The Cost-Effectiveness of Continuous Glucose Monitoring in Type 1 Diabetes

The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group*

*The members of the writing committee and the full listing of the members of the study group are included in the on line appendix available at http://care.diabetesjournals.org.

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**Objective:** Continuous glucose monitoring (CGM) has been found to improve glucose control in type 1 diabetes patients. We estimated the cost-effectiveness of CGM versus standard glucose monitoring in type 1 diabetes.

**Research Design and Methods:** This societal cost-effectiveness analysis was conducted in trial populations where CGM has produced a significant glycemic benefit (HbA\textsubscript{1C} \geq 7.0% cohort-adults \geq 25 years, HbA\textsubscript{1C} < 7.0% cohort- all ages). Trial data were integrated into a simulation model of type 1 diabetes complications. The main outcome was the cost per quality-adjusted life year (QALY) gained.

**Results:** During the trials, CGM patients experienced an immediate quality of life benefit (HbA\textsubscript{1C} \geq 7.0% cohort: 0.70 quality-adjusted life weeks (QALWs) p=0.49; HbA\textsubscript{1C} < 7.0% cohort: 1.39 QALWs, p=0.04) and improved glucose control. In the long-term CEA for the HbA\textsubscript{1C} \geq 7.0% cohort, CGM was projected to reduce the lifetime probability of microvascular complications; the average gain in QALYs was 0.60. The incremental cost effectiveness ratio (ICER) was $98,679/QALY (95% confidence intervals (CI), -60K (4\textsuperscript{th} quadrant), -87K (2\textsuperscript{nd} quadrant)). For the HbA\textsubscript{1C} < 7.0% cohort, the average gain in QALYs was 1.11. The ICER was $78,943/QALY (95% CI, 15k (1\textsuperscript{st} quadrant), -291K (2\textsuperscript{nd} quadrant)). If the benefit of CGM had been limited to the long-term effects of improved glucose control, the ICER would exceed $700,000/QALY. If test strip use had been 2 per day with CGM long-term, the ICER for CGM would improve significantly.

**Conclusions:** Long-term projections indicate that CGM is cost-effective among type 1 patients at the $100,000/QALY threshold, although considerable uncertainty surrounds these estimates.
The Diabetes Control and Complication Trial (DCCT) established the clinical benefits of intensive glucose control in type 1 diabetes (1). Despite the availability of insulin pumps and insulin analogues, achieving optimal glucose control, while avoiding hypoglycemia, continues to be a significant challenge for patients. An important component of glucose control is glucose monitoring. Conventional self-glucose monitoring permits patients to periodically measure capillary glucose. This leaves patients unaware of post-prandial hyperglycemia and asymptomatic nocturnal hypoglycemia (2). Newer continuous glucose monitoring (CGM) technology, which measures glucose levels in subcutaneous tissue, has the potential to overcome these challenges and increase the likelihood that patients with diabetes can achieve and maintain optimal glucose control without symptomatic hypoglycemia. While there are potential advantages of CGM, the technology does have some disadvantages including discomfort from the probe, ongoing use of conventional monitoring, potential overestimation of the frequency of overnight low glucose levels, and high costs (3).

Recently, parallel multi-center trials comparing CGM with conventional self-glucose monitoring alone were conducted in patients with glycated hemoglobin (HbA1c) levels at or above 7.0% (HbA1c≥7.0% cohort) and in patients with HbA1c levels below 7.0% (HbA1c<7.0% cohort)(4). In the HbA1c≥7.0% cohort, CGM was found to significantly reduce average HbA1c levels (-0.53; 95% confidence interval (CI), -0.71 to -0.35, p<0.001) in adults (≥25 years of age)(5).

In the HbA1c<7.0% cohort, CGM helped intervention patients maintain their glycated hemoglobin at 6.5%, while control patients experienced an increase in glycated hemoglobin of 0.3% (6).

The purpose of this study is to evaluate the cost-effectiveness of CGM technology compared with standard glucose monitoring in the type 1 diabetes patients from the societal perspective.

