**APR 30, 2024**

# CRISTAL study published in The Lancet Diabetes & Endocrinology shows promising outcomes for pregnant women living with type 1 diabetes

Study shows the investigational use of the MiniMed™ 780G system improved glycemic control during pregnancy. Medtronic, a global leader in healthcare technology, today announced the results of...

*Study shows the investigational use of the MiniMed™ 780G system improved glycemic control during pregnancy.*

Medtronic, a global leader in healthcare technology, today announced the results of the randomized controlled Closed- loop insulin delivery in pregnant women with type 1 diabetes: a randomized controlled trial, also known as the CRISTAL study, published in *The Lancet Diabetes & Endocrinology*. This investigator-initiated, international, and multicenter trial evaluated the safety and efficacy of the MiniMed™ 780G system versus standard of care (multiple daily injections or insulin pump therapy both with CGM) in women with type 1 diabetes during pregnancy. The results showed that for pregnant women with type 1 diabetes, the introduction of the MiniMed™ 780G automated insulin delivery (AID) system improved overnight glucose control and reduced overall and nighttime risk of hypoglycemia. Those using the MiniMed™ 780G system also experienced higher treatment satisfaction compared to those on standard of care therapy.

**Overcoming the pregnancy-specific burden of diabetes**

There are over 42 factors that impact blood sugar levels on a day-to-day basis for individuals living with type 1 diabetes. This results in unpredictable variability in glucose levels, which can make diabetes management challenging. During pregnancy, the placenta produces hormones that result in extreme glycemic changes that can make management even more difficult. This unpredictability can pose risks to both the mother and the unborn baby. Pregnant women with type 1 diabetes are advised to aim for tighter control of their glucose levels, typically targeting a range of 63-140 mg/dL (3.5-7.8 mmol/L), to minimize the risk of high blood sugar levels, which can have adverse effects on the baby's development. However, achieving this level of control can be challenging due to the complex interplay of hormones, dietary changes, and other factors during pregnancy. Additionally, the limited treatment options available for pregnant women with type 1 diabetes contribute to the difficulty in managing blood sugar levels effectively. These challenges highlight the critical need for advanced and tailored

solutions, such as automated insulin delivery systems, like the MiniMed™ 780G system, to support pregnant women and their babies with type 1 diabetes in achieving optimal blood sugar management.

The study evaluated 95 pregnant women across 12 centers in Belgium and the Netherlands, 96% of whom were already using insulin pumps and had tight glycemic control (average HbA1c of 6.5 in early pregnancy). At study initiation, roughly half of the women were randomly assigned the MiniMed™ 780G system and were recommended to set the glucose target at 100 mg/dL (5.5 mmol/L) and active insulin time at 2 hours throughout pregnancy.

With respect to safety, the results suggested that the use of the MiniMed™ 780G system was safe for pregnant women with type 1 diabetes, a population for which previous data on the use of AID was limited. Primary endpoints included time spent in pregnancy-specific time in range (63-140 mg/dL, 3.5-7.8 mmol/L), number and duration of severe hypoglycemia and diabetic ketoacidosis (DKA) episodes, as well as device deficiencies.

“For women with type 1 diabetes, achieving tight glycemic control that can help improve pregnancy outcomes for mother and baby can be elusive,” said Prof. Katrien Benhalima, MD, PhD, University Hospitals Leuven, Belgium, the Principal Investigator of the CRISTAL study. “In this study, use of the latest Medtronic generation of automated insulin delivery systems – the MiniMed™ 780G system – showed promise of providing additional benefits compared to standard insulin therapy, with improved time in range overnight, less risk for hypoglycemia, and improved treatment satisfaction.”

Compared to standard of care, the MiniMed™ 780G system had a higher overnight time in pregnancy-specific range with study participants spending on average 6.6% more time within pregnancy range overnight. This is promising as managing highs during the night can be challenging for people living with type 1 diabetes. Those using the MiniMed™ 780G system also experienced on average 1.3% less time below range (time below range is generally 63 mg/dL or <3.5 mmol/L for pregnant women; <70 mg/dL or 3.9 mmol/L for non-pregnant women) and 1.9% less time below range overnight. Importantly, there were no hospitalizations for severe hypoglycemia in the MiniMed™ 780G system group, while five hospitalizations for severe hypoglycemia occurred amongst those managing their diabetes with standard of care.

| **OUTCOMES** | **BASELINE** | | **ANTENATAL PERIOD (OVER 4 VISITS) *** | | | |
|---|---|---|---|---|---|---|
| | **MiniMed™780G AID system N=46** | **Standard of Care N=49** | **MiniMed™ 780G AID system N=45** | **Standard of Care N=48** | **Adjusted Mean Difference#** | **P-values** |
| | | | | | | |

| OUTCOMES | BASELINE | | ANTENATAL PERIOD (OVER 4 VISITS) * | | | |
|---|---|---|---|---|---|---|
| | MiniMed™780G AID system N=46 | Standard of Care N=49 | MiniMed™ 780G AID system N=45 | Standard of Care N=48 | Adjusted Mean Difference[#] | P-values |
| Percentage of time within pregnancy range (63-140 mg/dL) | 60.5% | 57.6 % | 66.5% | 63.2 % | 1.9% | 0.17 |
| Percentage of overnight time within pregnancy range (63-140 mg/dL, midnight to 6 a.m.) | 64.8% | 60.4% | 75.1% | 67.2% | 6.6% | 0.0026 |
| Percentage of time below range (<63 mg/dL) | 5.3% | 5.1% | 2.5% | 4.1% | -1.3% | 0.002 |
| Percentage of overnight time below range (<63 mg/dL, midnight to 6 a.m.) | 5.3% | 4.0% | 1.9% | 4.2% | -1.9% | 0.0005 |

