

# RESEARCH HORIZONS

A Publication of the Cincinnati Children's Research Foundation

WINTER 2018



## ASTHMA ADMISSION RATES

CAMP WASHINGTON

WINTON HILLS

OVER-THE-RHINE

WALNUT HILLS

AVONDALE

MT. AUBURN

L. PRICE HILL/QUEENSGATE

EVANSTON

NORTHSIDE

COLLEGE HILL

EVANSTON-E. WALNUT HILLS

KENNEDY HTS.

E. PRICE HILL

CHEVIOT

CORRYVILLE

CLIFTON

MT. LOOKOUT

TERRACE PARK

Avondale

Price Hill

## THIRD-GRADE READING PROFICIENCY

KILGOUR 96%

MT. WASHINGTON 90%

CHASE 88%

SANDS MONT. 87%

CREATIVE & PERFORMING ARTS 78%

COLLEGE HILL FUND 76%

SAYLER PARK 74%

S. AVONDALE 70%

WILLIAM H. TAFT 67%

FRED. DOUGLASS 58%

BOND HILL ACADEMY 56%

CARSON 55%

CINCINNATI CITY 47%

REES E. PRICE 39%

## PRETERM BIRTH RATES

OTR-PENDLETON

RIVERSIDE-SEDAMSVILLE

KENNEDY HTS.

AVONDALE

N. COLLEGE HILL

S. CUMMINSVILLE-MILLVALE

ELMWOOD

EVANSTON

MADISONVILLE

E. PRICE HILL

SPRINGFIELD TWP.

WEST END

COLERAIN TWP.

SILVERTON

CLIFTON

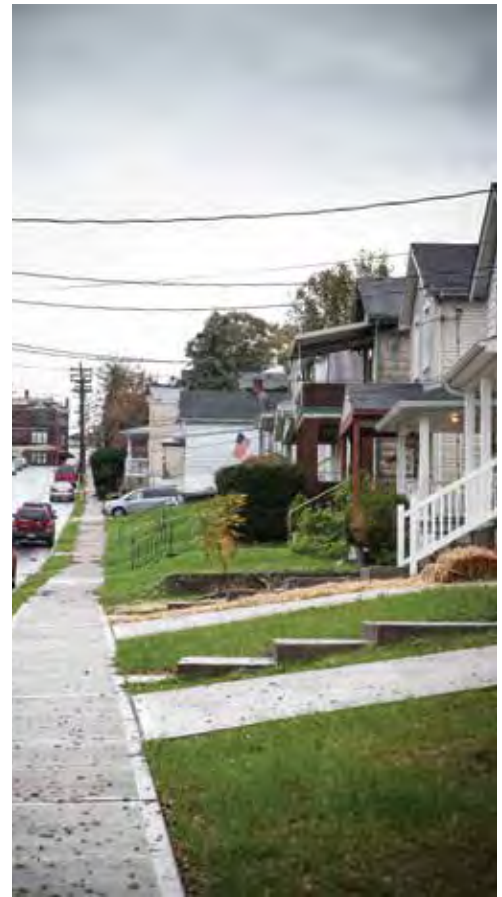
BLUE ASH

WHITEWATER TWP.

LOVELAND

Seemingly regional health problems actually vary widely among neighborhoods, suggesting a need for more-targeted solutions, researchers at Cincinnati Children's say.

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# Cincinnati Children's Opens Center for Stem Cell and Organoid Medicine

Eight years ago, Cincinnati Children's scientists first used pluripotent stem cells to mimic natural human development and grow working human intestine in a lab. Today medical center doctors can bioengineer the gastrointestinal tissues of sick children to find clues about a child's disease and how to treat it.

Building on this early research advancement in personalized medicine, Cincinnati Children's recently launched the Center for Stem Cell and Organoid Medicine (CuSTOM). The center will accelerate the transfer of stem cell-organoid technology from the research lab to practical clinical tool.

Organoid technology has the potential to solve several current medical and research challenges, according to Aaron Zorn, PhD, the new center's Director. The technology can address a shortage of organs available for transplant. It can eliminate the lack of human modeling systems for developing drugs and testing their safety and effectiveness before going into expensive clinical trials. The

technology also gives researchers a first-in-class physiological platform to conduct laboratory research on living diseased tissue, which cannot be done on patients.

## Organized to Collaborate

The new center is organized as a highly collaborative, multi-disciplinary center of excellence that integrates scientists, clinicians, geneticists, surgeons, bioengineers and entrepreneurs. It is believed to be the first dedicated facility at a pediatric medical center focused on advancing pluripotent stem cell-organoid technology and translating its potential to clinical practice.

"We have this convergence of transformative breakthroughs in organ-gener-

ation technology at Cincinnati Children's, and it's critical that we speed up the translation cycle so patients can benefit more quickly. This is, by definition, personalized medicine," Zorn says.

## Built on Science

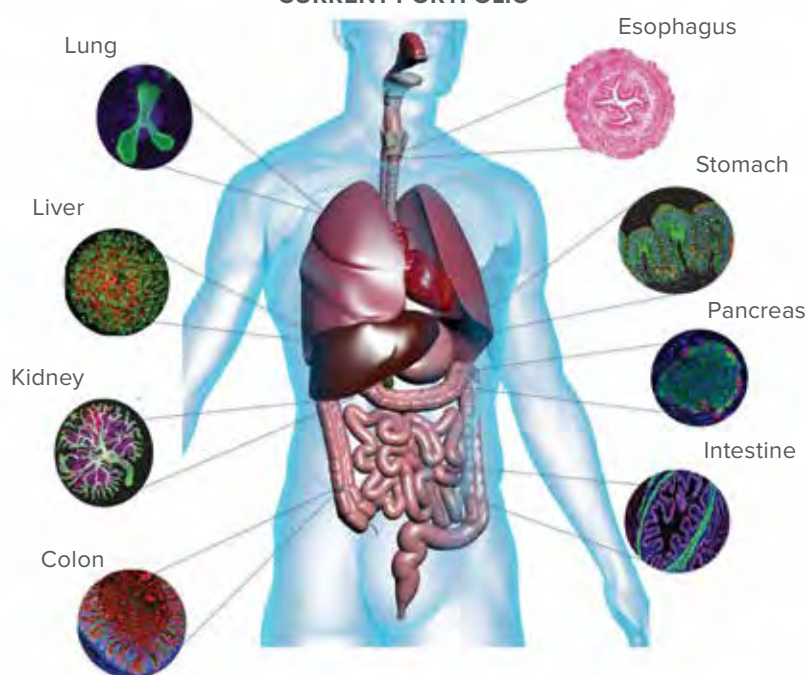
In a series of studies published since 2010, medical center researchers led by developmental biologist James Wells, PhD, the new center's Chief Scientific Officer, used human pluripotent stem cells to bioengineer gastrointestinal tract tissues that mimic natural human development in a laboratory. Scientists tissue engineered the small intestine, colon, stomach, and human intestine with functioning enteric nerves and then used these to study different gastrointestinal diseases.

Medical center researchers also bioengineered mini livers in landmark studies led by Takanori Takebe, MD, the center's Associate Director of Commercialization. Liver organoids hold the nearest-term clinical potential as a personalized platform to test the toxicity or efficacy of existing and new drugs in organoids grown from patients' cells for diseases such as drug-induced liver injury and steatohepatitis.

The lab-bioengineered tissues reveal the precise genetic and biological processes that cause disease, say researchers. Mini organs can identify the unique biological characteristics of a disease in a single person.

The overall effort to study potential applications for organoid technology is led by Michael Helmrath MD, MS, Division of Pediatric General and Thoracic Surgery, the new center's Associate Director for Translational Research .

## CURRENT PORTFOLIO





Louis Muglia, MD, PhD, and Ge Zhang, MD, PhD

## Six Gene Loci Linked to Preterm Birth in Landmark Study

A massive DNA analysis, based on data from more than 50,000 women, could lead to new ways to prevent the leading cause of infant mortality.

The study, published in September in *The New England Journal of Medicine*, identifies six gene regions that influence the length of pregnancy and the timing of birth. One of the gene regions indicates a potentially important role for the mineral selenium in the diets of pregnant women. Another suggests that cells within the lining of the uterus play a larger-than-expected role in the length of pregnancy, which in turn provides a new target for medications to help prevent preterm birth.

Louis Muglia, MD, PhD, Co-Director of the Perinatal Institute at Cincinnati Children's and principal investigator of the March of Dimes Prematurity Research Center—Ohio Collaborative, coordinated the study with first author Ge Zhang, MD, PhD, of the Division of Human Genetics. The globe-spanning team also included researchers from Norway, Denmark, Finland, Sweden, and the genetic testing company 23andMe.

"Previous research has suggested that about 30 to 40 percent of the risk for preterm birth is linked to genetic factors. This new study is the first to provide robust information as to what some of those genetic factors actually are," Muglia says.

## Tool Identifies Autism Risk Early

A tool that diagnoses autism spectrum disorders (ASD) identifies autism risk in patients with tuberous sclerosis complex (TSC) earlier than ever before possible.

TSC causes malformations and tumors in the brain and other vital organs. Children with TSC are more likely to have ASD.

A study published online in *Pediatric Neurology* evaluated 79 children up to 24 months old, all of whom had TSC. Researchers administered the Autism Observation Scale for Infants at 12 months of age, examining activities including visual tracking and response to facial emotion. They followed this with the Autism Diagnostic Observation Schedule-2 at 24 months.

Infants at greater risk of ASD scored significantly higher at 12 months than the non-ASD group, says Jamie Capal, MD, lead author, Division of Neurology, "demonstrating that it is a useful clinical tool in determining which infants with TSC are at increased risk of developing ASD."



Jamie Capal, MD

# Novel Potential Treatment for Obesity-Linked Disease

A blood thinner could play a surprising role in limiting weight gain and disease, according to a 2017 study in the *Journal of Clinical Investigation*.

In mice fed a high-fat diet and in the tissue of patients with fatty liver disease, scientists found that the glycoprotein fibrinogen binds with the leukocyte receptor M $\beta$ 2-integrin to fuel diet-induced obesity and disease.

With obesity, the clotting system can become overactive, converting fibrinogen into insoluble fibrin strands, or thrombin, which leads to inflammation and tissue damage.

