported by NICHD

Article:  

**Blood test for monitoring blood cancer**

Researchers designed a microfluidic chip that uses a blood sample to monitor the recurrence of acute lymphoblastic leukemia (ALL), the most common type of blood cancer in children. The technology was initially developed as a low-cost, reliable blood test to detect and monitor multiple myeloma, a different type of blood cancer more common in older people. This blood-based test could reduce or eliminate the need for painful biopsies to diagnose ALL in children.

Supported by NIBIB, NCI, NHLBI

Article:  

**Designing a rapid diagnostic for identifying nutrient deficiency**

A team of engineers and nutritionists supported have designed and tested a small, portable diagnostic system that can be used to identify vitamin A and iron deficiencies. One third of the world’s population are affected by vitamin and mineral deficiencies that can lead to health effects such as vision impairment or anemia. This newly developed system is a point-of-care device that generates three diagnostic results using a color-sensitive, disposable test strip. It signals iron and vitamin A deficiency, and can indicate inflammation, which can alter results and change a clinician’s interpretation of those results. In a small preliminary study, the researchers tested 43 human samples. The device gave accurate results when compared with standard test kit techniques and would be easier to use in low resource settings.

Supported by NIBIB

Article:  
**Human tissue platform to evaluate vaccine candidates**
NIAID-supported researchers recently developed a new modeling system to test age-specific immune responses to vaccines in target populations, such as newborns and the elderly. Using human components to model the immune system of a newborn or an adult, researchers have validated *in vivo* responses to vaccines for tuberculosis and hepatitis B virus. The study demonstrated that systems such as this can be used to model responses to vaccines and adjuvants in vulnerable populations, such as newborns, the elderly, and pregnant women.
Supported by NIAID

**New tool for targeted expression of mitochondrial genes**
Mitochondrial encephalomyopathies (MEs) are rare diseases that often appear in childhood and that result from mutations in genes that reside in mitochondria as opposed to the cell nucleus. Techniques to manipulate the expression of these genes and the proteins they encode could facilitate research and therapy development, but such methods have been limited. A new study describes a mitochondrial-targeted RNA expression vector for directing protein expression within mitochondria. The authors used the system to express a normal mitochondrial protein (ATP6) in a fly model of ME and showed that the targeted protein expression could rescue flies from disease when combined with a method to reduce expression of the mutant protein.
Supported by NIGMS, NINDS, NIA

**New map of brain scaling**
The size of the human brain varies over the course of development as the proportions of different brain regions naturally shift. Individual brain size can vary almost twofold among typically developing humans, but the consequences of this variation for brain organization remain poorly understood. Using in vivo neuroimaging data from more than 3,000 individuals, researchers found that differences in the brain’s total size are related to the brain’s shape and the way it is organized. This new scaling map of the typically developing brain may be used to better pinpoint emerging changes in brain structure amongst youth with developmental disorders.
Supported by NIMH, NINDS

**From new models to novel therapeutics**
Researchers used existing mouse models of two forms (CMT2D and CMT4J) of Charcot-Marie-Tooth (CMT) disease to perform preclinical gene therapy studies. CMT disease is a slowly progressive, inherited disorder of the peripheral nerves that control muscles, causing loss of function or sensation in the legs and arms. The scientists demonstrated the efficacy of gene therapy in mice for both forms of the disease, and pre-investigational new drug applications have been submitted to the Food and Drug Administration. It is hoped that clinical trials for both treatments can be initiated soon, including one targeting a specific patient with a severe, life-threatening case of CMT2D.
Supported by ORIP, NIGMS, NINDS
Global Pediatric Health

Understanding why iron can worsen malaria infection
For many years, scientists and public health officials have observed that iron supplements can sometimes worsen malaria infection. Researchers have now discovered a possible explanation for this mystery. By studying mice as well as samples from malaria patients, scientists found that extra iron interferes with ferroportin, a protein that prevents a toxic buildup of iron in red blood cells and helps protect these cells against malaria infection. They also found that a mutant form of ferroportin that occurs in African populations appears to protect against malaria. In one study of children hospitalized for malaria in Zambia, the research team found that 20 percent of the children had the mutation, and that they tended to have fewer malarial parasites in their blood and tolerated their fevers for a longer period before coming to the hospital. Another study of pregnant women in Ghana found that those with the mutation were significantly less likely to have pregnancy-associated malaria, which can cause adverse pregnancy and birth outcomes. These basic findings may help researchers and health care officials develop strategies to prevent and treat the infections, which numbered nearly 216 million worldwide in 2016.

Supported by NICHD, NIAID
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29599243
SELECTED NEW AND EXPANDED RESEARCH EFFORTS FOR FY 2018 IN PEDIATRICS

Selected New Pediatric Research Efforts

NIH ICOS launched a range of new research programs and efforts related to pediatrics in FY 2018. Selected highlights of new initiatives and funding opportunity announcements (FOAs) are given 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 treatments.

INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down Syndrome)
The INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down SyndromE) 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, such as Alzheimer’s disease/dementia, autism, cataracts, celiac disease, congenital heart disease and diabetes. Applying the expertise and resources from multiple NIH Institutes and Centers, INCLUDE will:

- Conduct targeted, high-risk, high-reward basic science studies on chromosome 21;
- Assemble a large study population (cohort) of individuals with Down syndrome; and
- Include individuals with Down syndrome in new and existing clinical trials.

Supported by NIH
Website:  https://www.nih.gov/include-project

HEAL Initiative: Preventing Opioid Use Disorder
As part of the NIH Helping to End Addiction Long-term (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.

Supported by 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 opioid withdrawal syndrome (NOWS). The study is a collaboration between NICHD’s Neonatal Research Network (which has over 30 years of experience in conducting clinical trials with newborns) and the IDEAS States Pediatric Clinical Trials Network, part of the Environmental influences on Child Health Outcomes (ECHO) program within the Office of the NIH Director, with sites located in rural and medically underserved communities. Together, they are assessing the prevalence of NOWS 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.

Supported by NICHD, OD
Website:  https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative/advancing-clinical-trials-neonatal-opioid-withdrawal-act-now
Risk for Opioid Abuse and Misuse in Adolescents Prescribed Opioids for Pain
Adolescents who are exposed to opioid medications through legitimate prescriptions are at increased 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 NIDA-funded study will follow adolescents ages 14-18 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.
Supported by NIDA
R01DA044778: https://projectreporter.nih.gov/project_info_description.cfm?aid=9472051

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) and led by NICHD, the Task Force reported in September 2018 to the Secretary and Congress on the state of the science and research gaps that need to be filled in order to inform the use of medications (pharmaceuticals and dietary supplements) by pregnant and lactating women. In addition to reporting extensive research gaps with regard to safety, efficacy, and dosing with regard to 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 dearth 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.
Supported by NICHD, NIMH, NIDDK, NIAID, NCATS, NHLBI, ORWH
Website: https://www.nichd.nih.gov/About/Advisory/PRGLAC

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 pregnant women about what they feel, think, do, and experience during pregnancy and after giving birth can provide more insights on pregnancy and how to improve care.
Supported by NICHD, NCCIH, NHLBI, NIEHS, NINR, NIMHD, OBSSR, ORWH
Website: https://pregsource.nih.gov/

Hurricane-Related Maternal Stress, Infant Outcomes and Resilience Factors
The Puerto Rican population endured tremendous stress following the Hurricane season of 2017-2018, as the result of lack of power and communications, interrupted services, scarcity of fuel, and abandoned streets, followed by a challenging response and reconstruction effort. Researchers supported by NIMHD will identify specific resilience factors to help ameliorate the negative impacts of stressful experiences on maternal and infant health.
Supported by NIMHD
R21MD013675: https://projectreporter.nih.gov/project_info_description.cfm?aid=9686209
Understanding Socioeconomic Disparities in Perinatal Risk: The Role of Epigenetic and Transcriptional Regulation in the Placenta

NIMHD-supported researchers plan to obtain wide-ranging data from an economically diverse sample of pregnant women, to specify connections among features of neighborhoods, families, and individuals. The researchers intend to use these data to characterize how these multiple factors are associated with epigenetic and transcriptional modifications in the placenta during pregnancy. The scientists anticipate that these relationships will provide insights on how health disparities are initiated and/or maintained. Supported by NIMHD
R01MD011749: https://projectreporter.nih.gov/project_info_description.cfm?aid=9572939

Advancing Understanding, Prevention, and Management of Infections Transmitted from Women to their Infants

This NICHD initiative encourages research studies and trials that improve the understanding, prevention, and clinical outcomes of non-HIV infections that can be transmitted from women to their offspring during pregnancy, labor, and delivery. High-priority perinatal infections of interest include, but are not limited to: cytomegalovirus, herpes simplex viruses, toxoplasmosis, viral hepatitis, Human T-cell lymphotropic viruses (HTLV-1/2), Trypanosoma cruzi (Chagas disease), enteroviruses and parvovirus B19. Supported by NICHD


Zika Virus Transport in Neuronal Axons

Zika virus (ZIKV) infections of pregnant women can lead to microcephaly and other neurodevelopmental abnormalities in infants. Also prominent in ZIKV-infected newborns is damage to the retina, which may lead to blindness. NEI researchers are studying the hypothesis that Zika virus co-opts axonal transport machinery to transport the virus from neuron to neuron. They will characterize zika virus transport in the neurons and the biochemical molecules (kinesin motors) that interact with the virus. Supported by NEI
R21EY029082: https://projectreporter.nih.gov/project_info_description.cfm?aid=9510533

Research for Prenatal and Pediatric Hydrocephalus

Hydrocephalus is a condition in which excess cerebrospinal fluid (CSF) accumulates in the brain, resulting in enlargement of the ventricles and functional impairments. At a scientific workshop held by NINDS, participants discussed the need for a clearer understanding of disease mechanisms involved in prenatal and pediatric hydrocephalus. Based on these discussions, NINDS developed two funding opportunity announcements (FOAs) to support research on the molecular, cellular, and developmental mechanisms involved in prenatal and/or pediatric hydrocephalus and to develop new and improved research tools. Supported by NINDS


Metabolomic Profiling in Children with Chronic Kidney Disease

Chronic kidney disease (CKD) is associated with neurocognitive dysfunction in children and young adults, including deficits in attention, memory, and executive function, which can have far-reaching and lifelong adverse consequences. The specific mechanisms leading to neurocognitive impairment in CKD remain unknown, but metabolic alterations caused by uremic toxins may have a significant impact on cognitive function. Recent advances in metabolomic technologies allow for high-throughput, high-resolution metabolic phenotyping of small volume human blood samples that offers great promise for the
discovery of highly discriminant biomarkers. NCCIH-supported researchers aim to discover novel metabolites associated with neurocognitive dysfunction in children and young adults with CKD, by analyzing blood metabolomic profiles of participants in two large cohorts. Supported by NCCIH R21AT009752: https://projectreporter.nih.gov/project_info_description.cfm?aid=9436602

**Pilot Clinical Trials Targeting HIV-1 Reservoirs in Children**
Long-term HIV suppression with antiretroviral treatment (ART) is difficult to maintain over the course of an entire lifetime, and significant toxicities to ART may accumulate with time. HIV-infected children who initiate ART in the first week of life may have both low viral reservoir and limited viral diversity, and therefore represent an ideal population to evaluate strategies other than ART for maintaining viral suppression. NIAID-supported scientists will investigate therapeutic HIV vaccines to reduce the HIV reservoirs in children with HIV. The researchers will characterize changes in viral reservoir and immune responses at each step of the intervention. Supported by NIAID FOA: https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-16-086.html

**Pediatric Clinical Trial of Universal Influenza Vaccine**
NIAID is supporting a Phase I trial of a live-attenuated influenza vaccine in 50 children and adolescents, 9-17 years old. In multiple preclinical models, this vaccine has demonstrated superior protection compared to other live or inactivated influenza vaccine technologies. Supported by NIAID Clinical Trial: https://clinicaltrials.gov/ct2/show/NCT03553940

**Accelerating Cellular Immunotherapy Development for Treatment of Life-Threatening Childhood Disorders**
Cellular immunotherapies are emerging as a paradigm shifting, personal and precise treatment for a range of fatal rare diseases in children. Early Phase 1 trials in refractory leukemia have provided proof of concept that this approach can be lifesaving. The scientists propose to establish a consortium of pediatric hospitals affiliated with other CTSA Program hubs, called the Consortium for Pediatric Cellular Immunotherapy, to accelerate production and delivery of these novel lifesaving therapies to children. Supported by NCATS U01TR002487: https://projectreporter.nih.gov/project_info_description.cfm?aid=9597782

**Juvenile Arthritis Pathogenesis Unit**
The goal of the Juvenile Arthritis Pathogenesis Unit, within the NIAMS intramural program, is to understand the mechanisms that underlie the development of inflammatory arthritis and cartilage inflammation in children. Researchers are studying severe, early-onset arthritis in children to learn more about the role of rare, highly penetrant variants to understand disease mechanisms that will inform individualized treatment approaches. In addition, they are working to understand pathogenic mechanisms underlying the development of relapsing polychondritis (RP), a systemic inflammatory disease of cartilage that can present with joint involvement. Supported by NIAMS ZIAAR041208: https://projectreporter.nih.gov/project_info_description.cfm?aid=9794586

**Assessing Speech Outcomes in Infants Who Have Undergone Primary Surgery to Repair Cleft Lip/Palate**
Children with cleft lip and palate (CL/P) undergo numerous repair surgeries, followed by orthodontic and behavioral treatments to improve speech. There are multiple surgical techniques, and it is currently unknown what approach has the best speech outcomes. NIDCR-supported researchers are developing a registry to compile data of surgical approaches to CL/P and subsequent inpatient and outpatient care,
including speech-language therapy practices. The two most common CL/P repair techniques will then be compared to determine their effect on speech outcomes and other complications following CL/P surgical repair. This multi-institutional, point-of-care data system will harmonize practice data from leading cleft care programs across North America and will synthesize data about surgical approaches to CL/P and subsequent inpatient and outpatient care, including speech-language therapy practices.

Supported by NIDCR
R01DE027493: https://projectreporter.nih.gov/project_info_details.cfm?aid=9427681

**Typical and Atypical Patterns of Language & Literacy in Dual Language Learners.**

About one of every five people ages 5 years 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 (DLLs), and account for greater than 9 percent of enrollment in grades K-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 (DLLs) in the United States.

Supported by NICHD, NIDCD
FOAs: https://grants.nih.gov/grants/guide/pa-files/PA-18-316.html

**Early Screening for Autism Spectrum Disorder**

Reliably detecting autism in young children is difficult and the average age of diagnosis for ASD remains at approximately four years of age. In 2018, NIH issued FOAs to encourage researchers to translate research methods for identifying risk markers of ASD into efficient, inexpensive screening tools for use in infants (0-12 months of age) that are readily deployable within the general population.

Supported by NICHD, NIMH, NIDCD, NIEHS, NINDS

**Monitoring Toe-Walking Severity in Children with Cerebral Palsy**

Equinus gait, or “toe-walking”, is commonly observed in children with cerebral palsy (CP), and can be treated by a variety of treatments. An SBIR grant supported by NLM will help researchers develop a wearable system to continuously monitor and analyze simple gait parameters in children with CP outside the clinical laboratory and during normal daily activities. With access to continuous data, the medical team will be better informed and can effectively plan treatment, thus improving the quality of care and the lives of children with CP and their families.

Supported by NLM
R43LM013104: https://projectreporter.nih.gov/project_info_description.cfm?aid=9467293

**Rare Mutations in Cystic Fibrosis: Overcoming Barriers to Personalized Medicine**

Cystic Fibrosis (CF) is a fatal genetic disorder affecting 1 in 2,500 to 3,500 white newborns in the U.S. annually. CF is caused by over 1,900 different gene defects in the CF Transmembrane Conductance Regulator (CFTR). This study focuses on gaps in knowledge that must be overcome to advance precision medicine and interventions for CF based on an individual's genes. Researchers will conduct a clinical trial in 22 patients with ultra-rare CFTR mutations to test the efficacy of a triple therapy drug (Symdeko, consisting of tezacaftor/ivacaftor and ivacaftor), which is currently used to treat patients with specific genetic mutations. This clinical trial is paired with additional assays to provide detailed understanding on how these drugs modulate CFTR for individuals with ultra-rare mutations in CF for which these treatments have not previously been evaluated.

Supported by NHLBI
R01HL139876: https://projectreporter.nih.gov/project_info_description.cfm?aid=9754239
**Mapping Environmental Contributions to Rapid Lung Disease Progression in Cystic Fibrosis**

Progressive lung disease is the leading cause of death in individuals with cystic fibrosis (CF). Accelerated loss of lung function is a common feature beginning in childhood for CF patients and cannot be explained or predicted by CFTR/gene dysfunction alone. This study leverages a rich CF registry, extant national and local environmental data sources, and prospectively collected study data to accurately forecast the onset of rapid decline in individual patients, and to develop a feasible medical monitoring tool that positively impacts CF point-of-care decision-making. Mapping the environmental exposures and community characteristics (geomarkers) that predict patient-specific rapid decline and providing tools for earlier detection and monitoring at the center level are essential to transforming the precision of CF clinical care and offer an opportunity to adjust interventions to prevent irreversible lung damage.

Supported by NHLBI


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**Testing Multi-Targeted Immunotherapy in Common Childhood Cancer**

NCI’s Pediatric Oncology Branch is conducting a new clinical trial at the NIH Clinical Center to determine whether modified CD19/CD22-targeted chimeric antigen receptor (CAR) T cells can be used as a treatment for hematologic cancers in children and young adults. This is one of the first trials in the country evaluating a multi-targeted CAR T cell approach, in an effort to prevent relapse and resistance to therapy that targets CD19 or CD22 alone.

Supported by NCI

Clinical Trial: [https://clinicaltrials.gov/ct2/show/NCT03448393](https://clinicaltrials.gov/ct2/show/NCT03448393)


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**Pediatric Genomic Data Inventory**

Pediatric cancer often is genetically and molecularly different from malignancies that may appear in similar organs in adults. NCI has developed a dynamic resource known as the Pediatric Genomic Data Inventory to allow scientists to more easily locate genomic datasets that could help identify new treatment targets specific to pediatric cancers. This resource lists 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 continually updated as new information is deposited by the research community.

Supported by NCI

Website: [https://ocg.cancer.gov/programs/target/pgdi/overview](https://ocg.cancer.gov/programs/target/pgdi/overview)

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**Rare Tumor Patient Engagement Network**

In 2018, NCI launched a network for cancer patients with rare tumors. The goal is to build a national network to study selected rare pediatric tumors along with adult CNS tumors and develop a network of clinical trials. The initiative will build shared infrastructure across sites to study selected rare tumors, with specific attention to connecting patients and scientists through advocacy groups and other means. Data on selected rare tumors will be collected and analyzed and shared with patients and their families, as well as researchers to better understand these tumors and develop new therapies.

Supported by NCI

Website: [https://ccr.cancer.gov/research/cancer-moonshot](https://ccr.cancer.gov/research/cancer-moonshot)

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**Pragmatic Trial of Parent-focused Prevention in Pediatric Primary Care: Implementation and Adolescent Health Outcomes in Three Health Systems**

Fifty percent of all adolescents will use some form of illicit drugs before the end of high school. One fifth to one quarter of adolescents meet criteria for depression, and many others will engage in health compromising behaviors like delinquency and violence with consequences for their long-term health. Evidence-based interventions shown to prevent these behavioral health concerns could improve
adolescent health trajectories if implemented widely in pediatric primary care. NIH is supporting an effort to test the feasibility and effectiveness of implementing Guiding Good Choices, a universal, evidence-based anticipatory guidance curriculum for parents of early adolescents, in three large, integrated healthcare systems serving socioeconomically diverse families. This intervention reduced adolescent alcohol, tobacco and marijuana use, depression, and general delinquency in two previous rigorous randomized controlled trials. This partnership with pediatricians and healthcare leaders in three large integrated healthcare systems, as well as the NIH Healthcare Systems Research Collaboratory, will help ensure this approach fits pediatric care workflows so that, if effective, it will be ready for broad dissemination to achieve public health impact.