*The antenatal period includes data over the four prespecified timepoints, corresponding with average over periods 14–17 weeks', 20–23 weeks', 26–29 weeks', and 33–36 weeks' gestation.

[#]Analysis was corrected for baseline time in pregnancy-specific range (63-140 mg/dL), HbA1c concentration, insulin delivery method, and clinic center. Difference > (<) 0: higher (lower) value with MiniMed™ 780G AID system compared to Standard of Care.

**Improving maternal and neonatal outcomes**

While the CRISTAL study was not powered for pregnancy outcomes, the study showed lower excessive gestational weight gain for participants using the MiniMed™ 780G system compared to those on standard therapies. Additionally, study results suggested that neonatal intensive care unit (NICU) admissions due to neonatal hypoglycemia occurred less frequently in the trial group using the MiniMed™ 780G system.

“Managing type 1 diabetes during pregnancy can be complex given the unpredictable and extreme changes to the body that can impact not only the person living with diabetes, but the unborn baby as well. There is an unmet need for technology to help women during this critical time,” said Ohad Cohen, M.D., senior global medical affairs director, Medtronic Diabetes. “As we continue to explore what is possible with the MiniMed™ 780G system, we are hopeful that it will demonstrate a reduction to the outcome disparities across diverse individuals with varying needs to making living life with diabetes easier for all.”

*The MiniMed™ 780G system has not been approved for use in pregnancy by FDA or other regulatory bodies.*

Benhalima K, Beunen K, Van Wilder N, et al. Comparing advanced
hybrid closed loop therapy and standard insulin therapy in pregnant women with
type 1 diabetes (CRISTAL): a parallel-group, open-label, randomised controlled trial.
Lancet Diabetes Endocrinol 2024; published online April 29.
https://www.thelancet.com/journals/landia/article/PIIS2213-8587(24)00089-5/abstract
S2213-8587(24)00089-5.

**About the MiniMed™ 780G system**

The MiniMed™ 780G system is the most advanced insulin pump system from Medtronic, currently approved for the treatment of type 1 diabetes in people aged 7 and older. The MiniMed™ 780G system's SmartGuard algorithm (also referred to as the advanced hybrid closed-loop algorithm) automates the delivery of insulin every five minutes – personalizing these doses to auto-correct† highs every five minutes based on CGM readings.§ The system is designed to be used at a target glucose of 100 mg/dl (5.5 mmol/L) that can be adjusted and personalized on an individual basis.

† Refers to auto correct, which provides bolus assistance. Can deliver all auto correction doses automatically without user interaction, feature can be turned on and off.
§ Refers to SmartGuard™ feature. Individual results may vary.

**About the Medtronic Diabetes** (www.medtronicdiabetes.com)

Medtronic Diabetes is on a mission to alleviate the burden of diabetes by empowering individuals to live life on their terms, with the most advanced diabetes technology and always-on support when and how they need it. We've pioneered first-of-its-kind innovations for over 40 years and are committed to designing the future of diabetes management through next-generation sensors (CGM), intelligent dosing systems, and the power of data science and AI while always putting the customer experience at the forefront.

**About Medtronic**

Bold thinking. Bolder actions. We are Medtronic. Medtronic plc, headquartered in Dublin, Ireland, is the leading global healthcare technology company that boldly attacks the most challenging health problems facing humanity by searching out and finding solutions. Our Mission – to alleviate pain, restore health, and extend life – unites a global team of 95,000+ passionate people across 150 countries. Our technologies and therapies treat 70 health conditions and include cardiac devices, surgical robotics, insulin pumps, surgical tools, patient monitoring systems, and more. Powered by our diverse knowledge, insatiable curiosity, and desire to help all those who need it, we deliver innovative technologies that transform the lives of two people every second, every hour, every day. Expect more from us as we empower insight-driven care, experiences that put people first, and better outcomes

for our world. In everything we do, we are engineering the extraordinary. For more information on Medtronic (NYSE:MDT), visit www.Medtronic.com and follow Medtronic on LinkedIn.

**Any forward-looking statements are subject to risks and uncertainties such as those described in Medtronic's periodic reports on file with the U.S. Securities and Exchange Commission. Actual results may differ materially from anticipated results.**

**Contacts:**

Ashley Patterson
Global Communications
+1-818-576-3025

Ryan Weispfenning
Investor Relations
+1-763-505-4626

https://news.medtronic.com/CRISTAL-study-published-in-The-Lancet-Diabetes-Endocrinology-shows-promising-outcomes-for-pregnant-women-living-with-type-1-diabetes