METHODS
Design of the Continuous Glucose Monitoring Trials. The design of the JDRF-CGM trials has been previously described (4-6). In brief, patients with type 1 diabetes were randomized to CGM versus standard glucose monitoring for six months. In the HbA1c≥7.0% study cohort, subjects were stratified into three pre-specified age groups (8-14, 15-24, and ≥25 years of age). The HbA1c<7.0% cohort was not stratified by age. We conducted cost-utility analyses (CUA) in the adult (≥25 years of age) HbA1c≥7.0% cohort and the overall HbA1c<7.0% cohort. For the remainder of this manuscript, the adult HbA1c≥7.0% cohort will be referred to as the HbA1c≥7.0% cohort.

Cost-utility analysis data collected during trials. Costs - Direct Cost Items: The primary costs of interest for this CUA are the costs of CGM technology and training. During the trial, investigative staff reported on time spent with patients during scheduled and non-scheduled encounters. We included staff time devoted to CGM training and diabetes management and excluded research time. The utilization of CGM was routinely collected as days of use per week. The use of standard glucose monitoring was recorded as number of tests per day.

Adult patients and caregivers of children were surveyed at baseline and 6 months regarding health service utilization outside of the trial. Survey data included items for routine office visits, after hours clinic visits, ER visits, 911 calls, and hospitalizations.

Indirect Cost Items. Apart from health service utilization, adult patients and caregivers of children were surveyed at baseline and 6 months on the number of hours devoted to diabetes care per day, number of days missed from work or school due to
diabetes, and number of days of work underperformance.

**Unit Costs.** The unit costs and their sources are listed in Online Appendix Table 1 available at [http://care.diabetesjournals.org](http://care.diabetesjournals.org). The daily cost of CGM technology was calculated based on FDA recommended frequency of sensor replacement and the expected frequency of receiver and transmitter replacement. The costs of the three devices (DexCom, Medtronic, Abbott) used during the trial were averaged to arrive at a daily cost of CGM of $13.85 in year one (Appendix Table 2). The costs of CGM equipment reflect full retail prices, with no insurer discounts. This daily cost was multiplied by the reported weekly use of CGM to arrive at an overall cost of CGM technology (e.g., 6 days of use/week = annual cost of $4,335).

**Measurement of quality of life effects.** The quality of life effects of CGM were expected to manifest themselves in terms of immediate changes in quality of life from using the device as well as from the occurrence of long-term complications of diabetes that might be altered by changes in glycemic control. We collected utilities from trial patients for both immediate (experienced) quality of life effects of CGM and for the quality of life effects of potential long-term complications (7).

We collected experienced utility data by using the Health Utility Index (8) and by eliciting time tradeoff (TTO) utilities for overall experience (7). In the TTO method, patients were asked to consider their current state of health in comparison to life in perfect health. Experienced utilities were elicited at baseline, 13 weeks, and 26 weeks. For children <18 years of age, parents served as surrogates in responding to questionnaires. *A priori*, we planned to use the time tradeoff utilities, as the most theoretically grounded measure, for the CUA.

For complication utilities, we used the TTO method to elicit utilities for life with blindness, end-stage renal disease (ESRD), lower extremity amputation, chronic angina, and stroke (7). Parents of children <18 years of age served as surrogates for their children during complication utility elicitation. For the CUA, we used the same set of overall population complication utility weights for both trial arms in long-term projections.

**Calculation of the Incremental Cost-Effectiveness Ratio.**

(1) *Within-trial analyses:* Experienced utilities at baseline, week 13 and week 26 were modeled using a random effects linear model (9; 10). In the regression, we adjusted for treatment arm indicator, time indicators for 13 and 26 weeks, interaction between time and treatment indicators and a variety of subject level confounders. Quality of life predictions were obtained at weeks 13 and 26 for all subjects (in both control and CGM arms) as if they belonged to either trial arm. This was necessary to account for the difference in baseline quality of life across treatment arms and was accomplished by the method of recycled predictions where the treatment indicator and its interaction with time were turned on and off subsequently. The total quality-adjusted life weeks (QALWs) were calculated as the area under the quality of life time trends under each arm. Total direct and indirect costs over the 6 month period were analyzed separately using generalized linear models with log link and gamma variances. Standard errors for both costs and effects were obtained simultaneously using 500 bootstrap replicates that were clustered by subjects. Estimates of costs and effects and their empirical distributions were used to calculate the overall incremental cost-effectiveness ratios and their 95% confidence intervals.

