

The Impact of Patient Preferences on the Cost-Effectiveness of Intensive Glucose Control in Older Patients With New-Onset Diabetes

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OBJECTIVE — Cost-effectiveness analyses have reported that intensive glucose control is not cost-effective in older patients with new-onset diabetes. However, these analyses have had limited data on patient preferences concerning diabetic health states. We examined how the cost-effectiveness of intensive glucose control changes with the incorporation of patient preferences.

RESEARCH DESIGN AND METHODS — We collected health state preferences/utilities from 519 older diabetic patients. We incorporated these utilities into an established cost-effectiveness model of intensive glucose control and compared incremental cost-effectiveness analyses ratios (ICERs) (cost divided by quality-adjusted life-year [QALY]) when using the original and patient-derived utilities for complications and treatments.

RESULTS — The mean utilities were ~0.40 for major complications, 0.76 (95% CI 0.74–0.78) for conventional glucose control, 0.77 (0.75–0.80) for intensive therapy with oral medications, and 0.64 (0.61–0.67) for intensive therapy with insulin. Incorporating our patient-derived complication utilities alone improved ICERs for intensive glucose control (e.g., patients aged 60–65 years at diagnosis, \$136,000/QALY→\$78,000/QALY), but intensive therapy was still not cost-effective at older ages. When patient-derived treatment utilities were also incorporated, the cost-effectiveness of intensive treatment depended on the method of glucose control. Intensive control with insulin generated fewer QALYs than conventional control. However, intensive control with oral medications was beneficial on average at all ages and had an ICER ≤\$100,000 to age 70.

CONCLUSIONS — The cost-effectiveness of intensive glucose control in older patients with new-onset diabetes is highly sensitive to assumptions regarding quality of life with treatments. Cost-effectiveness analyses of diabetes care should consider the sensitivity of results to alternative utility assumptions.

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Over 40% of people living with type 2 diabetes are over the age of 65. The condition represents a significant health burden for such patients (1–4), and the care of this population is a substantial economic burden for society (5,6). Despite the high prevalence of older individuals with diabetes, there is consid-

erable uncertainty regarding how intensively to control glucose levels in these patients (7). This uncertainty exists in part because elderly patients have been excluded from major trials of intensive glucose control (8).

Without such data, insight into the effectiveness and cost-effectiveness of in-

tensive glucose control in older patients has come from decision and cost-effectiveness analyses (9–11). Cost-effectiveness analysis is a policy analysis tool that provides an assessment of the relative social value of alternative medical interventions. Since clinical evidence may often not be adequate to fully characterize effects on final treatment outcomes, as is the case with diabetes treatments, simulation models are often used to extrapolate from the intermediate outcomes of clinical trials. Cost-effectiveness models of diabetes care have consistently reported that intensive glucose control compared with conventional glucose control produces minimal health benefits (9) and is not cost-effective in older patients with new-onset diabetes (10,11). Analysis of a model developed at the National Institutes of Health (NIH) showed that intensive glucose control was highly cost-effective compared with conventional control for patients with onset of diabetes before 50 years of age, while intensive glucose control was not cost-effective for patients with onset of diabetes at 65 years and older (10,12). These results were confirmed in analysis of an updated model of diabetes developed by the Centers for Disease Control Diabetes Cost-effectiveness Group (11).

The main result of such cost-effectiveness studies is the incremental cost-effectiveness ratio (ICER), which is the incremental cost per unit of health gained with one program compared with another. The unit of health that is typically used is a quality-adjusted life-year (QALY), which is a measure of health that captures changes in morbidity and mortality. QALYs are calculated by multiplying the time spent in specific health states by quality-of-life weights called utilities. A utility is a quantitative measure of preference on a scale from 0 to 1, where 0 is equivalent to death and 1 is equivalent to perfect health (13). Utilities can be elicited from patients or nonpatients and by several methods (13,14). To date, diabetes cost-effectiveness studies have had limited data on diabetes health state util-

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Abbreviations: ICER, incremental cost-effectiveness analyses ratio; NIH, National Institutes of Health; QALY, quality-adjusted life-year.

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

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ities and have not routinely evaluated the sensitivity of results to alternative utilities for complications (10–12,15,16). The National Institutes of Health (NIH) model used complication state utilities found in the literature that were obtained from patient and nonpatient populations, using several different utility elicitation methods (17–19). In the one sensitivity analysis that has been conducted, investigators found that the NIH model results for the overall diabetic population did not differ significantly whether or not quality-of-life adjustment for complications was included. However, no such analyses have ever been conducted for important subpopulations such as the elderly, for whom results may differ (10).

