# NOTE TO USERS

# QUALITY OF LIFE IN LIVER TRANSPLANT PATIENTS: RESPONSIVENESS OF THE SF-36, EQ-5D AND GHQ-30

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*Philip Wong*
*January, 2005*

## ABSTRACT

Health is defined as a state of complete physical, mental and social well-being, and not merely the absence of disease. Quality of life refers to a person's perception of well-being and life satisfaction. Chronic liver failure can have significant negative impact on a patient's cognitive abilities and can cause physical debilitation. Thus, it is not surprising that cirrhotic patients often have severe impairment in their quality of life (QOL). From the perspective of the health care system, patient's health-related quality of life (HRQL) is the more relevant construct. Success of liver transplantation (OLT) is often measured by length of survival, as opposed to patient perceptions of personal health.

The *primary objective* of this study is to identify which of the Short-Form Health Survey (SF-36), EuroQuol (EQ-5D) VAS, and General Health Questionnaire-30 (GHQ-30) is the most responsive for detecting HRQL change for patients pre- and post-liver transplantation. The *secondary objective* is to compare the relative efficiency of the HRQL measures to traditional liver biochemistry parameters.

All outpatients with advanced liver disease referred for OLT assessment from 1997 to 2004 were eligible for this prospective cohort study. Data was obtained on 219 patients, of which 44 had HRQL measures performed pre- and post-OLT. Study variables included all subcomponents of the SF-36, as well as the EQ-5D VAS and GHQ-30. Liver enzymes (AST, ALT, ALP) and function tests (albumin, total bilirubin, INR, PT) were analyzed and their relative efficiency compared to HRQL measures.

The instrument that best predicts HRQL change post-OLT will be the most responsive. Responsiveness was assessed by calculating effect size, standardized response mean (SRM), and the relative efficiency of each instrument when compared to each other as well as liver tests.

There was strong inter-instrument agreement for detection of impaired HRQL with advanced liver dysfunction, but little correlation between biochemical markers of poor liver function and HRQL scores. Albumin demonstrated the largest effect size (1.62), but the EQ-5D VAS had the highest SRM (0.58) and relative efficiency (1.1, GH as standard) of all measurement instruments. Laboratory parameters in general were poorly responsive for changes in HRQL.

The results of this study suggest that HRQL measurement tools are a responsive and efficient method for evaluating patient health status. The EQ-5D VAS was the most responsive HRQL tool, and was the most efficient measure for detection of HRQL change. In contrast, traditional liver function tests are poorly responsive to HRQL changes, and have poor correlation with a patient's views on personal health. The addition of the EQ-5D in clinic follow-up visits with liver transplant recipients will provide a more complete assessment of a patient's personal views of health.

## SOMMAIRE

L'insuffisance hépatique chronique peut avoir des répercutions néfastes sur les habilités intellectuelles du patient et peut causer un affaiblissement physique. Il n'est pas étonnant que les patients cirrhotiques constatent une détérioration sévère de leur qualité de vie. Le succès d'une transplantation hépatique (OLT) est fréquemment mesuré en terme de période de survie plutôt que basé sur la perception personnelle du patient.

Le premier objectif de cette étude est d'identifier quel instrument de mesure est le plus sensible aux changements pré- et post-transplantation hépatique sur la qualité de vie des patients en utilisant les questionnaires S.F.-36, E.Q.-5D et GHQ-30. L'étude avait pour objectif secondaire de comparer l'efficacité relative des mesures de la qualité de vie comparé aux marqueurs biochimiques hépatiques.

Les données ont été recueillies sur 219 patients référés pour une évaluation de transplantation hépatique, la qualité de vie pré- et post transplantation hépatique a été mesurée sur 44 patients. Les variables étudiées incluent toutes les sous-composantes des questionnaires S.F.-36, E.Q.-5D VAS et GHD-30. Les tests de fonction hépatique ont été analysés et leur efficacité comparée aux mesures de la qualité de vie liée à la santé.

Il existe une forte concordance inter-instrumentale dans la détection de la détérioration de la qualité de vie chez les patients ayant une dysfonction hépatique avancée. Il existe cependant peu de corrélation entre les marqueurs biochimiques hépatiques perturbés et des résultats des questionnaires portant sur de la qualité de vie. L'albumine a démontré la plus grande ampleur de l'effet (1.62), le E.Q.-5D VAS avait la meilleure réponse moyenne standardisée (0.58) et une meilleure efficacité relative (1.1,

selon le standard GH) parmi tous les instruments de mesure. Les paramètres de laboratoire étaient en général peu sensibles aux changements de la qualité de vie.

Les résultats de cette étude suggèrent que les instruments de mesures de qualité de vie liée à la santé sont sensibles et efficaces pour évaluer l'état de santé. Le questionnaire E.D.-5D VAS était l'outil le plus effficace dans l'évaluation de la qualité de vie et était l'outil le plus sensible aux changements d'états de santé.

