Cost-Effectiveness of Sensor-Augmented Pump Therapy in Adults with Type 1 Diabetes in the United States

Shital Kamble, PhD†, Kevin A. Schulman, MD1,2, Shelby D. Reed, PhD1,2,*
1Duke Clinical Research Institute and 2Department of Medicine, Duke University School of Medicine, Durham, NC, USA

A B S T R A C T

Objectives: A recent randomized trial demonstrated significant reductions in hemoglobin A1c (HbA1c) levels with sensor-augmented pump therapy (SAPT) compared with multiple daily injections of insulin (MDI) in type 1 diabetes. We analyzed resource use in the trial and estimated the long-term cost-effectiveness of SAPT from the perspective of the US health care system. Methods: We undertook a cost-effectiveness analysis combining estimates from the trial and the literature to populate the previously validated Center for Outcomes Research (CORE) Diabetes Model. Results represent the use of 3-day sensors, as in the trial, and 6-day sensors, approved in most markets but not yet approved in the United States. Results: Within-trial hospital days, emergency department visits, and outpatient visits did not differ significantly between the treatment groups. Assuming 65% use of 3-day sensors, treatment-related costs in year 1 were an estimated $10,760 for SAPT and $5072 for MDI. Discounted lifetime estimates were $253,493 in direct medical costs and 10.794 quality-adjusted life-years (QALYs) for SAPT and $167,170 in direct medical costs and 10.418 QALYs for MDI. For 3-day and 6-day sensors, the incremental cost-effectiveness ratios were $229,675 per QALY (95% confidence interval $139,071–$720,865) and $168,104 per QALY (95% confidence interval $102,819–$523,161), respectively. The ratios ranged from $69,837 to $211,113 per QALY with different strategies for incorporating utility benefits resulting from less fear of hypoglycemia with SAPT. Conclusion: Despite superior clinical benefits of SAPT compared with MDI, SAPT does not appear to be economically attractive in the United States for adults with type 1 diabetes in its current state of development. However, further clinical developments reducing disposable costs of the system could significantly improve its economic attractiveness. Keywords: insulin, type 1 diabetes mellitus.

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Introduction

Treatment to a target hemoglobin A1c (HbA1c) level of 7% or less through an intensive insulin regimen can help patients with type 1 diabetes minimize or delay the incidence of complications associated with the disease [1,2]. Existing intensive treatments, including continuous subcutaneous insulin infusion, are associated with improved glycemic control and fewer hypoglycemic events compared with multiple daily injections of insulin (MDI) [3,4]. Improvement in glycemic control may be related to accurate administration of rapid-acting insulin analogues at rates tailored to individual patients’ needs [4]. Although insulin pumps and insulin analogues are available, achieving optimal glucose control remains a challenge.

Continuous glucose monitoring (CGM), which uses a subcutaneous glucose sensor to measure interstitial glucose concentration, has been shown to be more effective than standard glucose monitoring in improving glycemic control, which leads to lower glycated hemoglobin (i.e., HbA1c) levels [5]. The Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) trial recently compared sensor-augmented pump therapy (SAPT) with MDI among adults and children in the United States and Canada. SAPT combines insulin pump therapy and CGM in an integrated system that allows monitoring through an Internet-based monitoring service. The STAR 3 trial demonstrated superior clinical outcomes with SAPT at 1 year, specifically reductions in mean HbA1c levels [6].

Given the significant direct costs associated with initiation and ongoing use of SAPT, it is important to evaluate its expected long-term effects on costs and health outcomes compared with MDI. We used data on medical resource use collected during the STAR 3 trial to estimate the long-term cost-effectiveness of SAPT versus MDI in adults with type 1 diabetes from the perspective of the US health care system.

Methods

The design of STAR 3 has been described previously [7]. During the 52-week follow-up period, data on medical resource use were collected at each study visit, including information on hospital admissions, emergency department visits, and outpatient visits by type of health care provider. Each visit was classified as related or...
unrelated to diabetes. In addition, the physicians, certified diabet- 
es educators, nurse practitioners, and registered nurses associ- 
ated with the study reported the amount of time they spent with 
patients for each study visit and for other activities, such as un-
scheduled visits, phone calls, and remote monitoring.