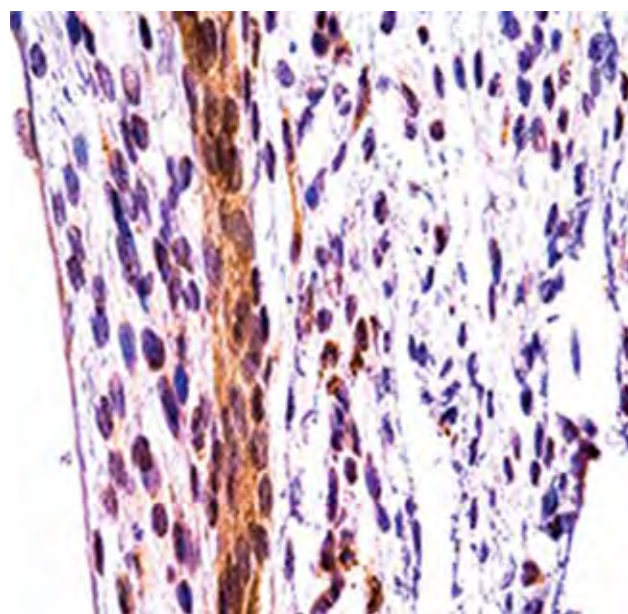
Matthew Flick, PhD, Division of Experimental Hematology and Cancer Biology, and his team used an FDA-approved blood thinner, dabigatran, to target the thrombin in the mice fed a high-fat diet. Dabigatran protected the mice from obesity-related disease.

The scientists are now exploring whether people currently taking dabigatran have less obesity and disease. If so, Flick says, it could provide strong rationale to use the drug as a preventive.



Matthew Flick, PhD

# MMP-7 Enzyme Shows Promise as Biomarker for Biliary Atresia



This image from the bile duct of a mouse model shows the expression MMP-7 (shown in brown), an enzyme that may serve as a biomarker for early diagnosis of biliary atresia, the most common cause of pediatric liver transplants in the United States.

After analyzing a collection of infant blood samples, scientists at Cincinnati Children's report that the enzyme matrix metalloproteinase-7 (MMP-7) served as an effective biomarker for biliary atresia, with greater than 90 percent sensitivity and specificity.

Findings appeared in November 2017, in *Science Translational Medicine*.

Biliary atresia is the most common cause of liver transplants for children in the United States. Finding a strong biomarker candidate could allow for earlier diagnosis and treatment, which could reduce the numbers of children who wind up on transplant waiting lists.

"From a broad screen of over 1,000 proteins, we found a unique protein associated with biliary atresia. Testing this protein as a diagnostic biomarker in two additional groups of babies to validate accuracy, it passed with flying colors," says senior investigator Jorge Bezerra, MD, Director, Gastroenterology, Hepatology and Nutrition.

The study's first author was Chatmanee Lertudomphonwanit, MD, who has appointments at Cincinnati Children's and Ramathibodi Hospital in Bangkok, Thailand.

In mouse models, the researchers learned that MMP-7 is released during bile duct injury, which promotes duct obstruction. Future research will explore whether an experimental MMP-7 inhibitor that worked in mice can serve as a potential treatment for infants.



# Exposure to Air Pollution Can Increase Birth Defect Risk

Women exposed to air pollution just prior to conception or during the first month of pregnancy face an increased risk of their children being born with birth defects.

The study compared birth defect rates and the distances women lived from sources of fine particulate pollution (PM2.5), based on data from 57 U.S. Environmental Protection Agency monitoring stations located throughout Ohio. Detailed results were published online in December 2017, in *The Journal of Pediatrics*.

Overall, the increased risk was modest. The strongest influences of PM2.5 on individual malformations were found with abdominal wall defects and hypospadias.

“The most susceptible time of exposure appears to be the one month before and after conception,” says senior author Emily DeFranco, DO, MS, an environmental health expert based at Cincinnati Children’s and the University of Cincinnati College of Medicine. “Public health efforts should continue to highlight the importance of minimizing population-level exposure to harmful particulate matter in the air.”



Emily DeFranco, DO, MS



Burns Blaxall, PhD

## Protein Inhibitor Could Prevent Heart Failure

Researchers report encouraging results in repairing scarred and poorly functioning heart tissues after cardiac injury.

In a study published online Aug. 14, 2017, in the *Journal of the American College of Cardiology*, researchers in our Heart Institute inhibited G $\beta$  $\gamma$  and GRK2, proteins that regulate the heart’s response to adrenaline. This alleviated disease processes in mouse models of human heart failure, and in cardiac cells of patients undergoing reparative surgery.

After a heart attack, chronic overstimulation of the adrenaline system produces hypertrophy and fibrosis in the heart. Blocking G $\beta$  $\gamma$  and GRK2 with the molecular inhibitor gallein preserved heart function and reduced enlargement and tissue scarring. Similar results were achieved when GRK2 was removed from cardiac fibroblasts in genetically altered mice.

The finding could revolutionize the treatment of heart failure, says senior investigator Burns Blaxall, PhD. Researchers are working on a compound that mimics gallein and is safe for use in animals and humans.

# Key Regulator of Male Fertility Revealed

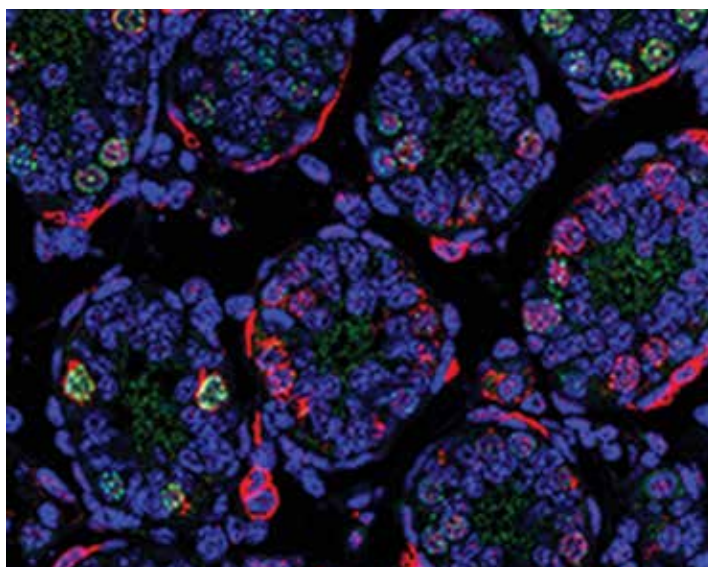
When it comes to male reproductive fertility, timing is everything.

Researchers at Cincinnati Children's report in *Genes & Development* that a protein complex called Polycomb Repressive Complex 1 (PRC1) acts as a molecular switch that activates production of healthy male sperm—but only when the time is right.

At birth, male mammals possess the germline cells needed to make sperm, but PRC1 represses activation during childhood. The new study, based on mouse models, shows that PRC1 changes at puberty, shedding the gene components that block sperm production and substituting in a component (Sall4) that starts spermatogenesis.

"A long-standing question has been how reproductive germline genes are activated in a precise and timely manner. Our study answers this fundamental question," says lead investigator Satoshi Namekawa, PhD, Division of Reproductive Sciences.

Future questions to explore include whether and how lifestyle or other environmental factors might affect this process; and whether Sall4 can serve as a biomarker for male infertility.



This confocal microscopic image of an 8-day-old mouse's testicular section shows evidence of the PRC1 subcomponent Sall4 (in green). Scientists report in *Genes & Development* that PRC1 is the key molecular and genetic switch that activates production of healthy male sperm.

## Healthy Guidelines Not Followed For Preschoolers

There is "ample room for improvement" in the diet and activity levels of preschool-age children, reports Amrik Singh Khalsa, MD, fellow in the Division of General and Community Pediatrics.

Khalsa's study, published online in *Preventive Medicine Reports*, found only one of nearly 400 preschoolers following daily 5-2-1-0 obesity prevention guidelines. Khalsa's team obtained objective measures of dietary intake, body mass index (BMI), activity levels, and screen time in 398 preschool children over 24 hours, in day care and at home.

Among their findings: one of every four children had a BMI in the overweight category; just 17 percent ate at least five servings of fruits and vegetables; and fewer than 1 percent met activity recommendations.

5-2-1-0 daily guidelines recommend at least five servings a day of fruits and vegetables, fewer than two hours of screen time, one hour of physical activity and no sugar-sweetened beverages.



Amrik Singh Khalsa, MD





Maha Almanan, first author and graduate student in the Division of Immunobiology

## CMV Latency Depends on Location, Location, Location

Findings reported Aug. 10, 2017, in *PLOS Pathogens* suggest that whether cytomegalovirus (CMV) goes dormant or reactivates depends on where it lodges in the body.

Immune system T-cells appear to encourage CMV's latency in the spleen, but not in the salivary gland, reports Maha Almanan, first author and graduate student in the Division of Immunobiology.

CMV infects more than half of adults by age 40. Usually it causes no symptoms, but it can reactivate in people with weakened immune systems.

Previous work showed that T-cells caused this reactivation; researchers tested this by infecting mice with CMV. Eight months after infection, they found latent CMV in the spleen, salivary gland, lung, and pancreas.

Then the team decreased levels of regulatory T-cells. In the spleen, depleting T-cells reduced the virus and boosted immune cell function; the opposite occurred in the salivary gland.

Findings are being investigated in immune-suppressed patients, and may eventually lead to developing improved treatments.

## Untapped Language Skills Detected Among the Deaf and Hard of Hearing

Universal screening of newborns for hearing loss is not enough to improve language skills of children who are deaf or hard of hearing, according to a study published online in the *Journal of Developmental and Behavioral Pediatrics*.

Research scientists at Cincinnati Children's report that at least 40 percent of children with a hearing loss have the capacity for higher language levels—beyond what test scores indicate.

"We have focused efforts for children who are deaf or hard of hearing on obtaining a language level that is often considered in the normal or average range on standardized assessments," says Jareen Meinzen-Derr, PhD, an epidemiologist and lead author. "But their language skills are not good enough if we account for their cognitive abilities."

The study enrolled 152 children. Language and neurocognitive assessments revealed significant disparities between language scores and nonverbal cognitive scores. With a slightly modified evaluation approach, therapists could begin to recognize these mismatches at younger ages and intervene, Meinzen-Derr says.



Jareen Meinzen-Derr, PhD

# A Higher Goal Helping Children Thrive

Cincinnati Children's Devotes Expertise and Resources  
to a Shared Community Mission

by Tim Bonfield

A new language is taking root among dozens of agencies and organizations dedicated to improving child health in Cincinnati.

The vocabulary includes terms such as community activation, family-centered design, co-production, quality improvement and social determinants of health. Now nurses, teachers, agency leaders, parents and neighbors are joining with physicians, scientists and other community health experts to talk about SMART aims, run charts, concurrent neighborhood controls, and more.

This is the language of the All Children Thrive Learning Network, a collaboration launched by Cincinnati Children's and more than 30 other organizations to apply the science of quality improvement to some of the toughest, most complex problems affecting community health.

"It's a way of working differently that we believe will lead to different results," says William Brinkman, MD, MEd, MSc, Director of Research, Division of General and Community Pediatrics. "It's a way of working together, as opposed to working in silos, to move the same dial with everyone using a shared system of measurement. It's a way of providing evidence for people to use in decision making, a method that can allow people to stop holding onto ideas that haven't worked."

## GOING BEYOND TREATING ILLNESS

The city of Cincinnati is home to about 66,000 children, more than 40 percent of whom live in poverty—the third highest rate in the nation.

