

Cost Efficiency of Canagliflozin Versus Sitagliptin for Type 2 Diabetes Mellitus

Varun U. Ektare, BPharm, MPH; Janice M. S. Lopez, PharmD, MPH; Silas C. Martin, MS; Dipen A. Patel, BPharm, PhD; Marcia F. T. Rupnow, PhD; Marc F. Botteman, MSc, MA

Abstract

Objectives: To compare 1-year clinical outcomes and cost efficiency of treating adults with type 2 diabetes mellitus (T2DM) with canagliflozin (300 mg/day) or sitagliptin (100 mg/day), both added on a background of metformin and sulfonylurea.

Study design: An economic model integrated data from an active-controlled, randomized trial, claims database analyses, and published literature.

Methods: The model adopted a US managed care payer perspective and included the clinical and economic impact of achieving specific clinical quality goals. The model was run separately for 2 single clinical quality metrics, glycated hemoglobin (A1C) <7% (used as base case) or <8%, and 4 composite metrics (A1C <7% or <8% combined with body mass index <30 kg/m² and blood pressure <140/90 mm Hg or low-density lipoprotein cholesterol <100 mg/dL). Cost savings of achieving versus not achieving metrics were derived from a claims database analysis. Drug and adverse event costs were included.

Results: In the base case, compared with sitagliptin 100 mg, treatment with canagliflozin 300 mg resulted in \$215 in annual cost savings and 12.3 absolute percentage points more patients achieving goal. Similar findings were found across all other quality metrics (difference in proportion achieving goal ranging from 6.7% to 19.0% and annual savings ranging from \$1 to \$669). Canagliflozin remained cost saving versus sitagliptin in sensitivity analyses.

Conclusions: Canagliflozin 300 mg may represent a cost-efficient T2DM treatment option versus sitagliptin 100 mg for patients on metformin plus sulfonylurea due to lower overall costs and better achievement of A1C and quality composite goals.

Am J Manag Care. 2014;20:S204-S215

For author information and disclosures, see end of text.

Type 2 diabetes mellitus (T2DM) is a chronic, progressive disease associated with substantial clinical and economic burdens, accounting for 69,000 deaths in 2010¹ and \$245 billion in total annual medical costs in 2012.² With the passage of the Affordable Care Act (ACA) and the adoption of the pay-for-performance model, the treatment of T2DM is increasingly focused on short-term quality measures such as achieving glycated hemoglobin (A1C), low-density lipoprotein cholesterol (LDL-C), and blood pressure (BP) targets. These short-term end points have been proved to be predictors of long-term clinical and economic outcomes.³ A relationship between achieving A1C and other goals (eg, weight loss, BP reduction, cholesterol control, smoking cessation) and reductions in costs has been consistently reported in published literature, including evaluations of managed care costs, claims database analyses, and findings from a panel of healthcare leaders working with the National Committee for Quality Assurance (NCQA) Diabetes Recognition Program.^{4,6} These attributes of the short-term quality measures make them useful tools to identify high-quality healthcare providers and organizations, and to incentivize pay-for-performance under programs such as the Pioneer Accountable Care Organization (ACO) model and the Medicare Shared Savings Program.^{5,7,9} The NCQA and the National Quality Forum (NQF) continue to develop and endorse measures to evaluate the quality and cost of care for use by the CMS and other US payers.^{5,8,10}

Given the importance of achieving the short-term quality measures, various prescription antihyperglycemic agents (AHAs) in the market should be compared for their ability to help patients reach these quality targets. The relative health economic benefit of AHAs can be compared using a single metric of “cost efficiency” that combines the key components of T2DM quality measures, such as the proportion of patients achieving targets, the length of time patients stay at their targets, and the total costs associated with reaching these targets.¹¹ Based on the analytic framework drafted by the

Agency for Healthcare Quality & Research (AHRQ),¹² cost efficiency can be defined as the cost of getting 1 patient to achieve a treatment target, such as A1C less than 7%. Economic analyses that compare the short-term cost efficiency of new and existing AHAs in achieving such targets may be useful to managed care payers.

Many cost-effectiveness studies of AHAs in T2DM have been conducted using various economic models (eg, ECHO-T2DM,¹³ CORE Diabetes,^{14,16} and DELTA^{17,18}). These models have used results from clinical trials of 52 weeks or less in duration to estimate long-term clinical and economic outcomes associated with various AHAs over periods of up to 35 years.¹³⁻¹⁸ While valuable, these “traditional” long-term T2DM cost-effectiveness models do not examine costs associated with achieving short-term intermediate quality measures.^{4,5} Previous economic models^{19,20} adopting a short-term perspective have compared glipizide versus metformin or acarbose,²¹ nateglinide versus metformin,¹¹ and insulin detemir versus NPH insulin.²² However, few models have incorporated the concept of quality measures of care as important components in overall cost efficiency.

Short-term cost per outcome analyses focusing on the efficient attainment of desired healthcare outcomes or quality of care measures can be useful decision-making tools for managed care payers. With this in mind, a simple model that follows in the framework of cost efficiency measures proposed by AHRQ¹² was developed to compare the 1-year clinical outcomes and cost efficiency of treating hyperglycemia associated with T2DM of the recently approved agent canagliflozin with an established therapy, sitagliptin, in patients inadequately controlled on a background therapy of metformin and sulfonylurea. Canagliflozin, a sodium glucose cotransporter 2 (SGLT2) inhibitor,²³ and sitagliptin, a dipeptidyl peptidase-4 inhibitor, are both approved for use in adults with T2DM to improve glycemic control.²⁴

METHODS

Model Overview

The analysis population was similar to the 755 adult patients with inadequately controlled T2DM (A1C $\geq 7.0\%$ to $\leq 10.5\%$) who participated in a randomized phase 3 trial²⁵ comparing therapy with canagliflozin (300 mg/day) or sitagliptin (100 mg/day) plus maximally tolerated metformin (2000 mg per day for most patients) and sulfonylurea (glimepiride 6 mg/day for most patients). Inclusion and exclusion criteria and the

demographic/clinical profile of study participants have been previously reported.²⁵ Study findings showed that after 52 weeks, canagliflozin 300 mg provided a greater reduction from baseline in A1C than sitagliptin 100 mg (-1.03% vs -0.66% ; $P < .05$). In addition, a greater percentage of patients achieved an A1C less than 7.0% with canagliflozin than with sitagliptin (48% vs 35%), and patients receiving canagliflozin had a mean body weight reduction of -2.3 kg (-5.1 lb) compared with a mean increase of 0.1 kg (0.2 lb) in sitagliptin-treated patients ($P < .05$). Incidences of adverse events (AEs), serious AEs, and study discontinuations attributable to AEs were similar for canagliflozin 300 mg and sitagliptin 100 mg.²⁵ Canagliflozin was associated with higher rates of genital mycotic infections than sitagliptin, which led to 1 study discontinuation and no serious AEs; these events responded to standard antifungal treatment.²⁵

Over a 52-week time horizon, the model adopted the perspective of a US managed care payer considering formulary decisions regarding a new AHA, focusing on short-term direct medical and pharmacy costs, and excluded indirect (ie, productivity) costs and other costs not typically borne by a managed care payer.