(2) *Lifetime analyses:* For the lifetime analyses, we extrapolated the findings from the clinical trials over the projected lifetime of patients. For these lifetime projections, we developed a Monte Carlo based Markov simulation model that employs a framework and data inputs shared by prior cost-effectiveness analyses of treatments in type 1
diabetes (Technical Appendix)(11). The model is framed by the simultaneous progression of disease through major categories of complications and their associated Markov states (Appendix Figure 1) (Microsoft Excel 2000, Microsoft, Seattle, WA and @Risk 4.0 for Windows, Palisades, Inc., Newfield, NY). After assignment of characteristics of hypothetical subjects, the model simulates the natural history of diabetes based on these characteristics. A detailed description of the model inputs is available in Appendix Table 3. For all microvascular complications, we used the original DCCT prediction models for intermediate complications that relate HbA$_1C$ with the cumulative probability of developing these intermediate complications (courtesy Richard Eastman) (12). For the transitions from intermediate to end-stage microvascular complications, we used annual probabilities found in the literature(13-15).

For cardiovascular complications, there were no published prediction models for patients with type 1 diabetes at the time of our analysis. In lieu of such models, we employed prediction models for type 2 diabetes patients for ischemic heart disease, myocardial infarction, congestive heart failure, and stroke (16). To calculate cardiovascular risk, we used age and gender stratified risk factor data from the study population whenever possible. For blood pressure and cholesterol inputs, we used data for the non-diabetes population from the National Health and Nutrition Examination Surveys. Observational studies have found that type 1 diabetes patients typically have blood pressure and cholesterol levels that are closer to the non-diabetes population than the type 2 diabetes population (17). For mortality related to diabetes complications, we used mortality prediction models developed with type 2 diabetes data (16). To calculate background mortality rates, we used National Vital Statistics Life Tables (18).

For the lifetime analysis, the main outcome of interest was the incremental cost-effectiveness ratio (ICER) using an intention-to-treat analysis ($/QALY$s). Unlike the within-trial analyses, the lifetime analysis accounted for lifetime costs and benefits with the assistance of the simulation model. We assumed a lifetime use of the CGM by patients in the CGM trial and no adoption by the control arm.

**Projected CGM effects.** From the clinical trial, we know that CGM had an impact on glucose levels as well as on immediate, experienced utility. Both effects were incorporated into lifetime simulations. For the impact of CGM on glucose levels, we evaluated CGM’s effect as a change in the distribution of HbA$_1C$ levels at 26 weeks and carried this difference in distribution over the remaining lifetime. For the impact of CGM on experienced utility, we evaluated CGM’s effect as a change in the distribution of experienced quality of life and carried this difference in distribution over the remaining lifetime. The assumption that both CGM effects are maintained over time is based on 12 month observational data that has revealed that glycemic control, mean experienced utilities, and utilization of the device were unchanged among CGM patients.

**Sensitivity Analyses.** To assess the relative contributions of immediate quality of life and long-term glucose control benefits, we ran analyses where the only benefit was due to improved glucose control. We also evaluated the impact of variation in the daily cost of CGM on the cost-effectiveness of the technology. CGM use may eventually lead to lower utilization of conventional blood glucose monitors and associated test strip use. To account for this possibility, we conducted a sensitivity analysis around the number of daily test strips used among patients on CGM. We separately evaluated the effect of future costs, including medical costs for unrelated illnesses, nonmedical costs, and future earnings, on the overall cost-effectiveness results (19).

**Uncertainty.** To express the degree of uncertainty around ICERs, we present 95%
confidence intervals, using the percentile method based on bootstrap replicates.(20)

RESULTS
A description of the HbA1C≥7.0% cohort and the HbA1C<7.0% cohort is provided in Table 1. The HbA1C≥7.0% cohort had a mean baseline HbA1C level of 7.5% while the overall secondary cohort had a mean HbA1C level of 6.3%. Over 80% of patients in both cohorts were insulin pump users.