Research led by Cincinnati Children's shows that children in the five least healthy of the county's 80-plus neighborhoods have a 20-fold higher hospital admission rate. As they grow, many

of these children are not well prepared to enter kindergarten. Many are not reading proficiently at third grade. Meanwhile, mothers in the five least healthy neighborhoods are three times more likely to have a preterm birth.

All Children Thrive represents an organized effort to reduce the massive health burdens caused by childhood poverty by involving the families these organizations are trying to help—not just as participants, but as leaders.

As a result, instead of a traditional focus on treating illness, the mission is more about helping children thrive. The network's goals:

- Ensure all children reach their first birthday
- Ensure that all 5-year-olds have a "healthy mind and body"
- Reduce disparities in hospital admissions across neighborhoods
- Ensure that all children are reading proficiently by the end of third grade

All Children Thrive, launched in 2015, is hosted by Cincinnati Children's and coordinated with leaders from multiple sectors. The network includes families, health care providers, educators, community service providers, and others. Members meet weekly to collaborate on systemic solutions carried out through numerous neighborhood-focused projects.

So far, more than 3,800 people have participated in collaborative events, training sessions and quality improvement "boot camps." More than 45 "parent partners" have become active in two of Cincinnati's most impoverished neighborhoods—Price Hill and Avondale.



More than 30 agency leaders have received quality improvement training through a program called Impact U in collaboration with the Strive Partnership. The United Way and the Greater Cincinnati Urban League are deeply involved.

Meanwhile, Cincinnati Public Schools has connected many of its elementary teachers to a reading-focused quality improvement program that has spread to a dozen schools in just two years.

The heavy emphasis on educational goals is a crucial element of the All Children Thrive approach. Experts at Cincinnati Children's and other centers have documented many of the brain development benefits that flow from early childhood reading. Social scientists have long known that when children fall behind in reading, they often fall behind on many other subjects, which can lead to lower high school graduation rates, increased poverty, and higher risks for a wide range of poor health outcomes.

The value of the learning network approach followed by All Children Thrive flows from assembling interested, committed people to work together towards improving measurable outcomes, says Uma Kotagal, MBBS, MSc, Executive Leader, Population and Community Health at Cincinnati Children's.

"Solving a problem like poverty is too big. Solving a problem like literacy is too big," Kotagal says. "What the network does is serve as a convener, a catalyst. For big problems, the network brings people together across multiple sectors to test different things and scale what works."

"All of our partners are deeply caring, very committed community leaders. We do not tell these people what they should do. We provide a structure they can use to bring quality improvement methods to their work. Providing these methods and co-producing with people in the community makes it possible to build energy and optimism."

"Instead of focusing  
narrowly on  
traditional health  
measures, the  
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– Robert Kahn, MD, MPH





(From left) Drs. Uma Kotagal, Robert Kahn and William Brinkman have spearheaded development of the All Children Thrive Learning Network, which brings together government and community agencies, neighborhood leaders, and families to co-produce interventions to improve complex health concerns.

(For more about the collaborative's partnership with Cincinnati Public Schools, see page 20.)

### AN EVOLUTION IN IMPROVEMENT SCIENCE

Cincinnati Children's recent involvement in community health issues reflects a years-long commitment to quality improvement science.

The roots of All Children Thrive reach back as far as 2002, when Cincinnati Children's received a \$1.9 million "Pursuing Perfection" grant from the Robert Wood Johnson Foundation.

That quality improvement effort started with an internal focus to transform cystic fibrosis care, then expanded to other hospital processes. This process led to the formation of the James M. Anderson Center for Health Systems Excellence, launched in 2010 under Kotagal's leadership, and now directed by Peter Margolis, MD, PhD, and Steve Muething, MD.

The Anderson Center develops and shares a wide range of evidence-based best practices for healthcare providers on topics ranging from hospital safety and capacity management to managing chronic disease. It has supported and facilitated more than a dozen learning networks involving hundreds of medical centers and physician practices, enabling Cincinnati Children's to collaborate across the country to get results at scale.

One of the most significant of those has been ImproveCareNow, a group co-founded by Margolis to focus on inflammatory bowel diseases (IBD). The network brings patients, families and experts together to accelerate the adoption of best practices. Since its origins in 2007, the network has grown from six participating

centers to more than 100 worldwide and has transformed care and outcomes for a generation of children with IBD.

This network approach has been extended to the All Children Thrive network in an effort to apply many of the concepts behind ImproveCareNow to a new level of complexity and challenge.

### DEVOTING RESOURCES TO THE EFFORT

Helping the children of Cincinnati become the healthiest in the nation through strong community partnerships is one of the pillars built into the medical center's 2020 strategic plan.

In addition to supporting the work of All Children Thrive, Cincinnati Children's is investing \$11 million over five years in community redevelopment in Avondale. The work ranges from working with partners to provide interest-free, forgivable loans for housing rehab projects to investing \$1.5 million in grants to smaller nonprofits to improve child health and expand workforce development.

Now, the medical center is expanding some of the successful projects that started in Avondale to another neighborhood: Price Hill. (For more about the work happening there, see page 24.)

"Instead of focusing narrowly on traditional health measures, the challenge," says Robert Kahn, MD, MPH, Associate Chair for Community Health at Cincinnati Children's, "is how do we reduce the barriers to family success? How do we get all the elements of a complex system—the job training agencies, the child welfare system, the health clinic, the schools, the housing groups—working hand in glove for a family? So we're working with agencies to ask them, 'How do we surface the systemic problems and change the rules?'" Experts at Cincinnati Children's

already have devoted extensive research resources, including geospatial mapping techniques and other approaches, to expose the neighborhood-by-neighborhood disparities hiding within aggregated city, county, and statewide health data sets.

“It’s one thing to look at asthma morbidity for the county,” Kahn says. “It’s quite another to say here’s the asthma admission rate this month, by neighborhood, and then add housing, pollution and pharmacy use data to track risk factors. This is a set of data that few others in the country could have put together—and it helped paint a pretty clear picture of where we could and should be doing more.”

(For more detail about asthma improvement work happening in the community, see page 12.)

### RESULTS BEGINNING TO SURFACE

What does thriving mean? In addition to disease-focused goals, the initiative has assembled a bundle of health measures that track immunization, obesity, dental, vision, speech, hearing, literacy and behavioral factors. Combined, the network seeks to achieve several specific goals by 2020, including:

- Raising the percentage of 5-year-olds meeting all the bundled targets from 13.4% to 40%
- Reducing infant mortality in Hamilton County to 6.0 per 1,000 births
- Increasing the percentage of Cincinnati Public Schools children achieving third-grade reading proficiency from 46.5 percent to 90 percent

Early progress has been documented for all of these and many other goals.

For example, in early 2006, the countywide infant mortality rate was as high as 13.24 per 1,000 births. By late 2016, after the launch of Cradle Cincinnati and other efforts, the rate had declined to 9.10. Within that countywide figure, the Start Strong pilot project in Avondale resulted in a dramatic decline in extreme preterm births. Now network leaders are working to expand the

program to other parts of the city, and beyond. (For more details about the community’s infant mortality efforts, see page 16.)

“Avondale is a prototype for success in preterm birth,” Kotagal says. “Now, we know the components that went into how to do that, which in turn inspires the rest of the learning network to do the work that’s needed to scale up.”

Meanwhile, some of the literacy work happening in Cincinnati is attracting national attention. Kotagal and other partners are working with the Carnegie Foundation for the Advancement of Learning to share the lessons learned in Cincinnati. Planning meetings are set for later this spring to launch a meta-literacy network that could include school districts in other states, including Maryland, Tennessee, California and Colorado.

“It may be that other people have already addressed some of the problems we’ve been talking about. It may be that we can offer insights,” Kotagal says. “That’s the core idea behind learning networks: to see them grow, share and improve outcomes as quickly as possible.” ■



Organizers of All Children Thrive established the Impact U program to train agency leaders and volunteers on quality improvement methods. So far, more than 3,800 people have participated in collaborative events, training sessions and quality improvement “boot camps.”

# Asthma Improvement

Collaborative Reduces Hospital Re-Visits by 41%

by Tim Bonfield

**Y**es, the needle can be moved. From a distance, the health disparities exacerbated by poverty can seem like a Gordian knot. Lack of educational opportunities. Lack of transportation. Lack of access to care. Increased dangers from pollution and poor housing conditions. Instability in the home. Racial disparities. Distrust of the health care system.

All of these factors, and more, make it hard for low-income families to fully follow their doctors' prescriptions for managing a serious chronic disease like asthma. Hospitals and clinics in big cities across America live this reality every day.

But outcomes can be improved. Children with poorly controlled asthma can achieve dramatically improved outcomes, even among families facing desperate situations. That's what a five-year improvement effort organized by Cincinnati Children's and a group of committed community organizations demonstrated with results published in November 2017 in *JAMA Pediatrics*.

The project involved forming a learning network of people working in hospital and outpatient care settings who collaborated with families, pharmacies, school nurses and city health officials. This virtual village recommended and supported changes that have improved day-to-day life for children with asthma while saving health care costs by reducing hospital re-admissions.

"I do think this study is fairly unique in the number of partners we brought together, the scope of the work, and the ability

to impact outcomes," says Mona Mansour, MD, MS, Director of Primary Care at Cincinnati Children's and a co-author of the study.

"One of the hardest metrics to move in asthma care is high utilization of emergency services," says Carolyn Kercsmar, MD, Director of the Asthma Center, and another co-author. "But beyond the statistics, what we're really doing is reducing the disruption that families face when their children get hospitalized or come to the emergency room for asthma exacerbations."

## BREAKING DOWN A BIG PROBLEM

The scale of the asthma challenge here is daunting. In Hamilton County, the home location of Cincinnati Children's, more than 36,000 children have asthma, including more than 13,000 covered by Medicaid. For years, those Medicaid children have endured poorer outcomes including less well-controlled symptoms, more missed days of school, more-frequent emergency visits, and more.

Cincinnati Children's provides more than 90 percent of inpatient services for the children of Hamilton County and an estimated 65 percent of their emergency needs. General pediatric clinics here provide primary care for about 34,000 Medicaid-insured children.

Within that sphere, asthma accounts for about 1,000 hospitalizations and 2,500 emergency department visits a year. In addition, more than 7,000 patients receive long-term asthma care from pulmonary specialists here.





Unsurprisingly, improving asthma outcomes has been an ongoing high priority for Cincinnati Children's.

The medical center launched its Asthma Improvement Collaborative in 2007, with improvement efforts kicking off in 2009. In 2010, medical center trustees made asthma improvement one of four core elements of a five-year strategic plan.

A three-phase set of improvements flowed from the collaborative's efforts. The first focused on hospital-based changes, the next on outpatient care, and the third on a wider set of community goals.

#### **INPATIENT FOCUS ON MEDS-IN-HAND**

Specific goals included reducing the asthma-related hospitalization rate from a rolling 12-month mean of 7.2 to 5.8 per 10,000 patients per month; and reducing emergency visits from 20.9 to 16.7 per 10,000 patients per month.