Supported by NCCIH, NIDA, OBSSR
UG3AT009838: https://projectreporter.nih.gov/project_info_description.cfm?aid=9493866

**Improving Care and Health Outcomes among Youth with HIV**

In FY 2018, NIMH and NIMHD issued two companion RFAs to improve care for young people with HIV. Funded studies utilize mobile applications to improve self-testing, engagement with care, medication adherence, and outcomes among vulnerable populations such as youth, men who have sex with men, and transgender women.

Supported by NIMH, NIMHD


**Optimizing a Mindful Intervention for Urban Minority Youth via Stress Physiology**

NCCIH-funded scientists will assess the mechanisms underlying effects of a mindfulness program designed to target youth at risk. Adolescents from schools serving high poverty neighborhoods in Baltimore City, where adversity and experiences of trauma and maltreatment are common, will participate in a mindfulness-based program for youth. Changes in emotion regulation have been reported with this intervention. However, like most mindfulness programs, mechanisms of effects have not yet been delineated, particularly in disadvantaged youth.

Supported by NCCIH

R61AT009856: https://projectreporter.nih.gov/project_info_description.cfm?aid=9494140

**Mind-Body Interventions to Mitigate Effects of Media Use on Sleep in Early Adolescents**

Eliminating electronic media use is neither feasible nor perhaps even desirable given the role it plays in the lives of youth and adults, but mind-body interventions have the potential to reduce negative impacts of electronic media use on sleep. Given emerging literature on links between intensive media use, sensory and interoceptive awareness, and self-regulation, this research will study two related mind-body approaches: mindfulness sensory awareness exercises, and mindful body awareness check-ins, to guide media use choices. NCCIH-supported scientists will examine the effects of these mind-body strategies independently, jointly, and in combination with other strategies to mitigate the effects of media use on sleep, including amber glasses to block short wavelength light during evening media use, avoiding content with high vigilance demands or violence, and external controls to time-out media access.

Supported by NCCIH

R61AT009859: https://projectreporter.nih.gov/project_info_description.cfm?aid=9495512
Innovative Approaches to the Study of Social Determinants of Health in Children
Exposure to chronic psychosocial stress is a risk factor for poor physical health in adulthood, but little is known about how these stressful experiences are associated with physical health in children. Researchers supported by NIMHD will examine how chronic and acute stress exposures are linked to children's antibody response to vaccination. This study also will explore the relations between psychosocial stress and antibody production, capitalizing on an ongoing longitudinal study of rural African Americans. Supported by NIMHD
DP2MD013947: https://projectreporter.nih.gov/project_info_description.cfm?aid=9561526

Selected Expanded Pediatric Research Efforts
In addition to launching new research programs, NIH ICOs built on successful programs to expand research efforts related to pediatrics. Selected highlights of expanded research efforts are given below. As with the new programs, the majority of these expanded initiatives are concerned with developing and delivering evidence-based interventions.

The Human Placenta Project
Designed to provide information about placental health noninvasively and in real time, NICHD's 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. NICHD also launched the Placental Atlas Tool in 2018, a curated dataset that serves as a resource for placental research. Current funding opportunity announcements emphasize novel approaches to safe, non-invasive, real time assessment of human placenta development and function across pregnancy.
Supported by NICHD
Websites:  https://www.nichd.nih.gov/research/supported/HPP/default
https://pat.nichd.nih.gov/

Environmental Health Sciences and Hurricane Response Research
The unprecedented and widespread damage caused by recent hurricanes is substantial. Consequently, the potential for exposures to biological (such as mold, biotoxins from harmful algal blooms) and chemical hazards, as well as social stressors (e.g., displacement, social isolation, racial/ethnic and cultural factors) and subsequent effects on human health for first responders, volunteer workers and residents is of significant concern. NIEHS is supporting research grants that focus on questions of public health importance that will provide insights into exposures and/or potential health effects (e.g., physical and behavioral) as an aftermath of Hurricanes. Examples of funded projects include determining the impact of Hurricane Harvey on the maternal and fetal microbiome and birth outcomes, as well as environmental exposures and prenatal stress related to Hurricane Maria among pregnant women in Puerto Rico.
Supported by NIEHS, NIMHD
FOAs:  https://grants.nih.gov/grants/guide/rfa-files/RFA-ES-16-005.html

Effects of Exposures during Pregnancy on Perinatal Outcomes
A new analysis will combine cohorts in the ECHO consortium to provide a large, diverse sample for determining the effect of prenatal exposure to per- and polyfluorinated alkyl substances (PFAS) and psychological stress on infant outcomes. The analysis will explore whether (1) higher prenatal exposure to multiple PFAS is associated with reduced birthweight and gestational age; (2) prenatal psychosocial
stressors are associated with similar adverse birth outcomes; and (3) observed associations between prenatal PFAS exposures and adverse perinatal outcomes interact with maternal psychosocial stress and maternal socioeconomic status.

Supported by OD, NIEHS

**Human Health Exposure Analysis Resource (HHEAR)**

A continuation of Children’s Health Exposure Analysis Resource (CHEAR), this consortium will provide the research community access to laboratory and statistical analyses to add or expand the inclusion of environmental exposures in their research and make the data publicly available.

Supported by NIEHS, NCI

FOAs:  

**Type 1 Diabetes TrialNet**

Launched in 2001, the 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 disease (at high or moderate risk of developing clinical symptoms within 5 years), which has enabled TrialNet to initiate clinical trials of promising prevention strategies. In FY 2018, TrialNet began recruiting for a new prevention trial testing hydroxychloroquine, a drug that has shown efficacy in treatment of other autoimmune diseases, such as lupus. Two other ongoing TrialNet prevention studies (anti-CD3 and abatacept) are testing treatments that showed efficacy in preserving insulin secretion in new-onset type 1 diabetes.

Supported by NIDDK, NIAID

Website:  
[https://www.trialnet.org/](https://www.trialnet.org/)

**A Web-based Non-Pharmacological Pain Intervention for Pediatric Chronic Pancreatitis**

Abdominal pain is common in children with chronic pancreatitis, and as they continue into adulthood, the disease progresses with increased pain and greater exposure to opioids. Despite the relevancy of early pain self-management for childhood chronic pancreatitis, there have been no studies of non-pharmacological pain intervention in this population. This study will evaluate a web-based cognitive behavioral pain management program delivered to a cohort of children with chronic pancreatitis to reduce pain, pain-related disability and enhance health-related quality of life. Researchers will identify genetic risk factors and clinical and behavioral phenotypic factors associated with treatment response to enable precision medicine approaches.

Supported by NIDDK

R01DK118752:  

**The Cure Glomerulopathy Network (CureGN)**

Launched in 2013, the multi-site, prospective observational research network supported by NIDDK is following 2,400 children and adults with the following glomerular diseases (minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, and IgA nephropathy) over time. Scientists will use these data to better understand the causes of disease, response to therapy, and disease progression. The network has expanded to include ancillary studies which will help inform new diagnostic and treatment strategies.

Supported by NIDDK

Website:  
[https://curegn.org/default.aspx](https://curegn.org/default.aspx)
**Nephrotic Syndrome Rare Disease Clinical Research Network (NEPTUNE)**

The longitudinal, observational NEPTUNE program focuses on three glomerular diseases associated with the nephrotic syndrome: minimal change disease (MCD), FSGS, and MN. Participants are enrolled before their first clinically indicated biopsy, and 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.

Supported by NIDDK, NCATS

Website:  [https://www.rarediseasesnetwork.org/cms/neptune](https://www.rarediseasesnetwork.org/cms/neptune)

**Chronic Kidney Disease in Children (CKiD)**

This prospective cohort study of kidney disease in children and adolescents seeks to identify risk factors for disease progression, as well as the impact of chronic kidney disease on neurocognitive development, cardiovascular disease, and growth. CKiD has been renewed through 2023 and expanded to allow for the recruitment of additional study participants.

Supported by NIDDK, NICHD, NHLBI

FOAs:  

Clinical Trial:  [https://clinicaltrials.gov/ct2/show/NCT00327860](https://clinicaltrials.gov/ct2/show/NCT00327860)

**Pediatric Acute Liver Failure Treatment**

An abnormal immune response has been implicated in the development of PALF, a rare yet life-threatening condition in children. NIDDK-funded scientists will determine if suppressing inflammatory responses with either corticosteroids or equine anti-thymocyte globulin therapy improves survival for children with acute liver failure.

Supported by NIDDK


**Genetic Disorders of Mucociliary Clearance Consortium (GDMCC)**

The GDMCC is a clinical research network jointly funded by NCATS-NHLBI as part of the Rare Diseases Clinical Research Network (RDCRN), an initiative of the Office of Rare Diseases Research (ORDR), NCATS. The consortium is in its fifteenth year of NIH support and currently consists of nine primary sites in North America and Canada with expertise in studying the genetics and pathogenesis of airway diseases, design of clinical trials, and development of novel therapeutics for defective lung defenses and chronic pus-producing respiratory diseases. The GDMCC consists of programs created to improve the diagnostic testing and treatment of rare airway diseases, including primary ciliary dyskinesia (PCD), variant forms of cystic fibrosis (CF), pseudohypoaldosteronism (PHA), idiopathic bronchiectasis and non-tuberculosis mycobacterium (NTM) pulmonary disease. Based on findings by the investigators within the consortium that bronchiectasis and NTM were common in primary immune deficiencies (PID), the program was expanded to include PID patients with respiratory involvement in FY2018.

Supported by NHLBI, NCATS

Website:  [https://www.rarediseasesnetwork.org/cms/gdmcc/](https://www.rarediseasesnetwork.org/cms/gdmcc/)

**Inner City Asthma Consortium (ICAC)**

This program focuses on ways to reduce asthma severity and prevent disease among predominantly minority children living in low-income, urban environments. NIAID-funded scientists are conducting clinical trials and mechanistic studies in order to understand the immunopathogenesis of the disease and evaluate and develop effective interventions. As part of a large-scale systematic analysis of 700 children with asthma, they were recently able to identify 5 distinct clusters that track well with asthma severity outcomes. This study was expanded to employ whole genome sequencing to identify genetic differences between children with mild versus severe asthma within this population of children. If a gene of interest is identified, replication studies will commence on additional ICAC pediatric cohorts.

Supported by NIAID

Website:  [http://www.medicine.wisc.edu/asthma/icacmain](http://www.medicine.wisc.edu/asthma/icacmain)

**The Pediatric Heart Network**

NHLBI’s 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. PHN has launched the Do It! study to investigate whether pitavastatin can help improve cardiovascular outcomes in obese children and teens (10-17) who have a particular type of abnormal cholesterol because of their obesity.

Supported by NHLBI

Website:  [http://www.pediatricheartnetwork.org/](http://www.pediatricheartnetwork.org/)

**Channelopathy-Associated Epilepsy Research Center**

NINDS is supporting scientists at five academic medical centers and three free-standing research hospitals to focus 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 improve the accuracy of diagnosis of epilepsy and will work to identify optimal drug therapy for specific mutations.

Supported by NINDS

U54NS108874:  [https://projectreporter.nih.gov/project_info_description.cfm?aid=9626191](https://projectreporter.nih.gov/project_info_description.cfm?aid=9626191)

**Enzyme Replacement Therapy for Hypophosphatasia**

Hypophosphatasia (HPP) is a rare genetic disorder characterized by deficient bone and tooth mineralization (rickets or osteomalacia). NIDCR supported the basic and translational research that led to the development of a recombinant TNAP therapy (asfotase alfa). The therapy was then tested in an industry-sponsored Phase III clinical trial in infants and children under 5 years of age. The results were posted in 2018 and suggest Asfotase Alfa treatment promotes healing of HPP-associated rickets. The researchers are now working to improve the therapy to reduce side effects like calcification of the kidney parenchyma (nephrocalcinosis). Their studies will also provide data to help enhance clinical management of patients with life-threatening HPP and identify appropriate therapeutic approaches for patients with milder forms.

Supported by NIDCR


**NCI Clinical Trials Program for Children with Cancer**

Through the Children's Oncology Group (COG), the COG Phase I/Pilot Consortium (now the Pediatric Early Phase Clinical Trials Network) and the Pediatric Brain Tumor Consortium (PBTC), NCI is supporting nationwide clinical trials. The NCI intramural research program also conducts clinical trials at the NIH Clinical Center and internationally. During FY 2018, a number of clinical trials evaluating novel agents and new treatment approaches were initiated or expanded in scope. Examples of treatment interventions include radiation therapy, chemotherapy, molecularly targeted therapy. The trials focused on treating cancer in the brain stem, blood, brain, and liver. In particular, the NCI-COG Pediatric MATCH
trial that opened in July 2017, is enrolling children with advanced solid tumors that have progressed or recurred on standard therapy. Genetic sequencing is used to identify children and adolescents (ages of 1 to 21) whose tumors have a genetic abnormality for which either an approved or investigational targeted therapy exists. Currently, 10 treatment arms are open to accrual. New treatment arms will open as drugs become available. To date, almost 400 children and adolescents have been enrolled for screening. The trial is accessible at approximately 200 COG sites across the country, where the majority of pediatric cancer patients receive treatment.

Supported by NCI
Website:  https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/pediatric-match
Clinical Trial:  https://clinicaltrials.gov/ct2/show/NCT03155620

**Administrative Supplements to Support Pediatric Cancer Control Research**

Over 10,000 new cancer cases are estimated to be diagnosed among children ages 0-14 years; and about 70,000 adolescents and young adults ages 15-39 are diagnosed with cancer each year in the United States. Many cancers diagnosed in childhood and adolescence have unique genetic and biological features, as well as etiology. In addition, pediatric and young adult cancer survivors have potential for substantial late and long-term symptoms due to their cancer and its treatment(s). Extending currently funded NIH research to expand cancer control research on pediatric and young adult cancer can reduce burden for patients and their families.

Supported by NCI

**Pilot and Feasibility Studies in Preparation for Drug and Alcohol Abuse Prevention Trials**

Significant progress has been made in understanding effective approaches to the prevention of drug and alcohol use, misuse and related problems and alcohol and other substance use disorders over the past few decades. However, further research is needed to identify novel, highly effective prevention strategies for understudied groups and settings, including young adults and older adults, and populations and settings for which evidence-based interventions do not exist. NIDA and NIAAA have expanded their support for: (a) pilot and/or feasibility testing of innovative new, revised, or adapted prevention intervention approaches to prevent or delay the initiation and onset of drug and alcohol use, the progression to misuse or problem use or alcohol and other substance use disorder, reduce drinking and driving and deaths related to impaired driving, prevent suicide attempts (nonfatal and fatal), and the drug- or alcohol-related acquisition or transmission of HIV infection and viral hepatitis among diverse populations and settings; and, (b) pre-trial feasibility and acceptability testing for prevention services and systems research.

Supported by NIDA, NIAAA

**Safety and Outcome Measures of Pain Medications Used in Children and Pregnant Women**

NICHD aims to promote preclinical, translational, clinical and epidemiological research in pain medications use in children or in pregnant women and to develop effective approaches to evaluate maternal and child outcomes of pain medication treatments.

Supported by NICHD
Funding Opportunities for Pediatric Research

In FY 2018, NIH issued 346 Funding Opportunity Announcements (FOAs) that specifically called for applications related to pediatric research.1 These FOAs are listed in Table 3 of the Appendix to this report. Much of the NIH’s pediatric research portfolio comes from investigator-initiated research, and a large number of funded grants are associated with funding opportunities that do not have a pediatric focus. However, the FOAs listed in Table 3 provide information about the range of areas that NIH ICOs have taken steps to address in pediatric research. In FY 2018, NIH issued FOAs in research to advance safe and effective devices for neonatal, perinatal, and pediatric care settings; pediatric and neonatal resuscitation; HIV prevention and care; understanding, prevention, and management of infections and how immunity can be transmitted from women to their infants; the effects of maternal nutrition and pre-pregnancy obesity on mothers, infants, and children; prenatal and pediatric hydrocephalus; pain management; literacy in dual-language learners; early-life factors; cancer development, treatment, and survival in childhood cancers; early psychosis; managing asthma; pediatric drug dosing and formulations, among other areas.

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1 In 2018, changes to NIH’s policies on clinical trials required many FOAs to be re-issued. As a result, the number of FOAs is not comparable to those issued in prior years.
NIH supports a large number of ongoing programs in pediatric research. In FY 2018, NIH funded approximately 67 pediatric centers programs that supported pediatric research, with an additional 163 programs funded under cooperative agreement mechanisms that may be similar in structure to centers. Many, but not all, pediatric research programs were focused exclusively on child health. For example, the Gabriella Miller Kids First Pediatric Research Program is developing a large-scale data resource for the pediatric research community, providing access to vast amounts of genetic and clinical data from patient cohorts focused on childhood cancer and structural birth defects. The center/network programs supporting pediatric research at NIH include some that are targeted to a specific disease or condition, such as the Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers (MDCRCs). Others, like the pediatric component of the Clinical and Translational Science Awards, 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 and interagency agreements.

**Child Development**

**Adolescent Brain Cognitive Development (ABCD) Study**
NIH launched the Adolescent Brain Cognitive Development (ABCD) Study in September 2015 to gain better understanding of brain, cognitive, social, and emotional trajectories from childhood through adolescence. In September 2016, the ABCD Study began recruiting children ages 9-10, before they initiate substance use, targeting a total enrollment of ~10,000 participants by the end of 2018. Researchers will follow these children over the next decade, using non-invasive neuroimaging and cognitive, academic, social, emotional, and biological assessments to determine how childhood experiences (e.g., sleep; screen time; sports and arts involvement; alcohol, tobacco, and other substance use) interact with each other and with children’s changing biology to affect brain development and other outcomes (e.g., physical and mental health, academic achievement). The study allows researchers to examine how pre-existing differences in brain structure and function may contribute to substance misuse. Anonymized data will be released annually to the research community in an open science model to allow scientists worldwide to conduct analyses and pool resources to answer a variety of scientific questions that will guide education, substance use prevention, and other health promotion policies to ensure the well-being and success of the Nation’s children.

Supported by NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OBSSR, ORWH

Website: [https://abcdstudy.org/](https://abcdstudy.org/)

**The Add Health Study**
The Add Health Study, formerly the National Longitudinal Study of Adolescent Health and also known as the National Longitudinal Survey 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.

