

Emerging Technologies in Diabetes Research

The JDRF Emerging Technologies E-Newsletter No. 9

July 2009

New JDRF Trial Results: CGMs Benefit Patients with Good Blood Sugar Control

According to the results of another major multi-center clinical trial funded by JDRF, people with type 1 diabetes who have already been successful in achieving recommended blood sugar goals can further benefit from using continuous glucose monitoring (CGM) devices. Findings of the study were published online in May in the journal *Diabetes Care* and are available at <http://care.diabetesjournals.org/content/early/recent>.

The study found that CGMs enable people who have achieved excellent control (with HbA1c levels below seven percent) to continue to tightly manage their diabetes while cutting down on the frequency of low blood sugars, called hypoglycemia. Research has shown that good blood sugar control is a key factor in reducing the risk of the devastating long-term complications of the disease, such as blindness and kidney disease—but that the fear of low blood sugar emergencies often prevents people from achieving tight control, and remains a constant concern for those who manage their diabetes well. The landmark Diabetes Control and Complications Trial (DCCT) showed that with intensive insulin therapy, excellent blood sugar control could be obtained, but at the expense of a considerable increase in hypoglycemia. Today, the JDRF study has shown that, with CGMs, hypoglycemia can be reduced while maintaining excellent blood sugar control.

The CGM study was a randomized and controlled trial involving 129 adults and children ranging in age from eight to 69 years, and took place at 10 sites. Participants all had good diabetes control when they enrolled in the trial, and were randomly assigned to either a group that used CGM devices or one using standard finger-stick glucose testing for 26 weeks.

“The research suggests that CGM devices help people who are already doing an excellent job of managing their diabetes continue to do so, while lowering the risk of pushing their blood sugar so low it causes hypoglycemia,

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which can be life threatening,” said Dr. Bruce Bode of Atlanta Diabetes Associates and one of the lead authors of the *Diabetes Care* paper. “These trials are showing that CGMs not only help people get into control, which can have a significant positive impact on lowering the risk of complications, but it enables them to stay in control without increasing the near-term risk of hypoglycemia. That’s terrific news for people with diabetes and their families.”

(People with diabetes try to maintain their blood sugar levels between 70 mg/dL and 180 mg/dL. When blood sugar becomes very low, people can become confused, lethargic, and even slip into a coma or die. Very high blood sugars can also be dangerous. Long term, lack of control increases the risk of developing devastating complications, including eye, kidney, nerve, and heart disease. HbA1c is a measure of long-term blood sugar control; standards of good control are generally below seven percent for adults, and below 7.5 percent to eight percent for children, depending on age. According to the DCCT findings, every one-point reduction in HbA1c reduces the risk of long-term complications by approximately 40 percent.)

Main findings

According to the study, the amount of time spent with a blood sugar level below 70 mg/dL decreased by 37 minutes a day among the participants using CGM devices. This compared with a decrease in the control group of only five minutes a day. Ultimately, people in the CGM group spent almost two hours more per day in the target blood sugar range of 71 to 180 mg/dL compared with the control group, and about half an hour less per day with glucose values in the potentially dangerous hypoglycemia range. The authors demonstrated a number of other significant benefits in this population including:

- More people in the CGM group had an improvement in HbA1c of more than 0.3 percent (31 percent versus five percent in the control group)
- Fewer had a worsening of HbA1c greater than 0.3% (28 percent versus 52 percent)
- More CGM users had a HbA1c level below seven percent at 26 weeks (88 percent versus 63 percent)
- More people in the CGM group than the control group had a decrease in HbA1c of more than 0.3% without experiencing a severe hypoglycemic event (28 percent versus five percent).

Encouragingly, similar beneficial results were seen in children, adolescents, and adults spanning the ages of eight to 69 years.

Dr. Aaron Kowalski, program director for metabolic control at JDRF, explained that in planning this study, the change in HbA1c was not selected as the primary outcome measure because the researchers did not anticipate being able to lower HbA1c levels in the CGM group, given their already good level of control. He noted that the study group expected that there might even be small and clinically insignificant increases in HbA1c values in the CGM group if the devices were able to help them reduce the frequency of glucose levels below 70 mg/dL. Instead, the CGM group was able to maintain HbA1c levels with less hypoglycemia, whereas HbA1c levels rose over time in the control group. He noted that all the HbA1c outcomes favored the CGM over the control group.

Major eligibility criteria for the study included people over the age of eight who had type 1 diabetes for at least one year, who either used an insulin pump or took at least three daily insulin injections, and had HbA1c levels below seven percent. Subjects in the control group were given blood glucose meters and test strips and asked to perform blood glucose monitoring at least four times daily, and met with study personnel as often as the CGM group.

Why the study was conducted

The study is the second major publication resulting from JDRF's groundbreaking CGM trials, established to clinically document the benefits of CGM devices in helping people with type 1 diabetes manage their disease more effectively. In results published last fall in *The New England Journal of Medicine*, the JDRF Continuous Glucose Monitoring Study Group reported that CGM substantially improved

blood sugar levels without increasing the frequency of hypoglycemia in adults over 25 years of age in a randomized trial of 322 adults and children with type 1 diabetes and HbA1c levels above seven percent.

Because lowering HbA1c was the primary outcome of interest, that study excluded individuals already reaching target HbA1c levels lower than seven percent. As a result, the study group also conducted a separate, concurrent randomized trial to evaluate the efficacy and safety of CGM in adults and children with type 1 diabetes who already had successfully achieved HbA1c levels less than seven percent with intensive insulin therapy. More information on the initial results of JDRF's CGM trials and on the Artificial Pancreas Project is available online at www.jdrf.org/artificialpancreas.

