EXPERT CARE FOR HORMONE-RELATED CONDITIONS

children's health
Children's Medical Center

UT Southwestern
Pediatric Group

Specialty care provided by UT Southwestern physicians

BUILDING ON A LEGACY, LEANING INTO THE FUTURE

MISSION

Since 1913, the mission of Children's HealthSM has been to make life better for children. The flagship hospital of Children's Health, Children's Medical Center Dallas, along with Children's Medical Center Plano, 23 specialty centers and Our Children's House for inpatient and outpatient rehabilitation, compose the eighth-largest pediatric health care provider in the nation. In 2018, we saw nearly 300,000 children.

Our unique skill set and experience, combined with cutting-edge techniques and technology, allow us to provide definitive, comprehensive pediatric endocrinology care. These attributes, along with hard work, creativity and a dedication to research, patient care and medical education have allowed us to achieve our vision of making Children's Health among the very best medical centers, ranking in all 10 specialties by *U.S. News & World Report.* We believe there is no better affirmation of our mission than seeing healthy patients leave the hospital.

ACADEMIC AFFILIATION

Our success is the result of a close collaboration with UT Southwestern.

In addition to extending our academic mission of training the next generation of physicians, this one-of-a-kind relationship affords patients access to world-renowned expertise in every aspect of pediatric endocrinology care. With personalized treatment plans and leading research, we offer a full continuum of care from infancy through adulthood.

DEAR COLLEAGUES,

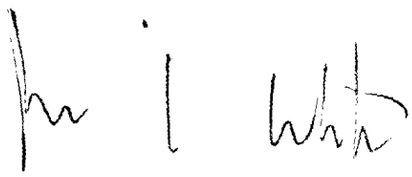
Perrin White, M.D., Division Director.

For over 25 years, I have been privileged to be the Director of the Division of Pediatric Endocrinology at Children's Health and UT Southwestern Medical Center. Before I arrived, there was only one pediatric endocrinologist on the staff; we have since grown to 17 physicians and 5 nurse practitioners, along with more than 20 endocrine nurses, diabetes educators, dieticians and social workers. We have 19,000 ambulatory patient encounters yearly including caring for over 2000 children with diabetes. We are one of the largest centers in the country for the care of transgender children, and see large numbers of children with medical complications of obesity, including elevated blood levels of lipids such as cholesterol.

In addition to delivering excellent patient care, we are proud of our efforts to improve care through our NIH-supported clinical research program. For example, we are one of 13 centers nationwide for TrialNet, a consortium to develop treatments to prevent type 1 diabetes. We are participating in a definitive clinical trial of a "bionic pancreas," a highly automated device to continuously deliver insulin in patients with type 1 diabetes at a rate that varies depending on the blood glucose level. Finally, we are trying to improve management of congenital adrenal hyperplasia, an inherited inability to synthesize the steroid hormone cortisol. As the lead site in a nationwide project at 4 institutions, we are studying whether abiraterone acetate, a drug that blocks the synthesis of androgens (male sex hormones), can help control the high levels of these hormones that are often found in patients with this disorder.

We leverage these activities in patient care and clinical research to provide educational experiences to learners of all levels, particularly in our fellowship program in pediatric endocrinology, which will celebrate its 25th anniversary in July 2020. For more about our fellowship program, see the inside back cover of this brochure.

After 25 years, coming to work every day and interacting with a great group of colleagues remains the highlight of my day. We look forward to continuing to serve the endocrinology needs of the North Texas region.



Perrin C. White, M.D.

Division Director at Children's Health
Professor at UT Southwestern Medical Center

POWERFUL OUTCOMES

RANKED NO. 18
BY *U.S. NEWS & WORLD REPORT*

CALLING DALLAS, TEXAS, HOME SINCE **1964**

17 Pediatric Endocrinologists, **5** APNs
and **9** Certified Diabetes Educators driving
breakthroughs in **8** distinct programs

- Center for Obesity and its Consequences in Health (COACH)
- Cystic Fibrosis-Related Diabetes
- Diabetes
- GENder Education and Interdisciplinary Support (GENECIS)
- General Endocrinology
- Lipid Disorders
- Thyroid Cancer
- 22q Deletion Syndrome

Practice Administrator Gayathri Ram with Nancy Gallegos and Diana Corral in the Endocrinology Clinic.