In addition, diabetes cost-effectiveness studies have, until very recently (20), generally assumed that life with intensive or conventional glucose control is equivalent to life in perfect health. This assumption does not acknowledge that achieving intensive glucose control typically requires greater use of insulin and multiple oral medications than otherwise would be required for conventional control (8,21). It also assumes that quality of life with therapies as distinct as insulin and metformin are equivalent (22). The quality-of-life impact of treatments may have a particularly large effect on the results of cost-effectiveness analyses of intensive glucose control because life with treatment is experienced by all patients, whereas the reduction in diabetes complications resulting from the treatment is experienced by only a minority of patients. This effect may be especially important for older patients who may have significant comorbid illnesses that further decrease their chances of experiencing long-term benefits.

We systematically obtained utilities from older diabetic patients and examined the impact of utilities for both complication and treatment health states on the results of the cost-effectiveness analysis of intensive glucose control in patients >65 years of age with new-onset diabetes.

RESEARCH DESIGN AND METHODS

Preferences of older diabetic patients

From December 2001 to January 2003, we collected preference data during face-to-face interviews with patients, ≥ 65 years of age, who were living with diabetes and attending the University of Chicago general medicine, endocrinology,

and geriatric clinics. Prospective subjects were identified through clinic scheduling software, and a diabetes diagnosis was confirmed through the medical record. We recruited by telephone, telephoning 1,067 patients and reaching 694, and completing interviews with 555 subjects.

Patients' utilities for blindness (no vision in either eye), end-stage renal disease requiring dialysis, lower-extremity amputation, conventional glucose control (one pill or single insulin injection with infrequent self-monitoring), intensive glucose control with oral therapy (two pills and periodic blood checks for side effects), and intensive glucose control with insulin (two insulin injections per day, daily home glucose monitoring, and severe hypoglycemic event every 2 years) were determined using time-tradeoff questions. For each time-tradeoff elicitation, patients were given a description of a health state and asked to consider life in that state. For the treatment utility questions, the subjects were asked to consider how the therapy would affect their daily lives and not consider the long-term effects of the treatments. During the time-tradeoff elicitation patients were asked to give their preference for 10 years in the health state of interest and a shorter period of time in perfect health. In a series of questions, using the ping-pong method, the time in perfect health was altered until the patient was indifferent between the two choices.

Medical records were abstracted for additional clinical data on current medications, comorbidities, and risk factor levels. The 519 individuals who completed all time-tradeoff questions and had complete chart abstraction data are the subjects of this analysis.

The results of the time-tradeoff questions are presented as means with 95% CIs. The differences between treatment utilities for individual patients were evaluated using paired *t* tests (SAS 8.1; SAS Institute, Cary, NC).

Model of diabetes

We used a previously validated model of the cost-effectiveness of intensive glucose control for type 2 diabetes created at the NIH (courtesy of R. Eastman) (10,12). The model compares conventional and intensive glucose control, defined as therapies designed to produce HbA_{1c} (A1C) levels of 10 and 7.2%. This Monte Carlo simulation model is framed by simultaneous progression of disease through nephropathy, neuropathy, retinopathy,

cardiovascular disease, and mortality. Within a 1-year cycle length, patients move from one disease state to another or stay in the current disease state until death or age 95 (Microsoft Excel 2000; Microsoft, Seattle, WA; and @Risk 4.0 for Windows; Palisades, Newfield, NY). When multiple health states occurred, we used the minimum health state method, which entails using the lowest single treatment or complication utility present during a given year for a simulated patient when calculating a QALY (23).

We performed simulations, as previously described in published reports, for hypothetical patients with new-onset type 2 diabetes at age 60–90 years of age (10,12). Cohorts were divided into 5-year age-groups. For each specific model setting, we ran 10,000 iterations.

Sensitivity analysis: complication and treatment utilities

For our sensitivity analysis, all simulations compare intensive and conventional glucose control for the hypothetical group of older patients mentioned above. Holding all other model assumptions constant, we compared model results using 1) original complication and treatment utilities, 2) our patient-derived complication utilities but original treatment utilities, 3) our patient-derived treatment utilities but original complication utilities, and 4) our patient-derived utilities for both complication and treatment states. In the case of intensive glucose control, we separately evaluated the impact of the utility for life with intensive insulin and the utility for life with intensive oral medications. In both analyses, we assumed that the same treatment benefits (A1C = 7.2%) and costs of intensive glucose control would be generated from intensive insulin and intensive oral medication therapy in comparison to conventional glucose control (A1C = 10%).