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

Website: [https://www.cpc.unc.edu/projects/addhealth](https://www.cpc.unc.edu/projects/addhealth)

**The NEXT Generation Health Study**
NICHD’s Division of Intramural Population Health Research coordinates the NEXT Generation Health Study, a nationally representative cohort of 2874 adolescents, recruited in 2010 and assessed annually up
to 22 years old for health, cardiovascular risk factors, and adolescent behaviors such as substance use, diet, physical activity, sleep, and driving.
Supported by NICHD, NHLBI, NIDA, NIAAA
Website: https://www.nichd.nih.gov/about/org/diphr/officebranch/sbsb/next

**Molecular Transducers of Physical Activity in Humans**
The NIH Common Fund’s Molecular Transducers of Physical Activity in Humans 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 key molecules. One of the clinical sites will focus on the molecular changes that occur when children and adolescents exercise. Scientists and clinicians increasingly recognize that physical activity is an essential component of health, growth, and development, and there are critical periods when exercise can lead to long-term improvements in health. When combined with data from the six clinical sites focusing on adults, this research will show whether the molecular transducers of health benefits differ in children and in adults and during different stages of development.
Supported by NIH Common Fund
Website: https://commonfund.nih.gov/MolecularTransducers

**Upstate KIDS Study and Follow-Up Study**
The Upstate KIDS study was designed to determine if fecundity and various infertility treatments adversely affect the growth, motor, and social development of children from birth through three years of age. Researchers tracked infants conceived with and without infertility treatment who resided in the 57 counties comprising Upstate New York State (exclusive of the five boroughs of New York City) using the “infertility check box” on the birth certificate for cohort selection. Parents and their infants were recruited at approximately 4-8 months of infant age, with 1,297 infants with reported infertility treatment and over 3,692 “unexposed” infants without reported 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. Through a follow-up study, the cohort will be followed to 8 years of age, focusing on childhood cardio-metabolic outcomes (i.e., obesity, high blood pressure, metabolism) and assessing epigenetic differences as measured by DNA methylation using collected biospecimens among approximately 900 children.
Supported by NICHD
Website: https://www.nichd.nih.gov/about/org/diphr/eb/research/pages/infant-development.aspx
Environmental and Social Influences

Environmental influences on Child Health Outcomes (ECHO)
In September 2016, NIH announced over $157 million in awards to establish 35 Pediatric Cohort projects, a Coordinating Center, a Data Analysis Center, a Patient/Person Reported Outcomes Core, six Children’s Health Exposure Analysis Resource projects, 17 IDEa States Pediatric Clinical Trials Network (ISPCTN) research sites, and the ISPCTN Data Coordination and Operating Center. The 35 ECHO Pediatric Cohort awards consist of many individual cohorts of mothers and children with a broad range of early life environmental exposures, including physical, chemical, biological, behavioral, social factors. ECHO focuses on five key high-impact pediatric outcomes: (1) Upper and lower airway, (2) Obesity, (3) Pre-, peri-, and postnatal outcomes, (4) Neurodevelopment, and (5) Positive health. By harmonizing the information gathered from existing cohort studies of mothers and children, complemented by new data that the cohorts will obtain from participants, ECHO will create a large ECHO-wide cohort – collectively > 50,000 children – that will greatly increase scientists’ ability to answer critical public health questions about the impact of early life exposures on children’s health.
Supported by OD
Website: https://www.nih.gov/echo

Clinical Sites for the IDEa States Pediatric Clinical Trials Network
The goal of the IDEa States Pediatric Clinical Trials Network is to provide medically underserved and rural populations with access to state-of-the-art clinical trials, apply findings from relevant pediatric cohort studies to children in IDEa state locations, and build pediatric research capacity at a national level.² Supported by OD

Children’s Health Exposure Analysis Resource (CHEAR)
This initiative has created a resource to provide the NIH-funded research community with access to laboratory and statistical analyses that will allow for the addition or expansion of environmental exposures as a component of ongoing epidemiological and clinical research, thereby creating a public resource of children’s exposures across the country. Exposures measured encompass the breadth of the exposome, the totality of biological, psychosocial, chemical, and physical factors to which humans are exposed.
Supported by NIEHS, NIH, NCI

Centers for Children’s Environmental Health and Disease Prevention Research
Since 1998, the Children’s Environmental Health and Disease Prevention Research Centers have studied individual, regional, national, and global environmental exposures and the effects on children’s health. The centers connect basic scientists, behavioral scientists, social scientists, pediatricians and other clinicians, and public health professionals, all working together to improve the health and environments of children.
Supported by NIEHS
Website: https://www.niehs.nih.gov/research/supported/centers/prevention/

² This network partially meets the requirement in Section 409D(d) of the PHS Act for a National Pediatric Research Network as part of the Pediatrics Research Initiative.
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. NIEHS provides support for the WHO Collaborating Centres for Children's Environmental Health Network, 14 research institutes around the world, each of which acts as a hub to strengthen national or regional capacity to advance children's environmental health.

Supported by NIEHS
Website:  https://www.niehs.nih.gov/research/programs/geh/partnerships/network/index.cfm

Stress Response, Socioemotional Development, and Health in Minority and Low Socioeconomic Status Children and Adolescents

Affecting a range of health conditions, health disparities can emerge across race, ethnicity, socioeconomic status, and many other factors, with different contexts for children, adolescents, and adults. Epigenetics holds great promise to help scientists uncover the origins of health disparities long before such disparities are normally observable. NIMHD is supporting a group of scientists that will assemble an epigenome-wide dataset with 2000 children to examine if DNA methylation partially mediates the effect of adverse social context (e.g., poverty, harsh parenting, neighborhood disorganization, family instability) on biological processes related to stress response and hormones levels.

Supported by NIMHD
Website:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9545862

Pediatric Patient Reported Outcomes in Chronic Diseases Consortium

Researchers will test several pediatric patient-reported outcome tools that measure aspects of physical, mental, and social well-being such as pain, anxiety, and peer relationships. The research will also help to improve understanding of the effects of environmental stressors on symptoms and quality of life in children who have a variety of chronic diseases or conditions. By validating the pediatric PROMIS measures, the Consortium will facilitate their adoption and meaningful use in research and clinical care settings, ultimately improving the treatment of chronic diseases in children.

Supported by NIAMS, OBSSR, ORWH, NICHD, NHLBI, NIDDK, NIMHD, NCI, NIMH
Website:  https://www.niams.nih.gov/newsroom/nih-funds-pediatric-patient-reported

Pregnancy and Health of the Newborn

Maternal-Fetal Medicines Unit (MFMU) Network

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 (RCTs) of preventing obstetrical hemorrhage after cesarean delivery, preventing effects from cytomegalovirus infection, and treating sleep apnea in pregnancy. Completed projects include RCTs on fetal heart rate monitoring, preventing preterm birth, and preventing preeclampsia.

Supported by NICHD
Website:  https://www.nichd.nih.gov/research/supported/mfmu

Neonatal Research Network (NRN)

The NICHD’s NRN is a collaborative network of neonatal intensive care units across the United States, comprising 18 clinical centers and a data coordinating center. Focused on newborns, particularly extremely low-birth-weight (ELBW) infants, the NRN conducts clinical trials and clinical studies in such
areas as sepsis and other infections, bronchopulmonary dysplasia and other lung conditions, and necrotizing enterocolitis (NEC), a condition in which the intestines lack oxygen or blood flow. Supported by NICHD
Website:  https://www.nichd.nih.gov/research/supported/nrn

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 to defining normal and abnormal fetal growth is the development of standards for fetal anthropometric (body measurement) parameters, measured longitudinally throughout gestation. The NICHD 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 actually are on track. Another project found that maternal stress levels, measured via survey, in low-risk pregnant women did not affect newborn growth. Supported by NICHD
Website:  https://www.nichd.nih.gov/about/org/diphr/officebranch/eb/fetal-growth-stud

Maternal Stress and Diesel Exhaust Interactions in Autism
Multiple prenatal/maternal environmental toxins and exposures have been linked to human autism spectrum disorders, but the associations of single agents are relatively weak, suggesting it is the combination of multiple maternal exposures that increases vulnerability in offspring. Researchers are using a new mouse model that combines the effects of maternal stress and exposure to diesel exhaust, both of which have been implicated in autism, to establish a causal link between prenatal environmental exposures and dysfunction of neural cells critical for normal brain development. Supported by NIEHS
R01ES025531:  https://projectreporter.nih.gov/project_info_details.cfm?aid=9552837

Center for the Health Assessment of Mothers and Children of Salinas
This is a pregnancy study examining the effects, including the cumulative effects, of chemicals and other factors in the environment on children’s health among pregnant women and children living in the Salinas Valley, California. Health outcomes studied include asthma, allergic response, birthweight, gestation length, metabolic syndrome, neurobehavioral outcomes, neurodevelopmental outcomes, obesity/body weight, premature/delayed puberty, respiratory outcomes, thyroid dysfunction, dental health, and risk-taking behavior. Supported by 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 (MONEAD) study supported by NINDS and NICHD follows over 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 FY2018, with new aims to determine the effects of breastfeeding while taking AEDs. Results from prior funding periods of this
project are already informing clinical practice for managing epilepsy in women of childbearing age, in order to optimize outcomes for both mother and child.
Supported by NINDS, NICHD
U01NS038455: https://projectreporter.nih.gov/project_info_description.cfm?aid=9524064

Zika in Infants and Pregnancy (ZIP) Cohort Study
The multi-country Zika in Infants and Pregnancy (ZIP) study is evaluating the extent of health risks that ZIKV infection poses to pregnant women and their developing fetuses and infants. The study is designed to follow the women throughout pregnancy as well as their infants, for at least a year after birth.
Supported by NICHD, NIAID, NIEHS
Clinical Trial: https://clinicaltrials.gov/ct2/show/NCT02856984

Immune Mechanisms at the Maternal-Fetal Interface
This program supports research to determine the roles and interactions of immune cells at the maternal-fetal interface throughout pregnancy, including mechanisms of responses to vaccination and infection, or ionizing radiation, that protect or impact the fetus and that may influence fetal immune system development.
Supported by NIAID, NICHD

Nutrition and Obesity in Pregnancy and Childhood

Dietary Supplement Label Database (DSLD)
Launched in June 2013, the DSLD is a searchable database of information taken from the labels of dietary supplement products. It is a joint project of the NIH Office of Dietary Supplements (ODS) and the National Library of Medicine (NLM) in collaboration with USDA, DCD, FDA, and DoD. About 1,000 new product labels are entered into the DSLD each month so that in time almost all of the dietary supplement products in the market will be included. There are currently more than 80,000 labels in the database.
Supported by NLM, ODS
Website: https://www.dsld.nlm.nih.gov/dsld/index.jsp

Factors in Infancy and Early Childhood that Influence Obesity Development
This initiative supports research to characterize or identify factors in early childhood (birth-24 months) that may increase or mitigate risk for obesity and/or excessive weight gain and/or to fill methodological research gaps relevant to the understanding of risk for development of obesity in children. Studies may also assess factors relevant to families and/or caregivers of children from birth to 24 months.
Supported by NIDDK, NICHD, NIMHD, NHLBI, OBSSR

Preventing Early Childhood Obesity in American Indian Populations
Childhood obesity is a major public health issue in the U.S., particularly among American Indian children. This NICHD study aims to assess the Family Spirit Nurture obesity prevention intervention, which incorporates infant and young child feeding practices and physical activity, among members of the White Mountain Apache Tribe and the Navajo Nation. Scientists will assess maternal feeding practices and behaviors, infant and toddlers’ diets, levels of physical activity, and BMI from birth to two years of age.
Supported by NICHD
R01HD087407: https://projectreporter.nih.gov/project_info_details.cfm?aid=9406321
**Body Weight & Puberty Study (Investigating 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. NIEHS-funded scientists are using breast ultrasound to better determine whether or not an overweight girl has breast tissue and to understand if overweight girls are truly entering puberty before normal weight girls.
Supported by NIEHS
Website:  https://www.niehs.nih.gov/research/clinical/studies/bwps/index.cfm

**National Collaborative on Childhood Obesity Research (NCCOR) Launches Youth Compendium of Physical Activities**
In October 2017, the National Collaborative on Childhood Obesity Research (NCCOR) launched the Youth Compendium of Physical Activities to help childhood obesity and physical activity researchers and practitioners estimate the associated energy expenditure of a variety of activities in which youth participate. The Youth Compendium of Physical Activities provides measures of energy expenditure for 196 common youth activities including sedentary activities, standing activities, playing and participating in games, and walking and running.
Supported by NIH
Website:  http://www.nccor.org/nccor-tools/youthcompendium/

**Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS)**
Teen-LABS was launched to assess the short- and long-term risks and benefits of bariatric surgery among teens with severe obesity. This is an observational study that enrolled teens who were already planning to have bariatric surgery.
Supported by NIDDK

**Diabetes**

**The Environmental Determinants of Diabetes in the Young (TEDDY)**
Insights about strategies to prevent type 1 diabetes could be identified through the NIDDK's ongoing TEDDY study. TEDDY is following over 6,000 children at high genetic risk of developing type 1 diabetes to identify environmental factors that trigger or protect against disease development. TEDDY 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. TEDDY researchers are also studying better ways to identify those individuals at high-risk, such as a recently developed genetic risk scoring model that may greatly improve clinicians’ ability to identify those likely to develop type 1 diabetes.
Supported by NIDDK, NIAID
Website:  https://teddy.epi.usf.edu
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29614081
Childhood Disease, Allergies, and Immunity

Childhood Liver Disease Research Network
NIDDK-supported researchers seek to improve understanding of pediatric liver diseases, including 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.
Supported by NIDDK
Website:  https://childrennetwork.org/

Genetic Analysis of Hirschsprung Disease
Hirschsprung disease, caused by missing nerve cells in the muscles of part of all of the large intestine, results in difficulty in having bowel movements. NICHD is supporting a genetic analysis of Hirschsprung disease, in order to describe the genes, sequence variants, and biochemical pathways that affect the disease. The researchers are using state-of-the-art technologies to screen the genome of patients with Hirschsprung's disease, as well as their affected relatives and their parents.
Supported by NICHD
R37HD028088: https://projectreporter.nih.gov/project_info_description.cfm?aid=9691015

INSPPIRE to Study Pediatric Chronic Pancreatitis
The multinational INSPPIRE (International Study Group of Pediatric Pancreatitis: In Search for a Cure) was established to investigate risk factors for and outcomes of pediatric pancreatitis. The Study Group is currently part of the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer. It 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 chronic pancreatitis in children.
Supported by NIDDK, NCI
U01DK108334: https://projectreporter.nih.gov/project_info_description.cfm?aid=9566165

Non-Operative Management of Pediatric Appendicitis: A Randomized Controlled Study
Pilot studies have found that initial non-operative management with antibiotics alone may resolve the majority of acute pediatric appendicitis. This NIDDK study is determining the complication rate, safety, and efficacy of this non-operative approach in children, investigate its potential cost and health utility benefits, and will examine the impact of specific clinical factors on the success rate of non-operative management.
Supported by NIDDK
U34DK112584: https://projectreporter.nih.gov/project_info_description.cfm?aid=9415134

The PROSpect Trial
The largest study of severe Pediatric Acute Respiratory Distress Syndrome is an NHLBI-funded multi-site Phase III clinical trial of this life-threatening condition in children with respiratory failure that compares two modes of ventilation, conventional and high frequency oscillatory ventilation, and supine versus prone positioning to determine the effect of each on outcomes.
Supported by NHLBI
Website:  https://prospect-network.org/

Controlling and Preventing Asthma Progression and Severity
Asthma remains one of the most important challenges to pediatric public health in the United States, and prevention of asthma is a high priority. NIAID is currently supporting a randomized trial of omalizumab, an anti-IgE monoclonal antibody, as a preventive therapy in 2 to 3-year old children at high risk for
asthma. This study will examine if treatment with omalizumab for two years prevents progression from allergic wheezing to asthma in the first two years after the treatment is completed.

Supported by NIAID
U01AI126614: https://projectreporter.nih.gov/project_info_description.cfm?aid=9517732

**Asthma and Allergic Diseases Cooperative Research Centers**

This initiative supports centers that integrate clinical and basic research to conduct studies on the mechanisms underlying the onset and progression of diseases of interest, including asthma, rhinitis (allergic and non-allergic), chronic rhinosinusitis, atopic dermatitis, food allergy, and drug allergy. A portion of the Asthma and Allergic Diseases Cooperative Research Centers was recompeted and four awards were made in FY2018, bringing the total number of grants encompassed under this program to ten. One additional cooperative agreement will be awarded in FY2019.

Supported by NIAID

**The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network:**

IMPAACT supports studies on prevention and treatment of HIV and its complications and co-infections, such as tuberculosis (TB), which is a major cause of death for HIV-infected infants, children, adolescents, and pregnant/postpartum women globally. IMPAACT's mission is to decrease HIV and HIV-associated infections, including mother-to-child transmission (MTCT), and to decrease mortality/morbidity due to HIV and HIV-associated infections and co-morbidities among infants, children, adolescents, and pregnant/postpartum women worldwide. The IMPAACT network has collaborated closely with the NICHD-funded Domestic & International Pediatric & Maternal HIV Clinical Studies Network (more details in the Global Pediatric Health section). This collaboration has made it possible to conduct an expanded clinical trial portfolio advancing pediatric HIV/AIDS clinical research.

Supported by NIAID, NICHD, NIMH
Website: https://impaactnetwork.org/

**Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN)**

The ATN 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 ATN has extensive experience in recruiting and retaining understudied youth populations in the United States. The primary mission of the ATN is to conduct both independent and collaborative research that explores promising behavioral, microbicidal, prophylactic, therapeutic, and vaccine modalities in HIV-infected and at-risk adolescents, ages 12 years through 24 years. ATN research informed FDA approval of Tenofovir (Truvada), a drug combination used in Pre-Exposure Prophylaxis (PrEP) for HIV, for use in at-risk adolescents.

Supported by NICHD, NIDA, NIMH, NIMHD, NIAID, OD
Website: https://www.nichd.nih.gov/research/supported/atan
Pediatric HIV/AIDS Cohort Study (PHACS)
PHACS began in 2005 to address two critical pediatric HIV research questions: (1) What is the long-term safety of fetal and infant exposure to antiretroviral therapy (ART)? and (2) What are the effects of perinatally acquired HIV infection in adolescents? The overall goals of PHACS are to: understand how HIV and its treatment affect growth and development, sexual maturation, organ function, and socialization of perinatally HIV-infected pre-adolescents, adolescents, and young adults; acquire more definitive information on the long-term safety of ART when used during pregnancy and in newborns; ensure a mechanism is in place to estimate the upper bounds of risk for children who were exposed to ART during maternal treatment to prevent perinatal HIV transmission; and continue the follow-up study of these populations.
Supported by NICHD, NIAAA, NIAID, NIDCD, NIDCR, NIDA, NIMH, NINDS
Website: https://www.nichd.nih.gov/research/supported/Pages/phacs.aspx

Primary Immune Deficiency (PID) Clinic
The PID clinic is the focal point for studies of the genetics, pathophysiology, and treatment of PID diseases, which are rare disorders of the immune system, often very severe in nature, that frequently manifest during infancy or childhood. The clinic conducts clinical trials to continuously improve bone marrow transplantation and gene therapy for the treatment of PID diseases.
Supported by NIAID, NIH Clinical Center
Website: https://www.niaid.nih.gov/clinical-trials/primary-immune-deficiency-clinic

Immune Tolerance Network (ITN)
The ITN develops treatment and prevention strategies for food allergy, autoimmune diseases, and organ transplantation, in adult and pediatric populations by inducing tolerance. The ITN is investigating whether the low rate of peanut allergy in children who began eating peanut-containing foods early in life persists until age 12. Additionally, a trial is being developed to assess whether early consumption of egg and milk will prevent allergy to these foods in young infants.
Supported by NIAID
Website: https://www.immunetolerance.org/

Clinical Trials in Organ Transplantation in Children (CTOTC)
The goal of NIAID’s CTOTC program is to promote understanding and reduce immune-mediated morbidity and mortality in vulnerable pediatric transplant recipients. In FY2018, the CTOTC program was extended for another three years to align with its companion program, Clinical Trials in Organ Transplantation (CTOT), which includes adult patients.
Supported by NIAID
Website: http://www.ctotstudies.org/

National Survey of Lead & Allergens in Housing (NSLAH)
NIEHS, in conjunction with the Department of Housing and Urban Development (HUD) Office of Lead Hazard Control, sponsored this study, which provided information to enable HUD and NIEHS scientists to assess the magnitude of the American public's exposure to household indoor allergens. NIEHS conducted the NSLAH in light of recent studies which suggested that cumulative exposure to indoor allergens can increase a person's risk for developing allergic disease and asthma.
NIEHS is using the allergen data from the NSLAH to: estimate indoor allergen exposures of the general population; assess the magnitude of levels of indoor allergens in the United States housing stock; evaluate differences in population exposure to allergens based on factors such as region/geography, ethnicity, socioeconomic status, and housing type.
Supported by NIEHS
Website: https://www.niehs.nih.gov/research/clinical/studies/nslah/index.cfm
**Bone and Muscle Health**

**The Microbiome and Juvenile Rheumatic Diseases**
The NIEHS Twin Sibling Study has enrolled more than 250 twins and same-gender (close in age) sibling pairs discordant for systemic rheumatic diseases to examine environmental risk factors in recently-diagnosed patients with juvenile and adult myositis, rheumatoid arthritis, lupus and scleroderma to examine risk factors common to these systemic rheumatic diseases in recently-diagnosed patients. To date, this study has identified peripheral blood gene and proteomic signatures common to these diseases, found epigenetic changes in a number of immune response genes in systemic lupus erythematosus patients, and identified herpes virus expression to be increased in the peripheral blood of affected patients. In one of the first studies of microbiome in pediatric rheumatic diseases, researchers will examine the oral microbiome in children with juvenile dermatomyositis as compared to their unaffected siblings and parents to see if changes in the microbiome may be associated with oral changes or disease outcomes. Supported by NIEHS
Website:  [https://www.niehs.nih.gov/research/clinical/studies/twin-sibs/index.cfm](https://www.niehs.nih.gov/research/clinical/studies/twin-sibs/index.cfm)

**Clinical Trial of Sodium Thiosulfate to Treat Calcinosis Associated with Juvenile Dermatomyositis**
Calciosis 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 calciosis after it occurs. Based on anecdotal experiences suggesting significant improvement in the calcifications of dermatomyositis with sodium thiosulfate treatment, NIEHS has opened a Phase 1-2 clinical pilot study to evaluate the efficacy of using sodium thiosulfate in juvenile and adult dermatomyositis with moderate to severe calciosis. Sodium thiosulfate is FDA-approved for the treatment of cyanide poisoning, but it also acts as a calcium chelator, an antioxidant, and a vasodilator. The study will also assess the safety of longer-term use of sodium thiosulfate in children and adults, and 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), as well as overall myositis disease activity and damage.
Supported by NIEHS
Clinical Trial:  [https://clinicaltrials.gov/ct2/show/NCT03267277](https://clinicaltrials.gov/ct2/show/NCT03267277)

**Structural Congenital Anomalies and Newborn Screening**

**Gabriella Miller Kids First Pediatric Research Program**
The NIH Common Fund's Gabriella Miller Kids First Pediatric Research Program (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 childhood cancer and structural birth defects patient 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. Over 2015-2018, the Kids First program selected 34 childhood cancer and structural birth defects patient cohorts for whole genome sequencing and sequenced more than 18,000 samples. The program will select additional cohorts in 2019-2022 pending available funding. In 2018, Kids First launched the Gabriella Miller Kids First Data Resource Portal. Clinical and genetic data from six of the Kids First projects are publicly available through the portal.
Supported by NIH Common Fund
Websites:  [https://commonfund.nih.gov/KidsFirst](https://commonfund.nih.gov/KidsFirst)
[https://commonfund.nih.gov/kidsfirst/x01projects](https://commonfund.nih.gov/kidsfirst/x01projects)
[https://kidsfirstdrc.org/portal/portal-features/](https://kidsfirstdrc.org/portal/portal-features/)
The Hunter Kelly Newborn Screening Research Program
This program funds an array of newborn screening related research 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.