Within-trial results. During the 6 month period of the trial, CGM improved experienced quality of life and increased costs in both cohorts (Table 2). For the HbA1C≥7.0% cohort, CGM patients had a higher quality of life than control patients (0.70 (Standard Error (SE) 1.03) quality-adjusted life weeks (QALWs), p=0.49) that was not statistically significant. They also incurred higher direct medical ($2391 (SE 376)) and total costs ($5951 (SE 5,847)). The societal ICER for the within trial period was $8,501/QALW or $442,052/QALY. There was considerable uncertainty around the ICER, such that 95% confidence intervals could not be defined.

For the HbA1C<7.0% cohort, CGM patients had a significantly higher quality of life during the trial (1.39 (SE 0.69) QALWs) (p=0.04) compared with control patients. CGM patients also incurred higher direct medical costs ($3,117 (SE 356)) and total costs ($10,991 (SE 7,113)). The societal ICER was $7,849/QALW or $408,148/QALY. Confidence intervals for the societal ICER ranged from dominant to $213,000/QALY. The confidence intervals for this ICER spanned the Northeast and Northwest quadrants of the cost-effectiveness plane (95% CI, -60,007 (4th quadrant, dominant), -86,582 (2nd quadrant, dominated)). The confidence intervals reflect a large degree of uncertainty about the ICER point estimate.

Long-term results: Base Case Analyses - In the lifetime analysis for both cohorts, CGM reduced the expected lifetime incidence of intermediate and end-stage complications of type 1 diabetes while also increasing costs. In the HbA1C≥7.0% cohort, the model predicted that the use of CGM would lead to reductions in lifetime risk of blindness (14.56%→12.00%), amputation (10.53%→9.13%) and end-stage renal disease (4.41% → 2.37%). Life expectancy for both intervention and control cohorts was around 27 years. The average improvement in quality of life was 0.60 QALYs. The ICER for the base case was $98,679/QALY. The confidence intervals for this ICER spanned the Southeast and Northwest quadrants of the cost-effectiveness plane (95% CI, -60,007 (4th quadrant, dominant), -86,582 (2nd quadrant, dominated)). The confidence intervals reflect a large degree of uncertainty around the ICER point estimate.

For the HbA1C<7.0% cohort, the model also predicted that CGM use would lead to reductions in blindness (16.19%→13.96%), amputation (12.92%→11.73%) and end-stage renal disease (2.40% → 1.44%). Life expectancy for both intervention and control cohorts was around 37 years. The average improvement in quality of life was 1.11 QALYs. The ICER for the base case was $78,943/QALY. The confidence intervals for this ICER spanned the Northeast and Northwest quadrants of the cost-effectiveness plane (95% CI, 14644 (1st quadrant), -290,780 (2nd quadrant, dominated)). The confidence intervals for this cohort were narrower than for the HbA1C≥7.0% cohort but still reflect considerable uncertainty around the ICER.

Sensitivity analysis. If the benefit of CGM was limited to glucose lowering and subsequent complication prevention, CGM would not be cost-effective by most conventional thresholds. In the HbA1C≥7.0% cohort, the average gain in QALYs would be 0.08 and the ICER would be $701,397/QALY. In the HbA1C<7.0% cohort, the average gain in QALYs would be 0.07 and the ICER would be $1,185,384/QALY. The benefits from improved glycemic control are relatively small due to the fact that complications are predicted to develop late in life, and the benefits of complication reduction are therefore heavily discounted.

We also performed sensitivity analyses on the average daily cost of CGM holding utilization
of the device constant (Appendix Figure 2). If the daily costs of CGM were reduced from $13.85/day ($4,335/year) to $9.89/day ($3096/year) or below, the ICER would be below $70,000/QALY for both study populations. In the test strip sensitivity analysis, if test strip use among CGM patients was 2 test strips per day as recommended for calibration, CGM would be cost saving compared to standard glucose monitoring. When accounting for future costs, the ICERs for the two populations did not qualitatively change from the base case.

