# Continuous Home Monitoring of Glucose

## Improved glycemic control with real-life use of continuous glucose sensors in adult subjects with type 1 diabetes

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Improving metabolic control reduces micro- and macrovascular complications of diabetes. However, intensive insulin therapy increases severe hypoglycemia more than threefold (1–3). Continuous glucose monitoring (CGM) is being introduced into routine clinical care despite a lack of reimbursement. Registration studies for the Food and Drug Administration (FDA) documented that subjects using real-time CGM improve glucose excursions, reduce variability, decrease time spent in hypoglycemia and hyperglycemia, and improve A1C values (4–9). Despite these reports, there are data unsupportive of new technologies such as CGM (10) or personal digital assistants (11) for reducing hypoglycemia. This study evaluates glucose control and its relationship with glucose target ranges with continuous home monitoring of glucose (CHMG).

## RESEARCH DESIGN AND METHODS

— Inclusion criteria limited analysis to subjects with A1C values and downloaded CHMG data at baseline and 3 months, as well as software to download receivers (not available for the first 9 months). Patients who were pregnant or planning a pregnancy were excluded.

A total of 24 subjects on CHMG were included in this analysis. All patients in this study used the DexCom STS sensor (DexCoM, San Diego, CA). Subjects were computer matched for baseline A1C (± 0.3%), sex, age, and duration of diabetes except for one subject in the CHMG group, who had diabetes for 57 years. Baseline demographics were similar between groups (Table 1). This protocol was institutional review board approved.

Subjects initiating CHMG attended a session on glucose trends, features of the CHMG receiver, and proper insertion techniques conducted by certified diabetes educators. All subjects were instructed not to change treatment based on their first week of CHMG use.

All subjects had baseline and 12-week A1C measurements (DCA 2000; Bayer, Tarrytown, NY). The CHMG data were downloaded prospectively at baseline and at 6 (± 2) and 12 (± 2) weeks, except for one subject who did not have 6-week data. Subjects wore sensors as they felt necessary. Subjects were taught to override the receiver every 3 days and use the same sensor for an additional 3 days. All subjects in the comparison group received similar diabetes care. No 6-week data or fingerstick SMBG measurements were available for the comparison group.

CHMG data were analyzed for within (WTRs) (60–150 mg/dl), above (ATRs) (>150 mg/dl), and below (BTRs) (<60 mg/dl) target ranges of blood glucose. The BTR of <60 mg/dl was used as a result of clinical observations that subjects using CHMG are more likely to treat glucose values of 60 mg/dl as opposed to 70 mg/dl, which was used for BTR in our previous self-monitoring of blood glucose (SMBG) publication (12). The ATR readings were further analyzed for 151–240 and >240 mg/dl. The percentages of readings within each target range were compared among baseline and 6- and 12-week data. The number of subjects reaching target A1C values was also analyzed. No subject had severe hypoglycemia needing glucagon or emergency room visits.

### Statistical analysis

Analyses of A1C change from baseline and time within glycemic ranges were performed using SAS software (version 9.1; SAS, Cary, NC). Two-tailed tests were used unless otherwise stated. Baseline characteristics were compared using independent-samples *t* tests. Fisher's exact tests were performed on the number of subjects reaching target A1C values at baseline. Logistic regression, with baseline A1C target as a covariate, was used to examine whether the experimental group was more likely than the comparison group to reach A1C targets by 3 months. Mixed-model repeated-measures analysis was used to evaluate the change over time in A1C, insulin dose, and the number of patients WTR, BTR, and ATR of blood glucose within the CHMG group.

## RESULTS

— Mean ± SD sensor use per subject was 17.6 ± 8.4 days per month. Subjects extended the use (despite 3-day approval and now FDA approval for 7 days) of sensors to 6.8 ± 1.6 days.