Supported by NICHD
Website:  https://www.nichd.nih.gov/health/topics/newborn

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. 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. https://nbstrn.org/research-tools/virtual-repository-of-dried-blood-spots

- **Longitudinal Pediatric Disease 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. https://nbstrn.org/research-tools/longitudinal-pediatric-data-resource

- **Laboratory Performance Database (R4S).** This web-based application for the collection and reporting of analytical results has been developed and widely adopted into the routine practice of newborn screening laboratories worldwide. https://nbstrn.org/research-tools/lab-performance-database

Supported by NICHD
Websites:  https://www.nichd.nih.gov/research/supported/Pages/nbstrn.aspx
https://nbstrn.org/

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 resource.

Supported by NLM
Website:  https://newbornscreeningcodes.nlm.nih.gov/nb/sc/constructingNBSHL7messages
FaceBase: Comprehensive Craniofacial Data and Resources
The FaceBase Consortium aims to advance craniofacial, genetic, and developmental research by generating large amounts of multi-omic and phenotypic data from model organisms and humans. The Consortium coordinating center curates and integrates the data on craniofacial development and the developmental disorders that lead to birth defects and facial malformations and disseminates the data with tools for using the data to do research via the FaceBase web site. These resources are free and openly accessible to the scientific community. The next phase of FaceBase will continue to enhance its data curation, integration, presentation, and search capabilities so that it better serves the craniofacial research community. In addition, it will expand the anatomical sites, types, and volumes of craniofacial data and make them available to the broad scientific community through effective outreach activities.
Supported by NIDCR
Website:  https://www.facebase.org

Vision, Hearing, and Speech
Newborn Hearing Screening: Impact and Federal Programs
Collectively, NIDCD, CDC, and HRSA meet to enhance collaboration and coordination so the federal Early Hearing Detection and Intervention (EHDI) program can continue to ensure early identification of and improved outcomes for deaf and hard-of-hearing infants. Federal agencies work with health care teams who provide diagnostic and early intervention services. This promotes critical care for these children, while minimizing the negative impact that hearing loss can have on their speech, language, emotional, and academic development.

- NIDCD-supported research has identified the most effective methods to screen for hearing loss in newborns, as well as demonstrated that early intervention can help children who are deaf or hard-of-hearing to meet age-appropriate language, social, and other communication development milestones.
- NIDCD has developed resources for parents about hearing screening in children, hearing loss, and communication development.

            https://www.nidcd.nih.gov/health/your-babys-hearing-screening

Preventing Progressive Hearing Loss in Infants Identified by Early Hearing Screening
Infants born with cytomegalovirus (CMV) infection are at higher risk for progressive hearing loss (hearing loss that is diagnosed, then becomes worse over time) and late-onset hearing loss. Antiviral therapy administered early in life has been shown to help prevent progressive hearing loss in infants born with symptoms of CMV infection. However, in most cases, infants infected with CMV show no symptoms of the virus, but approximately 6%-23% may have or develop hearing loss. A clinical trial aims to identify and treat asymptomatic infants born with CMV infection and hearing loss, with a targeted approach to identify CMV-infected infants who have failed their hearing screening, then treat them with antiviral valganciclovir therapy.
Supported by NIDCD
Clinical Trial:  https://clinicaltrials.gov/ct2/show/NCT03107871
Learning Disabilities

Learning Disabilities Research Centers (LDRC) Consortium
This program 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 on 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.

Supported by NICHD
Websites:  https://www.nichd.nih.gov/research/supported/Pages/ldrc.aspx
https://www.nichd.nih.gov/research/supported/Pages/ldhubs.aspx

Intellectual and Developmental Disabilities, Neurological Disorders, and Mental Health

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). Centers have cores to provide infrastructure support and must also support new research component projects that use the center cores, focusing on comprehensive "-omic" approaches to IDDs, outcomes measures for interventions or treatments, multi-modal treatment approaches, shared resources across IDDRCs for treatment or assessment, and/or public health approaches to IDDs. Examples of IDDs 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; disorders that involve biochemical processes and metabolic issues related to brain functioning, such as hypoxia and phenylketonuria.

Supported by NICHD
Website:  https://www.nichd.nih.gov/research/supported/eksiddrc

Centers for Collaborative Research in Fragile X (CCRFX)
The CCRFX program supports research to improve the diagnosis and treatment of Fragile X syndrome (FXS) 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.

Supported by NICHD, NINDS, NIMH
Website:  https://www.nichd.nih.gov/research/supported/Pages/ccrfx.aspx

Screening for Fragile X Syndrome
Early Check is a research program in which up to 120,000 North Carolina families each year will be offered voluntary screening for fragile X syndrome and other genetic conditions yet to be determined. Without evidence that a treatment is more effective when started earlier, a test for a genetic disease cannot be included in the standard newborn screening panel. But the evidence cannot be collected without a screening program. Rare disorders, like fragile X syndrome, pose an even greater challenge because of the tremendous difficulty identifying enough cases to conduct studies, especially before symptoms appear.

Supported by NCATS
Website:  https://ncats.nih.gov/pubs/features/newborn-screening
**Autism Centers of Excellence (ACE)**
Since 2007, this trans-NIH initiative supports large-scale multidisciplinary studies on autism spectrum disorders (ASDs), with the goal of determining the disorders' causes and best treatments. Research efforts are coordinated across NIH by the Autism Coordinating Committee. These ICs also participate in the NIMH-led Interagency Autism Coordinating Committee (IACC). Through the ACE program, NIH supports large research projects aimed at understanding autism spectrum disorder (ASD) and developing interventions. These awards seek to build upon prior knowledge by supporting the most innovative, multidisciplinary science. Among other topics, ACE projects are focused on studying the earliest brain and behavioral markers of ASD, identifying ASD subtypes, understanding the differences between males and females with ASD, evaluating screening practices for ASD, and developing innovative treatments.

**Supported by NICHD, NIDCD, NIEHS, NIMH, NINDS**

Website: [https://www.nichd.nih.gov/research/supported/ace](https://www.nichd.nih.gov/research/supported/ace)

**National Database for Autism Research (NDAR)**
This NIH-funded research data repository aims to accelerate progress in autism spectrum disorders (ASD) research through data sharing, data harmonization, and the reporting of research results. NDAR also serves as a scientific community platform and portal to multiple other research repositories, allowing for aggregation and secondary analysis of data. Data from over 100,000 consenting de-identified research participants are available for secondary analysis by other qualified researchers through NDAR. All data within NDAR are harmonized (e.g., the same names for each piece of data collected are used) and validated (e.g., reported values are consistent with other projects) to a community-established common data definition.

**Supported by NIMH, NICHD, NINDS, NIEHS**

Website: [https://ndar.nih.gov/](https://ndar.nih.gov/)


**The Down Syndrome (DS) Consortium**
Since 2011, NICHD has led this public-private collaboration to foster 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.

**Supported by NICHD, NCI, NHLBI, NHGRI, NIA, NIAID, NIDCD, NIDCR, NIDDK, NIMH, NIMHD, NINDS, NCATS**

Website: [https://downsyndrome.nih.gov/](https://downsyndrome.nih.gov/)

**DS-Connect®**
DS-Connect® is a web-based health registry that serves as a national health resource for individuals with DS and their families, researchers, and healthcare providers. The registry facilitates communication and online resource sharing through a secure, confidential database. With over 4,200 registrants to date, DS-Connect has allowed 35 researchers to successfully complete recruitment for their studies.

**Supported by NICHD, NCI, NHLBI, NHGRI, NIA, NIAID, NIDCD, NIDCR, NIDDK, NIMH, NIMHD, NINDS, NCATS**

Website: [https://dsconnect.nih.gov](https://dsconnect.nih.gov)

**Fetal Alcohol Spectrum Disorders (FASD)**
NIAAA supports research to improve the prevention, diagnosis, and treatment of FASD. For example, the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) 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. NIAAA is also encouraging studies on 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.

Supported by NIAAA

Websites:  https://cifasd.org/


Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers
The MDCRCs are designed to foster the translation of new scientific findings and technological developments into novel treatments for muscular dystrophies (MDs). The Centers promote basic, translational, and clinical research and 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 the specific projects and serve as a resource for the international research community.

Supported by NICHD, NINDS, NIAMS, NHLBI

Websites:  https://www.wellstonemdcenters.nih.gov/
https://www.nichd.nih.gov/research/supported/Pages/mdcrc.aspx

Genetic Risks for Common Neurodevelopment Disorders
The NIMH intramural research program is investigating multiple rare genetic disorders caused by the presence of too few or too many sex chromosomes. Understanding models of these disorders may help elucidate how genetic and brain changes lead to common neurodevelopment disorders (NDDs) such as autism, attention-deficit/hyperactivity disorder, and intellectual disability. The first phase of this study used brain scans to pinpoint when and where genetic risks for NDD impact brain maturation. The scans identified the initial cell types and stages to examine in order to understand how genetic risks impact individual brain cells. Due to advances in stem cell technology, scientists can now create these cells of interest from individuals and start to ask questions about human nerve cells that cannot be done in vivo or postmortem. NIMH researchers are collaborating with other scientists to induce neural tissue from the skin of individuals with certain genetic disorders. They plan to measure genome function from individual cells using new techniques for gene expression analysis. These efforts will identify molecular targets that could be acting at the cellular level, to ultimately give rise to disorders of brain structure and function. Identifying such targets is a key step in translating neuroscientific and genetic knowledge into tools that help improve health.

Supported by NIMH
ZIAMH002949:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9568282

Preventing Epilepsy in Infants with Tuberous Sclerosis Complex
Recent research showed that EEG biomarkers can predict seizure activity prior to onset in infants with Tuberous Sclerosis Complex (TSC). NINDS-supported scientists 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.

Supported by NINDS
U01NS092595:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9103780

Understanding the Brain Mechanisms Mediating Chronic, Severe Irritability in Youth to Develop New Treatments
Irritability is one of the most common reasons children present for psychiatric care and is associated with problems controlling behavior. There are no well-established treatments, and antipsychotic medication is frequently used to control irritability, despite significant side-effects and lack of an evidence base. NIMH intramural researchers are working to understand the brain mechanisms mediating irritability and to use
those insights to develop new treatments. Data indicate that irritable youth have a bias to interpret ambiguous faces as hostile, and to have abnormal brain responses to angry faces. These data motivated a clinical trial, which is now in progress, to determine whether computer-based training designed to address this bias can decrease irritability in children.
Supported by NIMH
Website: https://www.nimh.nih.gov/research/research-conducted-at-nimh/research-areas/clinics-and-labs/edb/smdn/index.shtml
ZIAMH002786: https://projectreporter.nih.gov/project_info_description.cfm?aid=9568255

**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. NICHD's 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.
Supported by NICHD
Website: https://www.nichd.nih.gov/research/supported/opru_network

**Rare Pediatric Diseases**

**Rare Diseases Clinical Research Network (RDCRN)**
The Rare Diseases Clinical Research Network conducts collaborative clinical research in rare diseases, including longitudinal studies of individuals with rare diseases, clinical studies, and clinical trials. The RDCRN is comprised of 21 distinctive Rare Diseases Clinical Research Consortia (RDCRC) 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. Half to two thirds of rare diseases manifest in children therefore, many of the rare diseases studied under this network occur primarily or frequently in children. Current consortia that study such disorders, include 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 and related disorders.
Supported by NCATS, NCI, NEI, NHLBI, NIAID, NIAMS, NICHD, NIDCR, NIDDK, NINDS
Website: https://ncats.nih.gov/rdcrn
The Undiagnosed Diseases Network (UDN)
The Undiagnosed Diseases Network (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 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 hopefully cures for these diseases will be increased. Approximately 58% of the participants enrolled in the UDN are pediatric. Examples of new developmental disorders recently discovered by the UDN include MTHFS-associated disorder and TBX2-related disorder.

Supported by NIH Common Fund
Website:  https://commonfund.nih.gov/diseases
Articles:  https://www.ncbi.nlm.nih.gov/pubmed/30031689

Treatment for Creatine Transporter Deficiency
Creatine serves as a crucial energy source in the brain, delivered to brain tissue by a specialized transport protein. Without this transporter, creatine cannot enter the brain, resulting in profound learning disabilities, autistic behavior, recurring epileptic seizures and lifelong care needs. There are no FDA-approved therapies for Creatine Transporter Deficiency (CTD). The prevalence of this rare disease is unknown, although more than 150 affected individuals have been identified. Two other creatine deficiency syndromes (GAMT and AGAT) have similar clinical manifestations to CTD and show significant clinical improvement when supplemented with creatine monohydrate. However, supplementation is not effective in CTD because the genetic defect prevents creatine transport across the blood-brain barrier. The lead collaborators at Lumos Pharma identified a creatine analog (LUM-001), shown in animal models to penetrate the brain and serve as an energy source. The goal of this project is to develop LUM-001 into an oral therapeutic to treat CTD. NIH support, combined with other funding, enabled Lumos to submit an Investigational New Drug application to the FDA and initiate a Phase 1 safety study in healthy volunteers. The team continues to collaborate on a prospective, multi-center natural history study to support future trials in CTD patients.

Supported by NCATS, NICHD
Website:  https://ncats.nih.gov/trnd/projects/active/cincy-creatine-transporter-defect

Gene Therapy for the Treatment of AADC Deficiency
Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare, inherited nervous system disorder. Children with the condition experience various symptoms, including severe developmental delays, weak muscle tone, involuntary movements of the arms and legs, and painful seizures. There are no approved treatments, and current practice – increasing dopamine levels through inhibition of monoamine oxidase (MAO) and direct stimulation of dopamine receptors with dopamine agonists – provides little benefit to patients. Scientists are now seeking to correct the underlying molecular defect in the DDC gene. The NCATS team retrieved and organized data from the three clinical trials conducted previously in Taiwan, conducting a rigorous statistical analysis. The clinical package and key preclinical safety, biodistribution, and chemistry, manufacturing and controls data developed by the NCATS scientists led FDA to agree that Agilis Biotherapeutics could submit a Biologics Licensing Application (BLA) for marketing approval in the U.S. AGIL-AADC has received the FDA Orphan Drug and Rare Pediatric Disease designations, as well as Orphan Medicinal Product status in Europe.

Supported by NCATS
Website:  https://ncats.nih.gov/trnd/projects/active/aadc-deficiency
Pediatric Cancer

Specialized Programs of Research Excellence (SPOREs) in Pediatric Oncology

SPOREs are a cornerstone of NCI’s 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 and currently nineteen organ sites, systems, or pathway-specific themes are represented in the SPORE portfolio, including: bladder, brain, breast, cervical, gastrointestinal, head and neck, kidney, leukemia, lung, lymphoma, myeloma, neuroendocrine, ovarian, pancreatic, prostate, sarcoma, skin, thyroid, and hyperactive RAS tumors. SPOREs focused on pediatric cancers include: pediatric astrocytoma, pediatric glioma, pediatric melanoma, and hyperactive RAS tumors (neurofibromatosis type 1, malignant peripheral nerve sheath tumors, and juvenile myelomonocytic leukemia).

Supported by NCI
Website:  https://trp.cancer.gov/spores/bylocation.htm

Beau Biden Cancer Moonshot

The Cancer Moonshot aims to accelerate cancer research to make more therapies available to more patients, while also improving our ability to prevent cancer and detect it at an early stage. In 2016, the report of the Cancer Moonshot Blue Ribbon Panel identified two specific high priority pediatric research opportunities that were uniquely poised for acceleration. The first was fusion oncoproteins in pediatric cancers, as these distinctive proteins are unique to childhood cancers and drive cancer growth and survival. In 2018, NCI funded the Fusion Oncoprotein Childhood Cancer Consortium (FusOnC2). This is a collaborative network of multi-disciplinary scientists working together to uncover the mechanisms governing how fusion oncoproteins drive childhood cancers. There are four research teams currently in the consortium with plans to expand in FY 2019. The second-high priority area was pediatric immunotherapy translational science. This is a critical area for research as many of the immunotherapy treatments being developed for adult cancers are not applicable to childhood cancers. Hence, NCI launched the Pediatric Immunotherapy Discovery and Development Network (PI-DDN) in 2018 to advance research in immunotherapy for pediatric cancers. There were 6 research projects funded in the network in 2018. Also, the Human Tumor Atlas Network which will describe important transitions in tumor formation for greater understanding of cancer includes on research team studying pediatric cancers (neuroblastoma, glioma, and high-risk B-cell acute lymphoblastic leukemia). Another Moonshot initiative aims to improve symptom management for pediatric cancer patients who experience Graft Versus Host Disease (GVHD) as a consequence of hematopoietic stem cell transplantation to treat their cancer. This initiative, led by a team of intramural scientists, is developing and validating a pediatric specific symptom scale for GVHD. A Patient Reported Outcome or PRO measure would represent an important step forward in outcomes measurement for both therapeutic trials and clinical practice, with the goal of delivering tailored symptom management to improve quality of life for these pediatric patients.

Supported by NCI
Website:  https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative

NCI Pediatric Provocative Question (Pediatric PQ) Program

In 2016, NCI published a Funding Opportunity Announcement (FOA) to invite applications for research projects designed to use sound and innovative strategies to solve specific problems and paradoxes in childhood cancer research identified by the NCI as the NCI’s Pediatric Provocative Questions (Pediatric PQs). This program is meant to challenge cancer researchers to think about and elucidate specific problems in key areas of pediatric cancer research that are deemed important but have not received sufficient attention. The FOA included 9 Pediatric PQs that represent diverse areas relevant to childhood cancer research ranging from basic research on mechanisms of cancer development to research addressing important issues for survivors of childhood cancers. Funded projects are investigating mechanisms of
Rhabdomyosarcoma and Acute Myeloid Leukemia oncogenesis, developing predictive models for long-term adverse effects of therapy, developing new model systems to study premature aging in pediatric cancer patients, identifying and validating non-coding drivers of pediatric cancer, identifying non-invasive predictors of neurocognitive impairment in leukemia patients, and developing models to identify patients most at highest risk for treatment related complications.