DIABETES APP HELPS FAMILIES DELIVER SICK-DAY CARE–ON THEIR OWN

It's hard for parents to care for children with type 1 diabetes (T1D) – and even harder when those kids have a cold or the flu. Soumya Adhikari, M.D., Pediatric Endocrinologist at Children's Health℠ and Associate Professor of Pediatrics at UT Southwestern, has seen this first-hand as an endocrinologist who fields questions about what to do when glucose and ketone levels fluctuate during illness. That's why he and his colleagues at Children's Health and UT Southwestern created an innovative solution: a mobile app called *Diabetes Advisor*.

Pictured above from left to right: Carlos Gomez, Data Analyst, Virtual Health; Soumya Adhikari, M.D., Endocrinology; Ronak Assadi, Program Manager, Virtual Health; Molly Beyer, Research Coordinator, Virtual Health; and Jamie Wood, Diabetes Educator, Endocrinology.

The app uses real-time biometric data, like blood sugar readings, to create sick day action plans. This empowers families to take charge of T1D care, and it helps them answer pressing questions without having to schedule an appointment or wait for our team to call them back.

"Our patients know they can reach a nurse or doctor day or night, but this just gives them one more tool to supplement our in-person availability, so we're excited about how this helps families manage sick days more independently and still get some immediate affirmation that they're doing the right thing," says Dr. Adhikari.

PERSONALIZED SICK DAY PLANS

To use Diabetes Advisor, parents enter their child's blood sugar levels, urine or blood ketone levels, and answer standardized questions about fluid and food intake. The app uses this information – plus the child's age, weight and normal insulin regimen – to calculate recommended insulin doses and fluid intake. It can then send optional reminder alarms to families to prompt them to recheck their child on a set schedule.

DIGITAL DIABETES CONGRESS APP AWARD

Families can also use the app to access the full diabetes education library that they receive from the Children's Health treatment team at their initial visit, along with some innovative, mobile-friendly content, such as links to selected podcasts and videos.

HOW AN ALGORITHM "AUTOMATES" TREATMENT

Dr. Adhikari and his team floated the idea for Diabetes Advisor during a department meeting about new diabetes sick day guidelines a few years ago.

"We know sick days are stressful, and we encourage parents to call us day or night," Dr. Adhikari says. "But we also want parents to feel empowered to manage care without us when appropriate, and we thought an app could help."

When he pitched the idea to our Virtual Health Team, they were on board and started working with Dr. Adhikari to turn the idea into usable technology. For example, he created a table that mapped out answers to questions that parents typically ask when their child is sick. Our developers turned these answers into an algorithm that calculates the treatment plan.

We launched Diabetes Advisor in November 2018, and we introduce it to families as part of their diabetes self-management education (DSME) sessions. Anyone can download the app and access the educational content, but the ketone manager is only available to Children's Health patients and families.

"More than 1,000 users have downloaded it so far, and we've received wonderful feedback from parents," Dr. Adhikari says.

THREE TIPS FOR DEVELOPING A HEALTHCARE APP

Diabetes Advisor was Dr. Adhikari's first foray into mobile healthcare tech and he has three pieces of advice for other would-be app builders:

1. Start with a needs and availability assessment. Our team scoured the app landscape to make sure a similar app didn't exist. "We didn't want to invest time in this if there was another app that we could refer patients to," Dr. Adhikari says.

2. Partner with people who have the right skills. Dr. Adhikari and our Virtual Health Team brought together experts in everything from design to user experience to writing code. "This was very much a partnership with other people who know far more about how to make an app than clinicians do," he says.

3. Decide what outcomes to track. "From day one, think about what you're going to track to know if your efforts have been worthwhile," Dr. Adhikari says. "For Diabetes Advisor, we're tracking app-related data — downloads, sick day utilizations and the number of families using the app. We're also looking at how the number of phone calls, ED visits and admission rates change before and after downloading the app."

MOBILE HEALTH WILL CHANGE HEALTHCARE DELIVERY

Dr. Adhikari is already mulling ideas for the next iteration of the app. One of those is the possibility of assessing a family's knowledge of their child's diabetes care through a "test" delivered via the app. The results would help providers tailor T1D educational content at the child's next visit to a family's demonstrated needs.