For each unique combination of age-group, utility assumptions, and glucose control treatment option, individual simulations were run for each of the 519 combinations of utilities available from our dataset. For each individual simulation, we again ran 10,000 iterations. Based on these simulation results, we calculated means and 95% CIs for the change in QALYs. In order to calculate 95% CIs for average incremental cost-effectiveness ratios, we used nonparametric bootstrapping methods (24). The original simulation results were sampled with replacement to generate new data-

Table 1—Comparison of original model and patient preferences for glucose control treatments and microvascular complications

Sources	Utilities for complications			Utilities for treatments		
	Blindness	Chronic renal failure with hemodialysis	Amputation	Conventional glucose control	Intensive glucose control	
				Oral medications	Insulin	
Original model utilities (refs. 17–19)	0.69	0.61	0.80	1	1	1
Patient utilities	0.39 (0.36–0.42)	0.36 (0.34–0.39)	0.45 (0.42–0.48)	0.76 (0.74–0.78)	0.77 (0.75–0.80)	0.64 (0.61–0.67)

Data are means (95% CI), unless otherwise indicated.

sets with distinct average ICERs. This was repeated 1,000 times.

RESULTS

Survey patient characteristics

The mean age of interview subjects was 74. The majority was female (63%) and African American (79%). The mean duration of diabetes was 13 years. The mean A1C was 7.7, and 40% had a A1C <7%. Forty percent of the group took insulin. Nineteen percent had diabetic nephropathy, 22% had diabetic neuropathy, and 15% had diabetic retinopathy.

Utilities

The mean for each of the complication health state utilities was ~0.4 in our study population and lower than utilities used in the original NIH model report (Table 1). For glucose control treatment states, the mean utilities were 0.76 (95% CI 0.74–0.78) for conventional glucose control, 0.77 (0.75–0.80) for intensive glucose control with oral medications, and 0.64 (0.61–0.67) for intensive glucose control with insulin. In comparisons of the treatment utilities, the only statistically significant difference was between utilities for conventional control and intensive glucose control with insulin ($P < 0.01$).

Model results

When using the original model utilities, intensive glucose control compared with conventional glucose control was most cost-effective in the youngest patients (60–65 years of age at disease onset) but became progressively less cost-effective as the age at diagnosis increased (Table 3, column 2). The ICER for intensive glucose control compared with conventional glucose control was \$136,000/QALY for patients 60–65 years of age and exceeded \$1,000,000/QALY after age 75.

When our patient-derived utilities for complications were incorporated, the dif-

ference in the QALYs generated under intensive versus conventional glucose control increased compared with those found in the original simulations (Table 2, columns 3 and 4). As a result, intensive glucose control became more cost-effective compared with conventional glucose control with a mean ICER of \$78,000/QALY (95% CI 75,000/QALY–81,000/QALY) for patients 60–65 year of age (Table 3, column 3). However, the mean ICER remained over \$100,000 per QALY for patients >65 years of age at the time of diagnosis.

When we incorporated patient utilities for treatments, the change in QALYs and ICERs for the treatment comparisons varied depending on which intensive therapy utility was incorporated (Tables 2 and 3). When patient utilities for intensive glucose control with insulin were used, intensive glucose control consistently generated fewer QALYs than conventional glucose control, with 95% CIs clearly in the negative range for all age-groups. Intensive therapy with insulin was consistently less beneficial and more expensive than conventional glucose control. These findings remained the same regardless of whether we used the original or our patient-derived complication utilities.

In contrast, when the utility for intensive glucose control with oral medications was examined, the mean change in QALYs indicated that intensive glucose control was beneficial at all ages compared with conventional glucose control. In addition, the mean ICERs for these simulations decreased compared with those using the original utility assumptions. However, the CIs for the change in QALYs above age 65 still included negative numbers, indicating that intensive therapy with oral medications could still be harmful and, similarly, the CIs for ICERs in patients aged >65 years included the possibility that conventional therapy would be preferred to intensive

therapy. When our patient-derived complication utilities were also incorporated into these analyses, the intensive therapy was clearly beneficial up to age 70 with mean ICERs \leq \$100,000/QALY. Above 70 years of age at disease onset, the mean ICERs remained $<$ \$160,000/QALY, but CIs still included the possibility that conventional therapy would be preferred to intensive therapy.