We valued provider time spent delivering diabetes-related care 
by assigning an hourly rate corresponding to total compensation 
(i.e., salary plus fringe) for each provider type [8]. During STAR 3, 
3-day glucose sensors were provided to patients in the SAPT 
group. By using information about the frequency of sensor use 
(i.e., percentage of time) reported in STAR 3 [6], we calculated a 
weighted average of 65% and estimated sensor costs on the basis 
of this level of use. All costs are reported in 2010 US dollars. Ap- 
pendix Table 1 in Supplemental Materials found at doi:10.1016/ 
j.jval.2012.02.011 shows the sources and assumptions we used to 
estimate the annual costs of SAPT and MDI.

Computer simulation model for studies of long-term cost- 
effectiveness
To extrapolate results from the clinical trial over the projected 
remaining lifetime of the participants, we used the Center for Out- 
comes Research (CORE) Diabetes Model version 7.0, a computer 
simulation model validated for type 1 and type 2 diabetes through 
66 internal and external validation analyses [9,10]. The model con-

sists of 15 submodels designed to simulate diabetes-related com-

plications, nonspecific mortality, and costs over time. Another 
submodel simulates treatment changes for patients with type 2 
diabetes who experience treatment failure or side effects. As the 
model simulates patients over time, it updates risk factors and 
complications to account for disease progression. The model can 
account for the development of multiple diabetes-related compli-
cations simultaneously and for the interactive effect of one com-

plication on the risk of developing another. The model also ac-
counts for first-order (i.e., patient-level) and second-order (i.e., 
parameter-level) uncertainty to represent the degree of uncer-
tainty associated with the results of the cost-effectiveness analy-
sis. Probabilities of heart failure, myocardial infarction, and stroke 
are based on data from the Framingham Heart Study or the UK 
Prospective Diabetes Study, whichever is selected by the analyst 
[9]. In this study, probabilities of heart failure and angina were 

based on Framingham data and probabilities of myocardial infar-
cion and stroke were based on data from the UK Prospective Dia-

betes Study.

Because the CORE Diabetes Model was developed from data for 
adult patients, we restricted the long-term cost-effectiveness analy-

sis to adults. We evaluated the use of both the 3-day sensors 
provided during the trial and the 6-day sensors currently available in 
Canada, Australia, and Europe but not yet approved for market-

ing in the United States.

Data sources for the cost-effectiveness model
Patient characteristics and management
Baseline characteristics, including preventive and therapeutic manage-

ment strategies used in the CORE Diabetes Model, are summarized in 
Appendix Table 2 in Supplemental Materials found at 
doi:10.1016/j.jval.2012.02.011. The primary source for the esti-
mates was the STAR 3 adult cohort (n = 329) [6]. We assumed that 
baseline characteristics were the same in both treatment arms. 
We assumed that use of aspirin, statins, and angiotensin-converting 
enzyme inhibitors represented primary prevention of diabetes 
complications, given the mean age of the STAR 3 adult cohort (i.e., 
41 years) and the low rates of preexisting comorbid conditions. For 
estimates not available from STAR 3, we relied on published sources.

Treatment effects
We used estimates of treatment effects in 329 adults from STAR 3. 

These included a change from baseline HbA1c level (i.e., 8.3 per-
tence points in both the SAPT and MDI groups) of −1.0 ± 0.7 
percentage points for the SAPT group and −0.4 ± 0.8 percentage 
points for the MDI group at 1 year, a difference of −0.6 percentage 
points (95% confidence interval [CI] −0.8 to −0.4; P < 0.001) in favor 
of SAPT, with no changes in body mass index [6]. To model 
changes in HbA1c over time for both treatment arms, we applied 
“table values” embedded in the CORE Diabetes Model, which rep-

resent HbA1c progression (i.e., increasing HbA1c levels) for type 1 
diabetes based on the longitudinal changes observed in the Dia-

betes Control and Complications Trial [11]. The change in HbA1c 
level is modeled as a linear change over time. With regard to 
changes in body mass index, we applied the default option in the 
CORE Diabetes Model representing no change in body mass index 
over time. We used the Framingham progression approach for 
changes in blood pressure and lipid levels.