Supported by NCI
Website:  https://provocativequestions.nci.nih.gov/

**NCI Research Programs for Children with Cancer**

NCI supports a comprehensive research program for children with cancer, ranging from basic molecular projects, through preclinical testing and clinical trials, to epidemiological studies to identify potential factors associated with childhood cancer development. An ultimate goal of this research is the identification of more effective and less toxic treatments so that all children diagnosed with cancer will survive their cancer and will grow to become healthy adults. Ongoing research initiatives include:

- **The Pediatric Brain Tumor Consortium (PBTC)**, a multidisciplinary cooperative research organization devoted to the identification of superior treatment strategies for children with primary brain tumors. [https://www.pbtc.org/](https://www.pbtc.org/)
- **The Pediatric Oncology Branch (POB)** conducts high-risk high-impact basic, translational and clinical studies. During this past year, the POB launched the Psychosocial Support and Research Program. This program 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 on research protocols in several NCI Branches and NIH Institutes. [https://ccr.cancer.gov/Pediatric-Oncology-Branch](https://ccr.cancer.gov/Pediatric-Oncology-Branch)
- **The Therapeutically Applicable Research to Generate Effective Treatments or 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](https://ocg.cancer.gov/programs/target)
- A comprehensive program of **Clinical Studies of Familial Cancer Syndromes**, several of which include children. [https://dceg.cancer.gov/research/what-we-study/hereditary-cancer-syndromes](https://dceg.cancer.gov/research/what-we-study/hereditary-cancer-syndromes)
- **The Children's Oncology Group (COG)**, part of the NCI National Clinical Trials Network, that develops and coordinates pediatric cancer clinical trials that are available at over 200 members institutions, including cancer centers throughout the United States and Canada. NCI is supporting many clinical trials of high-priority novel agents through the NCI clinical trials programs, including trials of targeted therapies and immunotherapies. The types of cancers addressed include relapsed/refractory solid tumors and lymphomas, newly diagnosed high-risk Hodgkin lymphoma, certain relapsed leukemias, osteosarcoma, and Ewing sarcoma, and certain pediatric brain tumors. [https://www.childrensoncologygroup.org/](https://www.childrensoncologygroup.org/)
- **The Pediatric Early Phase Clinical Trials Network (PEP-CTN)**, which builds upon the success of the Children's Oncology Group (COG) Phase 1 & 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 3 clinical trials. The PEP-CTN includes 21 core member institutions, representing many of the leading US childhood cancer centers. The PEP-CTN Operations and Data/Statistics Center (ODSC) is
embedded within the COG Operations and Data/Statistics center. Candidate agents for PEP-CTN evaluation are reviewed by the PEP-CTN Agent Prioritization Committee, which provides timely, rigorous, and transparent prioritization of investigational agents for evaluation through the PEP-CTN. Agents prioritized by the PEP-CTN Agent Prioritization Committee have protocols rapidly developed by the PEP-CTN. https://ctep.cancer.gov/initiativesPrograms/pep-ctn.htm

- The Pediatric Cancer Immunotherapy Trials Network (CITN) utilizes the clinical trials infrastructure of the CITN so that it can conduct clinical trials of immunotherapy agents of specific relevance to children and adolescents with cancer. Examples of the types of novel treatments to be investigated by the Pediatric CITN include cellular therapies (e.g., CAR T cells targeting pediatric cancer antigens) and antibody-based therapies, including antibody-drug conjugates, that target surface antigens preferentially expressed on childhood cancers. https://ctep.cancer.gov/MajorInitiatives/cancer_immunotherapy_trials_network.htm

- The New Approaches to Neuroblastoma Therapy (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, discovering targetable vulnerabilities driving resistance, and translating these insights into clinical trials. NANT works closely with COG to translate their experimental therapy findings into COG phase III clinical trials. Their findings regarding the tumor microenvironment, tumor response to therapy, and the application of cellular therapies to solid tumors have implications beyond neuroblastoma. http://www.nant.org/

- NCI Experimental Therapeutics Program (NExT). NCI has prioritized the development of new treatments for pediatric cancer in the NExT Program. This program focuses on advancing breakthrough discoveries in basic and clinical research into new therapies, and each agent accepted into the NExT Program is considered for its relevance to pediatric cancers. https://next.cancer.gov/

- Li-Fraumeni Syndrome Study. Li-Fraumeni Syndrome (LFS) is a rare, inherited disorder which 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 (called "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 cancers. Heritable disease-causing changes 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/

- Inherited Bone Marrow Failure Syndromes (IBMFS) Study. The inherited bone marrow failure syndromes (IBMFS) 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 which suggest a specific diagnosis. Patients with these syndromes have a very high risk of development of cancer (either leukemia or certain solid tumors). Scientists in the NCI Division of Epidemiology and Genetics have been leading an ongoing clinical study in order to better understand how cancers develop in persons with IBMFS, with the aim of improving the healthcare that can be offered to persons with these disorders. https://marrowfailure.cancer.gov/index.html

- Pleuropulmonary Blastoma DICER1 Syndrome Study. Pleuropulmonary blastoma (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/

- Retinoblastoma Survivors Follow-up Study. Scientists in the NCI Division of Epidemiology and Genetics are studying retinoblastoma (Rb), 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 younger than five years, and may be 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. [https://dceg.cancer.gov/research/cancer-types/retinoblastoma](https://dceg.cancer.gov/research/cancer-types/retinoblastoma)

- The *Childhood Cancer Survivor Study (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 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 children and adolescent cancer survivors. For example, to better understand the genetic risk of second cancers, researchers from the intramural Division of Cancer Epidemiology and Genetics (DCEG) and CCSS are collaborating on studies that aim to identify both common and rare genetic variants that may be associated with second cancers or other late adverse effects among survivors of childhood cancer. [https://www.cancer.gov/types/childhood-cancers/ccss](https://www.cancer.gov/types/childhood-cancers/ccss)

- Advancing RAS/RASopathy Therapies. The goal of this program is to accelerate the understanding of RASopathies/RAS mutated tumors and to develop effective therapies and prevention strategies. This includes a RASopathy clinic at the NIH Clinical Center for a natural history study and parallel trials with RAS targeting agents for RASopathies and pediatric cancers with somatic RAS mutations/Ras pathway activation in addition to employing a public health genomics approach to gain insights into prevalence, penetrance, phenotypes, and prediction of cancer risk.

**HPV Serology Standards Laboratory**

The Human Papillomavirus Serology Standards Laboratory (HPV-SSL) 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 Laboratory 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 and thus, it will facilitate vaccine development and implementation of new vaccine indications and new vaccine candidates.

Supported by NCI


**Childhood Injuries and Maltreatment**

**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 the following topics: 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. NCMRR also supports research on therapies and rehabilitative approaches for cerebral palsy. 
Supported by NICHD 
Website:  https://www.nichd.nih.gov/about/org/ncmrr/Pages/overview.aspx

**The Medical Rehabilitation Research Infrastructure Network (MRRIN)**
This network, funded through the National Center for Medical Rehabilitation Research with additional support from NINDS and NIBIB, 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. 
Supported by NICHD, NINDS, NIBIB 
Website:  https://www.nichd.nih.gov/research/supported/Pages/mrrin.aspx

**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. 

**Substance Misuse**
**Key Factors Contributing to Adolescent Substance Abuse**
In coordination with and co-funding from the NIH Office of Behavioral and Social Sciences Research, NIDA is supporting a study to use smartphone sensors and weekly surveys to assess substance use, executive function, disinhibition, risk-taking, and social context in a large sample during the transition from adolescence to young adulthood, to provide more detailed models of developmental change and their relationship with substance use. Using an adolescent twin design, this research is expected to distinguish whether and how environmental and social context disrupt normal development. 
Supported by NIDA, OBSSR 
U01DA046413:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9578133

**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. 
Supported by NICHD 
Website:  https://www.nichd.nih.gov/research/supported/Pages/cpccrn.aspx
Clinical Care, Outreach, and Services

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; approximately 5,000 youth emancipate from foster care annually. Health care outcomes are poor, in part due to 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 healthcare knowledge and utilization.
Supported by NLM
R01LM012816: https://projectreporter.nih.gov/project_info_description.cfm?aid=9565649

NIDCR Oral Health Disparities and Inequities Research Consortium
NIDCR funds a research consortium and data coordinating center aimed at reducing or eliminating inequities in access to care and improving the oral health of children. Current studies include financial incentives to improve oral health behaviors; multi-level oral health interventions in primary care settings; text-message based interventions to reduce caries in children; and family-focused oral health education and support from community health workers.
Supported by NIDCR
U01DE025507: https://projectreporter.nih.gov/project_info_description.cfm?aid=9544146

End-of-Life and Palliative Needs of Adolescents and Young Adults
NIH continues to support 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, their families and caregivers.
Supported by NINR, NCI, NICHD, ORWH
FOAs: https://grants.nih.gov/grants/guide/pa-files/PA-18-137.html

Pediatric Palliative Care Campaign
In FY2018, NINR released pediatric materials under its Palliative Care: Conversations Matter® Campaign, which was initially launched in 2014, including: a Pediatric Palliative Care Toolkit for Providers, which was developed to facilitate health care providers in providing guidance and presentations about pediatric palliative care to their colleagues; and a Pediatric Palliative Care Tear-Off Pad, updated based on suggestions made by health care providers, with answers to common questions about palliative care and offering resources to support conversations. The pads contain customizable patient education sheets that can be filled out during patient visits. The Tear-Off Pad is available in English and Spanish.
Supported by NINR
Websites: https://www.ninr.nih.gov/newsandinformation/conversationsmatter/provider-toolkit
https://www.ninr.nih.gov/sites/files/docs/NINR_Palliative_Care_ENG_Tear_Pad_508c.pdf

Safe to Sleep
This program is a public health campaign program to reduce the risk of SUID (sudden unexpected infant death). Many SUID cases are due to accidental suffocation, such as when an infant becomes trapped between a mattress and a wall, or when bedding material presses on or wraps around an infant's neck. In addition to placing infants on their backs to sleep, the Safe to Sleep Campaign emphasizes other ways to reduce the risk of sudden infant death. This includes placing infants in their own safe sleep environment and not on an adult bed, without any soft bedding such as blankets or quilts. Safe to Sleep also emphasizes breast feeding infants when possible, which has been associated with reduced SIDS risk, and
eliminating other risks to infant health that have been identified through research. These other risk factors include overheating, exposure to tobacco smoke, and a mother's use of alcohol and illicit drugs.

Supported by NICHD
Website:  https://www.nichd.nih.gov/sts/Pages/default.aspx

**Interventions to Prevent and Reduce Underage Drinking**

NIAAA continues to provide Alcohol Screening and Brief Intervention for Youth: A Practitioner’s Guide, a two-question screening tool and alcohol risk estimator designed to help primary care providers identify youth who are at risk for alcohol use, are using alcohol, or have alcohol use disorder (AUD). Six studies have been funded to evaluate the effectiveness of the Guide in various settings, such as juvenile justice, schools, and primary care. A recent study validated the Guide in primary care clinics serving racially and ethnically diverse patients. NIAAA also supports the development of a brief alcohol intervention for adolescents hospitalized for a suicide plan or attempt who also report recent alcohol use, and continues to encourage research on culturally-tailored interventions for preventing or reducing alcohol use among underserved youth.

R01AA021855:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9063017
R01AA021888:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9195613
R01AA021786:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9121338
R34AA025763:  https://projectreporter.nih.gov/project_info_description.cfm?aid=9486806
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29975071

**Technology and Tools**

**Data and Specimen Hub (DASH)**

NICHD's Data and Specimen Hub (DASH) is a centralized resource for researchers to store and access data from NICHD-funded research studies to use for secondary research. It serves as a mechanism for NICHD-funded extramural and intramural scientists to share research data from studies in accordance with the NIH Data Sharing Policy and the NIH Genomic Data Sharing Policy.

Supported by NICHD
Website:  https://dash.nichd.nih.gov/

**Data Sharing for Demographic Research (DSDR)**

Data Sharing for Demographic Research (DSDR) is a resource that aims to develop a scientifically rigorous data-sharing infrastructure that NICHD grantees and other researchers can use to facilitate data sharing, while maintaining respondent confidentiality. DSDR provides scientific expertise in dealing with complex data archiving and analysis, as well as supports researchers collecting data and those who wish to conduct subsequent analyses on these data. Datasets include information from many studies, including the National Longitudinal Study of Adolescent Health (Add Health), the Fragile Families and Child Wellbeing Study, and others.

Supported by NICHD
Website:  https://www.nichd.nih.gov/research/supported/dsdr
Detecting Tuberculosis in Children Using Saliva

Detecting tuberculosis (TB) in children requires invasive and time-consuming testing, which can be problematic to implement in resource-limited settings. Using a small business innovation grants, NICHD-supported researchers have set out to demonstrate the feasibility of rapid and sensitive detection of TB using a novel isothermal amplification technology in saliva. If successful, this project would enable routine early testing and screening of TB in children at home and in local community healthcare settings, in a rapid, cost-effective, and easy-to-use manner.

Supported by NICHD
R43HD090822: https://projectreporter.nih.gov/project_info_description.cfm?aid=9255903

Pumps for Kids, Infants, and Neonates (PumpKIN)

Researchers have developed a ventricular assist device (VAD) specifically for infants and small children awaiting a heart transplant. The PumpKIN implant is only 15mm wide (about the size of an AA battery) and fully implantable, and will, in future clinical use, allow children to remain active and at home. The device is being tested in two feasibility studies in 10 children with heart failure at up to 7 sites (5 children each with standard or challenging cardiac anatomy) in the U.S.

Supported by NHLBI
Clinical Trial: https://clinicaltrials.gov/ct2/show/NCT02954497

Computationally Modeling the Impact of Ontogeny on Drug Metabolic Fate

As an extension of prior work, scientists will build and test computational models and datasets for individual isozymes that accurately predict drug metabolites and the rate (kinetics) at which they form. Combining these models may yield an effective, low cost approach that simulates hepatic metabolism and takes into account age-dependent contributions from individual isozymes to assess the metabolic fate of drugs during child development.

Supported by NLM
R01LM012482: https://projectreporter.nih.gov/project_info_description.cfm?aid=9540939

Global Pediatric Health

Domestic & International Pediatric & 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 (DCC), 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 TB, malaria, hepatitis, and investigation of vaccines to prevent HIV-related or other high-priority infectious diseases in children, adolescents, and pregnant women, in addition to treatment of HIV infection. This NICHD-funded network has collaborated closely with the International Pediatric Maternal Adolescent AIDS Clinical Trials (IMPAACT) Network, funded by NIAID, NICHD, and NIMH. This collaboration has made it possible to conduct an expanded clinical trial portfolio advancing pediatric HIV/AIDS clinical research.

Supported by NICHD
Website: https://www.nichd.nih.gov/research/supported/Pages/pphsn.aspx

Global Network for Women’s and Children’s Health Research

The Global Network supports and conducts clinical trials in resource-limited countries by pairing foreign and United States researchers, with the goal of evaluating low-cost, sustainable interventions to improve maternal and child health and simultaneously building local research capacity and infrastructure. Today, the Global Network focuses on community-based common protocols, conducted at three or more sites, which 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.

Supported by NICHD
Website:  https://www.nichd.nih.gov/research/supported/Pages/globalnetwork.aspx

**International Centers for Excellence in Research**
The International Centers for Excellence in Research (ICER) program was launched in 2002 to develop and sustain research programs in disease-endemic countries through partnerships with local scientists. While the ICER program is focused on infectious disease clinical research, each center is enabled to address the research and training needs of relevance to the local population. Malaria caused by *Plasmodium falciparum* remains a major public health threat, claiming the lives of approximately 500,000 children each year in Africa alone, and is being investigated in multiple studies conducted out of the ICER in Mali. By applying recent advances in immunology and genomics-based technology, NIAID conducted longitudinal cohort studies in Mali, providing improved understanding of the human immune response to *P.* falciparum infection. This research is providing key insights into how malaria immunity can be enhanced through vaccination. NIAID also is conducting a large study of clinical isolates in which samples from children under five years of age were analyzed to explore key variables and endpoints related to malaria pathogenesis that are essential to the development of prophylactics and therapeutics.

Supported by NIAID
Website:  https://intramural.nih.gov/search/searchview.taf?ipid=105246&ts=1558520051
Article:  https://www.ncbi.nlm.nih.gov/pubmed/29066816

**Malaria Surveillance and Research Studies in Pregnant Women and Children in Liberia**
In FY 2018, NIAID began developing a protocol for a cross-sectional survey of malaria and helminth prevalence in pregnant women and children at two health care facilities in Liberia. The primary objective of the study is to estimate the burden of *P. falciparum* in these at-risk populations. The secondary objectives are to estimate the frequency of infections due to non-falciparum malaria and to helminths (such as *Strongyloides stercoralis*, filarial infections, or Schistosoma) in these cohorts.

Supported by NIAID
Website:  https://intramural.nih.gov/search/searchview.taf?ipid=105233&ts=1558519955
**Pediatric Research at the NIH Clinical Center**

**The NIH Clinical Center**
The NIH Clinical Center is the clinical research facility of NIH. It 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 FY 2018, 3,285 children seen on 353 research protocols were treated at the NIH Clinical Center. 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 1 and 2 trials that are the first studies of new treatments and therapies. To accommodate the growing number of pediatric intramural research subjects, The Children’s Inn at NIH can care for 64 families every night. In FY 2018, 1,703 families stayed at the Children's Inn while their children were being treated at the NIH Clinical Center.
Website: [https://clinicalcenter.nih.gov/](https://clinicalcenter.nih.gov/)

**The NIH Pediatric Rheumatology Clinic**
The NIH Pediatric Rheumatology Clinic is a specialty-care medical facility dedicated to evaluating and treating children with pediatric rheumatic diseases who are enrolled in clinical trials. Since the causes of these diseases are unknown, NIH also seeks to gain a better understanding of why some children develop them. The Clinic consists of two major parts: a clinic and a health information resource center. In the clinic, medical staff diagnose and treat children with arthritis, periodic fever syndromes, lupus, and other rheumatic diseases who are enrolled in clinical trials. The health information resource center provides written and oral information on signs and symptoms of arthritis and rheumatic diseases as well as tips for maintaining wellness and managing disease.
Supported NIAMS
Other Cross-Cutting Areas of Pediatric Research

**Pediatric Pharmacology and the Best Pharmaceuticals for Children Act**
Testing the safety and efficacy of drugs in children presents considerable 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 necessary 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, the majority of drugs used in children today are not approved for use in children and therefore are used without adequate understanding of appropriate dose, safety, or efficacy.

The Best Pharmaceuticals for Children Act (BPCA) established a process for NIH, 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 BPCA, NICHD and other NIH ICs support research to address the need.
Website:  https://bpca.nichd.nih.gov/

**Specialized Centers in Research in Pediatric Developmental Pharmacology (RPDP)**
NICHD supports the RPDP program to advance the science of pediatric pharmacology. The program’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 the conduct of translational research in high-priority areas of pediatric developmental pharmacology.
- Facilitate important community outreach and education efforts to increase awareness and convey the importance and implications of the research activities to the general public.

The RPDP 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 program performs nonclinical and clinical research to understand mechanisms of age- and developmentally 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. FDA is working closely with NIH to maximize the success of this important program.
Website:  https://www.nichd.nih.gov/research/supported/scrpdp

**Clinical and Translational Science Awards**
The NCATS Clinical and Translational Science Award (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 foster innovation in research training, new methodologies, and research participant engagement. Based on the recommendations of the IOM, 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 adult. 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 who are pediatric or child health clinical scientists. The authorizing legislation for the CTSA Program included a special provision to allow a pediatric principal investigator (co-PI) to be appointed at a CTSA Program
hub with a separate budget to support pediatric and child health translational research. Currently, at least eight CTSA Program hubs are led by scientists or co-PIs 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 include many pediatric studies, including scientific areas and conditions such as peanut allergy, Niemann-Pick type C1, fragile X, rare muscle diseases, cystic fibrosis, and Charcot-Marie-Tooth disease.
Website: https://ncats.nih.gov/ctsa

Research Training, Career Development, and Loan Repayment

Pediatric Clinical Pharmacology Postdoctoral Research Training Program
NICHD has set aside specific funding to support training grants awarded to institutions or organizations that seek to develop clinician-scientists who will be leaders in the field of pediatric clinical pharmacology research, through training and experience in basic science and clinical research.