CONCLUSIONS— Prior cost-effectiveness studies of intensive glucose control in older patients have made assumptions regarding the quality of life with complications and treatments related to diabetes that have not been previously examined with data on actual patient preferences (10–12). Our study provides systematically collected patient preference data and illustrates the sensitivity of the results of cost-effectiveness analysis to the incorporation of patient preferences and to assumptions about the quality of life with treatments.

Our most striking findings relate to the utilities of life with treatments. Our patient-derived treatment utilities indicate that life with diabetes treatments is far from equivalent to perfect health and that the utilities for different treatments vary. Incorporating these treatment state utilities into the NIH model had a large impact on the change in QALYs and consequently on the ICER of intensive glucose control. The effect of treatment utilities depended on the definition of intensive glucose control used when eliciting utilities and on the difference between the utility for intensive and conventional glucose control. In particular, when intensive glucose control was defined as intensive therapy with insulin, intensive therapy was consistently less beneficial than conventional therapy. On the other hand, when intensive glucose control was defined solely as oral medications, intensive glucose control was on average ben-

Table 2—Impact of patient complication and treatment utilities on the difference in QALYs of intensive glucose control versus conventional glucose control in older patients*

Age at onset (years)	Difference in costs (in dollars)	Difference in QALYs					
		Complication utilities			Treatment utilities		
		Original	Patient	Original	Patient	Original	Patient
		Original	Original	Patient, insulin	Patient, insulin	Patient, orals	Patient, orals
60–65	16,036	0.12	0.206 (0.198–0.213)	-1.04 (-1.25 to -0.82)	-0.96 (-1.18 to -0.75)	0.18 (0.01–0.35)	0.24 (0.07–0.41)
65–70	14,154	0.043	0.084 (0.081–0.088)	-0.88 (-1.06 to -0.70)	-0.84 (-1.02 to -0.67)	0.11 (-0.03 to 0.25)	0.14 (0.003–0.28)
70–75	12,185	0.016	0.034 (0.033–0.036)	-0.73 (-0.87 to -0.58)	-0.71 (-0.86 to -0.57)	0.081 (-0.033 to 0.20)	0.096 (-0.018 to 0.21)
75–80	9,897	0.0043	0.0104 (0.0098–0.0109)	-0.57 (-0.69 to -0.46)	-0.57 (-0.68 to -0.46)	0.060 (-0.029 to 0.15)	0.065 (-0.024 to 0.15)
80–85	7,310	0.00097	0.00256 (0.00242–0.00270)	-0.42 (-0.50 to -0.34)	-0.41 (-0.50 to -0.33)	0.046 (-0.019 to 0.11)	0.048 (-0.017 to 0.11)
85–90	4,962	0.00021	0.000557 (0.000527–0.000587)	-0.29 (-0.34 to -0.23)	-0.28 (-0.34 to -0.23)	0.035 (-0.010 to 0.08)	0.037 (-0.008 to 0.082)

Data are means (95% CIs). Columns 3–8 illustrate the impact of distinct combinations of original and patient utilities on the expected health benefit (difference in QALYs) of intensive glucose control versus conventional glucose control for hypothetical patients, 65–90 years of age at disease onset. Insulin, utility for intensive glucose control with insulin used; orals, utility for intensive glucose control with oral medications used.

eficial across all age-groups and cost-effective for the youngest patients.

Apart from the effects of treatment utilities, incorporating patient-derived utilities for major complications improved the cost-effectiveness of intensive glucose control for older patients with new diabetes. This occurred because our patient-derived utility values were lower than those used in the original NIH model (10,12). Our utilities for complications likely differ from prior preference measures because of differences in methods of utility ascertainment. The original utilities were acquired by diverse methods (17–19), while we used the time trade-off method to assess all of our utilities, providing a single, theoretically grounded, and widely accepted basis for the utilities in our analysis.

These results have implications for the conduct of cost-effectiveness analyses in type 2 diabetes. For older individuals and the general population of diabetic patients, future cost-effectiveness studies of diabetes-related treatments should incorporate formal sensitivity analyses of both treatment and complication state utilities. In particular, our results suggest that assumptions regarding the quality of life with treatments deserve careful examination. The assumption in earlier models that quality of life with different glucose control therapies is equivalent to life in perfect health was based on quality-of-life data from clinical trial populations, which showed that the overall quality of life of patients was altered most significantly by complications and much less by treatment assignment (25). This assumption is challenged not only by our study results but also by studies that show that the quality of life of diabetic patients who do not have complications is not equivalent to perfect health (26) and that increasing complexity of glucose therapies is associated with lower quality-of-life scores (27,28). The key insight that has not been recognized in previous cost-effectiveness analyses studies is that the negative quality-of-life effects of a treatment can outweigh its benefits over a population. In the case of diabetes, 30 patients need to be treated with intensive glucose control to prevent a diabetes-related outcome (8). All 30 will experience the burden of the treatment while only one will make a gain in quality of life.