## ABBREVIATIONS

| | |
|---|---|
| **AST** | aspartate aminotransferase |
| **ALT** | alanine aminotransferase |
| **ALP** | alkaline aminotransferase |
| **ALB** | albumin |
| **BP** | bodily pain |
| **CLDQ** | Chronic Liver Disease Questionnaire |
| **EQ-5D** | EuroQOL |
| **ES** | effect size |
| **GH** | general health |
| **GHQ-30** | General Health Questionnaire-30 |
| **GHQ1** | General Health Questionnaire-30, Likert Scale scoring |
| **GHQ2** | General Health Questionnaire-30, Bimodal Scale scoring |
| **HRQL** | Health Related Quality Of Life |
| **INR** | international normalized ratio |
| **LDQOL** | Liver Disease Quality Of Life |
| **MCS** | Mental Component Summary |
| **MH** | mental health |
| **OLT** | orthotopic liver transplantation |
| **PCS** | Physical Component Summary |
| **PF** | physical functioning |
| **PT** | prothrombin time |

| | |
|---|---|
| **QOL** | quality of life |
| **RE** | role emotional |
| **REff** | relative efficiency |
| **RP** | role physical |
| **SD** | standard deviation |
| **SF** | social functioning |
| **SF-36** | Short-Form Health Survey |
| **SRM** | standardized response mean |
| **TB** | total bilirubin |
| **VAS** | visual analogue scale |
| **VT** | vitality |
| **WHO** | World Health Organization |

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# CHAPTER I: INTRODUCTION

## 1.1 Overview of Liver Disease and Health Assessments in Liver Transplantation

Liver disease is a common cause of morbidity and mortality, and is one of the top ten leading causes of death worldwide[1]. One in twelve Canadians, over their lifetime, will develop a disorder of their liver or biliary tract. In spite of our best efforts for treatment, liver disease remains the ninth most common cause of death in the United States[2], and ranks fourth in Canada[3]. Despite important therapeutic advances[4 5 6], there remains a subgroup of patients that require orthotopic liver transplantation (OLT) to prevent an otherwise terminal course[7]. With current survival rates at 85%, 76% and 61% at 1, 4, and 10 years, OLT has become an essential option in the management of refractory, end-stage liver disease.

Chronic liver failure can negatively impact a patient's cognitive abilities, due to the development of encephalopathy, anxiety and depression[8 9]. Combined with the physical debility often seen in cirrhotic patients (Figure 1), it is not surprising that liver disease patients have severe impairment in their quality of life (QOL). As Medicine becomes more focused on chronic disease management, "the tradeoffs between the potential adverse consequences of a particular intervention and the anticipated benefits become increasingly dependent on how patients perceive and value different aspects of their health"[33]. With the lengthening survival of OLT patients, studies assessing the patient's view of personal health have become more important[10 11 12 13 14 15].

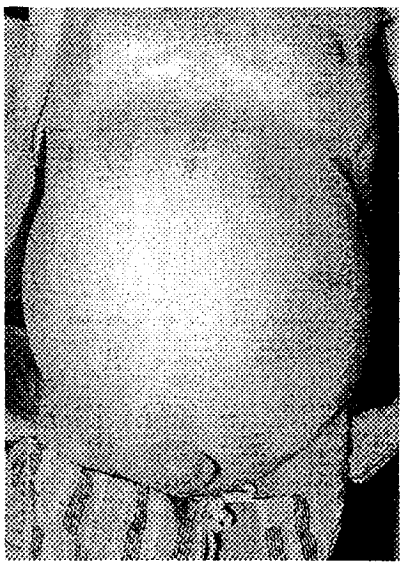

**Figure 1**. Liver failure with muscle wasting, development of intra-abdominal fluid accumulation (ascites), and an umbilical hernia

It is difficult to know, which of the wide variety of QOL instruments is most appropriate to use in the OLT setting. There is no consensus as to which is the "best scale" for QOL measures, as demonstrated by an informal Internet survey of experts in the area of QOL and liver disease[16]. Selection depends on the type of measurement needed, as some scales focus on characterizing physical abilities, while others concentrate more on mental health issues.

Hepatologists have traditionally relied on "hard" outcomes to gauge patient status post liver transplantation, such as mortality rates, laboratory indices (liver enzymes and liver function tests) and clinical assessments such as the Child-Pugh Score[17] [18] (See Appendix 6.1). These are directly observable and measurable.

Health Related Quality of Life (HRQL) measures can be used to supplement traditional laboratory parameters and clinical assessments in patients with liver disease. Although concerns have been raised about what actually is being measured and the relevance of this to clinical decision making, it is now well established that measures of

HRQL provide reliable and valid information about the impact on a health condition from the person's perspective[28 29 30 31]. Along with this understanding comes the acceptance that quality of life can only be measured using instruments that capture the patient's point of view – there are no other measurement options. Thus, HRQL measures are widely recognized as the gold standard for evaluation of life states[32].

## 1.2 Definition of Quality of Life

The World Health Organization (WHO) defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[19]. Quality of life on the other hand, has been defined as an "Individuals' perception of their position in life in the context of the culture in which they live and in relation to their goals, expectations, standards and concerns"[20]. In the context of the health field, Kaplan[21] defined HRQL as "the impact of disease and treatment on disability and daily functioning" and Bullinger et al.[22] defined it as "the impact of perceived health on an individual's ability to live a fulfilling life". Patrick and Erickson's[23], definition of HRQL is particularly important from a health services perspective; "... *a measure of the value assigned to duration of life as modified by impairments, functional states, perceptions and opportunities, as influenced by disease, injury, treatment and policy*". While the definitions differ, there is an emerging consensus that generic HRQL takes into account levels of physical, mental, social and role functioning, and includes abilities, relationships, perceptions, life satisfaction and well-being[24 28]. What distinguishes HRQL measures from others that capture some of these constructs is that HRQL must appraise at least the three core domains: physical, psychological and social[24].