Costs of genital mycotic infections and hypoglycemic events were also included in the model as AEs of interest. All costs are expressed in 2013 US dollars. The model was developed in Microsoft Excel.

For simplification, the model assumed that the average A1C reduction took effect only after 12 weeks; it was then assumed that this A1C reduction was sustained until the end of the 52-week model simulation period. No cost savings were accrued by any comparator during the first 12 weeks of therapy (when A1C declined but did not reach the full effect observed in weeks 12 to 52). Additionally, to simplify calculations, it was assumed that all patients received uniform doses of metformin 2000 mg per day and glimepiride 6 mg per day (these were the prescribed doses for the majority of trial patients)²⁵ as background therapy.

During the phase 3 trial,²⁵ 10.6% of patients in the canagliflozin 300-mg group and 22.5% in the sitagliptin 100-mg group discontinued the study drug due to treatment failure. This difference resulted in a longer duration of therapy with canagliflozin relative to sitagliptin. However, to ensure the highest level of simplicity and transparency in the base case analysis, it was assumed that all patients stayed on their assigned therapy for the entire 52-week duration of the analysis. In a sensitivity analysis, scenarios are presented in which discontinua-

■ **Table 1.** Main Clinical Inputs in the Canagliflozin Cost-Efficiency Model²⁵

	Canagliflozin 300 mg	Sitagliptin 100 mg
Patients achieving A1C <7% at week 52, %	47.6	35.3
Patients who met glycemic withdrawal criteria, % ^a	10.6	22.5
Patients with severe hypoglycemic event, % ^b	4.0	3.4
Patients with overall hypoglycemic event, %	43.2	40.7
Patients with female genital mycotic infections, %	6.9	1.9
Patients with male genital mycotic infections, %	5.0	0.3
Patients with urinary tract infections, %	4.0	5.6
Mean duration of exposure to study drug, weeks	42.64	41.44

A1C indicates glycated hemoglobin.

^aGlycemic withdrawal criteria correspond to patients needing glycemic rescue therapy due to lack of efficacy of the study treatment.

^bSevere hypoglycemic events were events coded in the trial as requiring assistance from another person.

tions occurred at rates reported in the clinical trial, and patients discontinuing the study drug are assumed to switch their medication to either liraglutide or pioglitazone from the time of discontinuation until the end of the 52-week analysis.

Outcomes

The main outcome measures included the total cost of each therapy, the cost per proportion of patients achieving defined therapeutic goals (cost per responder), and the incremental cost per additional patient reaching goal. Clinical outcomes analyzed included the proportion of patients achieving individual or composite quality metrics: (1) A1C less than 7% (used in the base-case analysis); (2) A1C less than 7%, body mass index (BMI) less than 30 kg/m², and BP less than 140/90 mm Hg; (3) A1C less than 7%, BP less than 140/90 mm Hg, and LDL-C less than 100 mg/dL; (4) A1C less than 8%; (5) A1C less than 8%, BMI less than 30 kg/m², and BP less than 140/90 mm Hg; and (6) A1C less than 8%, BP less than 140/90 mm Hg, and LDL-C less than 100 mg/dL. Similar to actual practice, this model does not control for medications used for cholesterol or BP (eg, statin or ACE inhibitor use), though these agents were used at the discretion of the treating physician in similar proportions of patients in both treatment arms during the clinical trial.

For all outcomes, cost efficiency was assessed in terms of average per-patient cost divided by the average proportion of patients achieving each quality metric. Incremental cost efficiency ratios were also computed, in which the difference in average per-patient cost was divided by the difference in the average proportion of patients achieving each quality metric.

Model Simulations

Multivariate, probabilistic sensitivity analyses were conducted whereby the model was run an arbitrarily large number of times (here, 5000 times) via Monte Carlo simulation techniques. In each of the 5000 model runs, input parameter values were selected from prespecified distributions. For instance, the probability of reaching A1C less than 7% may be represented with a beta distribution, while the cost savings of reaching (relative to not achieving) this goal may be represented with a different distribution (eg, normal). Distributions for the parameters were selected to represent the uncertainty surrounding the mean value of each parameter. The distribution of the results of the 5000 model runs was analyzed using estimated nonparametric bootstrapped 95th percentile credible intervals (95% CIs) around mean outcome values.

The analysis also recorded the proportion of model runs in which, relative to sitagliptin, canagliflozin treatment resulted in cost savings, higher efficacy, and both cost savings and higher efficacy. Finally, the 5000 model outcomes were plotted in 2 dimensions (with the proportion achieving goals on the x-axis and cost on the y-axis) to visually depict the distribution of outcomes.