One of the most important learnings uncovered by the network was that vital asthma medications often went unfilled at local pharmacies, even in the days after hospitalizations. So one of the first steps was to change practices within the hospital so that families left with a full month's supply of medications in-hand.

In 2008, just 50 percent of asthma patients went home with a 30-day supply of inhaled controller medications in-hand. By 2010, that figure had climbed to 90 percent. In 2008, no child started on a short course of oral corticosteroids in the hospital

“If compensation for more care delivery systems becomes tied to keeping patients out of the hospital, this type of work may become all the more important.”

— Andrew Beck, MD, MPH

## Emergency room visits from 2007-2015



Since launching the Asthma Improvement Collaborative in 2007, a study in *JAMA Pediatrics* shows that the asthma-related hospitalizations for Medicaid-insured pediatric patients in Hamilton County declined from a rolling 12-month mean of 7.2 to 5.8 per 10,000 patients per month while emergency visits dropped from 20.9 to 16.7 per 10,000 patients per month.

went home with their remaining doses in hand. By March 2011, that figure had climbed to 70 percent.

“We believe that providing a 30-day supply of all daily asthma medications at discharge was key to observed improvements,” the co-authors wrote in the *JAMA Pediatrics* paper.

Providing asthma medications at discharge helped overcome difficulties many urban, indigent families can face, be it the simple lack of a neighborhood pharmacy or a complex litany of potential lifestyle-related disruptions.

The change in practice produced results. Among Medicaid-insured children, the rate of return visits to the hospital within 30 days of initial discharge decreased by 41 percent; from 12 percent to 7 percent.

### OUTPATIENT FOCUS ON ACTION PLANS

Phase Two improvements focused on baseline asthma control among children served by the medical center’s primary care clinics. Teams implemented a bundle of asthma best practices that included consistent collection of asthma control testing data, working with families to create asthma action plans, and enrolling the highest-risk families in care coordination programs.

Two challenges surfaced. Some families needed stepped-up training on how to manage asthma at home, whether or not they had easy access to a pharmacy. Others faced clear, ongoing trouble picking up medications. This led to working with a local pharmacy to create a targeted delivery service for high-risk asthma families.

By the end of June 2015, the effort enrolled 763 patients into care coordination programs. Of those, 394 “graduated” with demonstrated improved understanding of asthma management.

Meanwhile, 345 families received medication delivery through the pharmacy partner.

These efforts made a difference: the percentage of primary care patients with well-controlled asthma improved from 48 percent to 54 percent during the study period.

### COMMUNITY FOCUS ON SCHOOL-BASED SUPPORT

At the wider population level, the learning network identified shortfalls—and opportunities—related to screening and communication. In response, the network focused on building a deeper relationship between Cincinnati Children’s, the Cincinnati Health Department, and the Cincinnati Public Schools, the county’s largest school system.

“School nurses were crucial,” says Mansour. “We were fortunate that we could build strong relationships with our partners in the health department and the school district who shared a common vision.”

The hospital helped school nurses identify all of the students known to have asthma, many of whom had not been revealed by routine school information requests. Then the hospital provided training, equipment—and in some cases extra sets of hands—to help school nurses do more asthma control testing.

With family permission, school nurses also received limited access to the hospital’s patient records so that nurses could coordinate care and stay informed about changes in medications and treatment plans. This allowed nurses to intervene in some cases long before lingering miscommunications and other care disruptions escalated into a serious asthma exacerbation.

By the end of the study period, more than 80 percent of CPS students with asthma had been screened. Those scores indicating

poor control were referred to their existing doctors, or to new medical homes, including school-based health centers.

“We believe that the bundle, which included in-depth risk assessment, directed education, medication delivery, and robust connections with hospital- and community-based partners, including schools, promoted lasting relationships with families and extended the reach of primary care,” the co-authors wrote.

Two well-established, local healthy housing programs also played roles. The CLEAR program supports families facing home-related asthma risks, while the Child HeLP program connects families with legal aid services when housing concerns emerge. Both programs help get city health officials involved when code violations affect child health.

### THE WORK CONTINUES

Overall, this five-year, phased approach contributed to decreasing asthma-related hospitalizations from 8.1 to 4.7 per 10,000 Medicaid patients per month. Asthma-related emergency visits fell from 21.5 to 12.4.

“This approach is now baked into how we do our work,” Mansour says. “Would other communities do this exactly the same way? Perhaps not. But if you have leaders with the will, and partners with a shared vision, I do believe this approach is replicable.”

Andrew Beck, MD, MPH, a study co-author based in the Divisions of General and Community Pediatrics, and Hospital Medicine, says economic incentives also may influence how far this asthma care model spreads beyond Cincinnati.

“A unique aspect of this project was the taking ownership for a population-wide metric. This went beyond just the children within the care of Cincinnati Children’s,” Beck says. “If compensation for more care delivery systems becomes tied to keeping patients out of the hospital, this type of work may become all the more important.”

Looking ahead, work to enhance school-based asthma care continues.

A two-year program that ended in 2017 followed 21 CPS students at three schools located in neighborhoods with high asthma hospitalization rates. The project included teleconferencing conducted at school between children and asthma specialists, providing patients with electronic inhaler monitors, and providing medication bottles with digital caps that can be synced with smart phones.

“Overall, we showed that reducing asthma exacerbations with a program like this is feasible,” says Theresa Guilbert, MD, MS, a pulmonologist who oversaw the program.

Now Guilbert is applying for a grant to expand the program to 26 schools.

Mansour says it was both sobering to recognize just how complicated life can be for families covered by Medicaid, and a joy to be able to make a difference.

“As we helped eliminate some barriers, these families were able to see their children do better and feel better,” Mansour says. “For some of these families, their kids had been living in such chronically poor control that they didn’t even know what life with a healthier child could look like. There was real joy in hearing those stories.” ■

Mona Mansour, MD, MS, (top left), Andrew Beck, MD, MPH, and Carolyn Kerckmar, MD, played leading roles in an asthma improvement collaborative that reduced hospital admissions and emergency visits while standardizing outpatient care practices. The effort went further to arrange pharmacy delivery services for some families while engaging school nurses in community-focused efforts to manage asthma care.





# HOW TO SAVE Babies? FIND EVERY MOTHER

Community-Wide Interventions Push Back  
Against Preterm Birth, Infant Mortality

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By Nick Miller

If the first step to solving a problem is admitting it exists, officials in Hamilton County, Ohio—where Cincinnati Children’s calls home—know they have one whopper of a wicked problem.

Infant mortality and preterm birth rates here are among the nation’s worst. Some neighborhoods, especially in Cincinnati’s inner city, have rates rivaling third-world countries. From the years 2007 to 2011, Hamilton County’s infant mortality was 10.8 per 1,000 live births. That ranks among the worst 10 percent of all counties nationwide.

Hidden within that overall statistic, an estimated 40 percent of premature infants born at 25 weeks gestation or earlier die within their first day.

“Many of these babies don’t even get out of the delivery room. The most modern and sophisticated interventions on the planet can’t help them,” says James Greenberg, MD, Co-Director of the Perinatal Institute, and a devoted disciple to saving as many babies as possible through collaborative human endeavor.

## A ‘WICKED’ PROBLEM

“There is literature around something that is actually called a ‘wicked problem,’” Greenberg says. “Infant mortality is a wicked problem. It means the problems are complex, they have a lot of variables, some variables confound others, and they are hard to solve.”

In Hamilton County, debate continues over the possible reasons behind the high infant mortality rate and its related instigator, extreme preterm birth (defined as births at less than 28 weeks gestation). Solid answers remain elusive.

For example, statistics clearly show that mortality rates run much higher for black babies. Experts still debate the cause, which is not adequately explained by biomedical factors or economic disadvantage.

Experts also differ over how specific behaviors may influence infant mortality, such as smoking during pregnancy, following safe sleep practices for infants, spacing between pregnancies, and access to prenatal care. Only recently have suspected gene loci emerged from a large study of expectant mothers that may explain how the length of pregnancy and onset of labor are controlled.

Meanwhile, ongoing research pokes holes in other suspected causes.

Take pregnant teenagers, who have a higher risk of giving birth to a preterm baby. Teenage pregnancy once was thought to be an important driver of infant mortality, but Greenberg notes that teenage pregnancy rates have dropped in the last decade while infant mortality rates remain stubbornly high.

Another example is opioid addiction, which had been suspected as a contributing factor in infant mortality. Subsequent research shows maternal addiction does not on its own significantly impact infant mortality, although other health behaviors



associated with opioid addiction (like smoking cigarettes) have strong links to infant mortality.

Both examples underscore the shifting layers of complexity that come with tackling wicked problems like infant mortality and premature birth.

#### **CRADLING CINCINNATI**

When Greenberg and Cincinnati Children's colleagues started the Perinatal Institute in 2009, a chief new objective was confronting infant mortality. This included Perinatal Institute co-founder and Co-Director Jeffrey Whitsett, MD, a pioneer in neonatal pulmonary research and care.

Data from previous years had made Hamilton County's high infant mortality rates appallingly clear. The problem even plagued Cincinnati Children's home turf, the socioeconomically challenged, mostly black neighborhood of Avondale.

Considered an anchor institution in the city and a global leader in child health, "the unique position of Cincinnati Children's comes with responsibilities," Greenberg says. Still, the hugeness of the challenge was obvious, as was the abundant realization that help was needed.

A new level of community involvement arrived in 2012 through a collaboration called Cradle Cincinnati. The organization was co-founded by Greenberg and Elizabeth Kelly, MD, Director of the Community Women's Health Division at

“We centered the work around what moms need and want as opposed to technically perfect medical care. It’s about them, not our busy clinical schedule.”

– Robert Kahn, MD, MPH



Clinical staff at the UC Health Women's Health Clinic huddle to review patient cases. (From left) Toni Mays, RN, William Moravec, MD, Marianne DiNapoli, MD, and Dawn Denno of Cincinnati Children's. Stephanie Ralston, case manager, is shown with back to camera.

the University of Cincinnati's Department of Obstetrics and Gynecology.

The collaboration is based at Cincinnati Children's but has grown to include all the city's hospital birthing centers, the Cincinnati Health Department, and other city and county officials. Several community health agencies including Every Child Succeeds and Healthy Moms and Babes participate as well.

Just a few years into the effort, Cradle Cincinnati began delivering results. During the years 2012 to 2016, Hamilton County's infant mortality rate dropped to 8.96 per 1,000 births, down from 10.8 in 2007-2011. That lower figure remains one of the highest rates in Ohio and nationally, but represents clear progress.

Even so, the work remains far from complete, says Ryan Adcock, Cradle Cincinnati's Executive Director, and an example in his own right of going against convention to find a path to success.