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 them 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.
Supported by NIMH
T32MH073517: https://projectreporter.nih.gov/project_info_description.cfm?aid=9280686

New Paths for Biomedical Informatics: A Mini-Symposium for High School Scholars
The future of health care in the United States will depend on a workforce of biomedical informatics professionals. This project aims to develop a mini-symposium for high school scholars and thus provide inspiration for future generations to consider STEM-C careers, especially in health care and biomedicine.
Supported by NLM
R13LM012214: https://projectreporter.nih.gov/project_info_description.cfm?icde=0&aid=9335446

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 three-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. This is a combined program sponsored by Wayne State University and the Perinatology Research Branch of NICHD. The program is housed at the Detroit Medical Center and the Wayne State University campus in Detroit, Michigan, where the Branch is located. The program includes 18 months dedicated to laboratory and clinical research. The Fellowship emphasizes a multi-disciplinary 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 villous sampling, and intravascular transfusion.
Supported by NICHD
Website: https://www.nichd.nih.gov/about/org/dir/osd/tp/mfmftp

Pediatric Endocrinology Inter-Institute Training Program
The Fellowship in Pediatric Endocrinology is a three-year, ACGME– 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 based at the National Institutes of Health Clinical Center, which is one of the largest and most sophisticated research institutions in the United States. The program is conducted in partnership with Children’s National Health System in Washington, DC. 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.

Supported by NICHD
Website: http://pe.nichd.nih.gov

Fellowship in Pediatric Hematology/Oncology
The Pediatric Hematology/Oncology Fellowship is a joint program of the Pediatric Oncology Branch, NCI, NIH and Johns Hopkins University. Fellows receive combined clinical training during their first year at both Johns Hopkins Hospital and the NIH Clinical Center, with exposure to clinical issues in pediatric hematology/oncology. Patients seen at both institutions are largely non-overlapping, giving 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 available at both campuses during subsequent years of the program.

Pediatric Scientist Development Program (PSDP)
This program provides scientific research experience (particularly in basic science areas) for pediatricians wishing to pursue careers in academic medicine. The PSDP 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.

Supported by NICHD
Website: https://www.cincinnatichildrens.org/education/research/psdp

Child Health Research Career Development Award (CHRCDA) Program
The CHRCDA 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.

Supported by NICHD
Website: https://www.nichd.nih.gov/research/supported/Pages/chrcda.aspx

Child Neurologist Career Development Program (CNCDP)
NINDS supports a Child Neurologist Career Development Program (CNCDP) for child neurologists who have made a commitment to independent research careers. The CNCDP is a single national program currently based at the Hugo Moser Research Institute, Kennedy Krieger Institute and Johns Hopkins University School of Medicine. The CNCDP provides up to three 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.

Supported by NINDS

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.

Website: https://www.lrp.nih.gov/eligibility-programs
ADDITIONAL PEDIATRIC COLLABORATIONS

Pediatric research at NIH involves various collaborations between NIH ICOs and with other HHS and federal agencies. During FY 2018, NIH spearheaded and participated in a broad array of workshops, committees, working groups, and task forces encompassing many pediatric health domains. Notably, the Trans-NIH Pediatric Research Consortium (N-PeRC) was established in June 2018 with the goals of coordinating pediatric research programs, best practices, and training opportunities across all NIH ICOs, and exploring gaps in the current NIH pediatrics portfolio. A selection of additional key collaborative efforts for pediatric populations follows.

NIH collaborations address multiple aspects of the obesity crisis among children and adolescents, as well as broader areas of nutrition for pregnant women and children. The Pregnancy and Birth to 24 Months Project conducts dietary reviews and makes dietary recommendations for pregnant women and infants under 2 (current collaborators are USDA, CDC, HRSA, FDA, OS, NIDDK, NCI, and NHLBI). The Joint Agency Nutrition Working Group supports dietary supplementation and nutritional research for pregnant women and children (current collaborators are NICHD, NIDDK, ODP, ODS, and FDA). The National Collaborative on Childhood Obesity Research (NCCOR), a multiagency and public-private collaboration between the CDC, USDA, NIH ICOs (NCI, NHLBI, NICHD, NIDDK, OBSSR, and ODP), and private foundations speeds progress in reducing childhood obesity through surveillance, policies, research, and interventions.

NIH also collaborates to better understand pediatric pain and pain medication abuse. The NIH Pain Consortium was established to support and enhance pain research activities across NIH (member ICOs are CC, NCCIH, NCI, NEI, NIA, NIAAA, NIAMS, NIBIB, NICHD, NIDA, NIDCD, NIDCR, NIDDK, NIGMS, NIMH, NIMHD, NINR, OBSSR, ORWH). The Pain Consortium is coordinating the Helping to End Addiction Long-termSM (HEAL) Initiative, a trans-NIH effort (involving NCATS, NCCIH, NHLBI, NIAAA, NIAID, NIAMS, NIBIB, NICHD, NIDA, NIDDK, NIMH, NIMHD, NINDS, and ODP) to accelerate the development of scientific strategies to combat the opioid crisis. In addition, NIDA, OD, SAMHSA, and OS participate in the Adolescent Medication-Assisted Treatment and Opioids Committee, which provides federal agencies with a better understanding of medication-assisted treatment policy, research, and practice for adolescents affected by opioids.

Development, assessment, and optimization of pediatric drugs and devices are the subjects of multiple collaborative activities at NIH. NICHD, OS, and FDA are part of the Critical Path Institute’s Pediatric Trials Consortium, which delivers regulatory-quality data needed for product labeling of innovative drugs, biologics, and devices for children. These same agencies participate in the FDA’s Pediatric Device Consortia Grants Program, which facilitates the development, production, and distribution of pediatric medical devices through funding of nonprofit consortia. NICHD and FDA work with the American Academy of Pediatrics’ Committee on Drugs, which focuses on all aspects of pediatric pharmacology. NCCIH, NICHD, CDC, HRSA, and SAMHSA collaborate on bioresource development, validation tools, and integration of high-throughput screening technology standards in complementary and alternative medicine product use in children.

There are numerous trans-NIH collaborations that enhance our understanding of diseases and conditions that affect pediatric populations. For example, FIC, NIAID, NICHD, NIMH, OAR, OGAC, and USAID are members of the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA). NHGRI, NINDS, NCATS, NIDCR, NHLBI, NIGMS, OD, NICHD, NIAID, NIDDK, NINR, NCI, NIMH, and the NIH Common Fund support the Undiagnosed Disease Network, which seeks to enhance and accelerate diagnosis of rare and heretofore undiagnosed conditions and diseases. NIH also supports the Down Syndrome Consortium, which brings together NIH ICOs (NCATS, NCI, NHGRI, NHLBI, NIA, NIAID, NICHD, NIDCD, NIDCR, NIDDK, NIMH, NIMHD, and NINDS) and external
stakeholders working in pediatrics and Down syndrome in order to facilitate the exchange of ideas and information between these collaborators and the Down syndrome community. NIH also launched the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome) project in June 2018 to expand research on Down syndrome and associated conditions like autism and diabetes. NCI, NEI, NHLBI, NHGRI, NIA, NIAID, NICHD, NIAMS, NIDCD, NIDCR, NIDDK, NIEHS, NIMH, NIMHD, NINDS, NINR, NCATS, NCCIH, ORIP, and the NIH Common Fund all participate in INCLUDE.

NIH also works with other federal agencies to address multiple forms of violence. The Federal Interagency Workgroup on Child Abuse and Neglect provides a forum for discussion of ideas and funding for child maltreatment-related activities (members include NIAAA, NICHD, NIDA, NIMH, OBSSR, and the ACF at HHS, as well as the USDA, DOD, EDUC, HUD, DOI, DOJ, DOS, USAID, and USICH). The Federal Partners in Bullying Prevention (NIAAA, NICHD, NIDA, OBSSR, OS, CDC, HRSA, SAMHSA, DOD, DOI, DOJ, EDUC, FTC, USDA, and WHIAAPI) provide information on the identification and prevention of and ways to respond to bullying and cyberbullying. NIMH and SAMHSA sit on the Task Force to Develop Best Practices for Trauma-Informed Identification, Referral, and Support for children and families who have experienced or are at risk of experiencing trauma. The National Action Alliance for Suicide Prevention (NAASP) is a public-private partnership, which aims to advance the National Strategy for Suicide Prevention, a comprehensive, long-term approach to preventing suicide (NIAAA, NIDA, NIMH, OBSSR, ODP, ACL, CDC, HRSA, IHS, OS, OSG, and SAMHSA all participate).

Environmental factors and conditions are the subject of several NIH collaborations. For example, 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 to best deliver care to children impacted by disasters. The CHILD Working Group involves the efforts of 6 NIH ICos (NIAID, NICHD, NIDA, NIGMS, NIMH, NIEHS), ACF, CDC, HRSA, SAMHSA, and the Assistant Secretary for Preparedness and Response. NICHD and NIGMS at NIH collaborate on the Public Health Emergency Medical Countermeasures Enterprise Integrated Program Team for Pediatrics and Obstetrics along with CDC, FDA, and the Office of the Assistant Secretary for Health (OASH) within the HHS, as well as the DOD, VA, USDA, and the Department of Homeland Security. This Team develops, stockpiles, and monitors the safety and effectiveness of medical countermeasures for children and pregnant mothers in preparation for immediate or future public health threats. The Trans-NIH Working Group on Household Air Pollution is made up of FIC, NCI, NEI, NHLBI, NICHD, NIEHS, OBSSR, and ORWH at NIH. This Work Group seeks to integrate and accelerate NIH-sponsored and -administered research in exposure response relationships of particulate matter and other pollutants to childhood pneumonia, low birth weight heart disease, lung cancer, stroke, eye disorders, and other conditions. The President’s Task Force on Environmental Health Risks and Safety Risks to Children is the focal point for coordinating federal government efforts to explore, understand, and act together to improve children’s environmental health. Major efforts of the group have focused on asthma, environmental issues in housing and daycares, identifying chemical exposures of particular concern for children, and climate impacts on children’s health. In December 2018, the Task Force released “The Federal Action Plan to Reduce Childhood Lead Exposures and Associated Health Impacts.” The Task Force is co-chaired by HHS and EPA. Several NIH ICs participate on the Senior Steering Committee and Subcommittees including NIEHS, NICHD, and NHLBI.

NIH brings together subject matter experts to better understand physiological processes. NHLBI, NCI, and NICHD also put together a workshop on pediatric hematopoietic stem cell transplantation to describe associated pulmonary complications, identify gaps in our knowledge base, and to explore avenues for research to advance care and optimize outcomes for transplant patients.
APPENDIX

Table 1: All NIH Pediatric Research, FY 2018
Table 2: NIH Funding Opportunity Announcements That Solicited Applications for Pediatric Research, Released in FY 2018
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 2018

The totals below were derived from NIH’s 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 2018 NIH-funded grants and projects in pediatric research is available at:


The term “Common Fund” refers to research funded through the Office of Strategic Coordination, OD, NIH, to address key scientific issues that no one ICO is positioned to address alone.

<table>
<thead>
<tr>
<th>NIH ICO</th>
<th>Fiscal Year 2018</th>
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### Table 2: NIH Funding Opportunity Announcements That Solicited Applications for Pediatric Research, Published in FY 2018