**DISCUSSION**

Real-time continuous glucose monitors have been found to improve glycemic control in type 1 diabetes in recent trials. In study populations where CGM improved glycemic control, our within-trial analysis revealed that CGM improved experienced quality of life (significant for the HbA1c<7.0% cohort and non-significant for the HbA1c≥7.0% cohort) and increased costs. Based on ICER point estimates, CGM was not cost-effective by conventional metrics during the first 6 months of use of the device, although there was considerable uncertainty around these results. When extrapolating benefits in experienced quality of life and glycemic control over a lifetime, the ICER point estimates from our analyses suggest that CGM is a cost-effective technology, based on the ICERs of commonly accepted diabetes therapies (21). Recent studies suggest that the acceptable ICER threshold is between $109,000-$297,000/QALY, above the commonly discussed $50,000/QALY threshold (22). While the ICER point estimates suggest that CGM is a good value relative to the $109,000 threshold, the confidence intervals were wide reflecting considerable uncertainty. For example, for the HbA1c≥7.0% cohort, the confidence intervals include the possibility that CGM is dominant (i.e., beneficial and cost-saving) but also include the possibility that CGM is dominated (i.e., harmful and cost-increasing). Most of the incremental cost of CGM is due to adding the RT-CGM system ($4,335 in year 1), while maintaining confirmatory blood glucose testing. If CGM were to lead to less confirmatory testing, the ICER for CGM would improve dramatically. One important insight from our analysis is that the overall quality of life effect of CGM arises from its ability both to improve the immediate quality of life of diabetes patients as well as reduce future complications through enhanced glycemic management. The immediate quality of life effect of CGM was responsible for the majority of projected lifetime benefit of the technology. For many patients, CGM provides some of the first insights into their dynamic patterns of glucose control. The provision of greater glucose control data may have improved the quality of life of patients by facilitating decisions related to food intake and insulin regimens as well as by reducing the risks and fears of hypoglycemia. These improvements occurred during the 6 month trial despite the fact that a large proportion of patients enrolled in these trials had very high baseline quality of life (Appendix Figure 3).

The analysis of quality of life data also suggests that the quality of life effect of the CGM differed between the HbA1c≥7.0% and HbA1c<7.0% cohorts. In comparison to the adult patients with sub-optimal glucose control, patients who were already at optimal glucose control levels achieved a significant immediate quality of life benefit from CGM. This difference could have been due to a lack of statistical power for the adult HbA1c≥7.0% cohort, but may also have been due to a relatively larger improvement in quality of life for the HbA1c<7.0% cohort. The exact reasons for the larger improvement in quality of life for the HbA1c<7.0% cohort are not entirely known. Quality of life of CGM subjects may have improved due to a reduction in time spent with biochemical hypoglycemia (median 54 minutes/day vs. 91 minutes/day), although this difference was not statistically significant (6). The difference in experiences for these two trial cohorts
suggests that the effect of CGM may differ across diabetes subpopulations varying by diabetes type, baseline glucose control, and current therapy. Our study has a number of important limitations. Criticism could still be leveled against our model choices. The DCCT models of microvascular complications may not reflect the modern natural history of type 1 diabetes (23). For cardiovascular complications, we relied on type 2 diabetes cardiovascular models due to a lack of type 1 diabetes cardiovascular models (24). Despite this limitation, we found that the cardiovascular event rate predicted by our model for the DCCT population were very similar to CVD rates observed in 20 year follow-up of DCCT-EDIC (25). Our model also does not account for the potential impact of long-term reductions in hypoglycemia that may be produced by CGM. And finally, as mentioned earlier, the patient in our cohorts had high baseline utilities, measured by the TTO method, which effectively placed a ceiling on the magnitude of potential quality of life benefit that could be brought about by CGM.

