## A COMPARISON OF THE EQ-5D AND SF-6D SINGLE INDEX IN ASSESSING THE HEALTH RELATED QUALITY OF LIFE OF LIVER TRANSPLANT PATIENTS

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## **INTRODUCTION**

Liver transplantation has become the main treatment of choice for patients with end-stage liver disease. Survival rates of adult patients undergoing liver transplantation in the UK are approximately eighty per cent at two-years post-transplantation [Department of Health Report, 2000]. Aside from its effect upon survival rates, liver transplantation is also widely believed to have a positive effect upon health-related quality of life [Bryan S *et al 1998*, Painter P *et al* 2001, Bravata DM *et al* 1999]

The data presented here forms part of a wider economic evaluation of liver transplantation in England and Wales. The study included two generic measures of health-related quality of life, the EuroQol EQ-5D and the Short-form (SF) 36. Both of these measures can be translated into one-dimensional preference-based scores, which may be applied to survival data to calculate the overall health improvement derived from liver transplantation (QALYs).

It is of course possible that the results from surveys evaluating the health-related quality of life in liver transplant patients will differ according to the choice of instrument used. This may in turn affect the conclusions drawn about the impact of liver transplantation upon patients' healthrelated quality of life and of their overall health improvement.

This study has two related aims. The first aim is to compare the results of health-related preference scores, using the EuroQol EQ-5D (with 'York' MVH tariff) and the SF-6D single index, in patients listed for liver transplantation. A secondary aim is to explore the reason for any difference between the two measures.

Changes in patients' reported preference scores will be examined using paired comparisons to assess the change in health-related quality of life over time post-transplantation, and to assess change pre- and post-transplantation. Differences between the preference scores resulting from the two measures will be explored through graphical means, and through examining ceiling effects on both measures.

## METHODS

Each of the six NHS designated transplant centres in England & Wales participated in the study, with start dates ranging between December 1995 and December 1996. All adult patients listed for a cadaveric liver transplant over the period of one year were included in the study. Patients listed for multi-organ transplantation were excluded from the study. Patients were followed from point of listing to transplantation, and then for two years following transplantation.

The survey was administered by postal questionnaire. Questionnaires were sent to all English speaking patients at point of listing, and then at 3 monthly intervals until transplantation. Following transplantation questionnaires were sent at 3, 6, 12 and 24 months. One reminder was sent to all non-responders approximately three weeks after their initial questionnaire. Patients who were too ill, in the opinion of a research nurse based at the centre, were excluded from being asked to respond to the survey at that point in time as it was felt they would be unable to respond. Excluding these potential responses will bias scores upwards, however the total number of these was small (34 questionnaires from all time-points).

The questionnaire included the EuroQol EQ-5D five-domain descriptive system and 'thermometer' [Brooks, 1996], and the Short-form 36 (SF-36) health profile [Ware *et al*, 1993]. The 'York' MVH tariff derived from general population scores was applied to the EQ-5D to generate one-dimensional preference scores [Dolan P, 1997]. The SF-6D was formed from the SF-36 data and an algorithm was applied to generate the single-index [Brazier *et al*, 1998]. The

SF-6D single index scores presented here are based upon a developmental version of the scoring algorithm based upon general population scores [personal communication, J Brazier].

When comparing patients' scores over time, values of zero were imposed on both scales to indicate patients who had died post-transplantation. However, when making direct comparisons between the EQ-5D tariff scores and the SF-6D single index, this imposition was not made.

All statistical tests are 2-tailed unless stated otherwise and the statistical level of significance was taken where p < 0.05. All statistical tests were non-parametric (Wilcoxon test) unless stated otherwise. The data were analysed using STATA version 6 [Statacorp, 1999] and SPSS version 6.1 [SPSS Inc, 1994].

# RESULTS

#### Sample population

585 patients were identified as eligible to participate in the study. Of these 523 patients (89%) returned at least one questionnaire during the course of the study, resulting in a total of 1779 (76%) returned questionnaires. This resulted in 1462 pairs of data consisting of both the EQ-5D tariff and SF-6D single index scores (82% of returned questionnaires).

Table 1 details the characteristics of respondents. 24 per cent of responders died during the course of the study. The proportion of males and females was relatively equal. The median age of responders was 51 years.

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Characteristic	N (%) of responders
Total number of responders	523 (100%)
Males	265 (50.7%)
Age	
Mean (SD)	49.02 (11.94)
Median (IQR)	51 (42 to 58)
Range	17 to 70
Centre 1	161 (30.8%)
Centre 2	85 (16.3%)
Centre 3	100 (19.1%)
Centre 4	51 (9.8%)
Centre 5	82 (15.7%)
Centre 6	44 (8.41%)
Number of respondents who died	126 (22.9%)

Table 1: Characteristics of respondents

Details of patients' classification by primary liver disease at the time of referral are shown in Table 2. The largest group of respondents exhibited alcoholic liver disease, followed by primary biliary sclerosis and primary sclerosing cholangitis.