"When it comes to chronic disease management, we've just touched the surface of what services might be deliverable through apps," he says. "Mobile health is truly a game changer."

CAN AN INNOVATIVE DRUG HELP KIDS WITH CONGENITAL ADRENAL HYPERPLASIA REACH NORMAL HEIGHT?

Children with congenital adrenal hyperplasia (CAH) often have elevated androgen levels, which leads to early puberty, accelerated bone maturation and short adult stature. Traditional glucocorticoid treatment, including hydrocortisone, is a Catch-22: It controls androgen levels, but high daily doses slow patients' linear growth and puts them at risk for excess weight gain.

Dr. Perrin White in the Edocrinology Clinic.

Researchers at Children's Health℠ and UT Southwestern are working to improve on this: They're leading a Phase I multicenter study to determine if abiraterone acetate, an oral androgen biosynthesis inhibitor, can safely lower patients' androgen levels and reduce hydrocortisone doses.

"Kids do pretty well with hydrocortisone and fludrocortisone, but we're hopeful that this new approach will lower patients' exposure to excess androgens and glucocorticoids and, ultimately, improve their quality of life," says Perrin White, M.D., Director of the Division of Pediatric Endocrinology at Children's Health and Professor at UT Southwestern. Dr. White is the principal investigator for the study.

CAH REDUCES PATIENTS' ADULT HEIGHTS

More than 90 percent of CAH cases are caused by 21-hydroxylase deficiency. Children with the disorder are unable to synthesize cortisol normally. This leads the adrenal cortex to overproduce cortisol precursors, which are then metabolized to androgen precursors and subsequently to testosterone.

Melissa Ham, M.D with patient Jimena Ojeda. age 6, in the Edocrinology Clinic.

Left untreated, CAH exposes patients to high levels of androgens and leads to rapid growth in childhood. Their bones mature faster than normal, causing the growth plates to close too early. Children with poorly controlled CAH tend to be tall children, but short adults.

THE CATCH-22 OF CAH TREATMENT

Controlling androgen levels requires supraphysiological doses of hydrocortisone – generally 50 percent more than needed for other forms of adrenal insufficiency.

While treatment replaces cortisol and controls androgen levels, the high doses themselves may slow down growth. On average, patients with CAH will be around three inches shorter than their expected adult height.

REPURPOSING A PROSTATE CANCER TREATMENT

A few years ago, Dr. White and his colleagues began brainstorming ways to solve this. "We got the idea of short circuiting this problem by using a drug that would block the synthesis of all sex hormones," he says.

This idea led them to abiraterone acetate, an FDA-approved treatment for prostate cancer that inhibits a key enzyme required for testosterone synthesis. The idea is that abiraterone acetate would minimize androgen secretion in patients with CAH. This, in turn, would slow down bone maturation, as well as reduce the amount of hydrocortisone needed.

"We would use this before a child is supposed to go through puberty," Dr. White says. "Once they go into puberty, they need to make testosterone or estrogen. But prepubertal kids don't make a lot of sex hormones normally, so there's no problem with blocking it."

Children with CAH often achieve a final height 1-2 SD's below their genetic potential

PHASE I TRIAL

Dr. White is the principal investigator for the multicenter Phase I study, which began recruiting participants – prepubescent children with classic 21-hydroxylase deficiency – in 2018.

The study aims to determine the minimum effective dose of oral abiraterone acetate that normalizes testosterone precursor levels. The 7-day treatment is an adjunct to approved CAH therapy (oral hydrocortisone and fludrocortisone).

The study completion date is slated for 2020. In Phase II, the researchers aim to determine if, over 24 months, the treatment slows bone age advancement and, ultimately, improves adult height prognosis.

LEVEL I COMPREHENSIVE CARE CENTER FOR CAH

GOAL:
TRANSFORM ENDOCRINE CARE

For Dr. White, this trial is part of a larger goal to transform care for children with endocrine disorders. He's also leading studies on gene expression in white blood cells from children with either type 1 or type 2 diabetes mellitus. The endocrinology group is planning participation in two multicenter studies for patients with type 1 diabetes; one will test an advanced "bionic pancreas" insulin pump, and the other will use a new drug in patients with newly diagnosed diabetes in an attempt to slow the loss of insulin-producing cells in the pancreas.