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**Abbreviations:** ATR, above target range; BTR, below target range; CGM, continuous glucose monitoring; CHMG, continuous home monitoring of glucose; WTR, within target range.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

**Table 1—*Demographics and results***

| | Baseline | | | 3 months | | |
|---|---|---|---|---|---|---|
| | CHMG | Comparison | *P* | CHMG | Comparison | *P* |
| *n* | 24 | 23 | NS | | | |
| Age (years) | 45.8 ± 13.2 | 44.3 ± 13.4 | 0.703 | | | |
| Duration (years) | 27.2 ± 16.6 | 24.0 ± 15.8 | 0.513 | | | |
| Sex (male/female) | 11/13 | 10/13 | 0.871 | | | |
| BMI (kg/m$^2$) | 26.1 ± 4.1 | 26.9 ± 4.8 | 0.565 | | | |
| Treatment | | | | | | |
| MDI | 18 | 16 | 0.677 | | | |
| CSII | 6 | 7 | 0.677 | | | |
| A1C (%) | 7.43 ± 1.0* | 7.39 ± 1.0 | 0.896 | 7.06 ± 0.8* | 7.73 ± 1.4 | 0.039 |
| Target A1C | | | | | | |
| <7.5% | 14 of 24 | 13 of 23 | 0.900 | 20 of 24 | 12 of 23 | 0.023 |
| <7.0% | 7 of 24 | 6 of 23 | 0.814 | 12 of 24 | 6 of 23 | 0.211 |
| <6.5% | 4 of 24 | 4 of 23 | 1.000 | 4 of 24 | 3 of 23 | 1.000 |
| Insulin dose | 51.9 ± 31.4† | 45.7 ± 28.6† | 0.413 | 50.1 ± 31.4† | 49.0 ± 33.4† | 0.310 |
| Glucose target ranges (%) | | | | | | |
| WTR‡ | 42.6 ± 19.5 | NA | NA | 49.1 ± 16.7 | NA | 0.0353§ |
| ATR | 53.2 ± 20.4 | NA | NA | 47.6 ± 17.0 | NA | 0.0355§ |
| BTR | 4.2 ± 3.5 | NA | NA | 3.4 ± 6.7 | NA | 0.638§ |

Data are means ± SD or *n* unless otherwise indicated. *There was a significant decrease ($P = 0.047$) in A1C in the CHMG group from baseline to 3 months. †There was no significant change in total insulin dose in the CHMG or comparison group from baseline to 3 months. ‡WTR glycemia was defined as 60–150 mg/dl (3.3–8.3 mmol/l). §These *P* values represent differences in glucose target ranges from baseline to 3 months in the CHMG group using mixed-model repeated-measures analysis. CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injection; NA, not applicable; NS, not significant.

### Changes in A1C

A1C values at baseline were 7.43 ± 1.0 and 7.39 ± 1.0% for the CHMG and comparison groups, respectively ($P = 0.896$) (Table 1). There was a significant decrease in A1C in the CHMG group (0.4 ± 0.5%; $P = 0.047$, mixed repeated-measures analysis) at 12 weeks, with a nonsignificant increase in A1C (0.3 ± 1.1%; $P = 0.0710$) in the comparison group. Also, at 12 weeks there was a difference in A1C values between groups ($P = 0.0385$) despite the fact that there was no change in insulin dose. The number of subjects achieving A1C values <7.5% was higher in the CHMG group at 12 weeks (OR 7.229; $P = 0.0234$) (13).

### Glucose target ranges

Subjects using CHMG increased WTR glucose readings by 6.5 ± 15.0% ($P = 0.0353$) and reduced mean ATR glucose readings by 5.6 ± 16.7% ($P = 0.0355$) at 12 weeks compared with baseline. ATR glucose values also showed a significant reduction in readings >240 mg/dl by 6.4 ± 14.0% ($P = 0.0351$) at 12 weeks. Results were similar for subjects using multiple daily injections or insulin pumps. Pie charts for glucose ranges are available in an online appendix at http://dx.doi.org/10.2337/dc07-1436.

**CONCLUSIONS** — This study demonstrates that use of real-time CHMG is associated with improved metabolic control over 12 weeks in adults with type 1 diabetes, as previously documented (8,14–19). This study supports previous findings carrying over to real-life use of CHMG in subjects with reasonable glucose control (A1C ~7.4%). The modest improvement in A1C of 0.4% could be due to the subject population, the short-term nature of the study, and near-target baseline A1C values of 7.43%.

Improvements in metabolic control with CHMG were not associated with increased hypoglycemia, supporting earlier findings (8,14–19). The mean increase in WTR glucose readings of 6.5% and decrease in ATR glucose readings of 5.6% at 3 months corresponded with a 0.4% decline in A1C, which is lower than was expected based on our previous self-monitoring of blood glucose data (12). This could be due to lower A1C values at baseline.

Limitations of this study include a small sample size, shorter follow-up, and lack of a randomized control group. However, the data show that CHMG use results in a small A1C reduction without increasing hypoglycemia, most likely due to behavioral changes.