Model Inputs

Table 1 shows key clinical inputs taken from the phase 3 trial comparing canagliflozin with sitagliptin in patients with T2DM receiving background therapy of metformin plus sulfonylurea,²⁵ and the **Appendix Table** provides the wholesale acquisition costs (WAC)²⁶ used in the model for canagliflozin (300 mg/day; \$9.64), sitagliptin (100 mg/day; \$9.46), and background metformin (2000 mg/day) with glimepiride (6 mg/day). Drug doses and frequency

Table 2. Cost Differences Associated With Achieving Versus Not Achieving Treatment Quality Metrics End Points⁴

Scenario and quality metrics considered	(1, base case)	(2)	(3)	(4)	(5)	(6)
A1C	<7%	<7%	<7%	<8%	<8%	<8%
BP	—	<140/90 mm Hg	<140/90 mm Hg	—	<140/90 mm Hg	<140/90 mm Hg
BMI	—	<30 kg/m ²	—	—	<30 kg/m ²	—
LDL-C	—	—	<100 mg/dL	—	—	<100 mg/dL
Total medical costs	-\$3130	-\$8464	-\$1554	-\$5132	-\$6784	-\$1940
ED	-\$278	-\$343	-\$135	-\$538	-\$131	-\$295
Inpatient	-\$1350	-\$3824	\$1521	-\$2357	-\$5019	\$341
Outpatient/other ^a	-\$1502	-\$4298	-\$2940	-\$2238	-\$1634	-\$1986
Diabetes-related medical costs	-\$1691	-\$4571	-\$2097	-\$2034	-\$2791	-\$1573
ED	-\$158	-\$132	-\$202	-\$158	\$62	-\$118
Inpatient	-\$385	-\$2683	-\$1011	-\$762	-\$2340	-\$442
Outpatient/other ^a	-\$1148	-\$1756	-\$884	-\$1113	-\$513	-\$1012

A1C indicates glycated hemoglobin; BP, blood pressure; BMI, body mass index; ED, emergency department; LDL-C, low-density lipoprotein cholesterol; —, criterion not included.

^aExcluding pharmacy costs.

of administration were obtained from product labels. In the base-case scenario, the cost of switching treatment was assumed to be zero, as the model assumed that no patient discontinued treatment. In the sensitivity analysis, it was assumed that patients would receive either liraglutide or pioglitazone as rescue medication. In the sensitivity analysis, the costs of liraglutide or pioglitazone treatment were included in the drug treatment costs starting from the average duration of study drug exposure (canagliflozin or sitagliptin) in weeks up through 52 weeks (end of study) in accordance with the randomized controlled trial data source. This was from 42.6 weeks in the canagliflozin arm and 41.4 weeks in the sitagliptin arm.

The cost impact of achieving versus not achieving univariate and composite A1C targets (with adjustments for covariates, including age, gender, year of index date, race, payer type, and Charlson Comorbidity Index) was obtained from a separate claims database analysis that studied annual direct medical costs (excluding drug costs, because these are included separately in the model) for patients with T2DM above or below an A1C threshold (Table 2).⁴ In the base case, results are presented for adjusted costs (diabetes-related or not). These costs were further categorized by emergency department, inpatient, and outpatient/other costs. A separate sensitivity analysis that included only diabetes-related medical costs—defined as costs from claims associated with a diagnosis of diabetes—was performed.

Costs of genital mycotic infections (ie, vulvovaginal candidiasis and balanitis or balanoposthitis), urinary tract infections, and hypoglycemic events were included

based on estimates from a separate analysis.²⁷ The cost for genital mycotic infections included 1 course of generic topical antifungal treatment (topical clotrimazole, 15-g tube) and 1 physician visit (Current Procedural Terminology code 99214 [ie, level 4 outpatient visit for an established patient]).²⁸ Estimated costs per event for female genital mycotic infections, male genital mycotic infections, and urinary tract infections were \$118, \$164, and \$111, respectively. Only hypoglycemic events reported as severe, which by definition in the clinical trial required assistance, were assumed to incur cost. Severe hypoglycemic events were further categorized as level 1 (71% of all severe events), requiring nonmedical intervention by a family member or another individual (cost assumed to be \$0); level 2 (28% of all severe events), requiring an emergency department visit (\$1392 per visit); or level 3 (1% of all severe events), requiring an inpatient stay (\$17,502 per visit).^{27,29}

RESULTS

Primary Analysis

Net per patient per year (PPPY) costs for the base-case scenario, using the A1C less than 7% end point, were lower with canagliflozin 300 mg than with sitagliptin 100 mg (Table 3). Total medical cost was the largest component of overall costs for both canagliflozin (82.8%) and sitagliptin (83.4%), and consisted of emergency department, inpatient, and outpatient costs. Medical costs were followed by drug costs (\$3735 for canagliflozin and \$3669 for sitagliptin). Costs associated with genital mycotic

■ **Table 3.** Net Annual Cost of Treatment for the Base-Case Scenario^a

	Canagliflozin 300 mg + MET + SU	Sitagliptin 100 mg + MET + SU	Difference
Study drug cost	\$3735	\$3669	\$66
Cost of switching therapy (excluded in base case; see text)	\$0	\$0	\$0
Total medical cost	\$18,269	\$18,566	−\$296
ED costs	\$873	\$900	−\$26
Inpatient costs	\$8332	\$8460	−\$128
Outpatient/other costs	\$9064	\$9206	−\$142
Severe hypoglycemia cost	\$23	\$19	\$3
Cost of genital mycotic infections	\$16	\$3	\$13
Cost of urinary tract infections	\$4	\$6	−\$2
Net total cost	\$22,047	\$22,263	−\$215

ED indicates emergency department; MET, metformin; SU, sulfonylurea.

^aBase-case scenario: glycosylated hemoglobin (A1C) <7% end point, total medical costs, and no discontinuations selected.

infections, urinary tract infections, and severe hypoglycemia were \$43 for canagliflozin 300 mg, representing 0.20% of total costs; these costs were lower for sitagliptin 100 mg (\$28), representing 0.13% of total costs.

Table 4 provides aggregate results for the base case and the other 5 analyses using different clinical quality measures to define treatment success. Canagliflozin treatment resulted in a higher proportion of patients achieving goals and lower costs across all quality end points.

Based on these results, average and incremental costs per responder were calculated for each quality metric (Table 4). For instance, the cost per patient achieving an A1C less than 7% was \$46,318 for canagliflozin 300 mg and \$63,068 for sitagliptin 100 mg. Average costs per responder were systematically higher for sitagliptin 100 mg than for canagliflozin 300 mg. For both drugs, average costs per responder were highest for the A1C less than 7%, BP less than 140/90 mm Hg, LDL-C less than 100 mg/dL criterion (\$98,201 for canagliflozin and \$142,653 for sitagliptin) and lowest for the A1C less than 8% criterion (\$24,551 for canagliflozin and \$32,633 for sitagliptin). When considering the incremental cost per responder, canagliflozin 300 mg was dominant, as it was both cost saving and more effective than sitagliptin in all scenarios.

