to 7.08 in the liraglutide 1.8-mg group and OR, 2.11; 95% CI, 1.24 to 3.59 in the 1.2-mg group; achievement of HbA1C <7.0% OR, 4.50; 95% CI, 2.90 to 6.97 in the liraglutide 1.8-mg group and OR, 2.75; 95% CI, 1.78 to 4.25 in the 1.2-mg group) compared with the sitagliptin cohort. The liraglutide groups also experienced significantly greater mean decreases in fasting plasma glucose (p<0.0001 for both).
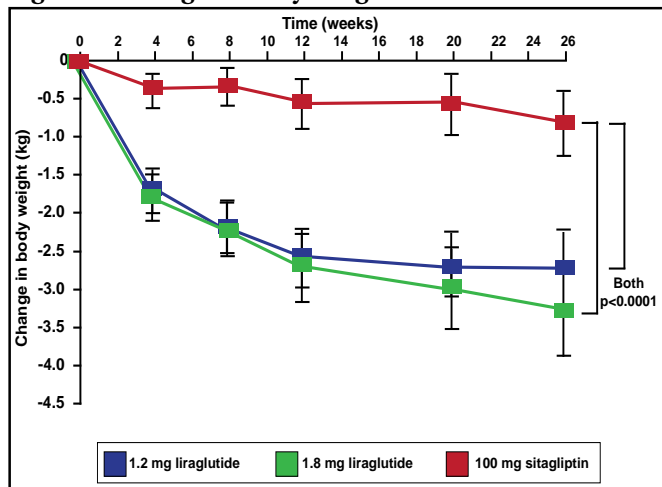
Figure 2. Proportion of Participants Achieving HbA1C Target Values.
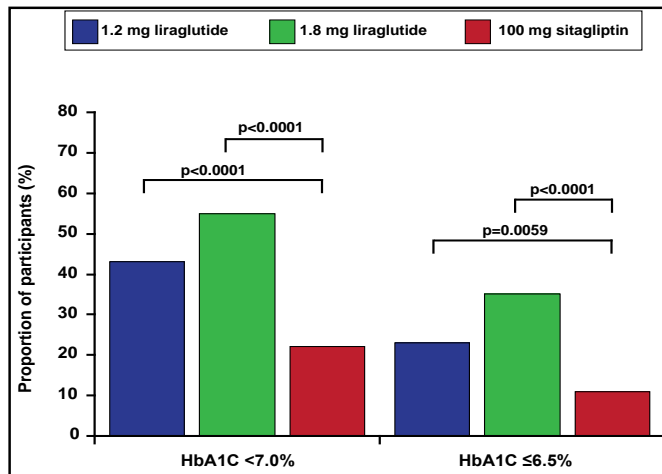
Of particular interest was the change in body weight between the liraglutide and sitagliptin cohorts (Figure 3). The liraglutide 1.8-mg group lost a mean of 3.38 kg, and the 1.2-mg group lost a mean of 2.86 kg, while the sitagliptin group lost a mean of 0.96 kg (p<0.0001 for both).

Figure 3. Change in Body Weight.

Despite the daily injection that was required with liraglutide, there was no difference in the perceived convenience of the two compounds between participants.

More treatment-emergent adverse events occurred with liraglutide than sitagliptin, although serious events occurred in 3% or fewer of the participants. The most common adverse events were gastrointestinal problems, particularly nausea, which were higher in the liraglutide groups, and infections and infestations, which occurred equally between all groups. The mean duration of nausea in the liraglutide 1.2-mg group was 13 days versus 8 days among the 1.8-mg group and 26 days among the sitagliptin group.

One major hypoglycemic episode occurred in a participant in the 1.8 mg liraglutide cohort. However, no seizures or coma resulted. Similar proportions of patients in each group experienced mild hypoglycemia.

In conclusion, liraglutide 1.2 mg and 1.8 mg provided superior glycemic control and body weight loss compared with sitagliptin 100 mg with no increase in hypoglycemia, although a greater proportion of patients who received liraglutide reported transient nausea that lasted a mean of 8 or 13 days, depending upon the dose.

Complications of Diabetes Have a Significant Long-Term Impact on QoL

The United Kingdom Prospective Diabetes Study (UKPDS) was a landmark randomized, multicenter trial of glycemic therapies in 5102 patients with newly diagnosed type 2 diabetes mellitus (T2DM). The study was conducted between 1977 and 1997 at 23 clinical sites in the United Kingdom. The final results, published in 1998, showed for the first time that the complications of T2DM could be reduced by improving blood glucose and/or blood pressure control [UKPDS Group. *Lancet* 1998].