We conclude that use of CHMG can further improve glucose control in subjects with relatively well-controlled type 1 diabetes, with no increase in hypoglycemia. Prospective randomized clinical trials using CHMG with a large sample size need to be conducted.

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### References

1. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus: The Diabetes Control and Complications Trial Research Group. *N Engl J Med* 329:977–986, 1993
2. UK Prospective Diabetes Study (UKPDS) Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352:837–

853, 1998
3. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA* 290:2159–2167, 2003
4. Garg SK, Schwartz S, Edelman SV: Improved glucose excursions using an implantable real-time continuous glucose sensor in adults with type 1 diabetes. *Diabetes Care* 27:734–738, 2004
5. Garg S, Jovanovic L: Relationship of fasting and hourly blood glucose levels to $HbA_{1c}$ values: safety, accuracy, and improvements in glucose profiles obtained using a 7-day continuous glucose sensor. *Diabetes Care* 29:2644–2649, 2006
6. Diess D, Bolinder J, Riveline JP, Battelino T, Bosi E, Tubiana-Rufi N, Kerr D, Phillip M: Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. *Diabetes Care* 29:2730–2732, 2006
7. Bailey T, Zisser H, Garg S: Reduction in hemoglobin A1c with real-time continuous glucose monitoring: results from a 12-week observational study. *Diabetes Technol Ther* 8:203–210, 2007
8. Chase HP, Kim LM, Owen SL, MacKenzie TA, Klingensmith GJ, Murtfeldt R, Garg SK: Continuous subcutaneous glucose monitoring in children with type 1 diabetes. *Pediatrics* 107:222–226, 2001
9. Kaufman FR, Austin J, Neinstein A, Jeng L, Halvorson M, Devoe DJ, Pitukcheewanont P: Nocturnal hypoglycemia detected with the continuous glucose monitoring system in pediatric patients with type 1 diabetes. *J Pediatr* 141:625–630, 2002
10. Hirsch I, Bode B, Abelseth J, Fischer J, Kaufman F, Mastrototaro J, Wolpert H, Buckingham B: Sensor augmented pump therapy: results of the first treat-to-target study (Abstract). *Diabetes* 56 (Supp1. 1): A24, 2007
11. Ellis S, Beatson C, Gottlieb P, Gutin R, Bookout T, Figal C, Snyder B, Garg S: Improved glycemic control in intensively treated subjects with type 1 diabetes using Accu-Chek® Advisor insulin guidance software (Abstract). *Diabetes* 56 (Suppl. 1):A8, 2007
12. Brewer KW, Chase HP, Owen S, Garg SK: Slicing the pie. Correlating $HbA_{1c}$ values with average blood glucose values in a pie chart form. *Diabetes Care* 21:209–212, 1998
13. American Diabetes Association: Standards of medical care in diabetes–2006. *Diabetes Care* 29 (Suppl. 1):S4–S42, 2006
14. Bode BW, Gross TM, Thornton KR, Mastrototaro JJ: Continuous glucose monitoring used to adjust diabetes therapy improves glycosylated hemoglobin: a pilot study. *Diabetes Res Clin Pract* 46:183–190, 1999
15. Chase HP, Roberts MD, Wightman C, Klingensmith G, Garg SK, Van Wyhe M, Desai S, Harper W, Lopatin M, Bartkowiak M, Tamada J, Eastman RC: Use of the GlucoWatch Biographer in children with type 1 diabetes. *Pediatrics* 111:790–794, 2003
16. Ludvigsson J, Hanas R: Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study. *Pediatrics* 111:933–938, 2003
17. Schaepelynck-Belicar P, Vague P, Simonin G, Lassmann-Vague V: Improved metabolic control in diabetic adolescents using the continuous glucose monitoring system (CHMGS). *Diabet Metab* 29:608–612, 2003
18. Schiaffini R, Ciampalini P, Fierabracci A, Spera S, Borrelli P, Bottazzo GF, Crino A: The continuous glucose monitoring system (CHMGS) in type 1 diabetic children is the way to reduce hypoglycemic risk. *Diabetes Metab Res Rev* 18:324–329, 2002
19. Tanenberg R, Bode B, Lane W, Levetan C, Mestman J, Harmel AP, Tobian J, Gross T, Mastrototaro J: Use of the continuous glucose monitoring system to guide therapy in patients with insulin-treated diabetes: a randomized controlled trial. *Mayo Clin Proc* 79:1521–1526, 2004