Despite these limitations, this study provides some of the first formal estimates of the cost-effectiveness of CGM technology. These estimates will require future revision as the prices and functionality of this technology evolves over time. The limitations of the current study highlight important areas of future research for the economic evaluation of chronic disease self-management technologies. The value of such technologies depends in part on their ability to improve the immediate quality of life of patients. Commonly accepted approaches to quantifying quality of life effects are designed to measure changes in traditional symptoms such as pain and daily functions such as walking. These approaches may not accurately reflect the subtle, but important, effects new devices have on addressing transient symptoms, reducing anxiety, and providing greater convenience for disease management. This study also raises fundamental questions about the approach to assessing the economic value of a technology that may be highly valuable to patients willing to use the technology but not to others.

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REFERENCES
1. The Diabetes Control and Complications Trial Research Group: The Effect Of Intensive Treatment Of Diabetes On The Development And Progression Of Long-Term Complications In Insulin-Dependent Diabetes Mellitus. *New England Journal of Medicine* 329:977-986, 1993
2. Boland E, Monsod T, Delucia M, Brandt CA, Fernando S, Tamborlane WV: Limitations of conventional methods of self-monitoring of blood glucose: lessons learned from 3 days of continuous glucose sensing in pediatric patients with type 1 diabetes. *Diabetes Care* 24:1858-1862, 2001
3. Fiallo-Scharer R: Eight-point glucose testing versus the continuous glucose monitoring system in evaluation of glycemic control in type 1 diabetes. *J Clin Endocrinol Metab* 90:3387-3391, 2005
4. JDRF randomized clinical trial to assess the efficacy of real-time continuous glucose monitoring in the management of type 1 diabetes: research design and methods. *Diabetes Technol Ther* 10:310-321, 2008
5. Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam HK, Hirsch IB, Huang ES, Kollman C, Kowalski AJ, Laffel L, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsakilian E, Weinzimer S, Wilson DM, Wolpert H, Wysocki T, Xing D: Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 359:1464-1476, 2008
6. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care* 32:1378-1383, 2009
7. Huang ES, Brown SE, Ewigman BG, Foley EC, Meltzer DO: Patient perceptions of quality of life with diabetes-related complications and treatments. *Diabetes Care* 30:2478-2483, 2007
8. Feeny D, Furlong W, Torrance GW, Goldsmith CH, Zhu Z, DePauw S, Denton M, Boyle M: Multiatribute and single-attribute utility functions for the health utilities index mark 3 system. *Med Care* 40:113-128, 2002
9. Longford NT: *Random Coefficient Models*. New York, NY, Oxford University Press Inc., 1993
10. Mallinckrodt CH, Clark WS, David SR: Accounting for dropout bias using mixed-effects models. *J Biopharm Stat* 11:9-21, 2001
11. The Diabetes Control and Complications Trial Research Group: Lifetime benefits and costs of intensive therapy as practiced in the Diabetes Control and Complications Trial. *JAMA* 276:1409-1415, 1996
12. Eastman RC, Javitt JC, Herman WH, Dasbach EJ, Zbrozek AS, Dong F, Manninen D, Garfield SA, Copley-Merriman C, Maier W, Eastman JF, Kotsanos J, Cowie CC, Harris M: Model of complications of NIDDM. I. Model construction and assumptions. *Diabetes Care* 20:725-734, 1997
13. Vijan S, Hofer TP, Hayward RA: Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. *Journal of the American Medical Association* 283:889-896, 2000
14. Humphrey LL, Ballard DJ, Frohnert PP, Chu CP, O'Fallon WM, Palumbo PJ: Chronic renal failure in non-insulin-dependent diabetes mellitus. A population-based study in Rochester, Minnesota. *Annals of Internal Medicine* 111:788-796, 1989
15. Peters EJG, Lavery LA: Effectiveness of the diabetic foot risk classification system of the international working group on the diabetic foot. *Diabetes Care* 24:1442-1447, 2001
16. Clarke PM, Gray AM, Briggs A, Farmer AJ, Fenn P, Stevens RJ, Matthews DR, Stratton IM, Holman RR: A model to estimate the lifetime health outcomes of patients with type 2 diabetes:
the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia* 47:1747-1759, 2004