Utilities
For health state utilities, we used the CORE Diabetes Model default 
values to maintain consistency with previous studies (see Appen-
dix Table 3 in Supplemental Materials found at doi:10.1016/j. 
jval.2012.02.011) [9]. We assumed that the disutility for acute keto-
acidosi was the same as for a major hypoglycemic event.

Costs
We used the costs of glucose meters and test strips, lancets, insu-
lin, and provider time to obtain annual treatment costs. For the 
SAPT group, we also included costs of insulin pumps, transmit-
ers, sensors, insertion devices, and other pump supplies. We used 
published estimates of insulin dose and annual use of glucose 

meter test strips for both groups [4,12]. We reduced the costs of 
insulin, devices, related supplies, and medications for diabetes 
management by 16% [13] to represent lower prices paid by larger 
private and public payers. Detailed cost estimates are shown in 
Appendix Tables 1, 4, and 5 in Supplemental Materials found at 

Discounting
We applied a discount rate of 3% per year to costs and clinical 
outcomes [14].

Time horizon
We applied a 60-year time horizon, consistent with previous stud-
ies [12,15–18]. This time horizon allows for development of all re-
levant complications during the remainder of a patient’s lifetime.

Sensitivity analyses
We performed numerous sensitivity analyses to evaluate the im-

pact of varying model inputs and assumptions. Given the multi-

tude of sensitivity analyses performed, our reporting focuses on 
those that we and others found to have the most impact on the 
resulting cost-effectiveness ratios, including impact on HbA1c 
level, fear of hypoglycemia, and scenarios that may better repre-

sent how SAPT is used in practice [18,19]. We varied the percent-

age use of sensors and the corresponding reduction in HbA1c levels 
[6]. We also examined the impact of less frequent use of glucose 
meter test strips in the SAPT group than in the MDI group (i.e., two 
test strips per day as recommended for calibration [12], and two 
fewer test strips per day than in the base case). To evaluate 
the influence of potential technological advances, we ran the model 
assuming that only one test strip would be required when the 
sensor is replaced (i.e., one test strip every 3 days for a 3-day sen-

sor and every 6 days for a 6-day sensor).
In another set of sensitivity analyses, we evaluated the impact of differences between the treatment groups on the Hypoglycemia Fear Survey 98. The survey was administered during STAR 3 at weeks 1, 13, 26, 39, and 52. Patients in the SAPT group reported an improvement from baseline of 4.7 points (95% CI 2.5 to 6.9; \( P = 0.001 \)), compared with the MDI group, on the “worry” subscale. Therefore, we estimated the utility benefit associated with less fear of hypoglycemia in the SAPT group from a separate study that examined the independent relationship between the “worry” subscale and the EuroQol five-dimensional questionnaire index (regression coefficient \( 0.007 \) [standard error 0.001]; \( P = 0.001 \)) from a sample of 1305 patients with diabetes in the United Kingdom [20].

We applied the utility increment of 0.0329 (i.e., \( 4.7 \times 0.007 \)) to the SAPT group in three ways. In approach 1, the utility increment represented an additive benefit in health-related quality of life with SAPT until patients experienced one or more complications. Beyond that point, we assigned the lowest corresponding utility weight. In approach 2, we applied the utility increment throughout the remaining lifetimes of patients in the SAPT group, even after they experienced one or more complications. In approach 3, we applied the utility increment to the first year of treatment in the SAPT group.

Other sensitivity analyses included varying the annual costs of SAPT by 20%, changing the baseline HbA1c level in the SAPT group [7], extending the replacement period for insulin pumps to 8 years [15–19, 21], reducing the hypoglycemia event rate in the SAPT group, varying discount rates for costs and quality-adjusted life-years (QALYs), choosing alternative sources to model progression for blood pressure and lipid parameters, and doubling the direct costs of complications. In addition, we adopted a societal perspective by incorporating patient time costs associated with treatment and days lost from work because of complications. Patients reported the total amount of time per week spent on diabetes-related care throughout the trial. To estimate patient time costs, we valued patient time spent on diabetes-related care on the basis of mean wages [22]. The incremental cost-effectiveness ratios (ICERs) for sensitivity analyses were obtained from 1000 bootstrap iterations.