For the purposes of this thesis, which considers the impact of liver disease and liver transplantation on the individual, the relevant construct is HRQL. HRQL may be more relevant in this context than length of life, as patients are frequently more concerned about life quality and disability than about longevity[25].

## 1.3 Measures of Health-related Quality of Life

Research in HRQL has risen exponentially over the last few decades[26], with the development of numerous generic and disease specific HRQL instruments. HRQL measures are generally of two types: 1) *profiles*, which report on several domains of health and 2) *indexes*, which report health status as one number[27].

While profiles capture more extensive descriptive information, they generally lack the capacity to balance gains and losses on the dimensions on which they are based. This is a particularly important constraint if change in health status is the desired objective. A gain in one dimension may be offset by a loss in another. Notwithstanding this important limitation, instruments of this type are widely reported in the clinical literature (e.g. MOS SF-36).

Health indexes use the concept of utility to represent health, which is defined as a value between 0 and 1, representing the strength of preference an individual has for a given multi-dimensional health state. The closer the value is to 1, the more the health state is seen as being the best possible one. When linked to life expectancy, utility values lead to quality adjusted life-years (QALYs). A key feature of utility is that it summarizes information about many health domains by one number, thus, the term "multidimensional". In this way, gains (or losses) in one domain can be offset by losses

(or gains) in another domain. The value placed on this health state is derived by techniques such as "Time Trade-off". This is the estimated amount of lifespan a patient is willing to "trade" for perfect health.

Generic measures are developed without considering a specific health condition but impact of health events in general. These are widely used in population health and health services research and also clinically. Examples of generic measures are the Short-Form Health Survey (SF-36), EuroQOL (EQ-5D) and General Health Questionnaire (GHQ)[28 29 30 31 32]. On the other hand, disease specific instruments are designed to capture the specific effects of a condition and, therefore, may more closely relate with traditional clinical disease measures. The Liver Disease Quality Of Life (LDQOL)[33], Chronic Liver Disease Questionnaire (CLDQ)[34] and Hepatitis Quality of Life Questionnaire for Hepatitis C Virus (HQLQ)[35] are examples of disease specific measures recently developed, but are still less commonly employed than the generic instruments.

Notwithstanding the value of HRQL to understanding the impact of a health condition on the individual, their use is not routine in clinical practice – but would be considered the exception rather than the rule. In 1997, the liver disease and transplantation program at McGill University recognized the need to develop standard procedures for recording the health and outcomes of the patients attending these clinics. At this time, liver disease specific measures for HRQL were limited – most of the current measures were non-existent or in the development phase. Therefore, in consultation with a quality of life measurement expert, Dr. Nancy Mayo, well-established and validated generic health status measures were chosen. All patients attending regular visits to the clinic were provided with these questionnaires to fill out. As part of ongoing quality

assurance, the research team asked the relevant question, "What is the best measure of HRQL for this population?" Further thought revealed that pivotal component of "best" was ability to identify change over time, particularly change pre to post-transplant, and the ability of the HRQL measure to reflect clinical indicators of disease, as this would add face value to the HRQL measure. This property of a measure is termed "responsiveness".

### 1.4 Responsiveness of Health Measures

Responsiveness is defined as the ability of an instrument to detect clinically important changes over time[36 37], even if the changes are small. Husted et al[38] reviewed the methods for assessing responsiveness, and the lack of consensus as to how one should measure it, has led to a proliferation of responsiveness statistics, often with several being reported in the same study.

Several responsiveness statistics are available, including paired t-test, relative efficiency, effect size, standardized response mean, Guyatt's responsiveness index, Receiver Operating Characteristic curves (ROCs), correlation (Pearson Product Moment) analyses, and regression modeling. Each statistic has its own strengths, and the choice of test is often dependent on personal preference and what the investigator wishes to demonstrate.

For this analysis, we used paired t-test, effect size, standardized response mean and relative efficiency. Their formulae are found in Table 1. The paired t-statistic tests the hypothesis that there is no change in the response between 2 time points, with

significant values therefore rejecting the null hypothesis and demonstrating a statistically significant change.

Effect size is a popular method for assessing responsiveness, and is the difference between the baseline measurement and follow-up scores of the measure, divided by the standard deviation of the baseline scores. In contrast to the t-test and standardized response mean, this provides a direct assessment of the magnitude of change. Although there is no universal consensus for quantifying a specific level of effect size, previous published work, by Cohen[39], has suggested that an effect size of 0.2 is considered small, 0.5 to be moderate, and 0.80 or > to demonstrate a large effect, representing at least 4/5 of a SD from the baseline.

Liang et al has proposed the use of the standardized response mean[40] (SRM) and the relative efficiency index[41] (REff) as responsiveness statistics. Both methods are advantageous in studies with missing data or small sample size, for the SRM is the ratio of observed change and the standard deviation of the change in scores, whereas the Reff is calculated by squaring of the ratio of paired t-tests for 2 measures, with one serving as the reference standard. The REff accounts for small sample sizes as t-statistics have a sample size factor in their calculation.

Guyatt's Responsiveness Index is considered by some to be a superior responsiveness statistic, but is dependent on knowledge of the minimally clinically important change on a measure. ROC curves may be useful overviews of the relationship between a measure and an external indicator of change, but their major disadvantage is their dependence on a dichotomous external criterion (i.e. Patient is worse, not worse), which may require a separate analysis to determine responsiveness. Correlation analyses

with Pearson Product Moment correlations are well suited to responsiveness as it examines how well changes in one measure predict changes in another. As a natural extension, if correlations are found, then regression modeling may provide more information about the relationship.