Our findings also have important implications for quality-of-care policies as well as for the routine care of older patients with diabetes. From a policy per-

Table 3—Impact of patient complication and treatment utilities on the incremental cost-effectiveness ratio of intensive glucose control versus conventional glucose control in older patients*

Age at onset (years)	Incremental cost-effectiveness ratio					
	Complication utilities					
	Original	Patient	Original	Patient	Original	Patient
	Treatment utilities					
	Original	Original	Patient, insulin	Patient, insulin	Patient, orals	Patient, orals
60–65	136	78 (75–81)	Dom.	Dom.	90 (38–537)	67 (39–209)
65–70	328	168 (161–176)	Dom.	Dom.	127 (Dom. –987)	101 (39–670)
70–75	746	354 (339–371)	Dom.	Dom.	149 (Dom. –1,470)	127 (Dom. –834)
75–80	2,284	953 (907–1,006)	Dom.	Dom.	165 (Dom. –1,200)	152 (Dom. –1,294)
80–85	7,544	2,852 (2,709–3,019)	Dom.	Dom.	159 (Dom. –1,602)	152 (Dom. –1,281)
85–90	24,205	8,912 (8,446–9,449)	Dom.	Dom.	142 (Dom. –1,190)	134 (Dom. –931)

Data are means (95% CI) in thousands of dollars/QALY, unless otherwise indicated. *Columns 2–7 illustrate the impact of distinct combinations of original and patient utilities on the relative cost-effectiveness of intensive glucose control versus conventional glucose control for hypothetical patients 65–90 years of age at disease onset. Dom., dominated (the alternative therapy is both harmful and more expensive); insulin, utility for intensive glucose control with insulin used; orals, utility for intensive glucose control with oral medications used.

spective, current attempts to measure the quality of diabetes care (29) or create incentives to improve diabetes care generally do not acknowledge the clinical heterogeneity of older diabetic patients (30) or the quality-of-life burden of treatments (22). Policies that promote the uniform achievement of general population goals for all diabetic patients, regardless of age, comorbidities, and preferences, run the risk of delivering intensive care to all patients even when it may not be clinically beneficial or cost-effective. In recent years, multiple diabetes care guidelines (7), including those published by the American Diabetes Association (31), have acknowledged the heterogeneity of older patients and specifically recommended that care of patients >65 years of age be individualized. Our results indicate that a key component of individualizing diabetes care should be the acknowledgment of a patient's perceptions of the quality-of-life effects of various treatment options.

Several limitations of this study should be considered when interpreting these results. The preferences were elicited in a largely urban, African-American patient population attending an academic medical center. To the extent that preference measurements are specific to certain subpopulations of older diabetic patients, either by specific ethnicity, age, or current treatment, this may limit the generalizability of these findings. Next, the validity of utility measurements cannot be directly assessed because there is no gold standard for preference measurement. However, the order of our utility measurements has face validity and our utility elicitation

methods represent a more direct measure of preference (32). Lastly, we utilized an older model of type 2 diabetes and did not substantially update the model. Current model assumptions regarding the difference between conventional and intensive glucose control may exaggerate the size of the benefits of intensive control and lower the incremental cost-effectiveness ratio of this therapy. Despite these potential limitations, our study does indicate that the incorporation of patient preferences can influence the results of this classic cost-effectiveness analysis. Whether patient preferences will have the same impact in other models that assess smaller differences in glucose control, in evaluations of other treatments such as intensive blood pressure or cholesterol lowering, or in nonelderly patient populations needs to be confirmed in future studies (11).

We have found that incorporating patient-derived preferences regarding complications and treatments of diabetes has important effects on the cost-effectiveness of glucose control in older type 2 diabetic patients. In particular, the model results are sensitive to the incorporation of utilities for the various glucose control therapies, and the exact definition of what constitutes intensive glucose control is an important determinant of the effect of including these treatment utilities. Future cost-effectiveness analysis that incorporates detailed analysis of patient preferences concerning both complications and treatments will provide important information on the value of individualizing the intensity of diabetes care in the burgeon-

ing population of patients >65 years of age.

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