17. Wadwa RP, Kinney GL, Maahs DM, Snell-Bergeon J, Hokanson JE, Garg SK, Eckel RH, Rewers M: Awareness and treatment of dyslipidemia in young adults with type 1 diabetes. *Diabetes Care* 28:1051-1056, 2005

18. Centers for Disease Control, National Center for Health Statistics: Compressed Mortality File 1999-2005.

19. Meltzer DO, Egleston B, Stoffel D, Dasbach EJ: Effect of future costs on cost-effectiveness of medical interventions among young adults: the example of intensive therapy for type 1 diabetes mellitus. *Medical Care* 38:679-685, 2000

20. Polsky D, Glick HA, Willke R, Schulman K: Confidence intervals for cost-effectiveness ratios: a comparison of four methods. *Health Econ* 6:243-252, 1997

21. The CDC Diabetes Cost-effectiveness Group: Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction, for type 2 diabetes. *Jama* 287:2542-2551, 2002

22. Braithwaite RS, Meltzer DO, King JT, Jr., Leslie D, Roberts MS: What does the value of modern medicine say about the $50,000 per quality-adjusted life-year decision rule? *Med Care* 46:349-356, 2008

23. Nathan DM, Zinman B, Cleary PA, Backlund JY, Genuth S, Miller R, Orchard TJ: Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and pittsburgh epidemiology of diabetes complications experience (1983-2005). *Arch Intern Med* 169:1307-1316, 2009

24. Zgibor JC, Piatt GA, Ruppert K, Orchard TJ, Roberts MS: Deficiencies of cardiovascular risk prediction models for type 1 diabetes. *Diabetes Care* 29:1860-1865, 2006

25. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 353:2643-2653, 2005
### Table 1. Baseline characteristics of the study populations

|                        | HbA<sub>1C</sub>≥ 7.0% Cohort | HbA<sub>1C</sub>≥ 7.0% Cohort |
|------------------------|-------------------------------|-------------------------------|
|                        | Control (N=46) | CGM (N=52) | Control (N=63) | CGM (N=67) |
| Female sex- no. (%)    | 26 (57)          | 31 (60)      | 33 (52)        | 36 (54)     |
| Age-yr                 | 44.69 ± 12.35    | 41.23 ± 11.21| 31.84 ± 17.63  | 29.38 ± 16.29|
| Non-Hispanic white race – no. (%) | 42 (91)          | 52 (100)     | 61 (97)        | 64 (96)     |
| Duration of diabetes – year, mean (standard deviation (SD)) | 21.83 (10) | 23.57 (11) | 18.15 (15) | 16.28 (15) |
| Daily insulin dose – units, mean (SD) | 45.97 (24) | 43.20 (19) | 42.23 (17) | 39.72 (13) |
| Pump Users – no. (%)   | 39 (85)          | 43 (83)      | 50 (79)        | 62 (93)     |
| Glycated hemoglobin at baseline-%, mean (SD) | 7.61 (0.50) | 7.61 (0.49) | 6.50 (0.34) | 6.39 (0.49) |
| Daily home glucose-meter reading – no./day, mean (SD) | 6.19 (1.94) | 6.89 (3.17) | 6.31 (2.72) | 7.67 (3.07) |

HbA<sub>1C</sub>≥ 7.0% Cohort is only for ages ≥25.

The only statistically difference between Control and CGM patients was in the proportion of pump users among the HbA<sub>1C</sub>< 7.0% Cohort (p=0.03).