One of the principal uses of responsiveness measures for HRQL research is in the design of clinical trials for measurement of treatment effectiveness[42]. As the magnitude of most responsiveness measures is related to the number of subjects in a trial needed to achieve a certain statistical power, then knowledge of and the use of more responsive measures would allow the completion of a study with fewer patients.

A study for the most responsive HRQL measurement instrument in liver transplantation has yet to be undertaken. The data arising from this attempt at routine implementation of health assessment in the liver transplantation population provided the material to address this question.

**Table 1: Indices of Responsiveness**

| Index | Formula |
|---|---|
| **Effect Size** | Mean $\Delta$ / $SD_{initial\ scores}$ |
| **SRM** | Mean $\Delta$ / $SD_{change\ scores}$ |
| **Paired t statistic** | Mean $\Delta$ / $SD / \sqrt{n}$ |
| **Relative Efficiency** | $(t\ statistic_{(test\ 1)} / t\ statistic_{(test\ 2)})^2$ |

SD = standard deviation, $\Delta$ = change, SRM = standardized response mean

# CHAPTER II: MATERIALS AND METHODS

## 2.1 Objectives of the Study

### *2.1.1 Overall Objective*

The overall aim is to identify which instrument is the most responsive tool for detecting HRQL change for patients pre- and post-liver transplantation using the Short-Form Health Survey (SF-36), EuroQOL (EQ-5D) and General Health Questionnaire-30 (GHQ-30).

### *2.1.2 Specific Objective 1:*

To estimate the indices of responsiveness for each HRQL measure.

### *2.1.3 Specific Objective 2:*

To compare relative efficiencies of HRQL measures to traditional liver biochemistry parameters.

## 2.2 Study Design

This study used a prospective cohort study design. The cohort was established in 1997 and patients were assessed prospectively, at one or more times prior to transplant, and one or more times after transplant. The study is historical in the sense that the data, while collected prospectively, were not examined until now.

## 2.3 Ethical Approval

This study was reviewed and approved by the Royal Victoria Hospital Ethics committee. All subjects who completed questionnaires had agreed to the data collection procedures and provided written and informed consent (see Appendix 6.2).

## 2.4 Subjects

All outpatients referred to the McGill University Liver Transplant program from 1997 to February 2004, with advanced liver disease and meeting criteria for OLT listing were potentially eligible for this study. Subjects were included if they were ≥ 18 years of age and had completed HRQL questionnaires prior to and after OLT. Patients were excluded from the analysis if they did not have both pre- and post-transplantation questionnaires.

## 2.5 Description of Study Measures

### *2.5.1 Short-form Health Survey (SF-36)*

The SF-36 is a comprehensive measure of general health status, originally developed for use in the Medical Outcomes Study and the Rand Health Insurance Experiment Surveys. It is a non-disease specific method of describing and evaluating health status across several domains, with scores ranging from 0 (poor health) to 100 (good health). There are eight areas that are assessed, including: 1) physical functioning

(PF), 2) limitations to usual role activities due to physical health problems (role physical, RP), 3) bodily pain (BP), 4) general health perceptions (GH), 5) vitality (VT) as a summation of energy and fatigue, 6) social functioning (SF), 7) limitations to usual role activities due to emotional problems (role emotional, RE), and 8) mental health (MH). An additional physical (PCS) and mental health (MCS) component summary score can be derived from the previous items for a succinct assessment.

Its reliability and validity have been established through numerous clinical studies in a variety of patients [47 48 49 50 51 52 53 54 55 56] and it has been used in patients with liver disease[57 58 59 60 61 62] as well as in liver transplantation[63]. Reliability testing of its 8 scales and the 2 summary measures has often exceeded 0.80[64 65], with the minimum standard being 0.70[66]. Similarly, multiple aspects of validity including content, concurrent, criterion, construct and predictive evidence has been extensively supported through repeated study and has led to its acceptance and widespread use[65 67] in over 1000 publications[68].

Advantages include the availability of 'normal' data for the general population in many nations, allowing comparisons between sick and well persons. There are shortened versions (SF-20, SF-12) available and it has been translated into several languages (Appendix 6.3).

### *2.5.2 EuroQOL (EQ-5D)*

The EQ-5D was designed to complement other generic HRQL measures like the SF-36, Nottingham Health Profile, Sickness Impact Profile or disease specific instruments. It assesses health on the day of the interview, and produces a descriptive

profile with an index value of health status. The main domains tested are physical, mental and social functioning, with emphasis on mobility, self-care, usual activities, pain/discomfort and anxiety/depression, graded on a 3-point scale.

There are 2 sections to the EQ-5D: the EQ-5D index and EQ-5D VAS[69]. The EQ-5D Index provides a standardized, generic measure of HRQL and gives an overall utility value (from 0 to 1) based on population preferences for different health states. The EQ-5D VAS is a visual analogue scale, with the best imaginable health at the top and worst imaginable health being at the bottom. Patients rate their health between 0 (worst) and 100 (best). For the purposes of this study, we used only the VAS to reflect the patient's perspective of their health and not the EQ-5D Index as it reflects healthy persons weighting of different hypothetical health states.

