Effective Health Care Program

Diabetes Conditions
Diabetes

Insulin Delivery and Glucose Monitoring Methods for Diabetes Mellitus: Comparative Effectiveness

Focus of Research for Clinicians

In response to a public request regarding the benefits and harms of current modes of intensive insulin therapy (continuous subcutaneous insulin infusion [CSII] vs. multiple daily injections [MDI]) and modes of blood glucose monitoring (real-time continuous glucose monitoring [rt-CGM] vs. self-monitoring of blood glucose [SMBG]), the Agency for Healthcare Research and Quality (AHRQ) contracted with the Evidence-based Practice Center at Johns Hopkins University to conduct a systematic review of these modalities. Forty-one studies in 44 publications met the inclusion criteria. Outcomes including glycemic control, hypoglycemia, quality of life, and clinical outcomes were assessed in individuals with type 1 diabetes, type 2 diabetes, or pre-existing diabetes in pregnancy. The review did not include pregnant women with gestational diabetes and patients with maturity-onset diabetes of the young in its evaluation. The full report, listing all studies, is available at www.effectivehealthcare.ahrq.gov/glucose.cfm. This summary, based on the full report of research evidence, is provided to assist in decisionmaking along with consideration of a patient's values and preferences. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background

Diabetes mellitus is a group of metabolic diseases resulting from defects in insulin secretion from the pancreatic beta-cells, resistance to insulin action at the tissue level, or both. The resultant hyperglycemia, if untreated, can lead to long-term complications, including microvascular complications (retinopathy, nephropathy, and neuropathy) and macrovascular complications (coronary heart disease and cerebrovascular disease). In pregnant women with pre-existing diabetes, poor glycemic control is associated with poorer pregnancy outcomes, including fetal anomalies, macrosomia, delivery complications, stillbirth, and neonatal hypoglycemia.

The prevalence of diagnosed diabetes in the United States is currently 7.7 percent and is expected to increase to nearly 10 percent by 2050. Daily insulin therapy is vital in the 5 to 10 percent of patients with type 1 diabetes and may be required in the 90 to 95 percent of patients with type 2 diabetes.

For tight glycemic control, insulin is administered according to the basal-prandial strategy. This can be done either via MDI or CSII. Glycemic control with intensive insulin therapy (either via MDI or CSII) has been shown to reduce the risk of the microvascular and macrovascular complications of diabetes. However, tight glycemic control can be associated with an increased risk of hypoglycemia for glycemic control, while intensive insulin therapy can lead to weight gain.

While long-term glycemic control in individuals with type 1 or type 2 diabetes is assessed by measuring hemoglobin A_{1c} (HbA_{1c}), fasting and 2-hour postprandial blood glucose are measured for short-term adjustments in insulin therapy. Monitoring of blood glucose is performed either through SMBG or rt-CGM.

The comparative effectiveness of CSII and MDI in young and old patients with type 1 diabetes, patients with type 2 diabetes, and pregnant women with pre-existing diabetes have not been systematically assessed. Additionally, the relative benefits of glucose monitoring with SMBG versus rt-CGM remain to be systematically evaluated.

Conclusion

Both CSII and MDI had similar effects on glycemic control and rates of severe hypoglycemia in children and adolescents with type 1 diabetes and adults with type 2 diabetes. In contrast, some studies suggested that CSII was superior to MDI for glycemic control in adults with type 1 diabetes with no difference in hypoglycemia and weight gain. Limited evidence suggested that measures of quality of life or treatment satisfaction improved in patients with type 1 diabetes. The approach to intensive insulin therapy can therefore be individualized to the preferences of appropriate patients that will maximize their quality of life. Studies suggested that rt-CGM was superior to SMBG in lowering HbA_{1c} in nonpregnant individuals with type 1 diabetes, particularly when compliance was high, without affecting the risk of severe hypoglycemia. rt-CGM/CSII in the form of sensor-augmented pumps was superior to MDI/SMBG in lowering HbA_{1c} in the research studies analyzed in this review; however, other combinations of these insulin delivery and glucose monitoring modalities were not evaluated.