Sensitivity Analyses on Cost Output

Limiting the analysis to diabetes-related medical costs led to a reduction of annual costs for both treatment groups: with canagliflozin 300 mg, costs decreased from \$22,047 to \$10,449, whereas costs decreased from

\$22,263 to \$10,529 with sitagliptin 100 mg, resulting in a net cost savings of \$79 favoring canagliflozin 300 mg. However, the inclusion of treatment discontinuations slightly increased total PPPY costs for both arms. For canagliflozin 300 mg, including discontinuations resulted in a cost of \$22,149, while for sitagliptin 100 mg it was estimated to cost \$22,407, for a net cost savings of \$259 favoring canagliflozin 300 mg.

Sensitivity Analyses Using Monte Carlo Simulation

Treatment with canagliflozin 300 mg resulted in greater efficacy compared with sitagliptin 100 mg in all scenarios. In addition, canagliflozin 300 mg was associated with lower costs than sitagliptin 100 mg in the majority of simulations, with the exception of the A1C less than 7%, BP less than 140/90 mm Hg, LDL-C less than 100 mg/dL criterion. In this case, canagliflozin 300 mg resulted in lower costs in 47% of cases (**Figure 1A**). In multivariate probabilistic sensitivity analysis, results were similar to the base-case analysis. **Figure 1B** presents 95% CIs for both the difference in the proportion of patients reaching each specific goal and net cost.

Canagliflozin 300 mg was dominant (ie, both cost saving and more effective) in 95% of the simulations using the A1C less than 8% criterion and the less than 8%, BMI less than 30 kg/m², BP less than 140/90 mm Hg criteria (**Figure 1A**). In the other scenarios, 95% of the simulations resulted in an incremental cost per responder for canagliflozin 300 mg compared with sitagliptin 100 mg of \$800 or less for the A1C less than 7% criterion; \$500 or less for A1C less than 7%, BMI less than 30 kg/m², BP less than 140/90 mm Hg; \$5100 or

■ **Table 4.** Efficacy, Cost, and Average and Incremental Costs per Responder^{33,a}

Quality Measure	Efficacy			Costs			Cost per Responder		
	CANA 300 mg	SITA 100 mg	Difference	CANA 300 mg	SITA 100 mg	Difference	Average		Incremental
							CANA 300 mg	SITA 100 mg	
A1C <7% (base-case scenario)	47.6%	35.3%	12.3%	\$22,047	\$22,263	−\$215	\$46,318	\$63,068	CANA dominant
A1C <7%, BMI <30 kg/m ² , BP <140/90 mm Hg	22.1%	15.0%	7.1%	\$20,106	\$20,487	−\$382	\$90,976	\$136,582	CANA dominant
A1C <7%, BP <140/90 mm Hg, LDL-C <100 mg/dL	21.5%	14.8%	6.7%	\$21,113	\$21,113	−\$1	\$98,201	\$143,632	CANA dominant
A1C <8%	85.0%	66.0%	19.0%	\$20,868	\$21,538	−\$669	\$24,551	\$32,633	CANA dominant
A1C <8%, BMI <30 kg/m ² , BP <140/90 mm Hg	39.5%	25.3%	14.2%	\$18,510	\$19,170	−\$660	\$46,860	\$75,770	CANA dominant
A1C <8%, BP <140/90 mm Hg, LDL-C <100 mg/dL	35.5%	27.8%	7.7%	\$20,608	\$20,642	−\$34	\$58,050	\$74,251	CANA dominant

BMI indicates body mass index; BP, blood pressure; CANA, canagliflozin; LDL-C, low-density lipoprotein cholesterol; SITA, sitagliptin.

^aIncremental defined as difference in cost/difference in efficacy.

less for A1C less than 8%, BP less than 140/90 mm Hg, LDL-C less than 100 mg/dL; and \$12,000 or less for A1C less than 7%, BP less than 140/90 mm Hg, LDL-C less than 100 mg/dL.

DISCUSSION

The results of this 52-week cost efficiency model suggest that canagliflozin 300 mg may be a cost-saving option compared with sitagliptin 100 mg when used in combination with metformin plus sulfonyleurea for the treatment of adults with T2DM. The cost savings with canagliflozin over sitagliptin were attributable to better glycemic control (A1C), as well as improvement in other quality metrics such as BMI and BP. In sensitivity analyses, canagliflozin 300 mg remained a cost-saving option when including only diabetes-related costs, when analyzing the impact of achieving treatment goals, and when the cost impact of treatment discontinuations was included.

Previously published cost-effectiveness models comparing AHAs for the treatment of T2DM have focused mainly on comparing total medical costs and changes in quality-adjusted life-years for 1 therapy versus another.^{14,15,20,22} In contrast, the current model simulated short-term outcomes that may be relevant from the payer and provider perspectives by analyzing costs associated with current and emerging quality metrics^{5,8,9}; clinical outcomes of hypoglycemia, BP, and LDL-C; drug costs; overall medical costs; and costs of associated AEs.

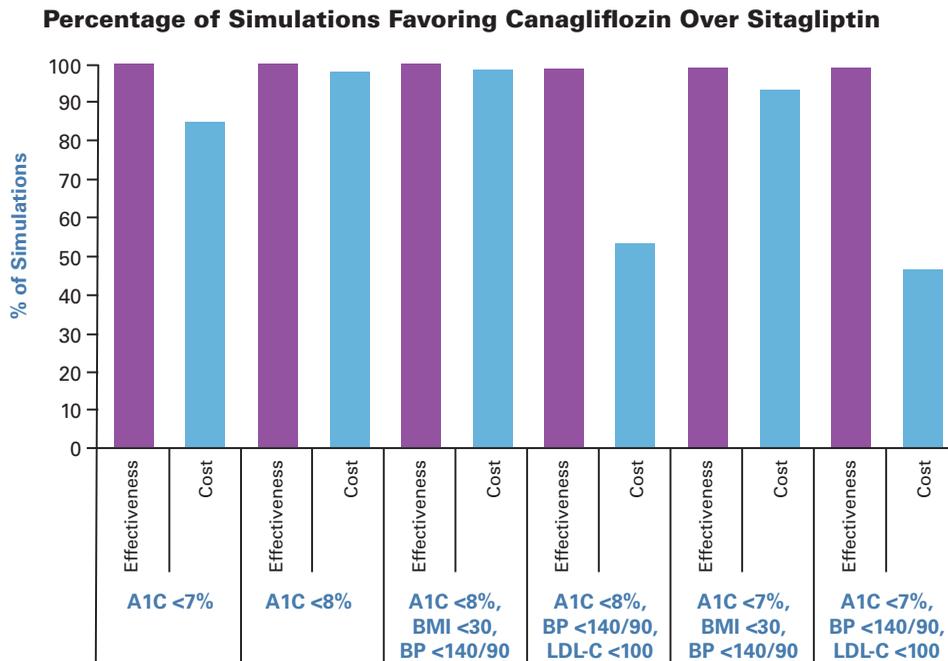
Using these clinical quality metrics anchored to A1C improvements and including measures of BMI, BP,