Advantages for the EQ-5D include its simplicity and ease of completion by patients, availability in several languages, and its calculation of a single measure of health status. It has been used in the general population and also many different illness populations[70 71 72 73 74 75 76 77 78 79]. (Appendix 6.4)

*2.5.3 General Health Questionnaire -30 (GHQ-30):*

Depression and anxiety are often the result of chronic illness and some method of assessment was desired by the transplant program. The GHQ is a measure of current mental health status, and is the most widely applied self-reporting instrument on psychiatric disturbance in the United Kingdom. Although it was originally developed as a sixty item questionnaire, several shorter versions have become available (GHQ-12, -20,

-28, -30). The GHQ-30 is used in this study as it was the most comprehensive version short of the original, more time-consuming 60 item questionnaire. (Appendix 6.5)

The questionnaire asks whether the respondent has recently experienced a particular symptom or behavior "over the last few weeks". Each item is rated on a four-point scale (less than usual, no more than usual, rather more than usual, or much more than usual), with the two most common scoring methods, being Likert (0-1-2-3) or Bi-modal (0-0-1-1) techniques. For example when using the GHQ-12 it gives a total score of 36 or 12 based on the selected scoring methods. For the GHQ-30, a total score of 90 or 30 would be possible, with higher scores indicating greater stress.

The GHQ was designed for use in general population surveys, primary medical care settings, or general medical outpatients, as a first stage screen for psychiatric disorders, not to diagnose mental illness. Four main areas of distress it covers are depression, anxiety, social impairment and hypochondrias. Patients are asked to compare their present state with usual or "normal" state[28 29 32]. It is not useful as a measure of chronic illness, and does not assess severity, due to the format in which questions are structured. Patients with chronic illness may grade themselves as "same as usual" and thus score zero for symptoms they are or have been experiencing for prolonged periods. This underestimation remains controversial, however, as Goldberg and Williams (1988)[32] point out that most people cling to the perception of themselves without disease.

### *2.5.4 Liver Biochemistry Measures*

Liver injury is suspected when there are elevated levels of liver enzymes in the serum. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline

phosphatase (ALP) enzymes reside within hepatocytes and are responsible for synthesis of cellular proteins. Liver function tests include the International Normalized Ratio (INR), albumin and bilirubin levels, for they reflect the metabolic capacity of the liver. An elevated INR or low serum albumin often indicates acute or chronic liver synthetic dysfunction, whereas elevated bilirubin levels may indicate decreased metabolism and conjugation of bilirubin to its more water soluble form.

Liver biochemistries were taken from the hospital computerized mainframe on the day patients completed the HRQL measures, or within a short time frame around this date (+/- 1 week).

## 2.6 Data Collection

The data collection period extended from July 1997 to February 2004. At their arrival to the Liver Transplant clinic, patients were asked by our research nurse to participate and complete a set of HRQL questionnaires consisting of the SF-36, EQ-5D and GHQ-30. These were completed either in the waiting room prior to their medical appointment, or were returned by mail in a self-addressed, stamped envelope. The completed questionnaires were collected and scored by a research data manager and results entered into a computerized database. The EQ-5D VAS score was recorded as well as results of the GHQ, scored by both Likert (GHQ1) and bi-modal (GHQ2) methods.

The attending physicians were not informed as to the results of the HRQL surveys. Patients were asked to fill out the questionnaires post transplant at a point when

acute medical issues were deemed stable or resolved. Socio-demographic data provided by the patients' included their name, age, gender, date of birth, medical record number (MRN), ethnicity, primary language of communication, height, weight, and the date of survey completion. Our study nurse retrieved additional clinical data (Child-Pugh Score, type of liver disease, unique transplant number (UTN), date of liver transplant, body mass index (BMI) from the patient's hospital chart. The primary type of liver disease was diagnosed by the patient's Hepatologist, and taken from the patient's medical file. It was then coded within SAS as 1 = viral hepatitis (Hepatitis B or C), 2 = alcoholic liver disease, 3 = cholestatic liver disease (Primary Biliary Cirrhosis or Primary Sclerosing Cholangitis) 4 = tumor (hepatocellular carcinoma) 5 = other (such as hemochromatosis, polycystic liver disease, sarcoidosis). Liver enzymes, AST, ALT, ALP, and liver function tests, albumin (ALB), total bilirubin (TB), and coagulation studies (International Normalized Ratio, INR and Prothrombin time, PT) were retrieved from the hospital records or institutional mainframe system for the date of their visit ± 7 days pre- or post-visit date (Reference ranges for normal laboratory values in Appendix 6.6).

The SF-36 was scored using the methods outlined by the developers of the measure[91]. The GHQ-30 was scored by 2 methods, the Likert (GHQ1) and Bimodal techniques (GHQ2) and the numeric value of the EQ-5D VAS was recorded. Missing data was left blank within the spreadsheet, and accounted for by SAS programming.

## 2.7 Statistical Analysis

The instrument that best predicts HRQL change post-liver transplantation will be the one that is most responsive to changes in health status. Indices of responsiveness were shown in Table 1, and include effect size and standardized response mean[80] (SRM). A paired t-statistic to assess significance of change between pre- and post-transplantation scores for the subcomponents of each instrument, will determine the one that detected the greatest magnitude of change. The relative efficiency[82] [83](that is, most effective for detecting HRQL change with a minimum of effort) of one measurement tool to the other will then subsequently be compared, for example, the SF-36 to the EQ-5D.

Pre-transplant vs. post-transplant liver biochemistries will be analyzed in a similar fashion as in Specific Objective 1, with indices of responsiveness to determine if traditional blood tests for liver injury and function are responsive to changes in health status when compared to HRQL measures.