In 2002, Clarke and colleagues published findings from a subanalysis of the UKPDS data that estimated the impact of 6 diabetes-related complications (myocardial infarction, blindness in one eye, ischemic heart disease, heart failure, stroke, and amputation) on quality of life (QoL) using the EuroQoL EQ-5D results from 3192 UKPDS participants [Clarke P et al. *Med Decis Making* 2002]. In this report, the effect on tariff values was ordered as follows: myocardial infarction, blindness in one eye, ischemic heart disease, heart failure, stroke, and amputation.

Maria L. Alva, PhD candidate, Department of Public Health, Health Economic Research Centre, Oxford, United Kingdom, presented updated results, drawing on the UKPDS Post Trial Monitoring Study, which was conducted between 1997 and 2007. During this time, the EQ-5D was administered annually with a final questionnaire that was administered to all surviving participants in October 2007. The current results are based on 11,614 fully completed EQ-5D questionnaires (from 3380 participants).

Compared with the original study, many more complications were available for analysis. Having repeated observations across time provided valuable additional information:

- Larger number of data points, which improves the efficiency of the estimates

- Ability to ask whether or not attrition and nonresponse over time are important

- Utilizing the information on both intertemporal and individual observations, provides ability to control for the effects of missing or unobservable time-invariant confounding factors that may otherwise bias results

Mean QoL declined from 0.77 at the first questionnaire in 1996/1997 to 0.64 in the last questionnaire in 2007, which was related to the increasing age of patients and an increasing proportion of patients with a history of complications (27% at first questionnaire compared with 55% at last questionnaire).

The different diabetes-related complications that were studied are assumed to have an additive impact on QoL. In this analysis, no evidence of interactions among the six complications that were studied was found. The variation in utilities was decomposed into two parts: variation across people, which is called between-, and variation across the questionnaires of a given person, which is called within-variation. The variation in utility across patients was more than twice that which was observed within a patient over time. If heterogeneity is correlated with the likelihood of having an event, then the results of an ordinary least squares (OLS) regression will be biased, which is why fixed effects (FE) analysis was used. Taking into account the fact that 26% of the questionnaires reported full health and thus the EQ-5D appears to have a ceiling effect, a Tobit FE was proposed. As seen in Table 1, the marginal effects are slightly lower using the FE type models compared with OLS. For example, in the case of stroke, values fluxuate from an absolute decrement of 0.19 points in utility with OLS to 0.16 points with FE and to 0.11 points on average with Tobit FE. In relative terms, this means that for the median person who, in this sample, has a utility of 0.72, stroke under OLS would put him in

the 19th percentile, while Tobit FE would put him in the 23rd percentile—a considerable drop.

These results suggest that complications from diabetes have substantial and long-lasting effects on patient QoL. In the current study, stroke, heart failure, and amputations had the largest impact. The other events did not significantly alter QoL, at least during the monitoring period of this study. Results also show that patients who had an event had a lower QoL before the event. Cross-sectional studies may have overestimated the impact of complications, because OLS pools together patients who never have events with patients who end up experiencing them, while FE only takes into account differences among people who experience a change in their history of complications. There is hope that this information may be used to estimate the outcome and cost-effectiveness of interventions that reduce diabetes-related complications in the future. More outcomes will be added to this analysis once the data become available.

Table 1: Preliminary Results of OLS, FE, and Tobit FE Regression Analysis of the Relationship Between Health State Utilities (EQ-5D Tariff Values) and Clinical Events.

	OLS		FE		Tobit FE	
	Coeff	Robust SE	Coeff	Robust SE	Coeff (MFX)	Robust SE
Constant	0.839**	(0.035)	1.774**	(0.046)		
Current age	-0.002**	(0.001)	-0.016	(0.001)	-0.012**	(0.001)
Male=1	0.081**	(0.010)				
Events						
MI (year before)	-0.088*	(0.036)	-0.066*	(0.030)	-0.036	(0.020)
MI (prior history)	-0.037*	(0.018)	0.008	(0.024)	0.011	(0.016)
IHD	-0.084**	(0.016)	-0.029	(0.022)	-0.020	(0.015)
Stroke	-0.189**	(0.029)	-0.165**	(0.035)	-0.111**	(0.029)
Heart Failure	-0.159**	(0.031)	-0.101**	(0.032)	-0.047*	(0.022)
Amputation	-0.203**	(0.039)	-0.172**	(0.045)	-0.106**	(0.035)
Blindness in 1 eye	-0.049	(0.022)	0.031	(0.027)	0.025	(0.017)
Observations	11614		11614		11614	
# of Participants			3380		3380	
R-squared	0.067		0.130		0.130	

**p<0.01; *p<0.05

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The Lifetime Risk of Nephropathy and Its Progression May Be Greater Than Previously Reported

The current worldwide prevalence of diabetes is estimated to be 366 million. One-third of these cases progress to nephropathy, a major cause of cardiovascular disease (CVD) and end-stage renal disease (ESRD). Progression through stages of nephropathy has not been well described in a large, well-characterized, population-based study.