and LDL-C, canagliflozin 300 mg was associated with higher proportions of patients achieving all efficacy criteria and lower costs than sitagliptin 100 mg. Model outcomes such as these provide relatively simple and accessible information to formulary decision makers in the absence of real-world utilization data, focusing on the efficiency of achieving individual and multiple short-term treatment goals that are relevant to payers, providers, and patients. These outcomes are also consistent with AHRQ recommendations, the NCQA Diabetes Recognition Program, endorsed NQF measures, and ACA/ACO quality metrics.^{5,8,9} Perhaps most notably, in this model, the value of each therapy is linked to the economic benefits of achieving short-term clinical goals, thereby providing ACOs and other payers with data that can be used to align reimbursement practices with execution of best clinical practices and achievement of quality metrics, with the overarching goals of reducing costs and improving clinical outcomes in patients with T2DM.³⁰⁻³²

A limitation of this analysis is that it relied on efficacy data from a clinical trial, which may not be representative of observations in real-world clinical practice. However, data from a randomized, active-controlled, phase 3 clinical trial is a stronger source for drug-to-drug comparisons than indirect comparisons often used for economic modeling. This analysis was also limited to representing only short-term outcomes and does not estimate long-term diabetes complications. However, given the results of this study, it is likely that the long-term cost-efficiency of canagliflozin 300 mg would have

■ **Figure 1.** (A) Percentage of Simulations Favoring Canagliflozin Over Sitagliptin, and (B) 95% Credible Intervals for Simulation Results for the Difference in the Proportion of Patients Reaching Each Specified Efficacy Goal and Net Cost of Achieving the Goal

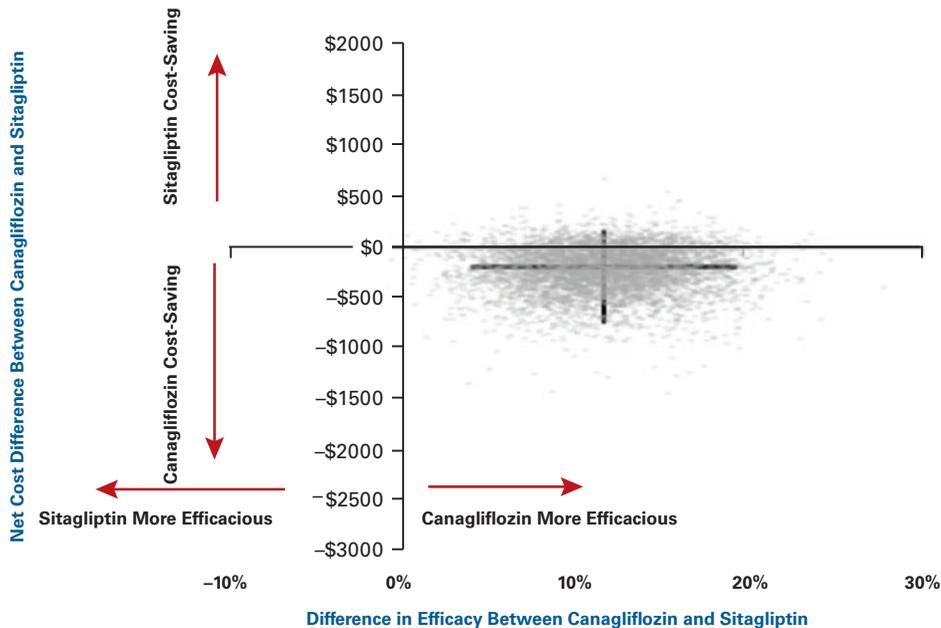
A.



A1C indicates glycated hemoglobin; BMI, body mass index; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol.

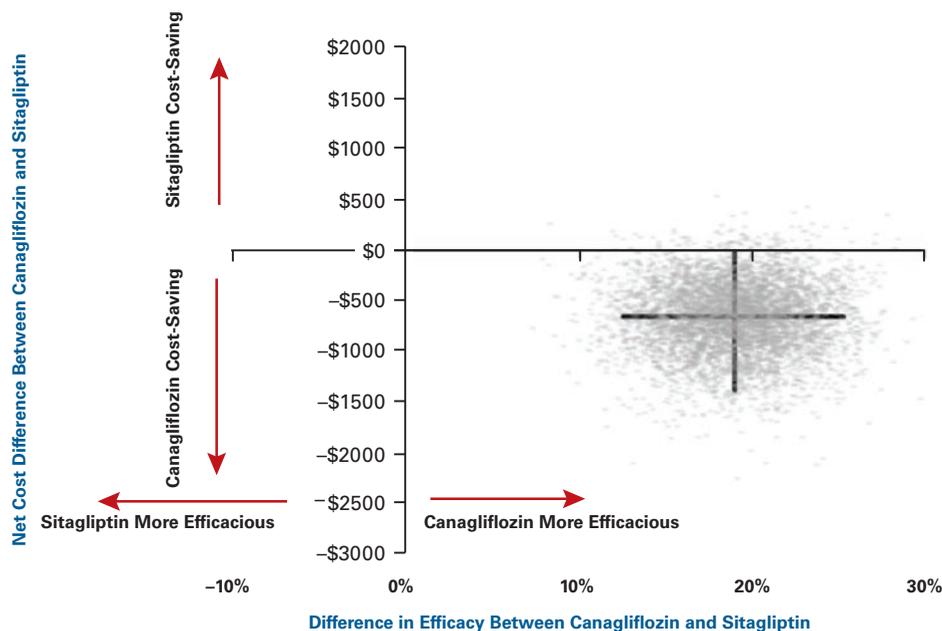
B.