Adcock was not trained as a public health professional. He is a former chief of staff for a Cincinnati mayor, and previously worked as a songwriter. Yet he plays a vital role in Cradle Cincinnati's success as a knowledgeable and enthusiastic convener of stakeholders, a catalyst, and a cheerleader for the community-wide effort.

"The message is, there is hope," Adcock says. "People sometimes come to this issue with hopelessness or thinking it's just too big. It is really hard and it takes a lot of intentionality. But we've shown when the right folks come together in the right way, it can make a difference."

#### STARTING STRONG IN AVONDALE

If the collective "who" of Cradle Cincinnati provides the strength, the "how" is the secret sauce to the collaborative's success so far.

Defanging the wickedness of the infant mortality problem requires changing the rules of engagement, leaders say. That

involves adherence to gathering good data, listening to the people most affected by the problem, and acting on the insights to get better at what we do every day, according to Robert Kahn, MD, MPH, a co-founder of the Start Strong initiative.

It was formed to apply these strategies to the problem of infant mortality. Launched in 2013 with \$5.2 million from donors, including \$3.2 million from the Bethesda Foundation, Start Strong serves as a learning network that informs the larger Cradle Cincinnati effort.

The new initiative's primary goal: decrease the high number of extreme preterm births occurring in Avondale.

When the initiative started, Avondale's infant mortality rate was 22.1 per 1,000 births—far higher than the U.S. average of 5 per 1,000. By 2016, the rate had plummeted to about three infant deaths per 1,000—including zero extremely premature births.

"Something special is happening in Avondale," Kahn says.

Kahn is Associate Chair for Community Health at Cincinnati Children's. He has a long track record of community health leadership including efforts to tackle substandard housing, childhood asthma, and other entrenched inner-city health challenges.

He credits the Start Strong success to an effort that placed emphasis on redesigning prenatal care to focus on mothers and their needs. This includes providing in-home support to every expectant mother in the neighborhood, and building trust by solving critical problems for women living in poverty.

The work started with an ethnography, a deep-dive listening exercise to understand the challenges facing expectant neighborhood moms. This increased insight and empathy between mothers and care providers, Kahn says. The Start Strong team held community dinners to meet people, hear their insights, share ideas, and get a sense of what does and does not work.



Caregivers learned many of the moms faced significant economic, social and environmental challenges to having a healthy pregnancy, Kahn says. Such challenges can produce toxic levels of stress, which experts theorize could be harming their yet-to-be-born babies.

Data from the listening exercise fed ideas that led to new approaches to supporting mothers. These were used to link and activate all the community providers serving women from Avondale. Community providers working with the neighborhood then learned from each other and customized their own approaches to meet the needs of expecting moms. According to Kahn, this created an engaged community outreach network of people who could talk, share information and help identify the women.

One goal of the program was to help participating obstetric clinics, home health visitors and community agencies to work together to reduce some of the barriers a mom might face in providing a healthy environment for her baby. These include streamlining access to prenatal care, enhancing referrals to community providers, or offering legal advocacy to address unstable housing or domestic violence.

“We centered the work around what moms need and want as opposed to technically perfect medical care,” Kahn says. “It’s about them, not our busy clinical schedule.”

But the first and primary barrier was finding every pregnant woman living in Avondale. Pregnant moms cannot be helped if no one knows who they are, Kahn says. It was finding moms that made other interventions possible.

## REDESIGN IN ACTION

One example of how these new approaches impacted the basic mechanics of health care delivery occurred at two clinics serving Avondale moms, one run by UC and another by Good Samaritan Hospital. The clinics transformed their clinical model of engagement, says Dawn Denno, Cincinnati Children’s Senior Director of Community and Population Health.

Depending on the clinic, a doctor or a nurse case manager was assigned to each expectant mom to serve as her central point

of contact and problem solver. Previously, a mom might see any number of different staff members during prenatal visits.

The new model called for building trust through forming more reliable relationships. Staff members have responded with enthusiasm to the change.

Denno recalls how staff at the Good Samaritan clinic reacted during a meeting when a pregnant mother with severe diabetes arrived after missing several previous appointments.

“One of the people in the room jumped up and said, ‘Ms. So and So just entered the building. I have to go where she is.’ It was like a surveillance system,” Denno says. “Moms come in, and they swarm them.”

## THE WORK CONTINUES

In January, Cradle Cincinnati officials announced the rate of fatal birth defects for Hamilton County, a leading cause of infant mortality. The report shows that from 2012 to 2016, when 486 infants died, 88 of those (18.7 percent) died from a fatal birth defect. According to the U.S. Centers for Disease Control and Prevention, one in 33 babies is born with a birth defect, but only a small percentage are fatal.

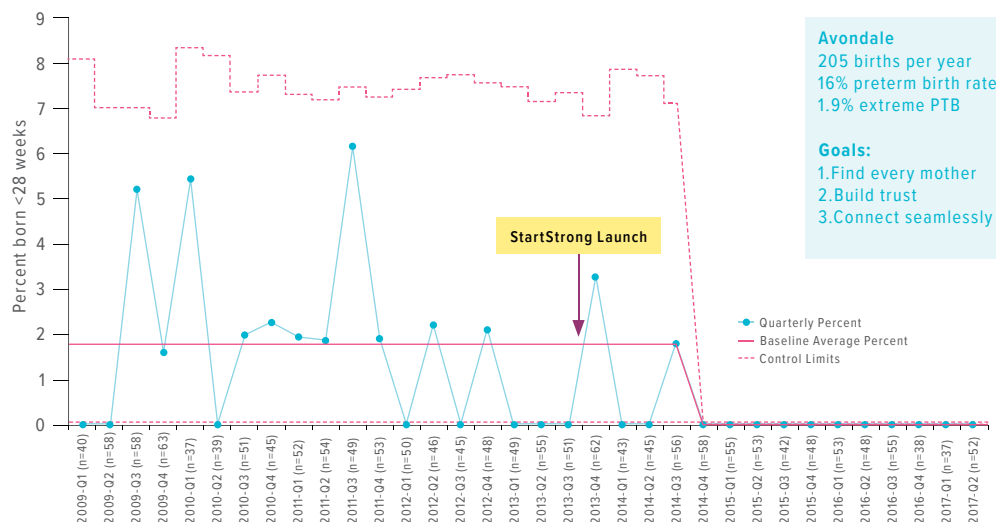
The announcement came with an urgent message from the community coalition that is Cradle Cincinnati to families in the Hamilton County-Cincinnati area. While not all birth defects can be prevented, families can take the steps to lower their risk of fatal birth defects.

These steps include: 1) controlling diabetes during pregnancy, because poor diabetes control during pregnancy increases the chance for birth defects and other problems, 2) take prenatal vitamins with folic acid, which can help prevent major birth defects of the developing brain and spine, 3) maintain a healthy weight, and 4) get a rubella vaccine, which can protect women against infections that can cause birth defects.

And very importantly, in the interest of finding every mother, officials urged women to see their health care provider as soon as they find out they are pregnant. ■

## Singleton Extreme Preterm Births in ZIP code 45229 (Avondale-North Avondale)

obstetric estimate of gestation <28 weeks



# The Light Bulb Called Reading

Cognitive Brain Research and Innovative Community Partnerships are Helping Schoolchildren Read by Helping Teachers Teach

by Tom O'Neill

**A**t birth, the human brain is wired to do some pretty instinctive things, like using fine motor skills to grasp a rattle or a parent's finger. But as babies become toddlers and beyond, grasping the abstract concepts of reading requires a bit more finesse.

The neural wiring must be developed and nurtured.

"And that makes sense," says Tom DeWitt, MD, Director of the Division of General and Community Pediatrics, "because you have to see and integrate all these visual and emotional parts. There's decoding. All these parts of the brain interact, so you have develop those pathways."

Today, research at Cincinnati Children's is driving an innovative partnership with Cincinnati Public Schools (CPS) to improve children's literacy, particularly the crucial benchmark of third-grade proficiency.

Our Reading and Literacy Discovery Center (RLDC) uses research to shape its evaluations and interventions for at-risk children at CPS and throughout the region. The RLDC specialists provide reports that describe each child's performance and suggest resources and strategies that parents, teachers and tutors can use to help improve proficiency.

A child's brain is a complicated canvas.

## READING ENERGIZES NEURAL CIRCUITS

In a widely cited May 2015 paper in *Pediatrics*, lead author John Hutton, MD, and colleagues including RLDC Program Director Tzipi Horowitz-Kraus, PhD, demonstrated for the first time positive correlation between exposure to books and reading at home

prior to kindergarten and differences in brain activity supporting literacy development and imagination. They have since published a series of groundbreaking, follow-up studies looking at other aspects of parent-child reading. This evidence has reinforced the view of reading as a critical aspect of brain development and health, and its integration into pediatric primary care.

Researchers at the RLDC have also provided new insights on the education front. Using regression maps, Horowitz-Kraus and colleagues illustrated positive correlation between narrative comprehension at ages 5 to 7 and subsequent scores on word-identification tests at age 11. These scientific insights are informing CPS' approach to better educating at-risk children.

"Honestly, getting access to Cincinnati Children's in this journey, it brought a different and wonderful perspective," says Cheryl Broadnax, Assistant Superintendent of Early Childhood Education at CPS. "It has allowed us to speed up interventions and better analyze data points. We're asking the deeper questions now."

"That's been a huge part of this partnership," she says. "It was fascinating to us, bringing all this knowledge together."

## TEACHING TEACHERS WORKS

The partnership began in 2016 with half-hour, twice-weekly "huddle calls" between Cincinnati Children's improvement experts, reading experts and a designated group of elementary school teachers. The goal was to provide teachers with access to real-time data on reading progress, along with training on novel intervention methods. The huddle approach made a rapid difference.



In four schools participating in the pilot program, the percentage of 3rd-graders reaching or exceeding national proficiency benchmarks grew from 43 percent in the fall quarter of 2016 to 61 percent by the winter quarter.

Conversely, in a control-group of four non-targeted schools with similar achievement levels, scores declined by four percentage points, to 35 percent from 39 percent.

The improvement at the targeted schools also contributed to an overall improvement for CPS in 3rd-grade reading proficiency from an “F” to a “C,” according to an Ohio report card on school performance released in September 2017.

“The things we learned,” Broadnax says, “spread rapidly throughout the district.”

Since starting with 15 teachers from five CPS elementary schools, the program has grown to more than 60 educators at 13 schools.

#### **AN UNEXPECTED “BOOST” FROM READING**

In a May 2017 study published in the journal *PLOS ONE*, a team of scientists led by Hutton demonstrated that engaging with 4-year-old children while reading books together seems to “turbocharge” their language and learning brain circuits.