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<td>Secondary Analyses in Obesity, Diabetes and Digestive and Kidney Diseases (R21 Clinical Trial Optional)</td>
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<td>Pilot and Feasibility Studies in Preparation for Drug and Alcohol Abuse Prevention Trials (R34 Clinical Trial Optional)</td>
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<td>R21</td>
<td>Tools to Enhance the Study of Prenatal and Pediatric Hydrocephalus (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-651</td>
<td>NIMH</td>
<td>R01</td>
<td>Developmentally Tailored HIV Prevention and Care Research for Adolescents and Young Adults (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-652</td>
<td>NIMH</td>
<td>R21</td>
<td>Developmentally Tailored HIV Prevention and Care Research for Adolescents and Young Adults (R21 Clinical Trial Not Allowed)</td>
</tr>
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<td>PA-18-653</td>
<td>NIMH</td>
<td>R34</td>
<td>Developmentally Tailored HIV Prevention and Care Research for Adolescents and Young Adults (R34 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-687</td>
<td>NICHD</td>
<td>R03</td>
<td>Developmental Pharmacodynamics and Models of Drug Effects in Pediatrics (R03 Clinical Trial Optional)</td>
</tr>
<tr>
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<tr>
<td>PA-18-688</td>
<td>NICHD</td>
<td>R01</td>
<td>Developmental Pharmacodynamics and Models of Drug Effects in Pediatrics (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-695</td>
<td>NIDCR</td>
<td>R21</td>
<td>Basic and Translational Oral Health Research Related to HIV/AIDS (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-699</td>
<td>NIDCR</td>
<td>R01</td>
<td>Basic and Translational Oral Health Research Related to HIV/AIDS (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-720</td>
<td>NIDDK</td>
<td>R21</td>
<td>Exploratory/Developmental Clinical Research Grants in Obesity (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-722</td>
<td>OBSSR</td>
<td>R01</td>
<td>Improving Patient Adherence to Treatment and Prevention Regimens to Promote Health (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-723</td>
<td>OBSSR</td>
<td>R21</td>
<td>Improving Patient Adherence to Treatment and Prevention Regimens to Promote Health (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-724</td>
<td>NIAID</td>
<td>R21</td>
<td>Generating New Insights and Mechanistic Understanding of Antibiotic Resistance Development (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-725</td>
<td>NIAID</td>
<td>R01</td>
<td>Generating New insights and Mechanistic Understanding of Antibiotic Resistance Development (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-728</td>
<td>NICHD</td>
<td>R21</td>
<td>Research on the Health of Transgender and Gender Nonconforming Populations (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-729</td>
<td>NICHD</td>
<td>R01</td>
<td>Research on the Health of Transgender and Gender Nonconforming Populations (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-741</td>
<td>NIDDK</td>
<td>R21</td>
<td>Secondary Analyses in Obesity, Diabetes and Digestive and Kidney Diseases (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-773</td>
<td>NIDA</td>
<td>R01</td>
<td>International Research Collaboration on Drug Abuse and Addiction Research (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-775</td>
<td>NIDA</td>
<td>R34</td>
<td>Pilot and Feasibility Studies in Preparation for Drug and Alcohol Abuse Prevention Trials (R34 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-776</td>
<td>NINR</td>
<td>R01</td>
<td>Maternal Nutrition and Pre-pregnancy Obesity: Effects on Mothers, Infants and Children (R01 Clinical Trial Optional)</td>
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<td>PA-18-780</td>
<td>NIDA</td>
<td>R34</td>
<td>Development and Testing of Novel Interventions to Improve HIV Prevention, Care, and Program Implementation (R34 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-783</td>
<td>NIEHS</td>
<td></td>
<td>Exposure Analysis Services for the Environmental Influences on Child Health Outcomes (ECHO) Program (Admin Supp - Clinical Trial Not Allowed)</td>
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<tr>
<td>PA-18-790</td>
<td>NICHD</td>
<td>R01</td>
<td>Patient Safety in the Context of Perinatal, Neonatal, and Pediatric Care (R01 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-791</td>
<td>NICHD</td>
<td>R03</td>
<td>Patient Safety in the Context of Perinatal, Neonatal, and Pediatric Care (R03 - Clinical Trial Optional)</td>
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<tr>
<td>PA-18-817</td>
<td>ODS</td>
<td></td>
<td>Administrative Supplements for Research on Dietary Supplements (Admin. Supp.- Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-861</td>
<td>NIAAA</td>
<td>R03</td>
<td>Alcohol and Other Drug Interactions: Unintentional Injuries and Overdoses: Epidemiology and Prevention (R03 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-862</td>
<td>NIAAA</td>
<td>R21</td>
<td>Alcohol and Other Drug Interactions: Unintentional Injuries and Overdoses: Epidemiology and Prevention (R21 - Clinical Trial Optional)</td>
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<tr>
<td>PA-18-863</td>
<td>NIAAA</td>
<td>R01</td>
<td>Alcohol and Other Drug Interactions: Unintentional Injuries and Overdoses: Epidemiology and Prevention (R01 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-872</td>
<td>NIAID</td>
<td>R21</td>
<td>Research to Advance Vaccine Safety (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-873</td>
<td>NIAID</td>
<td>R01</td>
<td>Research to Advance Vaccine Safety (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-874</td>
<td>NIDCR</td>
<td>R21</td>
<td>Biologic Factors Underlying Dental, Oral, and Craniofacial Health Disparities (R21 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-876</td>
<td>NIDCR</td>
<td>R01</td>
<td>Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome Research (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PA-18-902</td>
<td>NCI</td>
<td>R01</td>
<td>Advancing Translational and Clinical Probiotic/Prebiotic and Human Microbiome Research (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-927</td>
<td>NIMH</td>
<td>R41/R42</td>
<td>Innovative Technologies for HIV Behavioral and Social Science Research (R41/R42 Clinical Trial Optional)</td>
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<td>PA-18-928</td>
<td>NIMH</td>
<td>R43/R44</td>
<td>Innovative Technologies for HIV Behavioral and Social Science Research (R43/R44 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PA-18-932</td>
<td>ODP</td>
<td>R01</td>
<td>Increasing Uptake of Evidence-Based Screening in Diverse Adult Populations (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-008</td>
<td>NCI</td>
<td>R01</td>
<td>Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-019</td>
<td>NCI</td>
<td>R21</td>
<td>Linking the Provider Recommendation to Adolescent HPV Vaccine Uptake (R21 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-039</td>
<td>NICHD</td>
<td>R01</td>
<td>Outcome Measures for Use in Treatment Trials of Individuals with Intellectual and Developmental Disabilities (R01- Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-064</td>
<td>NIDA</td>
<td>R21</td>
<td>Mechanism for Time-Sensitive Drug Abuse Research (R21 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-084</td>
<td>NIDA</td>
<td>R21/R33</td>
<td>Integrative Research on Polysubstance Abuse and Addiction (R21/R33 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-090</td>
<td>NICHD</td>
<td>R01</td>
<td>Natural History of Disorders Identifiable by Screening of Newborns (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-091</td>
<td>NICHD</td>
<td>R01</td>
<td>Research to Advance the Understanding and Management of the Multiple Organ Dysfunction Syndrome in Children (R01 Clinical Trial Optional)</td>
</tr>
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<td>PAR-18-094</td>
<td>NICHD</td>
<td>R21</td>
<td>Research to Advance the Understanding and Management of the Multiple Organ Dysfunction Syndrome in Children (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-095</td>
<td>NICHD</td>
<td>R03</td>
<td>Research to Advance the Understanding and Management of the Multiple Organ Dysfunction Syndrome in Children (R03 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-106</td>
<td>NIDDK</td>
<td>R18</td>
<td>Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care (R18 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-107</td>
<td>NIDDK</td>
<td>R34</td>
<td>Planning Grants for Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care (R34 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-126</td>
<td>NHLBI</td>
<td>R01</td>
<td>Selected Topics in Transfusion Medicine (R01 Clinical Trial Optional)</td>
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<td>Announcement Number</td>
<td>Issuing Organization</td>
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<tr>
<td>PAR-18-132</td>
<td>NHLBI</td>
<td>R21</td>
<td>Selected Topics in Transfusion Medicine (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-133</td>
<td>NHLBI</td>
<td>R01</td>
<td>Strategies to Increase Delivery of Guideline-Based Care to Populations with Health Disparities (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-208</td>
<td>NIBIB</td>
<td>U01</td>
<td>Bioengineering Research Partnerships (U01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-211</td>
<td>NICHD</td>
<td>R03</td>
<td>NCMRR Early Career Research Award (R03 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-213</td>
<td>NICHD</td>
<td>R01</td>
<td>Human-Animal Interaction (HAI) Research (R01 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-214</td>
<td>NICHD</td>
<td>R21</td>
<td>Translational Research in Pediatric and Obstetric Pharmacology and Therapeutics (R21 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-215</td>
<td>NICHD</td>
<td>R01</td>
<td>Translational Research in Pediatric and Obstetric Pharmacology and Therapeutics (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-217</td>
<td>NICHD</td>
<td>R25</td>
<td>NICHD Research Education Programs (R25 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-220</td>
<td>NIDA</td>
<td>U01</td>
<td>Evaluating the NIDA Standardized Research E-Cigarette in Risk Reduction and Related Studies (U01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-222</td>
<td>NIDA</td>
<td>R01</td>
<td>Multi-Site Studies for System-Level Implementation of Substance Use Prevention and Treatment Services (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-223</td>
<td>NIDA</td>
<td>R34</td>
<td>Multi-Site Pilot and Feasibility Studies for System-Level Implementation of Substance Use Prevention and Treatment Services (R34 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-227</td>
<td>NIMH</td>
<td>R01</td>
<td>Development and Application of PET and SPECT Imaging Ligands as Biomarkers for Drug Discovery and for Pathophysiological Studies of CNS Disorders (R01 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-228</td>
<td>NIMH</td>
<td>R34</td>
<td>Pilot Studies to Detect and Prevent Suicide Behavior, Ideation and Self-Harm in Youth in Contact with the Juvenile Justice System (R34 Clinical Trial Required)</td>
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<tr>
<td>PAR-18-232</td>
<td>NIMH</td>
<td>R34</td>
<td>Reducing the Duration of Untreated Psychosis in the United States (R34 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-233</td>
<td>NIMH</td>
<td>R01</td>
<td>Reducing the Duration of Untreated Psychosis in the United States (R01 Clinical Trial Required)</td>
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<tr>
<td>PAR-18-242</td>
<td>FIC</td>
<td>R21</td>
<td>Mobile Health: Technology and Outcomes in Low and Middle Income Countries (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-254</td>
<td>NIAID</td>
<td>R01</td>
<td>Increased Knowledge and Innovative Strategies to Reduce HIV Incidence-iKnow Projects (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-286</td>
<td>NIMHD</td>
<td>R01</td>
<td>Health Services Research on Minority Health and Health Disparities (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-287</td>
<td>NIMHD</td>
<td>R21</td>
<td>Health Services Research on Minority Health and Health Disparities (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-313</td>
<td>NCI</td>
<td>P50</td>
<td>Specialized Programs of Research Excellence (SPOREs) in Human Cancers for years 2018, 2019 and 2020 (P50)</td>
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<tr>
<td>PAR-18-331</td>
<td>NIMHD</td>
<td>R01</td>
<td>Simulation Modeling and Systems Science to Address Health Disparities (R01-Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-332</td>
<td>NCATS</td>
<td>U01</td>
<td>Clinic Testing Therapeutic/Indication Pairing Strategies (U01 Clinical Trial Required)</td>
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<tr>
<td>PAR-18-333</td>
<td>NICHD</td>
<td>R01</td>
<td>Understanding the Early Development of the Immune System (R01 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-362</td>
<td>OBSSR</td>
<td>R21</td>
<td>Education and Health: New Frontiers (R21)-Clinical Trial Optional</td>
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<tr>
<td>PAR-18-387</td>
<td>OBSSR</td>
<td>R01</td>
<td>Education and Health: New Frontiers (R01)-Clinical Trial Optional</td>
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<tr>
<td>PAR-18-388</td>
<td>OBSSR</td>
<td>R03</td>
<td>Education and Health: New Frontiers (R03) - Clinical Trial Optional</td>
</tr>
<tr>
<td>PAR-18-402</td>
<td>NIGMS</td>
<td>R43/R44</td>
<td>Interactive Digital Media STEM Resources for Pre-College and Informal Science Education Audiences (SBIR) (R43/R44 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-403</td>
<td>NIGMS</td>
<td>R41/R42</td>
<td>Interactive Digital Media STEM Resources for Pre-College and Informal Science Education Audiences (STTR) (R41/R42 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-427</td>
<td>NIMH</td>
<td>U01</td>
<td>First in Human and Early Stage Clinical Trials of Novel Investigational Drugs or Devices for Psychiatric Disorders (U01-Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-428</td>
<td>NIMH</td>
<td>R01</td>
<td>Initiation of a Mental Health Family Navigator Model to Promote Early Access, Engagement and Coordination of Needed Mental Health Services for Children and Adolescents (R01-Clinical Trial Required)</td>
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<tr>
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<tr>
<td>PAR-18-429</td>
<td>NIMH</td>
<td>R34</td>
<td>Pilot Studies to Test the Initiation of a Mental Health, Family Navigator Model to Promote Early Access, Engagement and Coordination of needed Mental Health Services for Children and Adolescents (R34-Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-430</td>
<td>NIMH</td>
<td>R01</td>
<td>Effectiveness Trials for Post-Acute Interventions and Services and Services to Optimize Longer-Term Outcomes (R01-Clinical Trials Required)</td>
</tr>
<tr>
<td>PAR-18-431</td>
<td>NIMH</td>
<td>R34</td>
<td>Pilot Effectiveness Trials for Post-Acute Interventions and Services to Optimize Longer-Term Outcomes (R34-Clinical Trials Required)</td>
</tr>
<tr>
<td>PAR-18-479</td>
<td>NIMH</td>
<td>R01</td>
<td>Detecting and Preventing Suicide Behavior, Ideation and Self-Harm in Youth in Contact with the Juvenile Justice System (R01 - Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-506</td>
<td>NICHD</td>
<td>R01</td>
<td>Drug Repurposing for Conditions Affecting Neonates and Pregnant Women (R01 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-509</td>
<td>NIDA</td>
<td>R21</td>
<td>Synthetic Psychoactive Drugs and Strategic Approaches to Counteract Their Deleterious Effects (R21 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-510</td>
<td>NIDA</td>
<td>R01</td>
<td>Synthetic Psychoactive Drugs and Strategic Approaches to Counteract Their Deleterious Effects (R01)</td>
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<tr>
<td>PAR-18-511</td>
<td>NICHD</td>
<td>R01</td>
<td>Discovery of Molecular Targets for Pregnancy-Related/Induced Diseases and Development of Therapeutics to Prevent/Treat These Diseases (R01 - Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-527</td>
<td>NIDA</td>
<td>R03</td>
<td>Synthetic Psychoactive Drugs and Strategic Approaches to Counteract Their Deleterious Effects (R03 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-528</td>
<td>NINDS</td>
<td>U01</td>
<td>NeuroNEXT Clinical Trials (U01 - Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-541</td>
<td>NINDS</td>
<td>U44</td>
<td>Blueprint Neurotherapeutics Network (BPN): Small Molecule Drug Discovery and Development for Disorders of the Nervous System (U44) - Clinical Trial Optional</td>
</tr>
<tr>
<td>PAR-18-542</td>
<td>NINDS</td>
<td>U01</td>
<td>NINDS CREATE Bio Development Track: Preclinical Development for Biotechnology Products and Biologics (U01 - Clinical Trial Optional)</td>
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<tr>
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<tr>
<td>PAR-18-543</td>
<td>NINDS</td>
<td>U44</td>
<td>CREATE Bio Development Track: Preclinical and Early-Phase Clinical Development for Biologics (U44 SBIR- Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-561</td>
<td>NINDS</td>
<td>U01</td>
<td>NIH StrokeNet Clinical Trials and Biomarker Studies for Stroke Treatment, Recovery, and Prevention (U01 - Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-563</td>
<td>NINDS</td>
<td>U44</td>
<td>NIH StrokeNet Small Business Innovation Clinical Trials and Biomarker Studies for Stroke Treatment, Recovery, and Prevention (U44 - Clinical Trials Optional)</td>
</tr>
<tr>
<td>PAR-18-577</td>
<td>NHLBI</td>
<td>U01</td>
<td>New Epidemiology Cohort Studies in Heart, Lung, Blood, and Sleep Diseases and Disorders (U01 - Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-583</td>
<td>Roadmap</td>
<td>X01</td>
<td>Discovery of the Genetic Basis of Childhood Cancers and of Structural Birth Defects: Gabriella Miller Kids First Pediatric Research Program (X01, Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-612</td>
<td>ODP</td>
<td>R01</td>
<td>Electronic Nicotine Delivery Systems (ENDS): Population, Clinical and Applied Prevention Research (R01 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-628</td>
<td>NINDS</td>
<td>U44</td>
<td>NeuroNEXT Small Business Innovation in Clinical Trials (U44 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-643</td>
<td>NHLBI</td>
<td>R01</td>
<td>NHLBI Clinical Ancillary Studies (R01 - Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-644</td>
<td>NIA</td>
<td>R33</td>
<td>Advanced-Stage Development and Utilization of Research Infrastructure for Interdisciplinary Aging Studies (R33 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-645</td>
<td>NIA</td>
<td>R21/R33</td>
<td>Research Infrastructure Development for Interdisciplinary Aging Studies (R21/R33 - Clinical Trial Optional)</td>
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<td>PAR-18-646</td>
<td>NICHD</td>
<td>U01</td>
<td>Opportunities for Collaborative Research at the NIH Clinical Center (U01 - Clinical Trial Optional)</td>
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<td>PAR-18-649</td>
<td>NICHD</td>
<td>R03</td>
<td>Human-Animal Interaction (HAI) Research (R03 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-650</td>
<td>NICHD</td>
<td>R21</td>
<td>Human-Animal Interaction (HAI) Research (R21 - Clinical Trial Optional)</td>
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<td>PAR-18-654</td>
<td>NCI</td>
<td>R01</td>
<td>Basic Research in Cancer Health Disparities (R01 Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-655</td>
<td>NCI</td>
<td>R21</td>
<td>Basic Research in Cancer Health Disparities (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-657</td>
<td>NINDS</td>
<td>U54</td>
<td>Countermeasures Against Chemical Threats (CounterACT) Research Centers of Excellence (U54 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-674</td>
<td>NCI</td>
<td>R21</td>
<td>U.S. Tobacco Control Policies to Reduce Health Disparities (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-675</td>
<td>NCI</td>
<td>R01</td>
<td>U.S. Tobacco Control Policies to Reduce Health Disparities (R01 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-683</td>
<td>NHLBI</td>
<td>R61/R33</td>
<td>NHLBI Early Phase Clinical Trials for Therapeutics and/or Diagnostics (R61/R33 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-684</td>
<td>NHLBI</td>
<td>R33</td>
<td>NHLBI Early Phase Clinical Trials for Therapeutics and/or Diagnostics (R33 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-689</td>
<td>NICHD</td>
<td>R01</td>
<td>Innovative Therapies and Tools for Screenable Disorders (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-690</td>
<td>NICHD</td>
<td>R03</td>
<td>Innovative Therapies and Tools for Screenable Disorders (R03 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-691</td>
<td>NICHD</td>
<td>R21</td>
<td>Innovative Therapies and Tools for Screenable Disorders (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-694</td>
<td>OD</td>
<td>R24</td>
<td>Interdisciplinary Research Teams to Investigate Reciprocal Basic Behavioral and Social Linkages Between Sleep and Stress (R24 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-701</td>
<td>NIMH</td>
<td>P50</td>
<td>Advanced Laboratories for Accelerating the Reach and Impact of Treatments for Youth and Adults with Mental Illness (ALACRITY) Research Centers (P50 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-712</td>
<td>NIAID</td>
<td>R01</td>
<td>Investigations on Primary Immunodeficiency Diseases/Inborn Errors of Immunity (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-721</td>
<td>NINDS</td>
<td>R21</td>
<td>Countermeasures Against Chemical Threats (CounterACT) Exploratory/Developmental Projects in Translational Research (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-732</td>
<td>FIC</td>
<td>R21</td>
<td>Reducing Stigma to Improve HIV/AIDS Prevention, Treatment and Care in Low and Middle- Income Countries (R21 Clinical Trial Optional)</td>
</tr>
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<td>PAR-18-733</td>
<td>NICHD</td>
<td>R03</td>
<td>Small Research Grants for Analyses of Data for the Gabriella Miller Kids First Data Resource (R03 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-737</td>
<td>NIMH</td>
<td>P50</td>
<td>Silvio O. Conte Centers for Basic Neuroscience or Translational Mental Health Research (P50 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-740</td>
<td>NIH</td>
<td>SI2/R00</td>
<td>Lasker Clinical Research Scholars Program (SI2/R00 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-743</td>
<td>NIDDK</td>
<td>R21</td>
<td>Pilot and Feasibility Clinical Research Grants in Urologic Disorders (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-745</td>
<td>NIMHD</td>
<td>R21</td>
<td>Addressing the Challenges of the Opioid Epidemic in Minority Health and Health Disparities Research in the U.S. (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-747</td>
<td>NIMHD</td>
<td>R01</td>
<td>Addressing the Challenges of the Opioid Epidemic in Minority Health and Health Disparities Research in the U.S. (R01 Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-766</td>
<td>NICHD</td>
<td>R01</td>
<td>Identification and Management of Behavioral Symptoms and Mental Health Conditions in Individuals with Intellectual Disabilities (R01 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-767</td>
<td>NCI</td>
<td>U54</td>
<td>Comprehensive Partnerships to Advance Cancer Health Equity (CPACHE) (Collaborative U54 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-768</td>
<td>NHLBI</td>
<td>X01</td>
<td>Catalyzing Innovation in Late Phase Clinical Trial Design and Statistical Analysis Plans Resource Access (X01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-787</td>
<td>NIDCR</td>
<td>R01</td>
<td>Precision Imaging of Oral Lesions (R01- Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-835</td>
<td>FIC</td>
<td>R01</td>
<td>Global Brain and Nervous System Disorders Research Across the Lifespan (R01 Clinical Trials Optional)</td>
</tr>
<tr>
<td>PAR-18-836</td>
<td>FIC</td>
<td>R21</td>
<td>Global Brain and Nervous System Disorders Research Across the Lifespan (R21 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-845</td>
<td>ODP</td>
<td>R01</td>
<td>Electronic Nicotine Delivery Systems (ENDS): Basic Mechanisms of Health Effects (R01 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-847</td>
<td>ODP</td>
<td>R01</td>
<td>Electronic Nicotine Delivery Systems (ENDS): Population, Clinical and Applied Prevention Research (R01 - Clinical Trial Optional)</td>
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<tr>
<td>PAR-18-869</td>
<td>NCI</td>
<td>R01</td>
<td>Modular R01s in Cancer Control and Population Sciences (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-875</td>
<td>NIDCR</td>
<td>R01</td>
<td>Biologic Factors Underlying Dental, Oral, and Craniofacial Health Disparities (R01 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-884</td>
<td>NICHD</td>
<td>R01</td>
<td>Novel Approaches to Safe, Non-Invasive, Real Time Assessment of Human Placenta Development and Function Across Pregnancy (R01 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-885</td>
<td>NICHD</td>
<td>R21</td>
<td>Novel Approaches to Safe, Non-Invasive, Real Time Assessment of Human Placenta Development and Function Across Pregnancy (R21 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-909</td>
<td>NCATS</td>
<td>X02</td>
<td>Pre-application for the NIH-Industry Program: Discovering New Therapeutic Uses for Existing Molecules (X02 Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-910</td>
<td>NCATS</td>
<td>U01</td>
<td>Limited Competition for NIH-Industry Program: Discovering New Therapeutic Uses for Existing Molecules (U01) (Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-918</td>
<td>NIDA</td>
<td>R03</td>
<td>Imaging - Science Track Award for Research Transition (I/START) (R03 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAR-18-923</td>
<td>NIAID</td>
<td>R21</td>
<td>Characterization of Mycobacterial Induced Immunity in HIV-infected and Uninfected Individuals (R21 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-924</td>
<td>NIDDK</td>
<td>R34</td>
<td>Planning Grants for Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care (R34 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-925</td>
<td>NIDDK</td>
<td>R18</td>
<td>Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care (R18 Clinical Trial Required)</td>
</tr>
<tr>
<td>PAR-18-929</td>
<td>NIMH</td>
<td>R01</td>
<td>High-Priority Areas for Research Leveraging EHR and Large-Scale Data (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAR-18-930</td>
<td>NIMH</td>
<td>R01</td>
<td>Development and Optimization of Tasks and Measures for Functional Domains of Behavior (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>PAS-18-063</td>
<td>NIDA</td>
<td>R01</td>
<td>HIV/AIDS High Priority Drug Abuse Research (R01 Clinical Trial Optional)</td>
</tr>
<tr>
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<tr>
<td>PAS-18-120</td>
<td>NCCIH</td>
<td>R43/R44</td>
<td>Development and/or Validation of Devices or Electronic Systems to Monitor or Enhance Mind and Body Interventions (R43/R44 Clinical Trial Optional)</td>
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<tr>
<td>PAS-18-121</td>
<td>NCCIH</td>
<td>R41/R42</td>
<td>Development and/or Validation of Devices or Electronic Systems to Monitor or Enhance Mind and Body Interventions (R41/R42 Clinical Trial Optional)</td>
</tr>
<tr>
<td>PAS-18-557</td>
<td>NIAAA</td>
<td>R01</td>
<td>Research on Comparative Effectiveness and Implementation of HIV/AIDS and Alcohol Interventions (R01 - Clinical Trials Optional)</td>
</tr>
<tr>
<td>RFA-AI-17-034</td>
<td>NIAID</td>
<td>U01</td>
<td>Maintaining Immunity After Immunization (U01 - Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-AI-17-039</td>
<td>NIAID</td>
<td>R01</td>
<td>Understanding Immunopathogenesis of Tuberculosis in HIV-1 Infected and Exposed Children (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-AI-17-040</td>
<td>NIAID</td>
<td>U19</td>
<td>Cooperative Centers on Human Immunology (U19 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-AI-18-005</td>
<td>NIAID</td>
<td>U19</td>
<td>Sexually Transmitted Infections (STI) Cooperative Research Centers (CRC): Vaccine Development (U19 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-AI-18-006</td>
<td>NIAID</td>
<td>R61/R33</td>
<td>Sustained Release Innovation for HIV (SRI) (R61/R33 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-AI-18-010</td>
<td>NIAID</td>
<td>U01</td>
<td>Impact of Initial Influenza Exposure on Immunity in Infants (U01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-AI-18-022</td>
<td>NIAID</td>
<td>U01</td>
<td>Advancing mAbs to Achieve a Drug-free Sustained HIV Virologic Remission (U01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-AI-18-023</td>
<td>NIAID</td>
<td>R01</td>
<td>Immune Mechanisms at the Maternal-Fetal Interface (R01 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-AI-18-026</td>
<td>NIAID</td>
<td>R01</td>
<td>Modeling and Simulation to Optimize HIV Prevention Research (MS OPR) (R01 Clinical Trial not allowed)</td>
</tr>
<tr>
<td>RFA-CA-17-034</td>
<td>NCI</td>
<td>U2C</td>
<td>Human Tumor Atlases (HTA) Research Centers (U2C)</td>
</tr>
<tr>
<td>RFA-CA-17-035</td>
<td>NCI</td>
<td>U2C</td>
<td>Human Tumor Atlases (HTA) Precancer Atlas Research Centers (U2C)</td>
</tr>
<tr>
<td>RFA-CA-17-036</td>
<td>NCI</td>
<td>U24</td>
<td>Human Tumor Atlas Network: Data Coordinating Center (U24)</td>
</tr>
<tr>
<td>RFA-CA-17-056</td>
<td>NCI</td>
<td>U10</td>
<td>Limited Competition: NCI National Clinical Trials Network - Network Group Operations Centers (U10)</td>
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<tr>
<td>RFA-CA-17-057</td>
<td>NCI</td>
<td>U10</td>
<td>Limited Competition: NCI National Clinical Trials Network - Network Group Statistics and Data Management Centers (U10)</td>
</tr>
<tr>
<td>RFA-CA-17-058</td>
<td>NCI</td>
<td>U10</td>
<td>Limited Competition: NCI National Clinical Trials Network - Canadian Collaborating Clinical Trials Network (U10)</td>
</tr>
<tr>
<td>RFA-CA-17-059</td>
<td>NCI</td>
<td>UG1</td>
<td>NCI National Clinical Trials Network (NCTN)--Network Lead Academic Participating Sites (UG1)</td>
</tr>
<tr>
<td>RFA-CA-17-060</td>
<td>NCI</td>
<td>U24</td>
<td>Limited Competition: NCI National Clinical Trials Network - Network Radiotherapy and Imaging Core Services Center (U24)</td>
</tr>
<tr>
<td>RFA-CA-17-061</td>
<td>NCI</td>
<td>UG1</td>
<td>NCI National Clinical Trials Network - Network Group Integrated Translational Science Centers (UG1)</td>
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<tr>
<td>RFA-CA-18-015</td>
<td>NCI</td>
<td>UG1</td>
<td>NCI Community Oncology Research Program (NCORP) Research Bases (UG1 Clinical Trial Required)</td>
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<tr>
<td>RFA-CA-18-016</td>
<td>NCI</td>
<td>UG1</td>
<td>NCI Community Oncology Research Program (NCORP) Community Sites (UG1 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-CA-18-017</td>
<td>NCI</td>
<td>UG1</td>
<td>NCI Community Oncology Research Program (NCORP) Minority/Underserved Community Sites (UG1 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-CA-18-018</td>
<td>NCI</td>
<td>U54</td>
<td>Prevention of HPV-related Cancers in HIV-infected individuals: United States-Latin American-Caribbean Clinical Trials Network: Partnership Centers (U54 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-CA-19-003</td>
<td>NCI</td>
<td>U54</td>
<td>Pediatric Immunotherapy Discovery and Development Network (PI-DDN)(U54 - Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-CA-19-004</td>
<td>NCI</td>
<td>U01</td>
<td>Pediatric Immunotherapy Discovery and Development Network (PI-DDN)(U01 - No Clinical Trial Allowed)</td>
</tr>
<tr>
<td>RFA-CA-19-016</td>
<td>NCI</td>
<td>U54</td>
<td>Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium (U54 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-CA-19-017</td>
<td>NCI</td>
<td>U01</td>
<td>Approaches to Identify and Care for Individuals with Inherited Cancer Syndromes (U01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DA-19-002</td>
<td>NIDA</td>
<td>UG3/UH3</td>
<td>Development of Medications to Prevent and Treat Opioid Use Disorders and Overdose (UG3/UH3) (Clinical Trials Optional)</td>
</tr>
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<tr>
<td>RFA-DA-19-006</td>
<td>NIDA</td>
<td>R25</td>
<td>Workshop on the Use of Adolescent Brain Cognitive Development (ABCD) Data (R25 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DA-19-008</td>
<td>NIDA</td>
<td>UG1</td>
<td>The National Drug Abuse Treatment Clinical Trials Network (UG1 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-DA-19-013</td>
<td>NIDA</td>
<td>R61/R33</td>
<td>Responding to Opioid Use Disorders (OUD) in Tribal Communities in the Context of SAMHSA and CDC Funding (R61/R33 - Clinical Trials Optional)</td>
</tr>
<tr>
<td>RFA-DA-19-016</td>
<td>NIDA</td>
<td>UM1</td>
<td>HEALing Communities Study: Developing and Testing an Integrated Approach to Address the Opioid Crisis (Research Sites) (UM1 - Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DA-19-017</td>
<td>NIDA</td>
<td>UM1</td>
<td>HEALing Communities Study: Developing and Testing an Integrated Approach to Address the Opioid Crisis (Data Coordinating Center) (UM1 - Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>RFA-DE-19-003</td>
<td>NIDCR</td>
<td>U01</td>
<td>Limited Competition: FaceBase 3: Craniofacial Development and Dysmorphology Data Management and Integration Hub (U01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DK-17-020</td>
<td>NIDDK</td>
<td>R01</td>
<td>Immune System Engineering For Targeted Tolerance in Type 1 Diabetes (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DK-17-021</td>
<td>NIDDK</td>
<td>U01</td>
<td>Discovery of Early Type 1 Diabetes Disease Biomarkers in the Human Pancreas [HIRN Consortium on Beta Cell Death and Survival (CBDS)] (U01 - Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-DK-17-026</td>
<td>NIDDK</td>
<td>K12</td>
<td>Career Development Programs in Diabetes Research for Endocrinologists (K12 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-DK-17-027</td>
<td>NIDDK</td>
<td>R01</td>
<td>Incorporating Patient-Reported Outcomes into Clinical Care for Type 1 Diabetes (R01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DK-17-028</td>
<td>NIDDK</td>
<td>R01</td>
<td>Treating Diabetes Distress to Improve Glycemic Outcomes in Type 1 Diabetes (R01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DK-17-031</td>
<td>NIDDK</td>
<td>R01</td>
<td>The Characterization and Discovery of Novel Autoantigens and Epitopes in Type 1 Diabetes (R01 Clinical Trial Optional)</td>
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<tr>
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<td>RFA-DK-17-511</td>
<td>NIDDK</td>
<td>U01</td>
<td>Limited Competition for the Continuation of the Clinical Centers for The Environmental Determinants of Diabetes in the Young (TEDDY) Study (U01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DK-18-005</td>
<td>NIDDK</td>
<td>R01</td>
<td>Mechanisms Underlying the Contribution of Type 1 Diabetes Disease-associated Variants (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DK-18-501</td>
<td>NIDDK</td>
<td>U01</td>
<td>Limited Competition for the Continuation of the Childhood Liver Disease Research Network (ChiLDReN) Clinical Centers (U01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DK-18-502</td>
<td>NIDDK</td>
<td>U24</td>
<td>Limited Competition for the Continuation of the Childhood Liver Disease Research Network (ChiLDReN) Scientific and Data Coordinating Center (U24 Clinical Trial Optional)</td>
</tr>
<tr>
<td>RFA-DK-18-503</td>
<td>NIDDK</td>
<td>U01</td>
<td>Limited Competition for the Continuation of Cure Glomerulonephropathy (CureGN) Participating Clinical Centers (U01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-DK-18-504</td>
<td>NIDDK</td>
<td>U24</td>
<td>Limited Competition for the Continuation of Cure Glomerulonephropathy (CureGN) Data Coordinating Center (U24 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DK-18-505</td>
<td>NIDDK</td>
<td>U01</td>
<td>Limited Competition for the Continuation of the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Clinical Centers (U01 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-DK-18-506</td>
<td>NIDDK</td>
<td>U24</td>
<td>Limited Competition for the Continuation of the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Data Coordinating Center (U24 Clinical Trial Required)</td>
</tr>
<tr>
<td>RFA-ES-18-005</td>
<td>NIEHS</td>
<td>R01</td>
<td>The Role of the Microbiome in the Developmental Origins of Health and Disease (DOHaD) (R01 Clinical Trial Not Allowed)</td>
</tr>
<tr>
<td>RFA-ES-18-008</td>
<td>NIEHS</td>
<td>R43</td>
<td>Novel Approaches for Characterizing Exposure and Response to Engineered Nanomaterials (R43 Clinical Trials Not Allowed)</td>
</tr>
<tr>
<td>RFA-ES-18-010</td>
<td>NIEHS</td>
<td>U24</td>
<td>Human Health Exposure Analysis Resource: Coordinating Center (U24 Clinical Trial Not Allowed)</td>
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<td>Activity Code</td>
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<td>RFA-ES-18-011</td>
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<td>U2C</td>
<td>Human Health Exposure Analysis Resource: Targeted Exposure Analysis Laboratories (U2C Clinical Trial Not Allowed)</td>
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<td>RFA-ES-18-012</td>
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<td>RFA-ES-18-013</td>
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<td>RFA-ES-18-014</td>
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<td>U2C</td>
<td>Human Health Exposure Analysis Resource: Data Repository, Analysis and Science Center (U2C Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-HD-18-032</td>
<td>NICHD</td>
<td>UG3/UH3</td>
<td>Prevention and Treatment through a Comprehensive Care Continuum for HIV-affected Adolescents in Resource Constrained Settings (PATC3H) (UG3/UH3)</td>
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<tr>
<td>RFA-HD-18-102</td>
<td>NICHD</td>
<td>R43/R44</td>
<td>Advancing the Science of Multipurpose Technology for the Prevention of HIV and Unintended Pregnancy (R43/R44)</td>
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<tr>
<td>RFA-HD-19-001</td>
<td>NICHD</td>
<td>R43/R44</td>
<td>Safe and Effective Devices for Use In Neonatal, Perinatal and Pediatric Care Settings (R43/R44 Clinical Trial Optional)</td>
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<tr>
<td>RFA-HD-19-006</td>
<td>NICHD</td>
<td>R43/R44</td>
<td>Non-Invasive Diagnostics to Improve Gynecologic Health (R43/R44 - Clinical Trial Optional)</td>
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<td>RFA-HD-19-008</td>
<td>NICHD</td>
<td>K12</td>
<td>Pediatric Critical Care and Trauma Scientist Development Program (K12 Clinical Trial Optional)</td>
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<td>RFA-HD-19-017</td>
<td>NICHD</td>
<td>P50</td>
<td>National Centers for Translational Research in Reproduction and Infertility [NCTRI] (P50 - Clinical Trial Optional)</td>
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<tr>
<td>RFA-HD-19-018</td>
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<td>R21</td>
<td>Using Archived Data and Specimen Collections to Advance Maternal and Pediatric HIV/AIDS Research (R21 - Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-HL-19-005</td>
<td>NHLBI</td>
<td>UG3/UH3</td>
<td>Management of Asthma in Primary Care - Clinical Center (UG3/UH3 - Clinical Trial Required)</td>
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<tr>
<td>RFA-HL-19-006</td>
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<td>U24</td>
<td>Management of Asthma in Primary Care - Bioinformatics Center (U24 - Clinical Trial Required - Infrastructure)</td>
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<td>Announcement Number</td>
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<td>RFA-HL-19-014</td>
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<td>R01</td>
<td>Stimulating T4 Implementation Research to Optimize Integration of Proven-effective Interventions for Heart, Lung, and Blood Diseases and Sleep Disorders into Practice (STIMULATE) (R01 Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-HL-19-017</td>
<td>NHLBI</td>
<td>R44</td>
<td>NHLBI SBIR Phase IIB Bridge Awards to Accelerate the Commercialization of Technologies for Heart, Lung, Blood, and Sleep Disorders and Diseases (R44 - Clinical Trial Optional)</td>
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<td>RFA-HL-19-018</td>
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<td>NHLBI SBIR Phase IIB Small Market Awards to Accelerate the Commercialization of Technologies for Heart, Lung, Blood, and Sleep Disorders and Diseases (R44 Clinical Trial Optional)</td>
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<td>RFA-HL-19-020</td>
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<td>Molecular Atlas of Lung Development Program (LungMAP) Phase 2 Research Centers (U01-Clinical Trial Not Allowed)</td>
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<td>RFA-HL-19-021</td>
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<td>Molecular Atlas of Lung Development Program (LungMAP) Phase 2 - Human Tissue Core (U01-Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-HL-19-022</td>
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<td>Molecular Atlas of Lung Development Program (LungMAP) Phase 2 - Data Coordinating Center (U24-Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-HL-19-027</td>
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<td>U34</td>
<td>Catalyzing Innovation in Late Phase Clinical Trial Design and Statistical Analysis Plans (U34 Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-MD-18-004</td>
<td>NIMHD</td>
<td>R01</td>
<td>Prevention and Treatment Research to Address HIV/AIDS Disparities in Women in the US (R01-Accepting applications that either propose or do not propose clinical trial(s))</td>
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<td>RFA-MD-18-005</td>
<td>NIMHD</td>
<td>R01</td>
<td>Youth Violence Prevention Interventions that Incorporate Racism/Discrimination Prevention (R01-Clinical Trial Required)</td>
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<tr>
<td>RFA-MD-18-006</td>
<td>NIMHD</td>
<td>R21</td>
<td>Time-Sensitive Research on Health Risk and Resilience after Hurricanes Irma and Maria in Puerto Rico and the US Virgin Islands (R21 Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-MD-18-009</td>
<td>NIMHD</td>
<td>R43/R44</td>
<td>Innovations for Healthy Living - Improving Minority Health and Eliminating Health Disparities (R43/R44 - Clinical Trial Optional)</td>
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<td>RFA-MH-18-605</td>
<td>NIMH</td>
<td>R34</td>
<td>Mobile and Connected Health Interventions to Improve Care Continuum and Health Outcomes among Youth with HIV (R34)</td>
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<td>RFA-MH-18-606</td>
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<td>Mobile and Connected Health Interventions to Improve Care Continuum and Health Outcomes among Youth with HIV (R01)</td>
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<td>RFA-MH-18-700</td>
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<td>R01</td>
<td>Clinical Trials to Test the Effectiveness of Treatment, Preventive, and Services Interventions (Collaborative R01-Clinical Trial Required)</td>
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<tr>
<td>RFA-MH-18-701</td>
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<td>R01</td>
<td>Clinical Trials to Test the Effectiveness of Treatment, Preventive, and Services Interventions (R01- Clinical Trial Required)</td>
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<tr>
<td>RFA-MH-18-702</td>
<td>NIMH</td>
<td>R61/R33</td>
<td>Early Stage Testing of Pharmacologic or Device-based Interventions for the Treatment of Mental Disorders (R61/R33-Clinical Trial Required)</td>
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<td>RFA-MH-18-703</td>
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<td>R33</td>
<td>Early Stage Testing of Pharmacologic or Device-based Interventions for the Treatment of Mental Health Disorders (R33- Clinical Trial Required)</td>
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<td>RFA-MH-19-100</td>
<td>NIMH</td>
<td>K18</td>
<td>NIMH Career Enhancement Award to Advance Autism Services for Adults and Transition-Age Youth (K18 Clinical Trials Not Allowed)</td>
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<tr>
<td>RFA-MH-19-101</td>
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<td>K18</td>
<td>NIMH Career Enhancement Award to Advance Autism Services for Adults and Transition-Age Youth (K18 Clinical Trials Required)</td>
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<td>RFA-MH-19-150</td>
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<td>R01</td>
<td>Early Psychosis Intervention Network (EPINET): Practice-Based Research to Improve Treatment Outcomes (R01 Clinical Trial Optional)</td>
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<tr>
<td>RFA-MH-19-151</td>
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<td>Early Psychosis Intervention Network (EPINET): Data Coordinating Center (U24 Clinical Trial Not Allowed)</td>
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<td>RFA-MH-19-200</td>
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<td>Rare Genetic Syndromes as a Window into the Genetic Architecture of Mental Disorders (U01 Clinical Trial Not Allowed)</td>
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<tr>
<td>RFA-MH-19-201</td>
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<td>Rare Genetic Syndromes as a Window into the Genetic Architecture of Mental Disorders (Collaborative U01 Clinical Trial Not Allowed)</td>
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<td>RFA-NS-18-041</td>
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<td>R61/R33</td>
<td>Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain (R61/R33 Clinical Trial Optional)</td>
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<td>RFA-NS-18-046</td>
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<td>R61/R33</td>
<td>Analytical and/or Clinical Validation of a Candidate Biomarker for Pain (R61/R33 Clinical Trial Optional)</td>
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<td>RFA-OD-16-001</td>
<td>NIH</td>
<td>R03</td>
<td>Tobacco Regulatory Science Small Grant Program for New Investigators (R03 Clinical Trial Optional)</td>
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<td>RFA-OD-16-002</td>
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<td>R01</td>
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<td>NIH</td>
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<td>R03</td>
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<td>R01</td>
<td>Tobacco Regulatory Science (R01 Clinical Trial Optional)</td>
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<td>RFA-OD-18-003</td>
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<td>R21</td>
<td>Tobacco Regulatory Science (R21 Clinical Trial Optional)</td>
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<td>RFA-OD-18-004</td>
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<td>U54</td>
<td>Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)</td>
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<td>RFA-OD-18-005</td>
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<td>RFA-OD-18-006</td>
<td>ODP</td>
<td>K01</td>
<td>Mentored Research Scientist Career Development Award in Tobacco Regulatory Research (K01 - Independent Clinical Trial Required)</td>
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<td>RFA-OD-18-007</td>
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<td>Pathway to Independence Award in Tobacco Regulatory Research (K99/R00 - Independent Clinical Trial Not Allowed)</td>
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<td>RFA-RM-17-027</td>
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<td>Tissue Mapping Centers for the Human BioMolecular Atlas Program (U54 Clinical Trials Not Allowed)</td>
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<td>RFA-RM-18-030</td>
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<td>U24</td>
<td>Genome Sequencing Center for the Gabriella Miller Kids First Pediatric Research Program (U24 Clinical Trial Not Allowed)</td>
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Table 3: Acronyms for NIH Institutes, Centers, and Offices and Other Federal Agencies Referred to in This Report