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Clinical Bottom Line

Insulin Delivery: MDI Versus CSII

Children and Adolescents With Type 1 Diabetes

- HbA_{1c} lowering did not differ significantly between CSII and MDI (mean difference from baseline, -0.14%; 95% CI, -0.48 to 0.20; $p = 0.41$). ●●○
- Frequency of daytime hypoglycemia, frequency of nocturnal hypoglycemia, rate of severe hypoglycemia, weight gain, and quality of life did not differ significantly between CSII and MDI. ●○○
- CSII was associated with a significant improvement in diabetes treatment satisfaction versus MDI (mean difference, 5.7; 95% CI, 5.0 to 6.4; $p < 0.001$). ●○○

Adults With Type 1 Diabetes

- CSII resulted in a significant HbA_{1c}-lowering effect when compared with MDI (mean difference from baseline, -0.30%; 95% CI, -0.58 to -0.02), although results were heavily influenced by one study. ●○○
- Frequency of nocturnal hypoglycemia, severe hypoglycemia, other nonsevere hypoglycemia, hyperglycemia, and weight gain did not differ significantly between CSII and MDI. ●○○
- CSII resulted in a small decrease in postprandial glucose and an increase in symptomatic hypoglycemia when compared with MDI. ●○○
- CSII was associated with a significant improvement in diabetes-specific quality of life when compared with MDI (mean difference, 2.99; 95% CI, 0.006 to 5.97; $p = 0.05$). ●○○

Adults With Type 2 Diabetes

- HbA_{1c} lowering did not differ significantly between MDI and CSII (mean difference from baseline, -0.16%; 95% CI, -0.42 to 0.09; $p = 0.21$). ●●○
- No significant between-group differences in frequency of mild hypoglycemia (●●○) or severe hypoglycemia or in weight gain were observed in this population. ●○○

Pregnant Women With Pre-existing Type 1 Diabetes

- HbA_{1c} improved in both the CSII and MDI arms in all three trimesters, with no significant differences between the two arms. ●○○

Glucose Monitoring: rt-CGM Versus SMBG

Children and Adults With Type 1 Diabetes

- rt-CGM was associated with a significant HbA_{1c}-lowering effect when compared with SMBG (mean difference from baseline, -0.30%; 95% CI, -0.37 to -0.22%; $p < 0.001$). ●●●

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Glucose Monitoring: rt-CGM Versus SMBG *(Continued)*

- Time spent in the hypoglycemic range (mean difference, 2.11 minutes/day; 95% CI, -5.66 to 1.44 minutes/day) was similar in the rt-CGM and SMBG groups. ●●○
- A significant reduction in time spent in the hyperglycemic range occurred with rt-CGM when compared with SMBG (-68.56 minutes/day; 95% CI, -101.17 to -35.96). ●●○
- The evidence was inconsistent for the effect of rt-CGM versus SMBG on the ratio of basal to bolus* insulin in a daily insulin dose. ●○○
- The rt-CGM and SMBG groups exhibited similar rates of severe hypoglycemia, general quality of life, and diabetes-specific quality of life. ●○○

rt-CGM Plus CSII (Sensor-Augmented Pump) Versus MDI/SMBG

Children and Adults With Type 1 Diabetes

- Using a sensor-augmented pump was associated with a significant HbA_{1c}-lowering effect when compared with SMBG (mean difference from baseline, -0.68%; 95% CI, -0.81 to -0.54%; $p < 0.001$). ●●○
- Time spent with nonsevere hypoglycemia and incidence of severe hypoglycemia were similar between the sensor-augmented pump and the MDI/SMBG groups. ●●○
- Overall diabetes treatment satisfaction was greater among participants in the sensor-augmented pump arm when compared with the MDI/SMBG arm, while no significant difference was observed in weight gain between the two arms. ●○○
- Evidence from two randomized controlled trials suggests that time spent with hyperglycemia is significantly lower in the sensor-augmented pump group versus the MDI/SMBG group ($p < 0.001$). ●●○

*Basal insulin mimics normal physiological insulin secretion; bolus or meal-time insulin mimics the rapid release of insulin in response to meals.