A1C <7%



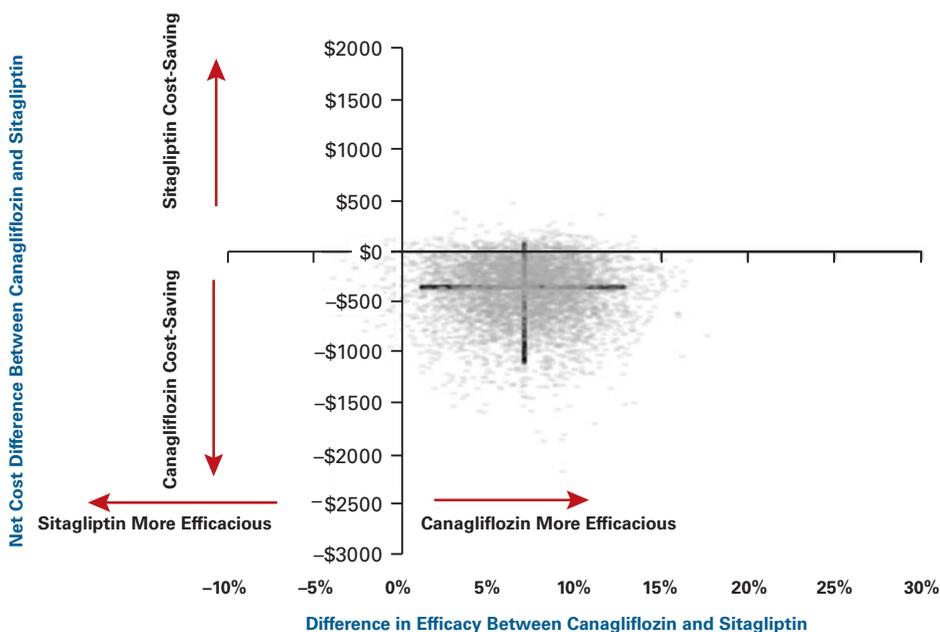
A1C indicates glycated hemoglobin. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

A1C <8%



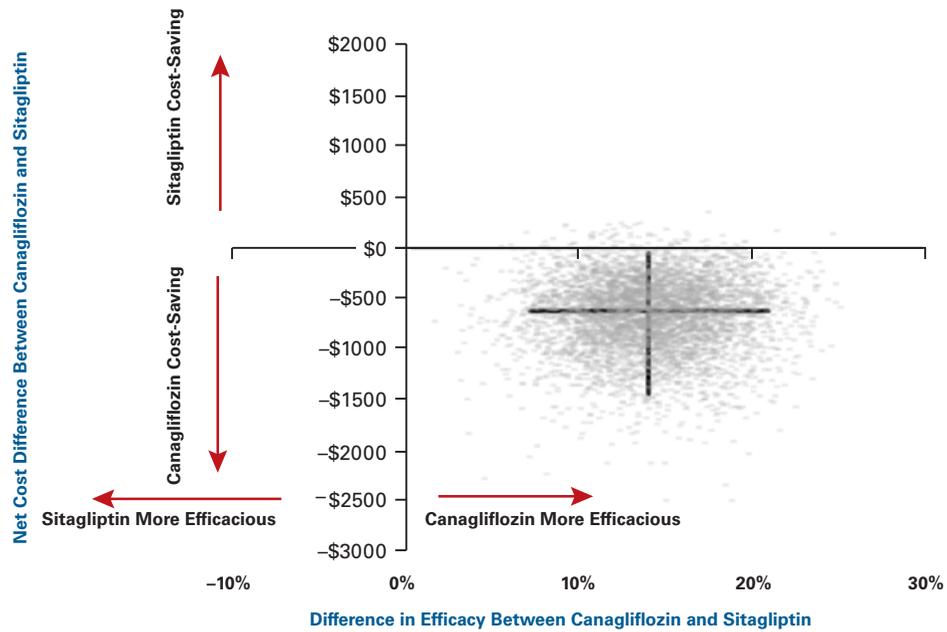
A1C indicates glycated hemoglobin. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

A1C <7%, BMI <30 kg/m², BP <140/90 mm Hg



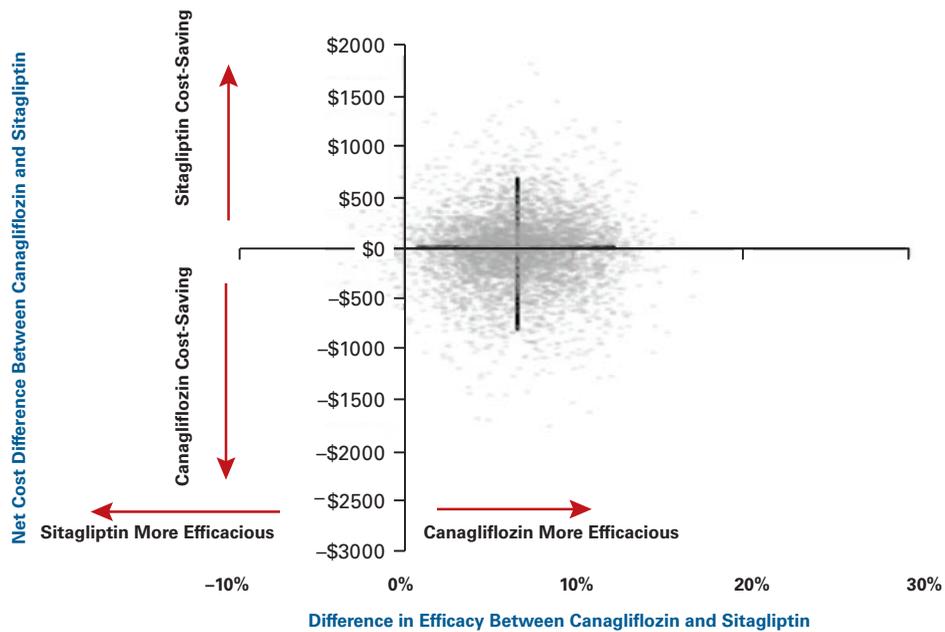
A1C indicates glycated hemoglobin; BMI, body mass index; BP, blood pressure. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