NEW HOPE FOR HYPERLIPOPROTEINEMIA: WEIGHT LOSS DRUG REDUCES TG LEVELS BY 50%

Type 1 hyperlipoproteinemia (T1HLP) is a rare genetic disorder characterized by extremely high serum triglycerides and chylomicronemia, which often leads to recurrent acute pancreatitis. Traditionally, the only effective therapy has been an extremely low-fat diet. But following this diet can be challenging and adherence doesn't guarantee success.

Patients may soon have a more effective option, thanks to research from Nivedita Patni, M.D., Pediatric Endocrinologist at Children's Health and Assistant Professor of Pediatrics at UT Southwestern, and Abhimanyu Garg, M.D., Division Chief of Nutrition and Metabolic Diseases at UT Southwestern.

In a small pilot trial, her team found that an FDA-approved weight loss drug called orlistat reduced participants' triglyceride levels by more than 50%. Now they're planning to build on these findings through a larger clinical study.

A BREAKTHROUGH HYPERLIPOPROTEINEMIA STUDY

Orlistat is a gastric and pancreatic lipase inhibitor that works by blocking dietary fat absorption. Dr. Patni and the research team reasoned that blocking dietary fat absorption would also help reduce blood triglyceride levels by reducing chylomicron production in the intestine.

Dr. Nivedita Patni discussing research data with Ms. Carmel Tovar in the laboratory.

To test this, they recruited two unrelated boys (9 and 11 years old) with T1HLP. A randomized, open-label, crossover trial with four periods and two sequences ("orlistat" and "off" for 3 months each) was conducted.

The results were impressive — orlistat reduced triglyceride levels by 53.3% and 53.0% in patient 1, and by 45.8% and 62.2% in patient 2, compared with the two "off" periods. Height and weight were not affected, and metabolic markers stayed safe throughout the trial.

What's more, the boys did not experience the typical side effects of orlistat (oily and loose stools, abdominal pain) because they maintained an extremely low-fat diet (~15% of the total energy from fat) throughout the study.

SEARCHING FOR THE GENETIC BASIS OF PEDIATRIC HYPERTRIGLYCERIDEMIA

A separate study by Drs. Patni and Garg aims to identify novel genes and variants involved in lipid metabolism that contribute to severe hypertriglyceridemia (sHTG) in children.

In adults, sHTG (serum triglycerides ≥ 500 mg/dL) is often caused or exacerbated by uncontrolled diabetes mellitus, alcohol abuse or obesity. But in children, the condition is more likely to be tied to genetic causes. Yet, the molecular basis of pediatric sHTG has not been studied systematically.

The research team aims to enroll 200 children with sHTG (excluding those with secondary sHTG) and their first-degree relatives. The researchers will perform whole exome sequencing on participants' DNA samples to pinpoint disease-causing mutations. The researchers will also study genotype-phenotype relationships, correlating genotypes with clinical features, body fat distribution, height, weight and serum metabolites.

"While there are medicines that can be helpful for patients with secondary causes, like diabetes, there is no specific therapy for genetic causes of sHTG," Dr. Patni says. "If we can identify these genes, we can start working on specific therapies to help patients decrease their blood triglyceride levels."

ORLISTAT REDUCES TRIGLYCERIDE LEVELS BY 50%

EXPERT CARE AND TECHNOLOGY HELP A YOUNG GIRL MANAGE TYPE 1 DIABETES

After 5-year-old Susanna was diagnosed with type 1 diabetes, she and her family turned to the team at Children's Health for support.

When Susanna was 5 years old, she started having regular accidents, even though she had been potty-trained since she was a toddler. At first, her parents thought the accidents may just stem from behavioral issues. But when Susanna began drinking an unusual amount of water and losing weight, her family began to suspect something more serious was going on.

"One Wednesday night after church, when we came to pick her up from class, her teacher told us that Susanna had used the bathroom nine times during the hour-long service," Susanna's mother, Tammy, says. "We made an appointment with her pediatrician the very next day."

Susanna's family copes with a surprising diagnosis

At the pediatrician's office, tests revealed Susanna's blood sugar levels were extremely elevated and there were high levels of ketones in her urine. Her doctor instructed her parents to bring her to the emergency room immediately.

Tammy drove Susanna to Children's Medical Center Dallas, where she was diagnosed with type 1 diabetes and admitted to the Endocrinology unit.