European Liver Disease Classification	N (%) of responders
Alcoholic liver disease	105 (20.1%)
Primary biliary cirrhosis	97 (18.5%)
Sclerosing cholangitis	49 (9.4%)
Post hepatic C cirrhosis	52 (9.9%)
Cirrhosis: unknown causes	27 (5.2%)
Autoimmune cirrhosis	26 (5.0%)
Post hepatic B cirrhosis	21 (4.0%)
Fulminant hepatitis	25 (4.8%)
Re-transplanted	21 (4.0%)
Acute hepatic failure	12 (2.3%)
Hepatocellular carcinoma	11(2.1%)
Secondary biliary cirrhosis	9 (1.7%)
Subacute hepatitis	9 (1.7%)
Other	59 (11.3%)

Table 2: Number of respondents by clinical indication

62 patients did not respond to any questionnaire sent during the study. The majority of nonresponders were male (63%) and the median age was 50 years. The largest group of nonresponders exhibited hepatitis C cirrhosis, followed by patients with alcoholic liver disease. Patients with both of these clinical indications are likely to have a history of substance abuse.

### Change in preference scores of liver transplant patients over time

Figure 1 shows the mean EQ-5D tariff and SF-6D scores at listing, 3 and 6 months post listing, and then at 3, 6, 12 and 24 months post-transplant for all observations. The error bars indicate 95 per cent confidence intervals around the mean.



Figure 1: EQ-5D tariff and SF-6D single index scores over time

The mean EQ-5D scores are lower post-listing than post-transplant (mean EQ-5D scores are 0.470 at listing and 0.544 at 3 months post-transplant), and they appear to increase steadily at 3, 6, 12 months post-transplant and tail off at 24 months post transplant. There is little difference in the SF-6D scores before transplantation compared to directly afterwards (mean SF-6D scores are 0.595 at listing and 0.580 at 3 months post-transplant), and they show little change over time until 24 months post-transplant where they decrease. The confidence intervals around the means at 3 and 6 months post -listing are larger as the number of observations at these time-points are small (N=86 and 33 respectively for EQ-5D scores).

The interpretation of Figure 1 is, however, complicated by missing values therefore, comparisons were made using related samples where patients have responded at more than one time point. The advantage of using related samples is that it is possible to test for change over time without the need to standardise for patient characteristics, such as gender or type of liver disease, as these remain constant for the individuals included in the analysis.

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	N	Mean score Pre-tx	Mean score Post-tx	P value
		(median)	(median)	
EQ-5D tariff	245	0.505	0.537	< 0.001
		(0.620)	(0.691)	

Table 3: Paired comparison of scores at 3 and 24 months post-transplantation

0.532

(0.650)

SF-6DSI

245

In order to assess the change in preference scores post-transplantation, paired comparisons were made of scores at listing and at two-years post-transplantation (Table 3). Both measures showed statistically significant changes in scores post-transplantation. Although the change in mean scores using both the SF6D single index and the EQ-5D tariff do not appear to be very large, the change was highly statistically significant as the distribution of scores changed between the two time points.

0.540

(0.670)

< 0.001

	N	Mean Pre-tx	Mean Post-tx	P value
EQ-5D tariff	152	0.531 (0.620)	0.586 (0.691)	0.029
SF-6DSI	152	0.622 (0.630)	0.577 (0.700)	0.392

Table 4: Paired comparison of scores at listing and 24 months post-transplantation

Paired scores at listing and 24 months post-transplantation were compared in order to assess the change in scores following transplantation (Table 4). The change in the EQ-5D tariff scores was statistically significant, however the SF-6D single index did not show a significant change. The results from these two measures are giving different messages to the change in health-related preferences following transplantation.

#### Direct comparison of the EQ-5D tariff and SF-6D single index scores

In order to explore why both measures produce different results the distributions of scores were examined further. Figures 2a and 2b depict histograms of the EQ-5D tariff and SF-6D single index scores across all time points in the study.

Figure 2a: Distribution of EQ-5D scores



Figure 2b: Distribution of SF-6D single index scores



The distributions of scores from both measures are clearly different. The EQ-5D scores are negatively skewed and bimodal. The SF6D single index scores are Normally distributed, but across a much smaller range than the EQ-5D tariff scores as the lowest possible score, other than death, that the SF-6D allows is 0.26, whereas the lowest possible scores on the EQ-5D using the 'York' tariff is -0.594.





The scatterplot in Figure 3 shows all paired observations where both EQ-5D and SF-6D single index scores are available. There is a large amount of variation in scores across both measures, particularly across the EQ-5D scale where the range is larger. The EQ-5D is able to predict scores in the lower range of the scale, including scores that are worse than death (zero). The gap between 0.883 and 1 on the EQ-5D tariff shows the range where it is not possible to discriminate between higher preference scores using the EQ-5D with the York tariff.