Data was analyzed using SAS® Software (SAS® Inc., Cary, N.C., USA). All statistical tests are two-tailed unless stated otherwise, and the level of significance is $p < 0.05$.

The datasets were sorted by the patient's unique medical record number and cleaned to remove duplicate entries, and impossible data (i.e. patients with HRQL scores outside of the maximum range). Datasets for the HRQL measurements, laboratory and demographic information (race, language) and primary disease diagnoses were merged and analyzed for demographic and baseline values. Ethnicity was classified into 5 groups: Caucasian, Asiatic, Indian, Black and "Other", which included small numbers of other ethnic groups.

Changes in each parameter were calculated as preoperative - postoperative score, with means and standard deviations. The Pearson-Product Moment Correlations were estimated for the HRQL indices to verify inter-instrument concordance in measuring poor health status. HRQL measures were also correlated with laboratory indices. Effect sizes were calculated by taking a ratio of the mean change in score pre-OLT vs. post-OLT, and dividing by the SD of the initial baseline value. The standardized response mean was calculated by the mean change in scores divided by the SD of change of the scores.

The efficiency of a measurement instrument can be thought of as its' ability to detect HRQL change "with a minimum of effort or waste"[81]. For relative efficiency, a paired t-statistic for significance of post-operative change was calculated for each parameter. General Health Perception (GH), was used as the comparator "standard", but this choice was arbitrary, and does not suggest any preference for GH. Based on the technique by Liang M et al[82 83], relative efficiency (REff) was calculated by squaring the ratio of appropriate t-statistics.

$$\text{i.e. REff of EQ-5D vs. GH} = (t_{\text{EQ-5D}}/t_{\text{GH}})^2$$

By basing the REff calculations on t-statistics, missing data is accounted for, as t-statistics include a sample-size factor. A REff > 1 would show the measurement tool or lab value was a more efficient tool for measuring change in HRQL than the GH, and the converse would be true if the REff was < 1. Any pair of instruments from the data in this study, including bloodwork, can be compared and REff calculated. The instrument with the highest REff should give the best trade-off between sample size and statistical power

to detect HRQL change. The one with the highest REff has the highest power for a fixed sample size, and requires fewer patients to achieve a fixed level of statistical power.[82]

# CHAPTER III: RESULTS

## 3.1 Patient Demographics

From July 1997 to February, 2004, there were 444 liver transplants in 435 patients. Nine patients received re-transplantation. Two hundred and nineteen patients completed at least one set of HRQL surveys for the study, giving an overall response rate of 50.3%. Of the 219 patients that had completed at least one HRQL measurement, 44 (20%) had HRQL measurements pre- and post-liver transplant, and are the main focus of this analysis. Twenty-two patients completed surveys up to the time of OLT (pre-transplant only) and there were 150 patients who had started completing surveys only after surgery (post-transplant only). Three patients were not classifiable into any of these 3 groups and removed, as they were recorded as completing HRQL measures on the day of their transplant, an unlikely situation. Baseline demographics, HRQL scores and laboratory indices are shown for the 3 groups in Tables 2 and 3. As the main analysis for this thesis pertains to the group of 44 patients with "matched" pre- and post-OLT data, the following discussion refers to this group unless otherwise specified.

The mean age of the patients was 54.5 years, with 63.6% of the patients being male, and 86.4% listing English as their primary language. Caucasians made up 84.1% of the cohort, Asians 11.3% and Indians 4.6%. Viral hepatitis was the main cause for liver disease, in 36.4% of the patients, followed by cholestatic liver diseases (Primary Biliary Cirrhosis or Sclerosing Cholangitis) and then Hepatocellular carcinoma. The majority of transplanted patients had severely decompensated liver disease, Child-Pugh Class 'C' (63.6%).

## 3.2 Baseline HRQL scores and Laboratory Indices

Table 4 provides simple statistics for the study group. Liver biochemistries were matched ± 7 days from the date of the HRQL assessment. Baseline HRQL subset scores and laboratory indices are provided, with Canadian population normal values for the SF-36 at age 55 years, for comparison.

**Table 2: Baseline Demographics of Patients Who Have Matched (Pre & Post), Pre-Transplant only and Post-Transplant only Data**

| Variable | Matched dataset (n = 44) | Pre-transplant only (n = 22) | Post-transplant only (n = 150) |
|---|---|---|---|
| Mean Age (years) | 54.5 | 52.9 | 53.9 |
| Male (%) | 63.6 | 36.4 | 72.0 |
| Anglophone (%) | 86.4 | 76.2 | 74.8 |
| **Ethnic Background** | | | |
| Caucasian (%) | 84.1 | 59.1 | 82.0 |
| Asian (%) | 11.3 | 4.6 | 4.7 |
| Indian (%) | 4.6 | 18.2 | 6.7 |
| Black (%) | --- | 4.6 | 5.3 |
| Other (%) | --- | 13.6 | 1.3 |
| **Disease Indication for Transplantation** | | | |
| Viral Hepatitis* | 36.4% | 18.2 | 29.3 |
| Cholestatic Liver Disease** | 20.5% | 27.3 | 12.7 |
| Hepatocellular Carcinoma | 15.9% | 13.6 | 18.0 |
| Alcoholic Liver Disease | 13.6% | 13.6 | 22.0 |
| Other | 13.6% | 27.3 | 18.0 |
| **Child-Pugh Class** | | | |
| A | --- | --- | 0.7 |
| B | 31.8% | 27.3 | 17.3 |
| C | 63.6% | 72.7 | 81.3 |
| Missing | 4.6% | --- | --- |