Dr. Kowalski noted that over the past 15 years, the use of rapid and long-acting insulin analogs, improvements in insulin pumps, and more frequent home blood glucose monitoring have had a positive impact on the ability of people with type 1 diabetes to achieve blood sugar control targets. However, the rates of severe hypoglycemia remain too high and the occurrence of such events is often followed by a decline in glycemic control due to fears of further hypoglycemic episodes. Hypoglycemia remains the major limiting factor for people with type 1 diabetes in trying to achieve and maintain good blood sugar control. These study results are extremely encouraging in showing that hypoglycemia can be reduced without sacrificing glycemic control.

In Brief: Updates from the Artificial Pancreas Project

For a wealth of articles and other updates about emerging technologies, visit JDRF's Artificial Pancreas Project web site at www.jdrf.org/artificialpancreas.

A Roadmap to Better Diabetes Outcomes

Aaron Kowalski, Ph.D., director of JDRF's Metabolic Control Program, recently wrote about the remaining steps that will bring the development of an artificial pancreas—asking and answering the questions, can we really close the loop, and how soon? Read the article, published in the journal *Diabetes Technology & Therapeutics*, at <http://www.liebertonline.com/doi/pdfplus/10.1089/dia.2008.0031>.

“Artificial Pancreas May Soon Be a Reality”

A review article on the ongoing efforts to develop an artificial pancreas was published this past April in the prestigious *Journal of the American Medical Association*. Providing an historical overview, the article features JDRF’s Artificial Pancreas Project as well as comments and insights by Dr. Kowalski. Included is a discussion of the technical obstacles to overcome in “closing the loop,” anticipated accomplishments in the near-term, and nontechnical hurdles such as broader coverage by health insurers. To read the article, follow the link at http://www.jdrf.org/files/General_Files/APP/2009/JAMA_AP.pdf.

The entire April 2009 issue of *JAMA* was devoted to the topic of diabetes to highlight the continued challenges of managing and living with the disease.

Health Plans Offer CGM Coverage

Five of the nation’s largest health plans—Aetna, CIGNA, United Healthcare, Wellpoint, and Kaiser Permanente—have broadened their coverage for continuous glucose monitors (CGM) based on the results of JDRF’s groundbreaking 2009 CGM clinical trial. Several influential regional plans are also offering reimbursement for the device, including Harvard Pilgrim. For further details, visit www.jdrf.org/cgmcoverage.

Video by JDRF Clinical Trial Participant To Be Used as Teaching Tool

Without question, Kris Bagwell is committed and determined to ease the burden of type 1 diabetes. A JDRF volunteer and president of the JDRF Georgia chapter, based in Atlanta, Kris recently participated in an Artificial Pancreas Project clinical trial at the University of Virginia and captured his experiences in a personalized video called *Pancreations, One Road to Hope*. Physicians and Artificial Pancreas Program researchers intend to use Kris’ video as an educational and teaching tool. If you wish to view the video, click here: www.jdrf.org/artificialpancreas.

Artificial Pancreas Project Is Highlighted by ABC News and U.S. News & World Report

In the last month, two major national news outlets featured JDRF-funded Artificial Pancreas Project researchers, highlighting the progress to date and prospects for the future:

- On July 9th, ABC News aired a two-and-half minute health story on the promise of the artificial pancreas. It featured teenager Sarah Carlow’s daily challenges in living with type 1 diabetes and her efforts to change things—she

is participating in a clinical trial of the artificial pancreas at the Yale-New Haven Hospital in Connecticut, led by Dr. Stuart Weinzimer. To view the ABC video, click here: <http://abcnews.go.com/video/playerIndex?id=8046559>.

- An article in *U.S. News & World Report* describes how the artificial pancreas could dramatically improve the lives of people with type 1 diabetes, and features University of Virginia researcher Boris Kovatchev, who is named a “Medical Pioneer.” To read the article, link to: <http://health.usnews.com/articles/health/diabetes/2009/06/30/boris-kovatchev-artificial-pancreas-could-help-diabetics.html>.

The two sites are part of the JDRF-funded Artificial Pancreas Consortium, a worldwide collaboration of diabetes researchers, mathematicians, and engineers that aims to speed and optimize the process of linking continuous glucose sensors and insulin pumps, including the development of various computer “algorithms” to communicate between the two devices. The consortium is now funding multiple sites to test the safety and effectiveness of various versions of a closed-loop system and make them more effective for real world situations such as meals, exercise, and stress. While the initial research is taking place in hospital-based clinical settings, the initiative will soon test artificial pancreas systems in every day life settings such as at home or school.

Consortium participants also include Cambridge University, Boston University, Oregon Health & Science University, Sansum Diabetes Research Institute, Stanford University, and the University of Colorado.

JDRF has launched the Artificial Pancreas Project to accelerate the availability of an artificial pancreas to people with diabetes, one of the foundation’s cure therapeutic pathways. The overall goal of the project is to accelerate the development, regulatory approval, health insurance coverage, and clinical acceptance of continuous glucose monitoring and artificial pancreas technology.

The long term goal is for broad patient access and a thriving competitive market for these devices and products.

For regular updates to the Artificial Pancreas Project, please visit www.jdrf.org/artificialpancreas.