### Results

#### Within-trial results

There were no significant differences between the treatment groups in the proportions of adult patients who were hospitalized or had one or more emergency department visits (Table 1). There also were no significant differences in the mean number of inpatient days or outpatient visits. During the 52-week trial, the total mean time spent by providers and patients on diabetes-related care was significantly higher in the SAPT group, a difference primarily attributable to the greater investment of time in SAPT initiation during the first few months.

#### Table 1 – Within-trial estimates of medical resource use and provider and patient time.

<table>
<thead>
<tr>
<th>Resource</th>
<th>SAPT (n = 166)</th>
<th>MDI (n = 163)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause resource use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital admissions, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>155 (93.4)</td>
<td>155 (95.1)</td>
<td>0.42*</td>
</tr>
<tr>
<td>1</td>
<td>7 (4.2)</td>
<td>8 (4.9)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (1.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 (1.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inpatient days, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.5 (2.4)</td>
<td>0.2 (0.7)</td>
<td>0.14†</td>
</tr>
<tr>
<td>1</td>
<td>136 (81.9)</td>
<td>139 (85.3)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>27 (16.3)</td>
<td>21 (12.9)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3 (2.1)</td>
<td>2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Emergency department visits, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>160 (94.7)</td>
<td>160 (97.5)</td>
<td>0.50*</td>
</tr>
<tr>
<td>1*</td>
<td>6 (3.6)</td>
<td>3 (1.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes-related resource use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital admissions, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>164 (98.8)</td>
<td>163 (100.0)</td>
<td>0.50*</td>
</tr>
<tr>
<td>1*</td>
<td>2 (1.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inpatient days, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.0 (0.4)</td>
<td>0</td>
<td>NA§</td>
</tr>
<tr>
<td>1*</td>
<td>0.4 (0.9)</td>
<td>0.4 (0.9)</td>
<td>0.18†</td>
</tr>
<tr>
<td>Emergency department visits, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>15.0 (6.5)</td>
<td>16.0 (7.5)</td>
<td>0.08†</td>
</tr>
<tr>
<td>1*</td>
<td>0.8 (1.6)</td>
<td>1.2 (2.8)</td>
<td>0.13†</td>
</tr>
<tr>
<td><strong>Outpatient visits, mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study site, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.4 (0.9)</td>
<td>0.3 (0.6)</td>
<td>0.08†</td>
</tr>
<tr>
<td>Nonstudy sites, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.8 (1.6)</td>
<td>1.2 (2.8)</td>
<td>0.13†</td>
<td></td>
</tr>
<tr>
<td>Provider time for diabetes-related care (h), mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.0 (6.5)</td>
<td>6.4 (3.2)</td>
<td>(&lt;0.001^1)</td>
<td></td>
</tr>
<tr>
<td>Patient time for diabetes-related care (h), mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>220.1 (168.6)</td>
<td>166.1 (159.5)</td>
<td>0.003^[1]</td>
<td></td>
</tr>
</tbody>
</table>

MDI, multiple daily injections of insulin; NA, not available; SAPT, sensor-augmented pump therapy.

* From Fisher exact test.
† From negative binomial test.
§ Zero patients experienced more than one hospital admission or emergency department visit due to diabetes-related events.
\^[1] Not reported because of small numbers.
\^[1] From t test.

In another set of sensitivity analyses, we evaluated the impact of differences between the treatment groups on the Hypoglycemia Fear Survey 98. The survey was administered during STAR 3 at weeks 1, 13, 26, 39, and 52. Patients in the SAPT group reported an improvement from baseline of 4.7 points (95% CI 2.5 to –6.9; \( P < 0.001 \)), compared with the MDI group, on the “worry” subscale. Therefore, we estimated the utility benefit associated with less fear of hypoglycemia in the SAPT group from a separate study that examined the independent relationship between the “worry” subscale and the EuroQol five-dimensional questionnaire index (regression coefficient \( –0.007 \) [standard error 0.001]; \( P < 0.001 \)) from a sample of 1305 patients with diabetes in the United Kingdom [20]. We applied the utility increment of 0.0329 (i.e., \( 4.7 \times –0.007 \)) to the SAPT group in three ways. In approach 1, the utility increment represented an additive benefit in health-related quality of life with SAPT until patients experienced one or more complications. Beyond that point, we assigned the lowest corresponding utility weight. In approach 2, we applied the utility increment throughout the remaining lifetimes of patients in the SAPT group, even after they experienced one or more complications. In approach 3, we applied the utility increment to the first year of treatment in the SAPT group.