A1C <8%, BMI <30 kg/m², BP <140/90 mm Hg



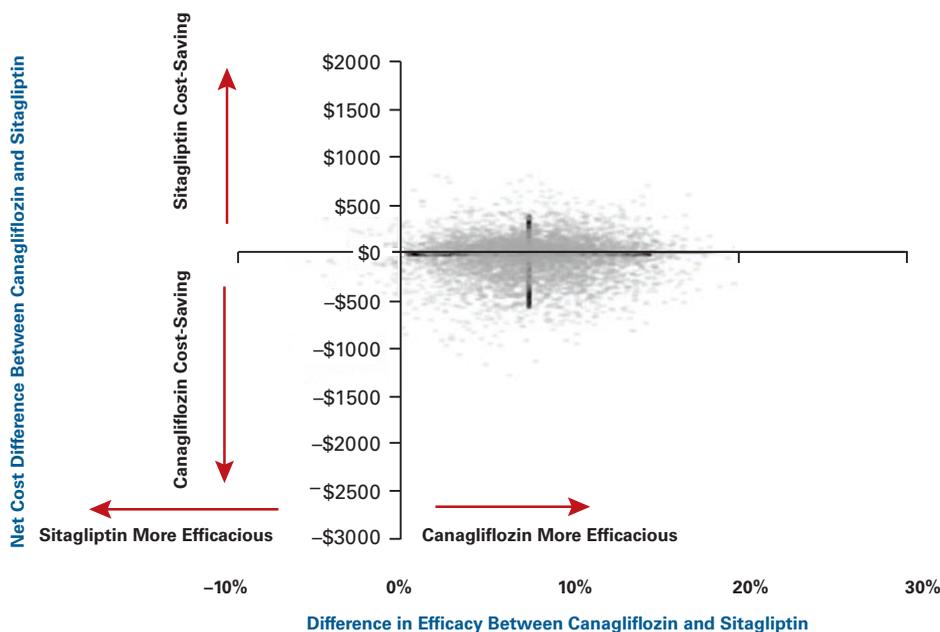
A1C indicates glycated hemoglobin; BMI, body mass index; BP, blood pressure. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

A1C <7%, BP <140/90 mm Hg, LDL-C <100 mg/dL



A1C indicates glycated hemoglobin; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

A1C <8%, BP <140/90 mm Hg, LDL-C <100 mg/dL



A1C indicates glycated hemoglobin; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol. Individual gray dots represent simulation results; the vertical and horizontal lines represent the 95% credible interval for simulated costs and simulated efficacy, respectively.

been better than that of sitagliptin 100 mg in this patient population as well.

In this analysis, we presented results for the cost per responder, including medical costs in the numerator. Had the cost difference associated with achieving clinical end points been excluded, the incremental cost per responder for canagliflozin 300 mg over sitagliptin 100 mg would have ranged from \$416 for the A1C less than 8% end point to \$1178 for the composite end point of A1C less than 7%, BP less than 140/90 mm Hg, and LDL-C less than 100 mg/dL. This incremental cost is minimal considering that the total medical cost savings for each additional responder ranged from \$1554 for the composite end point of A1C less than 7%, BP less than 140/90 mm Hg, and LDL-C less than 100 mg/dL, to \$8464 for the composite end point of A1C less than 7%, BMI less than 30 kg/m², and BP less than 140/90 mm Hg.

In conclusion, based on the inputs and assumptions used, the results of this 52-week economic analysis suggests that canagliflozin 300 mg may represent a cost-efficient treatment option versus sitagliptin 100 mg for patients with T2DM receiving background therapy of metformin plus a sulfonylurea due to lower costs; better

achievement of A1C, and composite quality-of-care goals including BMI, BP, and LDL-C; and fewer treatment failures.

Author affiliations: Pharmerit Interational, Bethesda, MD (MFB, VUE, DAP); Health Economics and Outcomes Research, Janssen Scientific Affairs, LLC (a Johnson & Johnson company), Raritan, NJ (JMSL, SCM, MFTR).

Funding source: This supplement was supported by Janssen Pharmaceuticals, Inc. This analysis was funded, in part, by Janssen Scientific Affairs, LLC, and was based on data from a study supported by Janssen Research & Development, LLC. Editorial support was provided by Cherie Koch, PhD, of MedErgy, and was funded by Janssen Scientific Affairs, LLC.

Author disclosures: Mr Botteman reports stock ownership with Pharmerit International. Drs Lopez and Rupnow and Mr Martin report employment with Janssen Scientific Affairs, LLC (a Johnson & Johnson company), and stock ownership with Johnson & Johnson. Dr Rupnow also reports meeting/conference attendance on behalf of Janssen Scientific Affairs, LLC (a Johnson & Johnson company). Mr Ektare and Dr Patel report no relationships or financial interests with any entity that would pose a conflict of interest with the subject matter of this supplement.

Authorship information: Concept and design (MFB, VUE, JMSL, SCM, DAP); acquisition of data (JMSL); analysis and interpretation of data (MFB, VUE, JMSL, SCM, DAP, MFTR); drafting of the manuscript (MFB, VUE, DAP); critical revision of the manuscript for important intellectual content (MFB, VUE, JMSL, SCM, DAP, MFTR); statistical analysis (MFB, VUE); obtaining funding (MFTR); administrative, technical, or logistic support (MFTR); and supervision (MFB, VUE, MFTR).

Address correspondence to: Marc F. Botteman, MSc, MA, 4350 E W Highway, Ste 430, Bethesda, MD 20814. E-mail: mbotteman@pharmerit.com.