Over the next few days, Susanna and her family met with Ximena Lopez, M.D., Pediatric Endocrinologist at Children's Health and Associate Professor at UT Southwestern. A team of diabetes educators, dietitians and other team members helped the family learn more about how to manage her disease.

"Her diagnosis totally just knocked us off our feet," says Tammy. "At first, the information was so overwhelming, but the team was so helpful in making sure we understood everything we needed to know. Susanna really bonded with her diabetes educator, and Dr. Lopez also took the time to answer all of Susanna's questions, which played a huge role in building their relationship right from the start."

Once home from the hospital, Susanna and her family continued to monitor her insulin levels throughout the day and count carbs with every snack and meal. She uses a continuous glucose monitor (CGM) to limit the number of finger pricks she endures each day, but does still require insulin injections with every meal and at nighttime.

The Diabetes Advisor App makes managing Susanna's care easier

Susanna's diabetes diagnosis affects every part of her family's life: interrupting their sleep to check Susanna's glucose monitor, affecting Susanna's concentration at times and even making it challenging to leave town for a spur-of-the-moment trip. But Tammy is grateful for the online tools and technology offered by Children's Health, like the Diabetes Advisor App, which helps her successfully manage Susanna's diagnosis at home.

For Tammy, the app, which provides real-time advice on how to manage many common issues related to diabetes, has been incredibly helpful, especially when Susanna is ill or has a higher-than-normal level of ketones in her urine.

Susanna doesn't let diabetes hold her back

"Susanna is able to do everything a kid with a working pancreas can do," says Tammy. "She just started taking piano lessons, loves everything to do with horses and is a very active young girl."

And that's music to the Endocrinology team's ears."By providing support – and the technology and tools to make the day-to-day easier – we want to empower our diabetes patients to manage their condition confidently and to live full, happy lives," says Dr. Lopez.

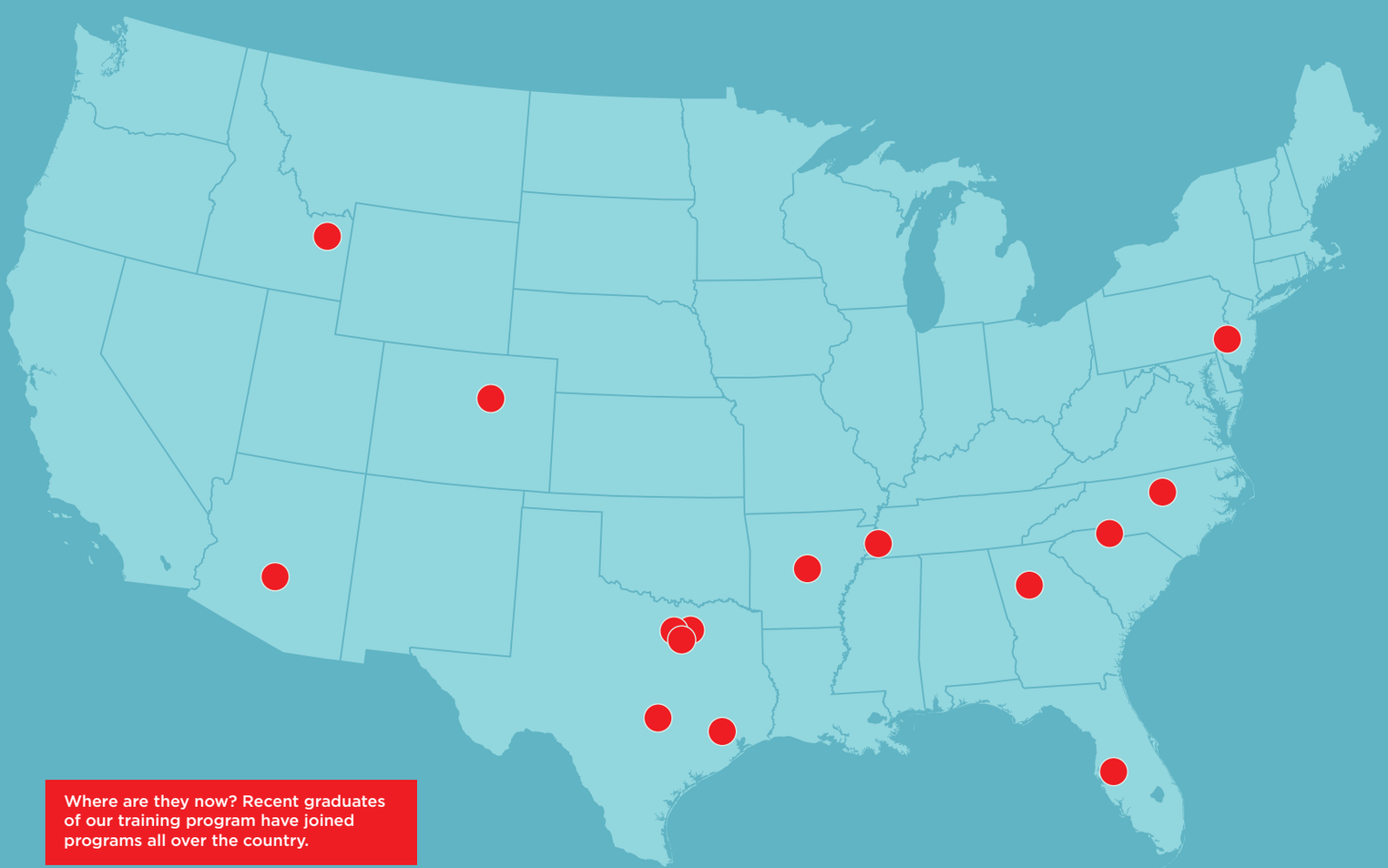
"BY PROVIDING SUPPORT – AND THE TECHNOLOGY AND TOOLS TO MAKE THE DAY-TO-DAY EASIER – WE WANT TO EMPOWER OUR DIABETES PATIENTS TO MANAGE THEIR CONDITION CONFIDENTLY AND TO LIVE FULL, HAPPY LIVES."