### Results

#### Within-trial results

There were no significant differences between the treatment groups in the proportions of adult patients who were hospitalized or had one or more emergency department visits (Table 1). There also were no significant differences in the mean number of inpatient days or outpatient visits. During the 52-week trial, the total mean time spent by providers and patients on diabetes-related care was significantly higher in the SAPT group, a difference primarily attributable to the greater investment of time in SAPT initiation during the first few months.
Long-Term Projections

Incidence of complications
Improved HbA1c levels associated with SAPT led to lower predicted incidence of several microvascular complications over patients’ lifetimes. During the 60-year simulation period, the cumulative incidence of proliferative diabetic retinopathy and end-stage renal disease decreased by 18.3% and 15.4% with SAPT versus MDI (see Appendix Table 6 in Supplemental Materials found at doi:10.1016/j.jval.2012.02.011).

Costs, QALYs, and incremental cost-effectiveness
With 3-day sensors, the discounted lifetime estimates of direct medical costs and QALYs were $253,493 and 10.794 for SAPT and $167,170 and 10.418 for MDI. The corresponding ICER was $229,675 per QALY (95% CI $139,071–$720,865). With 6-day sensors, direct medical costs were $230,352 for SAPT, or $168,104 per QALY (95% CI $102,819–$523,161) (Table 2). A scatter plot representing the estimated joint density of 1000 resampled estimates of incremental costs and QALYs is shown in Figure 1.

Fig. 1 – Scatter plot of estimated joint density of 1000 bootstrap replications of incremental costs and quality-adjusted life-years. QALYs, quality-adjusted life-years.

Sensitivity analyses
The large majority of sensitivity analyses had relatively little impact on the ICERs (Fig. 2; see Appendix Tables 7 and 8 in Supplemental Materials found at doi:10.1016/j.jval.2012.02.011). However, varying the number of glucose meter test strips for SAPT had a marked effect. With a 6-day sensor that requires one test strip per replacement for calibration, the ICER decreased from $168,104 to $72,417 per QALY. The ICERs ranged from $211,113 to $69,837 per QALY when we varied the utility benefit associated with less fear of hypoglycemia in the SAPT group across three approaches (see Appendix Tables 7 and 8 in Supplemental Materials found at doi:10.1016/j.jval.2012.02.011).

Table 2 – Treatment costs and summary results for the base-case scenarios.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SAPT</th>
<th>MDI</th>
<th>Difference (SAPT – MDI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment costs 3-d sensor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of treatment, year 1</td>
<td>10,760</td>
<td>5072</td>
<td>5689</td>
</tr>
<tr>
<td>Cost of treatment, year 2 and beyond</td>
<td>10,255</td>
<td>4944</td>
<td>5311</td>
</tr>
<tr>
<td>Treatment costs 6-d sensor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of treatment, year 1</td>
<td>9364</td>
<td>5072</td>
<td>4293</td>
</tr>
<tr>
<td>Cost of treatment, year 2 and beyond</td>
<td>8859</td>
<td>4944</td>
<td>3915</td>
</tr>
<tr>
<td>Long-term direct costs and QALYs SAPT with 3-d sensor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discounted direct total costs ($), mean (SD)</td>
<td>253,493 (3730)</td>
<td>167,170 (3058)</td>
<td>86,324 (4703)</td>
</tr>
<tr>
<td>Discounted QALYs (y), mean (SD)</td>
<td>10.794 (0.108)</td>
<td>10.418 (0.107)</td>
<td>0.376 (0.143)</td>
</tr>
<tr>
<td>Cost per QALY ($), mean (95% CI)</td>
<td>229,675 (139,071–720,865)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPT with 6-d sensor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discounted direct total costs ($), mean (SD)</td>
<td>230,352 (3568)</td>
<td>167,170 (3058)</td>
<td>63,182 (4583)</td>
</tr>
<tr>
<td>Discounted QALYs (y), mean (SD)</td>
<td>10.794 (0.108)</td>
<td>10.418 (0.107)</td>
<td>0.376 (0.143)</td>
</tr>
<tr>
<td>Cost per QALY ($), mean (95% CI)</td>
<td>168,104 (102,819–523,161)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval; MDI, multiple daily injections of insulin; QALY, quality-adjusted life-year; SAPT, sensor-augmented pump therapy.
Discussion