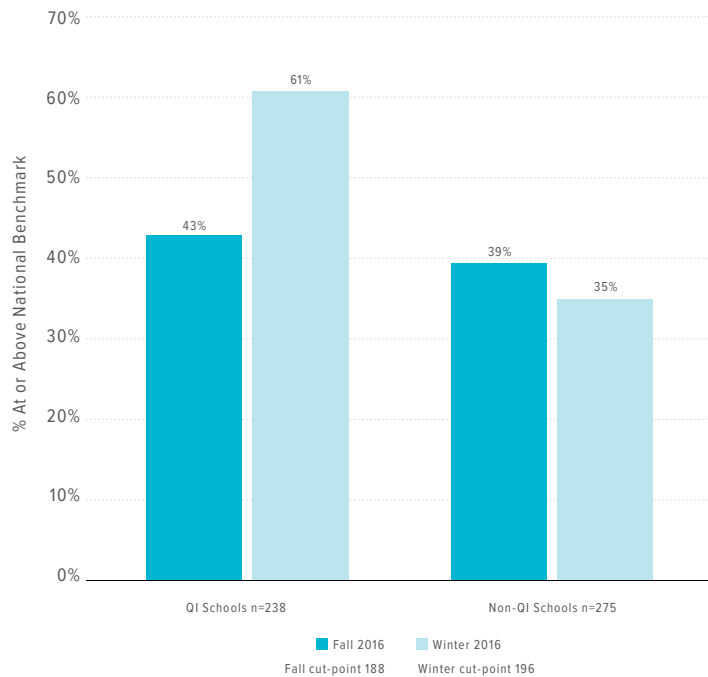
Using video observation and functional magnetic resonance imaging (fMRI), researchers found significantly greater brain activation in children who were more highly engaged during story listening. The study reinforces the value of “dialogic reading,” where the child is encouraged to actively participate in the story, and eventually becomes the storyteller. A related study published

“When you cannot  
read at third grade,  
you cannot do  
math at 10th grade.  
You cannot graduate.  
You cannot  
go to college.”

— Uma Kotagal, MBBS, MSc

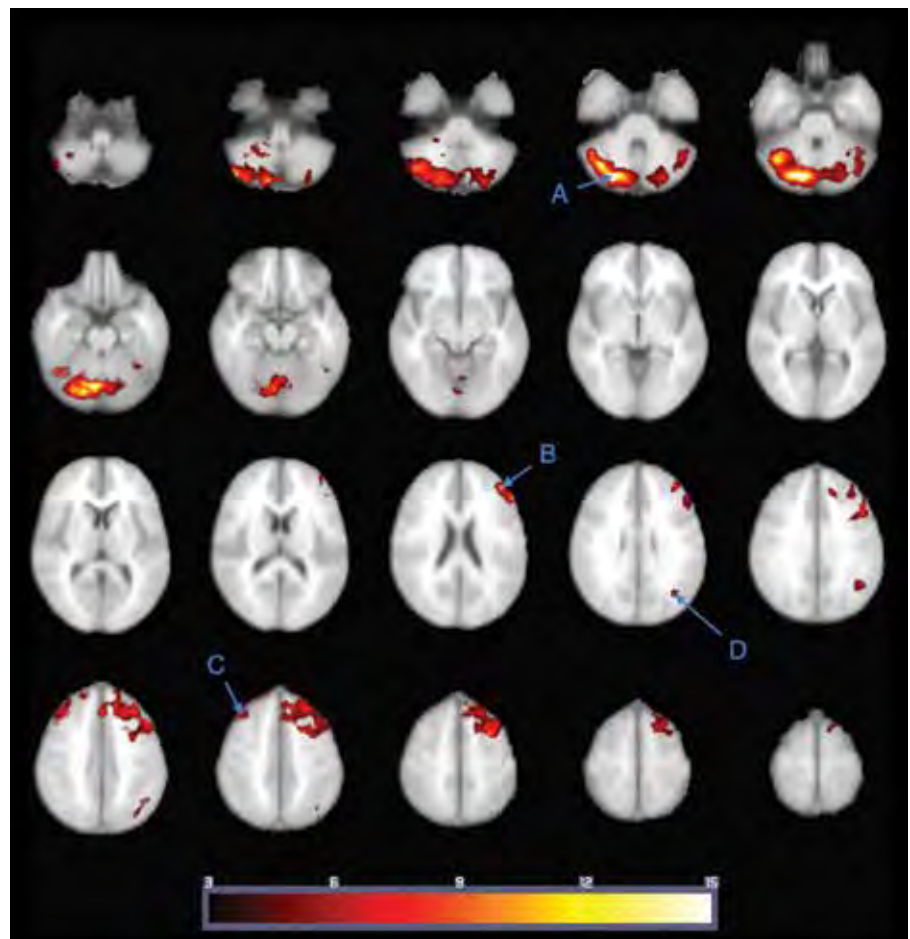


Cincinnati Public Schools 3rd Grade Students Meeting or Exceeding National Benchmark on MAP Reading Test  
4 QI Schools Compared to 4 Non-QI Schools



The chart (above) illustrates the significant rate of improvement in the percentage of targeted 3rd-graders who met national proficiency benchmarks (to 61 percent from 43 percent) in reading. In a control group, students with similar achievement levels at four non-targeted schools declined to 35 percent from 39 percent.

In research led by John Hutton, MD, scans (right) from a functional connectivity map of brain areas connected with a seed activation cluster illustrate how those areas correlate with child-engagement scores during story listening tasks. Clusters of activation are shown at coordinates: A (top row, image four), B, third row, image three), C (bottom row, image two) and D (third row, image four). Study authors note that while an estimated 5–12 percent of reading difficulty is rooted in an organic etiology such as dyslexia, the majority is attributable to inadequate motivation and/or stimulation required to learn to read.



in the *Journal of Pediatrics* in December 2017, which documented stronger brain function in children whose mothers read more interactively with them reinforced these findings. Coauthors included DeWitt, Horowitz-Kraus, Scott Holland, PhD, and Mekbib Altaye, PhD.

“The takeaway for parents is that they should engage more when reading with their child, ask questions, have them turn pages, and get more actively involved,” says Hutton, a clinical researcher in the RLDC and the Division of General and Community Pediatrics. “In turn, this helps ‘boost’ brain activation supporting critical early literacy skills such as imagery and comprehension. And it’s more fun, too!”

The studies and others conducted by the RLDC have focused on preschool-age children during a rapid span of brain growth and development who are preparing for kindergarten and beyond, emphasizing the major role of interactive reading at home. This is especially important given the disparities many children face, some arriving at kindergarten having never seen a book or with parents who are not strong readers themselves, DeWitt says.

**IT TAKES A VILLAGE ...  
OF RESEARCHERS, SPECIALISTS,  
EDUCATORS AND PARENTS**

Improving 3rd grade reading proficiency is one of the major priorities of the All Children Thrive Learning Network, an initiative launched by Cincinnati Children's in conjunction with several community agencies interested in child health.

Network participants focused on reading include teams of teachers, reading specialists, parents and agency partners including the United Way, the Success by Six Coalition, 4C's Child Care Resource Center, Community Action Agency/Head Start, and the Strive Partnership.

"Literacy at third grade is a very important predictor of future outcomes," says Uma Kotagal, MBBS, MSc, a senior fellow at Cincinnati Children's and Executive Leader for Population and Community Health. "When you cannot read at third grade, you cannot do math at 10th grade. You cannot graduate. You cannot go to college. As a result, long-term health outcomes decline, and life expectancy suffers."

While literacy can be seen as a vital measure of child health, Cincinnati Children's sees its role as being a convener and catalyst when it comes to tackling the issue, Kotagal says. Cincinnati Children's provides expertise in improvement science techniques, while educators, families, and community leaders play the central role in setting goals and doing the work.

With encouraging signs of progress so far, the All Children Thrive network plans to further expand the reading program within CPS in 2018 as well as to begin exporting lessons learned to school districts in other states.

"Community buy-in is fundamental," says DeWitt, who leads the 3rd-grade reading task force at Cincinnati Children's. "That's one of the exciting things going on in the community-health area. Block by block, leaders are creating a culture where reading is as important as anything you can do for a child."

At CPS, Broadnax calls these the 'ah-hah' moments of the classroom. "It just really changed our culture," she says. "It's powerful for teachers to have that space to be much more analytical."

"To ask, 'Am I giving every kid what they need?'" she says.

The answers to that question could help shape and nurture the "reading brains" of future researchers and doctors. Maybe even a reading specialist or two. ■

## ABOUT THE READING & LITERACY DISCOVERY CENTER

- For the past two summers, reading specialists and diagnosticians have partnered with the Cincinnati and Hamilton County Public Library to evaluate the reading difficulties of children from Cincinnati Public Schools considered at-risk of failing 3rd-grade reading guarantee measures.
- Reading specialists evaluated reading skills and responses to remediation programs for first-grade students at Rees E. Price Academy in the Price Hill neighborhood of Cincinnati.
- In the summer of 2017, reading specialists conducted individual and small group therapy programs for children recognized with reading difficulties.
- The center's clinical program introduced a reading science course at Xavier University and launched an internship program for graduate-level Xavier students pursuing reading certifications.



Jack Bekins, 9, of suburban Cincinnati, (above) was diagnosed three years ago with dyslexia, the most common form of language-based learning disabilities. Here, he has a reading session with Kimberly Rotundo, MEd, the clinical program manager at the Reading and Literacy Discovery Center. In an adjacent room, Jack's mom, Jennifer Bekins, watched the session on a computer screen while wearing headphones. She is a coordinator in Speech Pathology at Cincinnati Children's and once worked with Rotundo. "This has been invaluable for him," she says, "in helping to develop not only his reading skills, but him as a whole person."

# A Neighborhood Rises

An Innovative Collaboration Between Community Members and Cincinnati Children's is Transforming Price Hill's Health One Doorstep at a Time

by Tom O'Neill

**T**he October morning draped a fog blanket over Price Hill, a Cincinnati neighborhood where 52 percent of households live below the poverty line.

Here, health statistics have historically cast a long shadow. That is changing, driven by an unusual, two-way approach to scientific research, in which Cincinnati Children's and residents are co-investigators, actively shaping the direction—and execution—of research projects designed to improve health in Price Hill.

Healthy Homes, an initiative started in 2010 by Santa Maria Community Services and Cincinnati Children's, employs and empowers community leaders, called block captains, who live and work in the neighborhood.

Price Hill's children suffer from disproportionately high rates of preterm birth, infant mortality, and medical and

psychiatric hospitalization. To improve these disparities, Healthy Homes engages in the community by providing familiar faces to families who rarely, if ever, go to clinics or public health agencies.

"For most people," says Carley Riley, MD, MHS, of the Division of Critical Care Medicine, "including academics and community members alike, this kind of partnership and way of working is entirely new."

The collaborative structure has been an invaluable part of its success.

## RESIDENTS AS RESEARCHERS

"A community of families that are able to solve problems for themselves and each other, you cannot unlearn something like that," says Rachel Smith, a Price Hill mother of three and an integral member of the community-academic research team led by Riley.

Recently, Riley's team has brought block leaders and other neighbors into the research sphere, training them to serve as "peer researchers." In this role, block leaders co-conduct in-depth interviews of residents, and help Cincinnati Children's experts interpret responses.