### Ceiling effects

From Figure 3 it is apparent that where, the EQ-5D tariff scores indicate 'full health' there are a range of corresponding SF-6D single-index scores. There are a total of 237 paired observations where the EQ-5D shows full health (value equal to one). In 22 of these observations the SF-6D single index-scores also show a value corresponding to full health (equal to 1). The mean (SD) value of the remaining 215 observations is 0.854 (0.08), and the range of scores is from 0.63 to 0.96.

Where the SF-6D single index shows full health (value =1) all corresponding EQ-5D tariff values also show full health (value =1).

Table 5 details the proportion of responses for each domain of the SF-6D where respondents have given a value of one on the EQ-5D tariff but have given a value of less than one of the SF-6D single index. Large proportions of scores fall in the level two categories, particularly in the physical functioning and vitality domains.

	Physical	Role	Social	Pain	Mental	Vitality
1	20%	77%	82%	67%	49%	6%
2	60%	17%	12%	19%	43%	67%
3	16%	2%	6%	13%	7%	20%
4	1%	4%	<1%	<1%	0	4%
5	<1%	N/A	0	<1%	<1%	2%
6	1%	N/A	N/A	0	N/A	N/A

Table 5: SF-6D domains where EQ-5D shows full health (and SF-6D does not show full health)

### Patients' perceptions of their own change in health

It may be that the EQ-5D is identifying change in health-related quality of life pre- and posttransplantation where no 'true' change exists, for example, patients may be re-evaluating their interpretation of the EQ-5D dimensions over time. In order to assess whether this is the case patients' perceptions of their change in health over time were examined using part of the SF-36.

Question two in the SF-36 asks respondents "compared to one year ago, how would you rate your health in general now?". The five possible responses range from "much better now than one year ago" to "much worse than one year ago". The responses to this question at six months post-transplantation were examined to assess perceptions of change pre- and post-transplantation. Although, this is not a direct comparison of perceptions pre- and post-transplantation, and some patients would not have been listed for transplantation at six-months prior to transplantation, it was felt that six months post-transplant was the most appropriate proxy. Comparisons were made where respondents had both EQ-5D tariff and SF-6D single index scores.

Table 6 illustrates the number (percent) of responses indicating positive, negative or zero change on each of the measures. A negative change on either the EQ-5D tariff or SF-6D single index indicates that the score was less at six-months post-transplant compared to at time of listing. The histograms in Figures 4 show the differences in the EQ-5D tariff scores between listing and six-months post-transplantation for each of the possible responses to question two in the SF-36. Figure 5 shows the equivalent information for the SF-6D single index.

listing and 6-months post-transplant					
	'Worse than one year ago' (SF-36) / negative change (SF-6D SI or EO-5D)	'About the same' (SF- 36) / zero change (SF-6D SI or EQ-5D)	'Better than one year ago' (SF-36) / positive change (SF-6D SI or EQ-5D)		
SF-36 Question 2	7 (5%)	13 (9%)	117 (85%)		
EQ-5D tariff scores	33 (24%)	19 (14%)	85 (62%)		
SF-6D SI scores	31 (23%)	5(4%)	101 (74%)		

Table 6: Patients' perception of change in own health over the past year (at six months post-transplant), and the direction of change in EQ-5D and SF-6D scores between listing and 6-months post-transplant

Figure 4: Differences in EQ-5D tariff scores at 6 months post-transplant and listing



Figure 5: Differences in SF-6D single index scores at 6 months post-transplant and listing



From Table 6 it is clear that fewer patients perceive their own health to have worsened over the past year at six months post-transplantation (5%) than is indicated by either the EQ-5D (24%) or the SF-6D single index (23%). The majority of patients perceive their own health to be better post-transplantation (85%) which supports the change in health-related quality of life post-transplantation found by the EQ-5D tariff scores.

# CONCLUSION AND DISCUSSION

Different conclusions are drawn from the comparison of pre-and post- transplantation quality of life preference scores depending upon whether the EQ-5D using the York tariff or the SF-6D single index is used. The EQ-5D with the York tariff showed a statistically significant change using paired comparisons of scores listing and 24 months post-transplantation. The SF-6D single index scores however, did not show a significant change following post-transplantation.

Deaths in the sample would lead to an improvement in the EQ-5D scores if the patients who died were the same patients that previously had negative scores, yet this would show as a reduction in scores in SF-6D single index as negative scores are not possible. Examination of patients' own perceptions of the change in their health found that the majority of patients (85%) believed their own health had improved at six months post-transplant compared to the previous

year. This supports the change in the EQ-5D tariff scores when compared pre- and posttransplantation, and indicates that it is not solely due to patients dying.

A large amount of variation was found between the measures when examining paired comparisons of scores. The variation in scores is also apparent at the top end of the EQ-5D scale equivalent to 'full health', where the corresponding SF-6D single index scores ranged from 0.63 to 1. The ceiling effect is greater on EQ-5D tariff than on the SF-6D single index, making the SF-6D single index more sensitive to 'minor' changes away from full health. However, the EQ-5D tariff is able to reflect very severe health states, which had an obvious impact upon the results of this sample of patients, many of who were severely ill.

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