The relative improvement in HbA1c levels among adults in STAR 3 was 0.6 percentage points (−1.0 vs. −0.4 percentage points; \( P < 0.001 \)) with SAPT compared with MDI at 1 year [6]. This benefit was not associated with short-term differences in hospital admissions, emergency department visits, or outpatient visits. When we extrapolated the trial results over a lifetime (i.e., 60 years), the incremental cost-effectiveness of SAPT was an estimated $229,675 per QALY with 3-day sensors and $168,104 per QALY with 6-day sensors from the perspective of the US health care system.

To represent the use of 3-day sensors, we applied first-year treatment costs of $10,760 for the SAPT group, compared with $5072 for the MDI group, a difference of $5689. In the second and subsequent years, we applied $10,255 for SAPT and $4944 for MDI, a difference of $5311. The major drivers of the incremental direct cost were devices and supplies associated with SAPT, including pumps, sensors, transmitters, sensor insertion devices, reservoirs, and infusion sets ($6036 in year 1 for a 3-day sensor; see Appendix Table 1 in Supplemental Materials found at doi:10.1016/j.jval.2012.02.011), while maintaining the confirmatory blood glucose testing similar to patients in the MDI group. We tested key assumptions in the CORE Diabetes Model by performing numerous sensitivity analyses. With the technological advancement of a sensor with a 6-day replacement period with 65% usage and requiring only one test strip per replacement for calibration purposes, the ICER for SAPT would improve dramatically to less than $100,000 per QALY. In fact, however, when we increased the usage from 65% to 85% for a 6-day sensor with one test strip per replacement, the ICER remained below $100,000 per QALY.

When we incorporated the utility benefit of having less fear of hypoglycemia with SAPT prior to the development of complications (“approach 1”) and then throughout remaining survival (“approach 2”) (with 3-day sensors), the ICERs decreased from $229,675 to $181,181 to $95,416 per QALY. With 6-day sensors, the corresponding ICERs decreased from $168,104 to $132,611 to $69,837 per QALY. When we limited the benefit to the first year of treatment with SAPT (“approach 3”), there was relatively little change from the base-case ICERs. These results imply that the value of SAPT hinges on the handling of fear of hypoglycemia in the cost-effectiveness analysis. Applying an additive utility benefit of 0.0329 across all health states experienced by patients in the SAPT group is an optimistic scenario, suggesting that whatever diabetes-related complication patients may have incurred, they will continue to accumulate QALYs at a higher rate with SAPT because of less fear of hypoglycemia. Other studies that have evaluated utilities associated with joint health states have found that the minimum utility weight across health states best represents the utility of a joint health state rather than an additive function of utility weights [23,24]. Furthermore, patients in the SAPT group reported less fear of hypoglycemia than did patients in the MDI group, despite patients in the SAPT group having better glucose control, though actual rates of severe hypoglycemia were similar in STAR 3 (15.31 per 100 person-years with SAPT and 17.62 per 100 person-years with MDI) [6].

The results of the STAR 3 cost-effectiveness analysis are not directly comparable to the results of the recent Juvenile Diabetes Research Foundation (JDRF) trial, which showed that CGM was more effective than standard glucose monitoring in reducing HbA1c levels (mean difference in HbA1c level change −0.53; 95% CI −0.71 to −0.35; \( P < 0.001 \)) in adults 25 years and older with type 1 diabetes. However, the difference in HbA1c level change between CGM and standard glucose monitoring was not significant among patients aged 15 to 24 years (mean difference 0.08; 95% CI −0.17 to 0.33; \( P = 0.52 \)) or among those aged 8 to 14 years (mean difference −0.13; 95% CI −0.38 to 0.11; \( P = 0.29 \)) [5]. The JDRF trial compared the incremental value of CGM (i.e., sensor, transmitter, and receiver) with standard glucose monitoring. In that trial, more than 80% of patients in both treatment groups used insulin pumps at baseline [12]. Thus, incremental direct costs in the JDRF study be-