### Table 2. Within-trial results

|                        | HbA<sub>1C</sub>≥ 7.0% Cohort | HbA<sub>1C</sub>≥ 7.0% Cohort |
|------------------------|-------------------------------|-------------------------------|
|                        | Control | CGM | Control | CGM | Control | CGM | Control | CGM |
| Mean (SE)              | Mean (SE) | Difference (SE) | Mean (SE) | Mean (SE) | Difference (SE) | Mean (SE) | Mean (SE) | Difference (SE) |
| **Quality-adjusted life weeks (QALWs)** | 21.68 (0.60) | 22.38 (1.08) | 0.70 (1.03) | 21.84 (0.66) | 23.23 (0.81) | 1.39 (0.69)* |
| **Direct Costs**       | $3,984 (242) | $6,375 (302) | $2,391 (376)* | $3,412 (164) | $6,529 (277) | $3,117 (356)* |
| **Indirect Costs**     | $12,419 (3,478) | $15,979 (4,100) | $3,560 (5,781) | $17,352 (4,338) | $25,146 (6,238) | $7,794 (7,097) |
| **Total Costs**        | $16,403 (3,493) | $22,354 (4,127) | $5,951 (5,847) | $20,764 (4,351) | $31,675 (6,292) | $10,991 (7,163) |
| **Incremental cost-effectiveness ratio, $$/QALW, (95\% CI)$$ | $8,501 (Not defined) | $7,849 (-$3,397 (4th quadrant, dominant), $66,829 (1st quadrant)) |
| **Incremental cost-effectiveness ratio, $$/QALY, (95\% CI)$$ | $442,052 (Not defined) | $408,148 (-$176,644 (4th quadrant, dominant), $3,475,108 (1st quadrant)) |

HbA<sub>1C</sub>≥ 7.0% Cohort is only for ages ≥25.

Indirect costs are estimated from reports of subject and parent hours devoted to diabetes care per day, number of days missed from work or school due to diabetes, and number of days of work underperformance.

**SE= standard error; QALWs=quality-adjusted life weeks; * indicates a p<0.05; CI=confidence intervals.**

Dominant= intervention improves health at a lower cost compared to control.

Not defined= there is so much uncertainty around the ICER that a 95% CI cannot be defined.
Table 3. Lifetime cost-effectiveness analysis results

| Lifetime probability of:                | HbA\textsubscript{1C}≥7.0% Cohort* | HbA\textsubscript{1C}<7.0% Cohort |
|----------------------------------------|-----------------------------------|---------------------------------|
|                                        | Control   | CGM   | Control   | CGM   |
| Blindness                              | 14.56     | 12.00 | 16.19     | 13.96 |
| Neuropathy                             | 34.96     | 30.56 | 33.46     | 30.41 |
| Amputation                             | 10.53     | 9.13  | 12.92     | 11.73 |
| Microalbuminuria                       | 19.30     | 13.15 | 12.43     | 9.46  |
| End-stage renal failure                | 4.41      | 2.37  | 2.4       | 1.44  |
| Myocardial infarction                  | 11.53     | 11.24 | 11.24     | 11.04 |
| Ischemic heart disease                 | 10.41     | 10.22 | 10.82     | 10.66 |
| Congestive heart failure               | 2.08      | 2.04  | 1.67      | 1.65  |
| Stroke                                 | 1.94      | 1.92  | 1.84      | 1.81  |
| Life Expectancy, means                 | 26.79     | 26.84 | 36.54     | 36.58 |
| Discounted QALYs, means               | 13.75     | 14.35 | 16.69     | 17.80 |
| Difference in QALYs                    | 0.60      |       | 1.11      |       |
| Discounted Direct Costs, means         | $159,748  | $217,882 | $200,384 | $285,149 |
| Discounted Indirect Costs, means       | $441,322  | $441,955 | $1,911,155 | $1,913,776 |
| Discounted Total Costs, means          | $601,070  | $659,837 | $2,111,539 | $2,198,925 |
| Difference in Total Costs              | $58,767   |       | $87,386   |       |
| ICER, mean (95% Confidence Intervals (CI)) | $98,679 (-60,007 (4th quadrant, dominated), -86,582 (2nd quadrant, dominated)) | $78,943 (14,644 (1st quadrant), -290,780 (2nd quadrant, dominated)) |

Experienced quality of life benefit was not statistically significant during the 6 month trial for the HbA\textsubscript{1C}≥7.0% cohort. The HbA\textsubscript{1C}≥7.0% Cohort is only for ages ≥25. QALYs=quality-adjusted life years; ICER=incremental cost-effectiveness ratio; Dominant= intervention improves health at a lower cost compared to control; Dominated= intervention worsens health at increased cost compared to control.