Continued from page 17

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

Reproduced with permission from M. Alva, PhD candidate.

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.

Suma Vupputuri, PhD, The Center for Health Research, Kaiser Permanente Georgia, Atlanta, Georgia, USA, described the prevalence, incidence, and progression of nephropathy and identified demographic and clinical characteristics that are associated with progression in a US population-based sample.

A total of 11,562 members of a managed care organization (Kaiser Permanente), aged 18 years and older, with hypertension and type 2 diabetes, a urine-to-albumin creatinine ratio (UACR) measurement during 2001-2003, and at least one follow-up UACR, were independently assessed for different stages of nephropathy. Three baseline stages of nephropathy were defined: normal albumin (<30 µm/mg), microalbuminuria (30-299 µm/mg), and macroalbuminuria (≥300 µm/mg). Records through 2008 were searched for individuals who showed progression from baseline to a higher stage of nephropathy, including ESRD. Progression was defined as the first UACR value that was recorded in a stage that was higher than baseline. Incidence was calculated as the number of new cases over the sum of the person-time of the at-risk population. Independent predictors of time to progression were assessed using Cox regression.

At baseline, 59% of subjects had normal albumin (n=6853), 30% had microalbuminuria (n=3492), and 11% had macroalbuminuria (n=1217). The incidence of nephropathy progression (per 1000 person-years) was 94.6, 44.1, and 6.7 for normal albumin, microalbuminuria, and macroalbuminuria, respectively. Table 1 shows the number of patients who progressed to higher stages of nephropathy.

Table 1. Prevalence of Nephropathy and Progression to Subsequent Stages.

	Prevalent Normal Albumin n=6853	Prevalent Microalbuminuria n=3492	Prevalent Macroalbuminuria n=1217
Regressed to normal albumin, n (%)	–	932 (27%)	–
Regressed to microalbuminuria, n (%)	–	–	393 (32%)
No progression, n (%)	3244 (47%)	1656 (47%)	769 (63%)
Progressed to microalbumimuria, n (%)	3216 (47%)	–	–
Progressed to macroalbuminuria, n (%)	387 (6%)	890 (25%)	–
Progressed to ESRD, n (%)	6 (0.09%)	14 (0.4%)	55 (5%)

ESRD=end-stage renal disease

Predictors of progression of nephropathy included age (per 5 years), race (Caucasian), diabetes duration (per year), systolic and diastolic blood pressure (per 5 mm Hg), HbA1C (per 1%), body mass index (per 5 kg/m^2), estimated glomerular filtration rate (per 10 mL/min/1.73m^2), use of ACE inhibitors/ARBs, CVD, and active heart failure.

Although the ability to extend the results of this study to a broader population may be limited by the study sample (ie, only patients with diabetes and hypertension who had health insurance were included), Dr. Vupputuri concluded that in one of the first studies to examine the progression of nephropathy in a US population-based sample of adults with diabetes and hypertension, the lifetime risk of nephropathy and its progression may be greater than previously reported. Developing strategies to slow and/or prevent the progression of nephropathy may reduce the burden of disease.

The Association Between Arterial Stiffness and LV Diastolic Function in T2DM: 8-Year Follow-Up To the Hoorn Study

Individuals with diabetes are more likely to develop congestive heart failure (HF), particularly left-sided HF, than those without diabetes, but the underlying mechanisms remain controversial [Nichols GA et al. *Diabetes Care* 2004]. Arterial stiffness, which is more common in type 2 diabetes mellitus (T2DM), has been suggested as a potential cause of HF, while left ventricular (LV) mass has been shown to be a predictor [Stehouwer CD et al. *Diabetologia* 2008; de Simone G et al. *Eur Heart J* 2008]. Katja van den Hurk, PhD candidate, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands, presented data that addressed the issue of whether arterial stiffness was prospectively associated with a higher LV mass and worse LV diastolic function (indicated by increasing left atrial volume index [LAVI]) and whether this differed in individuals with or without T2DM.

These results were from an 8-year follow-up to the Hoorn Study, a population-based cohort study of diabetes and diabetes complications that began in 1989 [Henry RM et al. *Diabetes Care* 2004]. Echocardiography and arterial ultrasonography were performed in 2000 and again in 2008. Linear regression analyses were performed to