Since July 2016, the team has been conducting a mixed-methods study "Eliminating Health Disparities Block by Block," thanks in part to a Diversity and Health Disparities Research Award from Cincinnati Children's.

The aim is to identify the factors that can help block captains best identify and engage the most at-risk families, and develop trusting relationships with them.

Each family's "pilot package" includes identifying a safe place for every infant to sleep, offering information on safe-sleeping practices, providing smoke detectors and other home-safety equipment, and at





least 15 age-appropriate books for every child in the home.

The group also provides contact information for prenatal and pediatric medical resources.

#### **HOUSE-BY-HOUSE APPROACH**

Riley's team—including parents—is also co-creating a community-based research network, through a series of co-learning sessions and shared experiences that have researchers and community members learning with and from each other to co-produce research of relevance to the community.

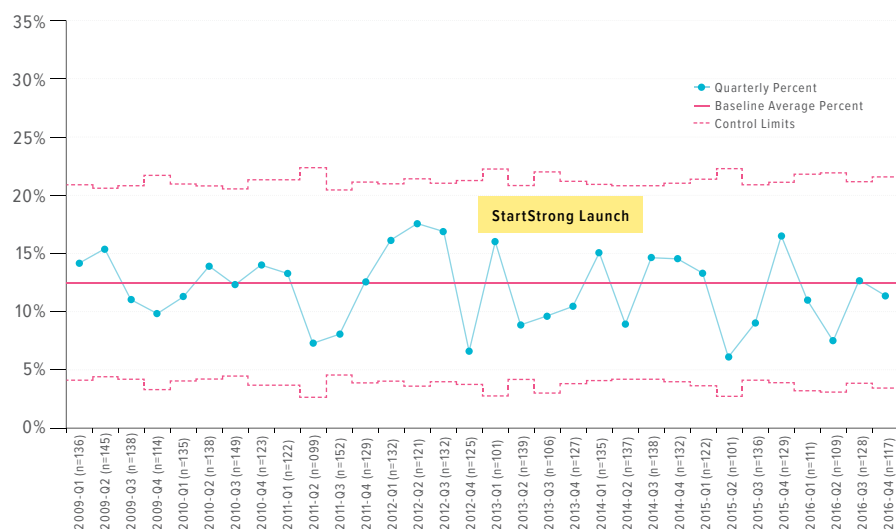
The network is supported, in part, by a Eugene Washington Engagement Award from the national Patient-Centered Outcomes Research Institute (PCORI).

Healthy Home's team members from Cincinnati Children's include a research assistant, a post-doctoral fellow and a

“Having the qualitative along with the quantitative gives us a more robust picture of what and how we impact lives in Price Hill.”

– Chellie McLellan,  
Executive Director at Healthy Homes

Resident Singleton Preterm Births in Zip Code 45204 & 45205  
(East/Lower Price Hill), by Quarter 2009-2016  
(Obstetric estimate of gestation <37 weeks)



Dates and Interventions

July 2013	Jan 2014	March 2015	June 2015	Aug 2015	Jan 2016
StartStrong launch	Mom's group	Home visits spread to Price Hill	Learning Collaborative	Nurse case manager spread to Price Hill	Community Health Worker/Home Visitor Shortage



Co-researchers in their Price Hill street-level element: (from left, Chellie McLellan, Executive Director at Healthy Homes; Carley Riley, MD, MHS, of Cincinnati Children's Division of Critical Care Medicine, and block captains Rachel Smith and Valerie Perez. The team focuses its research projects on pregnant women and those with children 6 and younger. The key, they say, is to meet people where they live, elevating "door-to-door science" from theory to practice.

clinical investigator. The community-based members include Executive Director Chellie McLellan and block captains such as Smith and Valerie Perez.

Progress has taken root. The Healthy Homes Block by Block initiative continues to grow its neighborhood-based social network, connecting families with pregnant women and children 6 and younger to resources and to each other.

"This type of research brings greater depth and meaning to statistical information," McLellan says. "Having the qualitative along with the quantitative gives us a more robust picture of what and how we impact lives in Price Hill."

In the first three years, the program grew from five blocks and 52 households to 18 blocks and 105 households. The ultimate goal is to identify and serve every at-risk household across Price Hill's 145 blocks.

"For Price Hill, it's of huge importance," says Perez, a mother of four. "More families need to be reached and educated on the health risks of not seeing a doctor can take on them and their children."

## THE POWER OF STORIES

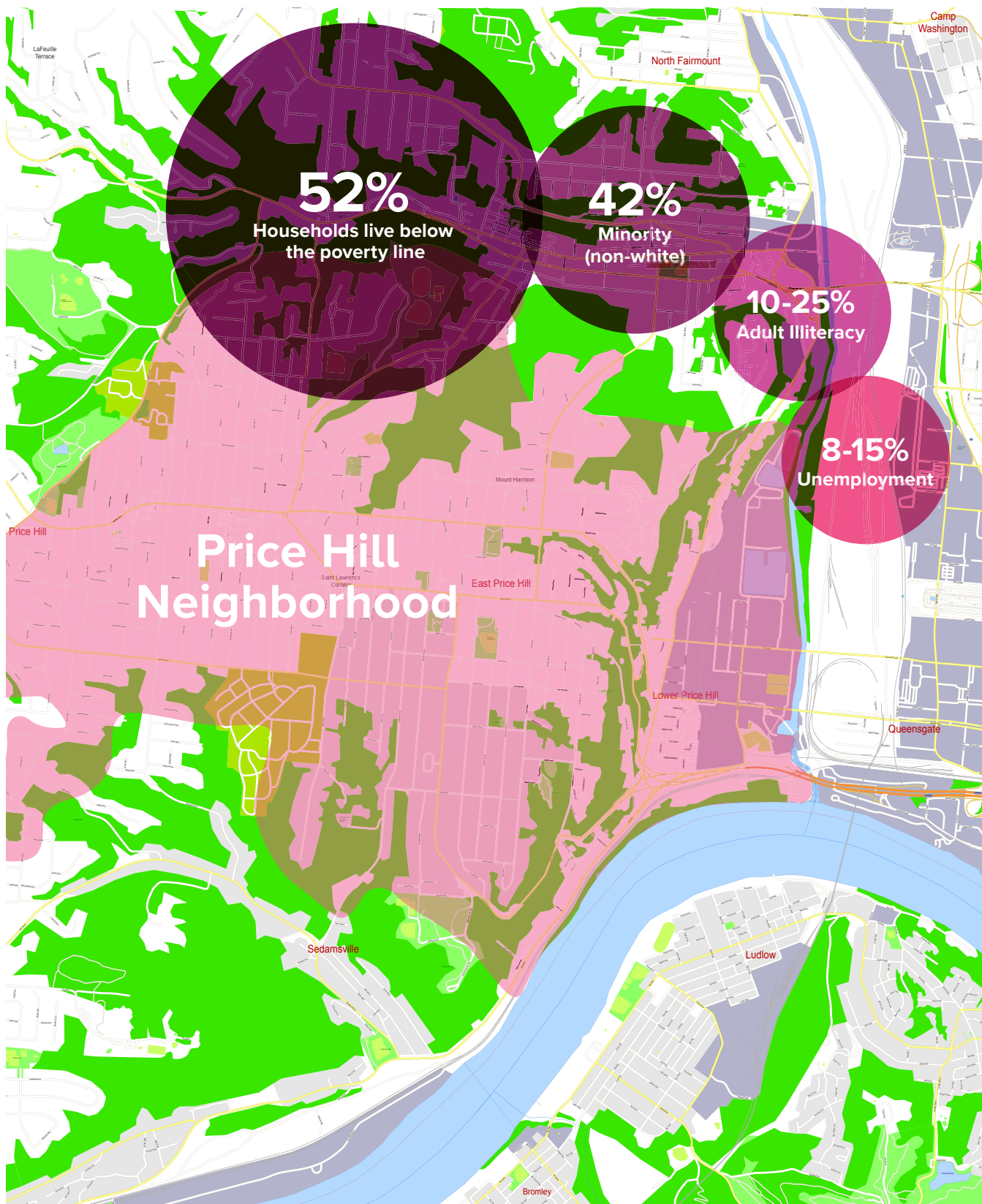
Such data, gathered through stories, helps inform the larger Cincinnati Community Health Initiative.

The network of block leaders and captains has been instrumental in overcoming skepticism among Price Hill residents about important health messages. Their involvement also enriches how health care providers understand the people behind the label "at risk."

"What's interesting," Smith says, "is the sense of community you get by living here and how the residents do not see themselves as living in poverty, even though from a societal standpoint, they by all means are. If they are rich in religion and in family, they do not see it as poverty."

For Riley, her involvement in the program brings a range of rewards.

"It has brought greater richness of understanding, increasing urgency for action, and a greater breadth and depth of potential solutions to our work," she says. "Seeing this evolution is deeply motivating and inspiring."



In the first three years, the Healthy Homes program has grown exponentially, from five blocks and 52 households to 18 blocks and 105 households. Fiscal year 2016-17 saw the creation of zones for targeted sections of neighborhoods, and the number of households served decrease by one, as families move away or their youngest child reaches age 7. The ultimate goal is to identify and serve every at-risk household across Price Hill's 145 blocks. *Neighborhood stats based on data from U.S. Census Bureau, American Community Survey.*



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# GRANTS

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From July 1 through Sept. 30, researchers at Cincinnati Children's were awarded 164 grants valued at \$118.4 million in total costs. Here are the recipients of grants of \$1 million or more in total costs:

**Matthew Alder, MD, PhD,**

**Critical Care**, will study the role of the glycoprotein olfactomedin 4 in septic shock, using a four-year, \$1 million grant from the National Institute of General Medicine Sciences.

**David Bernstein, MD, MA,**

**Infectious Diseases**, received a three-year, \$5.6 million grant from the National Institute of Allergy and Infectious Diseases for his role with the continued development of vaccine and treatment evaluation units, an agency program for which Cincinnati Children's is one of nine member hospitals.

**Jorge A. Bezerra, MD,**

**Director, Gastroenterology, Hepatology and Nutrition**, received a five-year, \$1.2 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases, for his role in the Digestive Health Center's Bench to Bedside Research in Pediatric Digestive Disease program.

**Samantha Brugmann, PhD,**

**Plastic Surgery**, received an eight-year, \$8 million grant from the National Institute of Dental and Craniofacial Research, to study the therapeutic potential of neural crest cells, which are formed from the embryonic ectoderm cell layer during fetal development.

**Prasad Devarajan, MD,**

**Director, Nephrology and Hypertension**, will explore critical translational studies in pediatric nephrology, using a five-year, \$1.2 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases.

**Judith Dexheimer, PhD,**

**Emergency Medicine**, received a four-year, \$1.5 million grant from the National Library of Medicine, for her work on the project "Personal Health Record for Youth Emancipating from Foster Care."