* Hepatitis B or C

** Primary Biliary Cirrhosis or Primary Sclerosing Cholangitis

**Table 3: Baseline HRQL Scores Between Patients Who Have Matched (Pre & Post), Pre-Transplant Only and Post-Transplant Only**

| Test | Subtest | Matched dataset (n = 44) | Pre-transplant only (n = 22) | Post-transplant only (n = 150) |
|---|---|---|---|---|
| SF 36 | BP | 50.9 | 57.6 | 56.0 |
| | GH | 41.4 | 40.1 | 51.3 |
| | MH | 58.7 | 60.7 | 61.0 |
| | PF | 50.1 | 44.1 | 54.4 |
| | RE | 59.1 | 47.0 | 55.5 |
| | RP | 22.6 | 35.2 | 37.9 |
| | SF | 48.4 | 46.4 | 53.7 |
| | VT | 35.6 | 33.7 | 41.0 |
| | MCS | 42.2 | 40.7 | 42.5 |
| | PCS | 33.2 | 34.8 | 37.5 |
| EQ5D | EQ5D VAS | 55.2 | 59.5 | 68.4 |
| GHQ-30 | GHQ1 (Likert) | 58.4 | 64.6 | 54.8 |
| | GHQ2 (Bi-modal) | 5.5 | 9.0 | 6.3 |
| Laboratory Indices | ALB | 32.0 | 31.5 | 40.2 |
| | ALP | 139.4 | 131.0 | 130.8 |
| | ALT | 78.6 | 110.0 | 53.7 |
| | AST | 84.8 | 76.7 | 31.7 |
| | INR | 1.4 | 1.4 | 1.0 |
| | PT | 15.0 | 14.7 | 11.9 |
| | TB | 41.7 | 95.6 | 18.9 |

**Table 4: Baseline Health-Related Quality of Life and Laboratory Indices In Dataset of 44 Matched Patients**

| Test | Subtest | N | SF-36 Normal Values (Age 55) | Mean | Standard Deviation |
|---|---|---|---|---|---|
| SF 36 | BP | 44 | 74.9 | 50.9 | 28.8 |
| | GH | 42 | 74.8 | 41.4 | 27.7 |
| | MH | 44 | 79.5 | 58.7 | 20.0 |
| | PF | 44 | 82.3 | 50.1 | 29.0 |
| | RE | 42 | 87.8 | 59.1 | 42.5 |
| | RP | 42 | 81.3 | 22.6 | 33.0 |
| | SF | 44 | 88.1 | 48.4 | 30.9 |
| | VT | 44 | 68.3 | 35.6 | 21.3 |
| | MCS | 44 | 53.7 | 42.2 | 10.7 |
| | PCS | 44 | 49.0 | 33.2 | 10.7 |
| | | | | | |
| EQ5D | EQ5D VAS | 32 | | 55.2 | 21.0 |
| | | | | | |
| GHQ-30 | GHQ1 (Likert) | 23 | | 58.4 | 13.3 |
| | GHQ2 (Bi-modal) | 23 | | 5.5 | 17.1 |
| | | | | | |
| Test | Subtest | N | Normal Range | Mean | Standard Deviation |
| Laboratory Indices | AST | 17 | 6-35 U/L | 84.8 | 72.1 |
| | ALT | 19 | 6-45 U/L | 78.6 | 74.0 |
| | ALP | 17 | 25-115 U/L | 139.4 | 76.8 |
| | ALB | 16 | 38-50 g/L | 32.0 | 7.8 |
| | INR | 18 | 0.8-1.2 | 1.4 | 0.3 |
| | PT | 15 | 11.2-15.7 s | 15.0 | 2.5 |
| | TB | 18 | 1.7-18.9 µmol/L | 41.7 | 32.0 |

## 3.3 Choice of HRQL Survey

The HRQL survey completed closest to the patient's liver transplant date was chosen as the baseline, initial survey, when they were expected to have the poorest functional status and lowest HRQL score. Initially, the second measurement survey was chosen if it fell within a suitable time frame for recovery of 6-12 months, but only 8 subjects completed measures within this period. Therefore, regardless of the time post transplant, the patient's completed second survey was chosen. Although the range in time post-OLT for completion of the second assessment varied between 1 and 70 months, the median time for all 44 patients to have completed the $2^{nd}$ survey was 5.3 months.

## 3.4 Inter-instrument Correlation and Correlation with Liver Dysfunction

Pearson Correlation Coefficients demonstrated strong inter-instrument agreement for detection of impaired HRQL with advanced liver dysfunction (Table 5). The EQ-5D showed high correlation and agreement with nearly all subcomponents of the SF-36 and the summary physical and mental health scores. There was also strong correlation for HRQL measurement by the EQ-5D VAS and the GHQ-30 (GHQ1 and GHQ2 denote scoring by the Likert and Bimodal systems, respectively), but less frequently between the SF-36 and GHQ-30. Table 6 illustrates correlations between some indices of liver dysfunction and the SF-36. Table 7 shows correlation between different markers of liver dysfunction. The full correlation matrix is included in Appendix 6.7 for review.