95% CI = 95-percent confidence interval; CSII = continuous subcutaneous insulin infusion; MDI = multiple daily injections; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose

Strength of Evidence Scale

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence either is unavailable or does not permit a conclusion.

Gaps in Knowledge

Several shortcomings exist in the studies examining the effects of insulin delivery and glucose monitoring devices reviewed for this report.

- Most randomized controlled trials identified in the literature were small, with the largest study including 322 participants.
- Most studies, particularly those comparing CSII with MDI, were fair to poor in quality and did not report most outcomes of interest.
- Most studies did not report the racial and ethnic composition of the study populations; for those that did, the study populations were mainly white and had limited numbers of participants from other ethnic groups in which diabetes is more prevalent.
- Few studies focused on or included children 12 years of age or younger or adults 65 years of age or older.
- The studies varied widely in definitions of nonsevere hypoglycemia, hyperglycemia, and weight gain, thus not permitting definitive conclusions about the effects of insulin delivery and glucose monitoring strategies on these intermediate outcomes.
- None of the studies included data on long-term microvascular and macrovascular complications associated with diabetes.
- Studies failed to evaluate insulin delivery and glucose monitoring devices in pregnant women with pre-existing type 2 diabetes, and the studies in pregnant women with pre-existing type 1 diabetes did not examine the effect of rt-CGM on maternal and fetal outcomes.
- Most of the studies did not report the extent of treatment adherence. High baseline HbA_{1c} values in both the CSII and MDI intervention groups may be related to poor adherence to previous treatments.
- The studies were not uniform in assessing and reporting quality-of-life outcomes, thus precluding quantification of the effects of insulin delivery methods and glucose monitoring devices on quality of life.
- Several studies excluded individuals with comorbidities such as impaired liver and renal function, microvascular complications, cardiovascular disease, mental disorders, recent severe hypoglycemia, or other chronic medical conditions, thereby limiting the applicability of the results to the entire population.

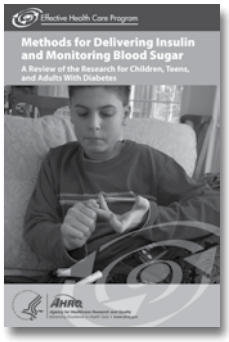
These shortcomings highlight the need for future large, well-designed studies with participants of all ages and from diverse ethnic groups, standard outcome measures including measures of vascular complications and quality of life, and long followup duration and for studies in pregnant women with pre-existing type 1 or type 2 diabetes.

What To Discuss With Your Patients

- The nature of his/her diabetes and the potential role of insulin therapy in its treatment
- The role of other lifestyle changes in managing the patient's diabetes
- The importance of glycemic control in managing the patient's diabetes
- The role of routine blood glucose monitoring in maintaining appropriate glycemic control
- The available strategies for insulin delivery and blood glucose monitoring
- The available evidence for the effectiveness of MDI versus CSII for insulin delivery
- The available evidence for the effectiveness of SMBG versus rt-CGM for glucose monitoring
- The available evidence for the effectiveness of rt-CGM plus CSII (sensor-augmented pump) versus MDI/SMBG
- The potential risks associated with intensive insulin therapy such as hypoglycemic events and weight gain, their impact on quality of life, and strategies for their management
- The potential out-of-pocket costs that the patient might incur with certain insulin delivery and glucose monitoring modalities based on his/her insurance coverage

Resource for Patients

Methods for Delivering Insulin and Monitoring Glucose, A Review of the Research for Children, Teens, and Adults With Diabetes is a companion to this clinician research summary. It can help adults with diabetes or caregivers of adults or children with diabetes talk with their health care professional about the benefits and harms of currently used modes of intensive insulin therapy and/or the mode of blood glucose monitoring used to manage diabetes.



Ordering Information

For electronic copies of *Methods for Delivering Insulin and Monitoring Glucose, A Review of the Research for Children, Teens, and Adults With Diabetes*, this clinician research summary, and the full systematic review, visit www.effectivehealthcare.ahrq.gov/glucose.cfm. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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