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**Fig. 2 – Summary results for sensitivity analyses.** QALY, quality-adjusted life-year; SAPT, sensor-augmented pump therapy. Details regarding estimated costs and QALYs in each treatment group are provided in Tables 6 and 7 in Supplemental Materials found at doi:10.1016/j.jval.2012.02.011.
between the two groups represented additional costs with CGM relative to standard monitoring. In STAR 3, the incremental direct cost represented additional costs with the combined use of insulin pumps and CGM versus MDI with standard monitoring. In addition, long-term projections of costs and health outcomes in the JDRF cost-effectiveness analysis were based on a newly developed disease simulation model, whereas we used the CORE Diabetes Model.

The ICERs in our study are significantly higher than those reported in previous studies that used the CORE Diabetes Model to evaluate the cost-effectiveness of pump therapy [17]. St Charles et al. [17] applied annual direct costs of $5358 for continuous subcutaneous insulin infusion, compared with $3776 for MDI, a difference of only $1582, and obtained an ICER of $16,992 per QALY. In our analysis, higher incremental costs with SAPT were attributable to sensors and transmitters needed for CGM and a higher cost assigned to insulin pumps. If we had applied treatment costs from St Charles et al. [17] in our study, the ICER would drop from $229,675 to $63,198 per QALY. St Charles et al. [17] also applied a 1.2 percentage point decrease in HbA1c level with continuous subcutaneous insulin infusion versus MDI on the basis of a meta-analysis of 52 studies published between 1979 and 2001, of which only 1 had a randomized parallel group design. If we applied a treatment effect of this magnitude, the ICER would have decreased to $29,037 per QALY. Thus, the difference between the two studies is attributable to higher estimates of incremental treatment costs and lower estimates of relative effectiveness in our study based on actual data from STAR 3.

Our study has several limitations. First, to predict the incidence of long-term complications of type 1 diabetes mellitus, the CORE Diabetes Model relies on data from the UK Prospective Diabetes Study, the Diabetes Control and Complications Trial, the Framingham Heart Study, and the Wisconsin Epidemiologic Study of Diabetic Retinopathy. Although these epidemiological data are widely used to model health outcomes of patients with diabetes, they may not reflect progression of more recently diagnosed patients with type 1 diabetes treated in the modern era [25]. Second, outcomes observed in clinical trials may not accurately reflect factors such as long-term adherence and varying standards of care that may influence costs and outcomes associated with diabetes. Third, because 6-day sensors are not marketed in the United States, our analyses evaluating 6-day sensors assumed that the cost per sensor would be the same as the cost per 3-day sensor. Similarly, although we made assumptions in an attempt to most accurately reflect expected costs for diabetes devices and supplies (e.g., $16 discount, 65% sensor use), actual costs may differ across patients, payers, and markets. There was also a slight difference between versions of the Hypoglycemia Fear Survey used to model utility benefits associated with less fear of hypoglycemia [19] and the version administered in STAR 3. The Hypoglycemia Fear Survey 98, rather than the original version, was administered in STAR 3 and includes an additional item in the “worry” subscale. Although we expect the impact on the incremental utility benefit to be small, it introduces additional uncertainty into the analysis. Finally, patients in both treatment groups received a high level of care and may have been particularly diligent with insulin therapy given their participation in the trial.

Conclusions

Data from STAR 3 demonstrated further reductions in HbA1c levels among patients receiving SAPT relative to MDI. The overall findings of our economic evaluation demonstrate that when considering the significant and ongoing costs associated with SAPT relative to MDI and costs of long-term complications in relation to expected health benefits, SAPT is not economically attractive over a number of scenarios for adult patients with type 1 diabetes. A surprising finding from the sensitivity analyses was that subtle differences in assumptions in the explicit modeling of patients’ fears about hypoglycemia can have a dramatic impact on the resulting cost-effectiveness ratios. Our base-case results demonstrate that replacing 3-day sensors with 6-day sensors without per-unit price increases would improve the cost-effectiveness of SAPT. The development of future technological advances that could allow for reduced use of glucose test strips with SAPT could further improve its economic attractiveness.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at doi:10.1016/j.jval.2012.02.011 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

References