—Dr. Ximena Lopez

TRAINING THE NEXT GENERATION OF PEDIATRIC ENDOCRINOLOGISTS

Since 1999, when the Division of Pediatric Endocrinology at UT Southwestern accepted its first extramural fellow, to 2019, when we matriculated our 30th and 31st trainees, we have always looked to foster a training environment which leverages our broad clinical base and the long history of scientific achievement at our institution to create the best training experience we can for tomorrow's pediatric endocrinologists.

From medical students to residents, we welcome you to explore our program in more depth through our elective offerings, our ongoing research and scholarly activities, or through a personal phone call or visit with any of our program leadership. If you're interested in learning more about our program, please visit: **www.utsouthwestern.edu/education/medical-school/departments/pediatrics/divisions/endocrinology/fellows/**or email us at PediatricEndocrinology@UTSouthwestern.edu to set up an in person visit to discuss your plans in further depth.



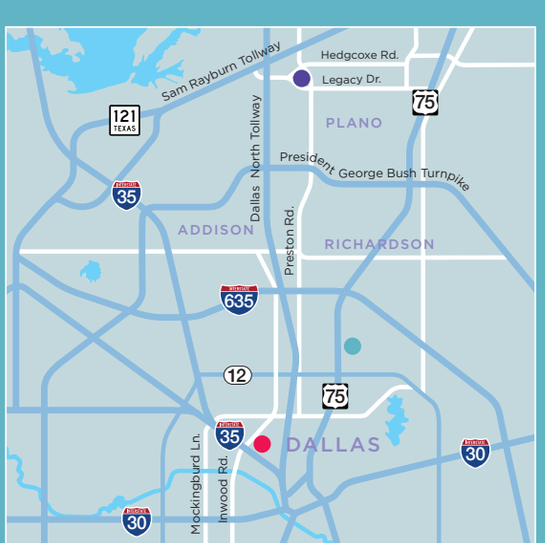
Where are they now? Recent graduates of our training program have joined programs all over the country.

LOCATIONS

- **Children's Health Specialty Center Dallas**
  2350 N. Stemmons Fwy.
  Dallas, TX 75207

- **Children's Health Specialty Center 1 Plano**
  7609 Preston Rd.
  Plano, TX 75024

- **Children's Health Specialty Center Park Cities**
  8160 Walnut Hill Ln, Suite 106
  Dallas, TX 75231



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Specialty care provided by UT Southwestern physicians