REFERENCES

- Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2010. *Natl Vital Stat Rep*. 2013;61(4):1-117.
- American Diabetes Association. Economic costs of diabetes in the US in 2012. *Diabetes Care*. 2013;36(4):1033-1046.
- De Berardis G, Pellegrini F, Franciosi M, et al. Quality of diabetes care predicts the development of cardiovascular events: results of the QuED study. *Nutr Metab Cardiovasc Dis*. 2008;18(1):57-65.
- Lafeuille MH, Grittner AM, Gravel J, et al. Quality measure attainment in patients with type 2 diabetes mellitus. *Am J Manag Care*. 2014;20(1 suppl):S5-S15.
- Curnow R, Knight TW, Harris R, Linscott K. Advancing care with NCOA's Diabetes Recognition Program. Washington, DC: NCOA's Diabetes Recognition Program (DRP) Summit: Leaders Advancing Quality of Care for Patients With Diabetes; May 18, 2012. http://www.ncqa.org/Portals/0/Programs/Recognition/NCOA%20White%20Paper%20Update%20201212_v2.pdf. Accessed July 15, 2014.
- Stephens JM, Botteman MF, Hay JW. Economic impact of antidiabetic medications and glycemic control on managed care organizations: a review of the literature. *J Manag Care Pharm*. 2006;12(2):130-142.
- CMS. Pioneer ACO Model. <http://innovation.cms.gov/initiatives/Pioneer-ACO-Model>. Accessed July 15, 2014.
- CMS. Guide to quality performance standards for Accountable Care Organizations starting in 2012: pay for reporting and pay for performance. <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/sharedsavingsprogram/Downloads/ACO-Guide-Quality-Performance-2012.pdf>. Accessed July 15, 2014.
- Coffey RM, Matthews TL, McDermott K. Diabetes care quality improvement: a resource guide for state action. AHRQ Publication No. 04-0072. <http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/diabguide/diabqguide.pdf>. Published September 2004. Accessed July 15, 2014.
- O'Connor PJ. Towards a comprehensive diabetes quality measure set: new measurement opportunities and methodological challenges. http://www.qualityforum.org/Publications/2008/11/White_Paper_Adding_Value_to_Diabetes_Quality_Measures_Opportunities_and_Methodological_Challenges.aspx. Published November 5, 2008. Accessed July 15, 2014.
- Caro JJ, Salas M, O'Brien JA, et al. Modeling the efficiency of reaching a target intermediate end point: a case study in type 2 diabetes in the United States. *Value Health*. 2004;7(1):13-21.
- Agency for Healthcare Research and Quality. Identifying, categorizing, and evaluating health care efficiency measures. AHRQ Publication No. 08-0030. <http://www.ahrq.gov/research/findings/final-reports/efficiency/hcemch2.html>. Published April 2008. Accessed July 15, 2014.
- Willis M, Asseburg C, He J. Validation of economic and health outcomes simulation model of type 2 diabetes mellitus (ECHO-T2DM). *J Med Econ*. 2013;16(8):1007-1021.
- Lee WC, Conner C, Hammer M. Cost-effectiveness of liraglutide versus rosiglitazone, both in combination with glimepiride in treatment of type 2 diabetes in the US. *Curr Med Res Opin*. 2011;27(5):897-906.
- Lee WC, Samyshkin Y, Langer J, Palmer JL. Long-term clinical and economic outcomes associated with liraglutide versus sitagliptin therapy when added to metformin in the treatment of type 2 diabetes: a CORE Diabetes Model analysis. *J Med Econ*. 2012;15(suppl 2):28-37.
- Palmer AJ, Roze S, Lammert M, et al. Comparing the long-term cost-effectiveness of repaglinide plus metformin versus nateglinide plus metformin in type 2 diabetes patients with inadequate glycaemic control: an application of the CORE Diabetes Model in type 2 diabetes. *Curr Med Res Opin*. 2004;20(suppl 1):S41-S51.
- van der Steen A, Verheggen BG, Heeg BMS, van Hout BA. Dealing with competing causes of death, illness and costs: the Disease Elimination Life Table Analysis (DELTA) model. *Value Health*. 2007;10:A454. Abstract PMC11.
- Verheggen BG, van der Steen A, Heeg BMS, Vos CBJ, van Hout BA. Cost-effectiveness of Januvia versus Avandia as supplementary treatment in combination with metformin for patients with type 2 diabetes. *Value Health*. 2007;10:A264. Abstract PDB33.
- Hood SC, Annemans L, Rutten-van Mölken M. A short term cost-effectiveness model for oral antidiabetic medicines in Europe. *Pharmacoeconomics*. 1998;13(3):317-326.
- Ramsdell JW, Braunstein SN, Stephens JM, et al. Economic model of first-line drug strategies to achieve recommended glycaemic control in newly diagnosed type 2 diabetes mellitus. *Pharmacoeconomics*. 2003;21(11):819-837.
- Ramsdell JW, Grossman JA, Stephens JM, Botteman MF, Arocho R. A short-term cost-of-treatment model for type 2 diabetes: comparison of glipizide gastrointestinal therapeutic system, metformin, and acarbose. *Am J Manag Care*. 1999;5(8):1007-1024.
- Ridderstråle M, Jensen MM, Gjesing RP, Niskanen L. Cost-effectiveness of insulin detemir compared with NPH insulin in people with type 2 diabetes in Denmark, Finland, Norway, and Sweden. *J Med Econ*. 2013;16(4):468-478.
- Invokana (canagliflozin) tablets, for oral use [package insert]. Titusville, NJ: Janssen Pharmaceuticals; 2013.
- Januvia (sitagliptin) tablets [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2012.
- Scherthaner G, Gross JL, Rosenstock J, et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. *Diabetes Care*. 2013;36(9):2508-2515.
- Truven Health Analytics. Red Book. <http://www.redbook.com/redbook/index.html>. Accessed July 15, 2014.
- Ward A, Alvarez P, Vo L, Martin S. Direct medical costs of complications of diabetes in the United States: estimates for event-year and annual state costs (USD 2012). *J Med Econ*. 2014;17(3):176-183.
- National Fee Analyzer: charge data for evaluating fees nationally, 2013 edition*. Salt Lake City, UT: Optuminsight Inc; 2012.
- O'Brien JA, Patrick AR, Caro J. Estimates of direct medical costs for microvascular and macrovascular complications resulting from type 2 diabetes mellitus in the United States in 2000. *Clin Ther*. 2003;25(3):1017-1038.
- Tzeel EA. Optimizing diabetes management: managed care strategies. *Am J Manag Care*. 2013;19(8 suppl):S149-S154.
- McClellan M, McKethan AN, Lewis JL, Roski J, Fisher ES. A national strategy to put accountable care into practice. *Health Aff (Millwood)*. 2010;29(5):982-990.
- Rice D, Roberts WL, Collinsworth A, Fleming N. Diabetes and accountable care organizations: an accountable care approach to diabetes management. *Clinical Diabetes*. 2011;29(2):70-72.
- Bailey RA, Damaraju CV, Martin SC, et al. Attainment of diabetes-related quality measures with canagliflozin versus sitagliptin. *Am J Manag Care*. 2014;20(1 suppl):S16-S24.