Health Care Special Report: Children's Mercy platform targets 'Goldilocks' doses
Kansas City Business Journal (online; Kansas City, Mo.)
By Elise Reuter
February 3, 2017

For some treatments, the perfect dose is a necessity. Leukemia patients, for example, take busulfan to prepare for a bone marrow transplant. Too little, and the patient's body won't accept the transplant. Too much, however, can cause irreversible liver damage.

"It's a really fine line," said Susan Abdel-Rahman, director of the pharmacokinetic and pharmacodynamics core laboratory at Children's Mercy.

Susan Abdel-Rahman (left) demonstrates how to calculate the right dose for a patient using the GOLDILOKs platform she created. Steven Leeder (right) came up with the idea while researching why some children respond better to ADHD medication than others.

She created a platform to help determine how much is "just right" based on a child's genome and age. Named GOLDILOKs after the children's story, the program gathers data about how pediatric patients process medication, looking at factors such as genetics and age.

"(We're) interested in making medications more effective for kids," said Steven Leeder, director of clinical pharmacology and therapeutic innovation for Children's Mercy. "People try to scale adult data for kids. ... How would you scale a dose from a 70-kilogram adult to a 1-year-old?"

As researchers gather data on a child's reactions to a medication, they also are able to gather population data to see how much variation there is among all pediatric patients.

"We're looking at how things change during growth and development," Leeder said. "The pathways to get rid of foreign chemicals come on after birth."

The project began when Leeder tested this concept with atomoxetine, a common ADHD drug better known as Strattera. The drug had gained a reputation for mixed success, but the results depended on a drug pathway with significant genetic variation between patients.

Although the recommended dose for a drug is based on the average amount needed for the desired effect in patients, this approach doesn't account for patients on either end of the bell curve. In the case of atomoxetine, 3 percent to 5 percent of the population processes the drug much quicker than average, experiencing less of the desired effect, whereas 7 percent lack the needed mechanisms to process the drug, resulting in too much of the drug.

Leeder's shocking finding: The variation between those two extremes was 50-fold.

"It's an extremely wide range," he said.

The discovery motivated him to start looking at the individual "bullet points," or patients, rather than the general response to the drug.

The key insight, Leeder said, was "trying to figure out what factors contribute to that data point being where it is — what we need to be doing to implement individualized therapeutics — rather than just lumping the data together to get a sense of how things are 'on average.'"

To the clinic

In 2013, Abdel-Rahman developed the platform to help physicians interpret this data, rather than keeping it isolated from the clinical side. With information on a patient's history and the general

population's reaction to a drug, the software can generate a line of best fit to tell physicians how much to prescribe.

"The value of the tool is to get (patients) managed more quickly and more efficiently," she said.

The platform gives real-time results and is fully integrated with the patient's electronic medical records for quick calculations. It essentially allows the physician to simulate a dose based on the desired effect for the patient. Although other hospitals have developed modeling tools, most don't make it into clinical practice, driving interest in the GOLDILOKs software.

"What we do here, the problems we work on are driven by clinicians," Leeder said. "Once you get to 100 kids, you start to see how much variability there is in (drug) exposure. That can drive a research question."

Child development and genetics are the current focus of the GOLDILOKs program, but Leeder said researchers may look at other variables, such as a child's environment.

"Part of the fun is coming up with these creative solutions," he said. "We're generating data where data doesn't exist."

For Leeder and Abdel-Rahman, this is just the beginning, as the program expands to several pediatric subspecialties. From Leeder's study on ADHD, the model now is applied to studying statin drugs for cardiology, histamines for asthma patients and studies on how obesity affects a child's response to medications.

"We've got a bunch of people who are not afraid to do something that hasn't been done before," Leeder said. "The information is there — we just need to pull it out."