**Robert Frenck, MD,**

**Infectious Diseases**, received a one-year, \$2.9 million grant from the National Institute of Allergy and Infectious Diseases, for his work with the vaccine and treatment evaluation units program. He also received a two-year, \$1 million grant from PATH Vaccine Solutions for a Phase 1 study on the safety and immunogenicity of live-attenuated universal flu vaccine followed by an inactivated version.

**Christina Gross, PhD,**

**Neurology**, received a four-year, \$1.9 million grant from the National Institute of Neurological Diseases and Stroke, to study MicroRNA-mediated silencing of the Kv4.2 complex in epilepsy.

**Margaret Hostetter, MD,**

**Director, Cincinnati Children's Research Foundation**, received a five-year, \$7.2 million grant from the National Institute of Child Health and Human Development, for her work with the Pediatric Scientist Development Program.

**Rulang Jiang, PhD,**

**Developmental Biology**, received a five-year, \$3.2 million grant from the National Institute of Dental and Craniofacial Research, to study the development of the mandible, or lower jaw.

**Helen Jones, PhD,**

**General and Thoracic Surgery**, will study placental-specific therapy for fetal growth restriction, with a five-year, \$1.9 million grant from the National Institute of Child Health and Human Development.

**Jane Khoury, PhD,**

**Biostatistics and Epidemiology**, received a five-year, \$3.5 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases, to study the level and timing of diabetic hyperglycemia *in utero*.

**Xinhua Lin, PhD,**

**Developmental Biology**, received a four-year, \$1.2 million grant from the National Institute of General Medical Sciences, to study the molecular mechanisms regulating intestinal stem cell activities and homeostasis.

**Qing Richard Lu, PhD,**

**Scientific Director, Brain Tumor Center**, will study chromatin remodeling control of myelination and remyelination, an insulating layer that surrounds the axon of some nerve cells, with a five-year, \$2.2 million grant from the National Institute of Neurological Disorders and Stroke.

**Satish Madala, PhD,**

**Pulmonary Medicine**, will study the therapeutic benefit of Hsp90 inhibition in pulmonary fibrosis, using a three-year, \$1.8 million grant from the Department of Defense.

**Peter Margolis, MD, PhD,**

**Co-Director, James M. Anderson Center for Health System Excellence**, received a two-year, \$1.6 million grant from the Patient-Centered Outcomes Research Institute for his work with the Pilot Learning Health System.

**Jeffery Molkentin, PhD,**

**Molecular Cardiovascular Biology**, received a five-year, \$1.8 million grant from the National Heart, Lung, and Blood Institute, to study the mechanisms of cardiovascular disease.

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## GRANTS

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Louis Muglia, MD, PhD,

**Co-Director, Perinatal Institute**, received a one-year, \$2.6 million grant from the Bill & Melinda Gates Foundation, to analyze the potential use of selenium supplementation, and possibly other micronutrients, to prevent preterm birth.

James Mulloy, PhD,

**Experimental Hematology and Cancer Biology**, will study leukemia stem cell polarity and differentiation therapy, using a five-year, \$2.4 million grant from the National Cancer Institute.

Ertugrul Ozbudak, PhD,

**Developmental Biology**, received a four-year, \$1.2 million grant from the National Institute of General Medicine Sciences, to examine elucidating the mechanism of precision in vertebral segmentation during embryonic development.

Qishen Pang, PhD,

**Experimental Hematology and Cancer Biology**, received a four-year, \$1.5 million grant from the National Institute of Child Health and Human Development, to study the FA DDR pathway in germline integrity that is vital for fertility and the health of offspring.

Nancy Ratner, PhD,

**Experimental Hematology and Cancer Biology**, will study the mitogenic activities in neurofibromatosis, a genetic disorder that causes tumors to form on nerve tissue, using a five-year, \$2.2 million grant from the National Institute of Neurological Diseases and Stroke.

Richard Ruddy, MD,

**Emergency Medicine**, received a four-year, \$2.7 million grant from the Health Resources and Services Administration for his role with the Pediatric Emergency Care Applied Research Network (PECARN) project.

Lisa Shook, MA, MCHES,

**Hematology**, received a four-year, \$2.1 million grant from the Health Resources & Services Administration, to study sickle cell treatment and outcomes research in the Midwest.

Paul Spearman, MD,

**Director, Infectious Diseases**, received a two-year, \$2.9 million grant from the National Institute of Allergy and Infectious Diseases, for his role in improving protocols for the continued development of vaccine and treatment evaluation units. The agency also awarded him a two-year, \$1.2 million grant to study mucosal protection against HIV generated by PIV5 priming.

Daniel Starczynowski, PhD,

**Experimental Hematology and Cancer Biology**, received a four-year, \$2 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases, to study targeting IRAK1 as a therapeutic approach for myelodysplastic syndromes, a group of blood disorders and precursor to leukemia.

Laura Walkup, PhD,

**Pulmonary Medicine**, received a two-year, \$1 million grant from the National Heart, Lung, and Blood Institute, to study early detection of regional bronchiolitis obliterans syndrome, an irreversible and obstructive lung condition, in bone marrow transplant patients using ultra-short echo time in methods for magnetic resonance imaging.

Russell Ware, MD, PhD,

**Director, Hematology**, received a five-year, \$3.5 million grant from the National Heart, Lung, and Blood Institute, for his role with the Phase I/II pilot study "Realizing Effectiveness Across Continents with Hydroxyurea (REACH)" in the treatment of children with sickle cell anemia.

Joshua Waxman, PhD,

**Molecular Cardiovascular Biology**, received a four-year, \$1.6 million grant from the National Heart, Lung, and Blood Institute, to study the molecular mechanisms of atrial development and regeneration.

Jeffrey Whitsett, MD,

**Co-Director, Perinatal Institute**, will study lung and cardiovascular development and disease pathogens, using a five-year, \$1.3 million grant from the National Heart, Lung, and Blood Institute.

Jason Woods, PhD,

**Director, Center for Pulmonary Imaging Research**, received a three-year, \$1.3 million grant from Polarean Inc., for his role in a Phase III trial on HP 129Xe magnetic resonance imaging as a functional pulmonary biomarker in pediatric lung disease.

Aaron Zorn, PhD,

**Developmental Biology**, will study the developmental mechanisms of trachea-esophageal birth defects, using a five-year, \$2.2 million grant from the National Institute of Child Health and Human Development.

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## HONORS

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### Boat Honored with Howland Award from American Pediatric Society

Thomas Boat, MD, Pulmonary Medicine, has been awarded the 2018 John Howland Award, the highest honor bestowed by the American Pediatric Society. The award honors leaders in academic pediatrics whose significant contributions have advanced the lives of children and the profession of pediatrics through clinical care, scientific discovery, mentorship and service.

Boat graduated from the University of Iowa Carver College of Medicine in 1966, where he also recently received a Distinguished Alumni Award. His long career began with years of pulmonary clinical care and cystic fibrosis research that led him to the University of North Carolina in Chapel Hill.

He advanced to chair the Department of Pediatrics there. In 1993, he moved to Cincinnati where he became Chair of Pediatrics, Director of the Research Foundation, and Physician-In-Chief as Cincinnati Children's. He recently resigned from roles as Dean of the University of Cincinnati College of Medicine and as chief executive officer of University of Cincinnati Physicians.



Thomas Boat, MD

[Katherine Auger, MD, MSc,](#)

**Hospital Medicine**, received the 2017 Outstanding Research Award during Pediatric Hospital Medicine 2017 in Nashville, an annual meeting sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

[Ray Bignall, MD,](#)

**Behavioral Medicine and Clinical Psychology**, received the William Cotton Pediatrician Advocate Award from the Ohio Chapter of the American Academy of Pediatrics. His advocacy work includes creating the “#100Words Project,” which collects and shares stories from pediatric patients, parents and child health professionals.

[Patrick Brady, MD, MSc,](#)

**Hospital Medicine**, received the 2017 Quality and Patient Safety Award during Pediatric Hospital Medicine 2017 in Nashville.

[Jose Cancelas, MD, PhD,](#)

**Deputy Director of the Hoxworth Blood Center** and stem cell group leader at the Cancer and Blood Diseases Institute, was selected as a 2017 inductee to the National Blood Foundation Hall of Fame.

[Alvin Crawford, MD,](#)

**Professor Emeritus, and Founding Director of the Crawford Spine Center**, received the Pioneer Award from the National Medical Fellowships organization, a nonprofit dedicated to increasing the number of underrepresented minority physicians and other professionals in health care.

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## HONORS

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Alexei Grom, MD,

**Research Director, Rheumatology,**

Grant Schulert, MD, PhD,

**Rheumatology,**

and Sherry Thornton, PhD,

**Rheumatology,** received the Gold Medal Suzanne Dehoche Prize from Kourir, a French organization for parents of children with JIA, at the European Pediatric Rheumatology Congress, in recognition of their work on discoveries that presage new treatments for JIA.

Donald Gilbert, MD, MS,

**Neurology,** was elected to the Board of Directors of the Child Neurology Society.

Ann Kummer, PhD,

**Speech-Language Pathology,** received a 2017 Honors of the Association award from the American Speech-Language-Hearing Association (ASHA). The group's highest honor recognizes her distinguished contributions to the field of communication sciences and disorders. Her achievements include several leadership positions within ASHA, developing a patented listening device, numerous peer-reviewed articles, 22 book chapters, and the textbook, "Cleft Palate and Craniofacial Anomalies."

Tesfaye Mersha, PhD,

**Asthma Research,** received the 2017 African Professionals Network Business and Professional Achievement Award in October for his distinguished research and professional contributions to pediatric genomics.

Daniel Starczynowski, PhD,

**Experimental Hematology and Cancer**

**Biology,** was inducted into the 2017 class of the *Cincinnati Business Courier's* "Forty Under 40."

### Takebe Receives High Honor from Japan

Takanori Takebe, MD, Gastroenterology, Hepatology and Nutrition, received the inaugural Japan Agency for Medical Research and Development (AMED) Chairperson Prize. The award, bestowed by Prime Minister Shinzo Abe, recognizes Takebe's leadership in developing innovative methods to produce liver buds from human iPS cells. In addition to his post at Cincinnati Children's, Takebe is an associate professor with the Department of Regenerative Medicine at Yokohama City University.



Takanori Takebe, MD

### Ware's Research in Africa Selected Among *Blood's* Top 10

Russell Ware, MD, PhD, Director, Division of Hematology, received a high honor from the editors of *Blood*, the journal of the American Society of Hematology, for his role as a senior author of this paper: Novel Use Of Hydroxyurea in an African Region With Malaria (NOHARM): a Trial for Children With Sickle Cell Anemia. The paper was selected as one of the journal's 10 most outstanding manuscripts of the year from more than 1,000 articles published by the journal in 2017.



Russell Ware, MD, PhD



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*Research Horizons* is published by the Cincinnati Children's Research Foundation to showcase work that changes outcomes for children.

Produced by:  
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Cincinnati Children's  
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