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<thead>
<tr>
<th>Acronym</th>
<th>Organization</th>
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<tbody>
<tr>
<td>ACF</td>
<td>Administration for Children and Families</td>
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<tr>
<td>ACL</td>
<td>Administration for Community Living</td>
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<tr>
<td>CC</td>
<td>Clinical Center, NIH</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CF</td>
<td>Office of Strategic Coordination Common Fund, DPCPSI, OD, NIH</td>
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<tr>
<td>DOD</td>
<td>United States Department of Defense</td>
</tr>
<tr>
<td>DOE</td>
<td>United States Department of Energy</td>
</tr>
<tr>
<td>DOI</td>
<td>United States Department of the Interior</td>
</tr>
<tr>
<td>DOJ</td>
<td>United States Department of Justice</td>
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<tr>
<td>DOS</td>
<td>United States Department of State</td>
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<tr>
<td>DPCPSI</td>
<td>Division of Program Coordination, Planning, and Strategic Initiatives, OD, NIH</td>
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<tr>
<td>EDUC</td>
<td>United States Department of Education</td>
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<tr>
<td>EPA</td>
<td>United States Environmental Protection Agency</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FIC</td>
<td>John E. Fogarty International Center, NIH</td>
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<tr>
<td>FTC</td>
<td>Federal Trade Commission</td>
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<tr>
<td>HHS</td>
<td>United States Department of Health and Human Services</td>
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<td>HRSA</td>
<td>Health Resources and Services Administration</td>
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<tr>
<td>HUD</td>
<td>United States Department of Housing and Urban Development</td>
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<tr>
<td>ICOS</td>
<td>NIH Institutes, Centers, and Offices</td>
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<td>IHS</td>
<td>Indian Health Service</td>
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<tr>
<td>NCATS</td>
<td>National Center for Advancing Translational Sciences, NIH</td>
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<td>NCCIH</td>
<td>National Center for Complementary and Integrative Health, NIH</td>
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<tr>
<td>NCI</td>
<td>National Cancer Institute, NIH</td>
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<td>NEI</td>
<td>National Eye Institute, NIH</td>
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<tr>
<td>NHLBI</td>
<td>National Heart, Lung, and Blood Institute, NIH</td>
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<tr>
<td>NHGRI</td>
<td>National Human Genome Research Institute, NIH</td>
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<tr>
<td>NIA</td>
<td>National Institute on Aging, NIH</td>
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<tr>
<td>NIAAA</td>
<td>National Institute on Alcohol Abuse and Alcoholism, NIH</td>
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<tr>
<td>NIAID</td>
<td>National Institute of Allergy and Infectious Diseases, NIH</td>
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<tr>
<td>NIAMS</td>
<td>National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH</td>
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<tr>
<td>NIBIB</td>
<td>National Institute of Biomedical Imaging and Bioengineering, NIH</td>
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<td>NICHD</td>
<td><em>Eunice Kennedy Shriver</em> National Institute of Child Health and Human Development, NIH</td>
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<td>NIDA</td>
<td>National Institute on Drug Abuse, NIH</td>
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<td>NIDCD</td>
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<td>NIDCR</td>
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<td>NIDDK</td>
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<td>NIMHD</td>
<td>National Institute on Minority Health and Health Disparities, NIH</td>
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<td>NINDS</td>
<td>National Institute of Neurological Disorders and Stroke, NIH</td>
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<td>NINR</td>
<td>National Institute of Nursing Research, NIH</td>
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<td>NLM</td>
<td>National Library of Medicine, NIH</td>
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<tr>
<td>OAR</td>
<td>Office of AIDS Research, DPCPSI, OD, NIH</td>
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<tr>
<td>OBSSR</td>
<td>Office of Behavioral and Social Sciences Research, DPCPSI, OD, NIH</td>
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<td>OD</td>
<td>Office of the Director, NIH</td>
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<tr>
<td>ODP</td>
<td>Office of Disease Prevention, DPCPSI, OD, NIH</td>
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<td>ODS</td>
<td>Office of Dietary Supplements, ODP, DPSCPSI, OD, NIH</td>
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<tr>
<td>OGAC</td>
<td>Office of the U.S. Global AIDS Coordinator and Health Diplomacy</td>
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<td>ORIP</td>
<td>Office of Research Infrastructure Programs, DPCPSI, OD, NIH</td>
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<td>ORWH</td>
<td>Office of Research on Women’s Health, DPCPSI, OD, NIH</td>
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<td>OS</td>
<td>Office of the Secretary of the HHS</td>
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<td>OSG</td>
<td>Office of the Surgeon General</td>
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<td>SAMHSA</td>
<td>Substance Abuse and Mental Health Services Administration</td>
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<td>SGMRO</td>
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<td>USAID</td>
<td>United States Agency for International Development</td>
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<td>USDA</td>
<td>United States Department of Agriculture</td>
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<tr>
<td>USICH</td>
<td>United States Interagency Council on Homelessness</td>
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<td>WHIAAPI</td>
<td>White House Initiative on Asian Americans and Pacific Islanders</td>
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