**Table 5: Significant Pearson Correlation Coefficients with Inter-instrument and Biochemistry Correlations**

| SF-36 Subcomponent | EQ-5D (R-value / *p*-value) | GHQ1 (R-value / *p*-value) | GHQ2 (R-value / *p*-value) |
|---|---|---|---|
| BP | 0.65 (<0.0001) | --- | --- |
| GH | --- | --- | --- |
| MH | 0.39 (0.03) | --- | --- |
| PF | 0.64 (<0.0001) | --- | --- |
| RE | 0.36 (0.047) | -0.53 (0.01) | -0.67 (0.0006) |
| RP | 0.5 (0.003) | -0.53 (0.01) | -0.58 (0.0038) |
| SF | 0.73 (<0.0001) | -0.52 (0.01) | --- |
| VT | --- | --- | -0.5 (0.015) |
| MCS | 0.42 (0.02) | -0.46 (0.03) | -0.53 (0.01) |
| PCS | 0.51 (0.003) | --- | --- |

| GHQ-30 Scores | EQ-5D (R-value / *p*-value) | GHQ1 (R-value / *p*-value) | GHQ2 (R-value / *p*-value) |
|---|---|---|---|
| GHQ1 Likert | -0.67 (0.0007) | n/a | n/a |
| GHQ2 Bimodal | -0.56 (0.006) | n/a | n/a |

**Table 6: Significant Pearson Correlation Coefficients with SF-36 and Laboratory Indices**

| Correlation Between HRQL instruments and Liver Dysfunction | | | |
|---|---|---|---|
| **Variables** | **R** | ***p*-value** | **Interpretation** |
| **INR*MH** | -0.61 | 0.007 | As the INR increases, MH decreases, which is consistent with worsening mental health as the liver becomes more dysfunctional. Anxiety and depression are often seen with chronic illness and liver disease. |
| **INR*VT** | -0.48 | 0.0043 | As the INR increases, feelings of vitality decrease, corresponding to the worsening liver function |
| **TB*PCS** | -0.49 | 0.04 | As the total bilirubin falls, overall physical status improves, reflecting improving liver function |

**Table 7: Significant Pearson Correlation Coefficients with Liver Biochemistry**

| Correlation Between Markers of Liver Injury and Liver Dysfunction | | | |
|---|---|---|---|
| **Variables** | **R** | ***p*-value** | **Interpretation** |
| **AST*TB** | 0.59 | 0.013 | Positive correlation between markers of liver injury |
| **ALT*ALP** | 0.55 | 0.028 | |
| **AST*ALT** | 0.81 | 0.0001 | |

AST = aspartate aminotransferase ALT = alanine aminotransferase

ALP = alkaline phosphatase TB = total bilirubin

## 3.5 Effect Sizes

The use of effect sizes (ES) allows comparison between interventions (i.e. Surgery vs. Drug X) by the removal of units of measurement. Comparisons across different studies can also be performed, in which, for example, the treatment effect size of a new drug can be calculated and compared to the effect size of another published, tested therapy, which may be the gold standard.

There is no universal consensus for quantifying a specific level of effect size, but previous published work, by Cohen[84], has suggested that an effect size of 0.2 is considered small, 0.5 to be moderate, and 0.80 or > to demonstrate a large effect, representing at least 4/5 of a SD from the baseline.

Albumin had the largest effect size, of 1.62, considered a very large value as judged by Cohen's reference system. This was then followed by the EQ-5D which had a large effect (0.81), and then by the GH (General Health Perception) subcomponent of the SF-36 (0.71). (Refer to Table 8)

**Table 8: Effect Sizes by Measurement Modality**

| Test | Subtest | Effect Sizes | Ranking |
|---|---|---|---|
| SF 36 | BP | 0.02 | 9 |
| | GH | 0.71 | 3 |
| | MH | 0.55 | 4 |
| | PF | -0.10 | |
| | RE | -0.08 | |
| | RP | 0.28 | 7 |
| | SF | -0.02 | |
| | VT | 0.44 | 5 |
| | MCS | 0.32 | 6 |
| | PCS | 0.08 | 8 |
| | | | |
| EQ5D | EQ5D VAS | 0.81 | 2 |
| | | | |
| GHQ | GHQ1 | -1.02 | |
| | GHQ2 | -0.54 | |
| | | | |
| Laboratory Indices | AST | -1.99 | |
| | ALT | -0.72 | |
| | ALP | -0.50 | |
| | ALB | 1.62 | 1 |
| | INR | -4.09 | |
| | PT | -1.70 | |
| | TB | -2.93 | |

**Effect Size = Mean $\Delta$ / $SD_{initial\ scores}$**

### 3.6 Standardized Response Means (SRM) and 3.7 Relative Efficiency

Although albumin showed the largest effect size of all the measures, the EQ-5D had the greatest SRM (0.58), followed by albumin (0.54) and the General Health (GH) perception subcomponent of the SF-36 (0.48). (Table 9)

General Health perception was chosen at random as an arbitrary "reference standard" for comparison and calculation of the relative efficiency. Its use does not denote any preference for this measure. The EQ-5D VAS had the highest relative efficiency for detection of HRQL changes (1.10) followed by the GH (1.0), and then Mental Health (MH) at 0.99. (Table 10)

**Table 9: Standardized Response Mean of Different Measurement Modalities**

| Test | Subtest | Mean Change | SD | SRM | Ranking |
|---|---|---|---|---|---|
| SF 36 | BP | 0.57 | 38.08 | 0.01 | 9 |
| | GH | 16.02 | 33.52 | 0.48 | 3 |
| | MH | 9.98 | 21.78 | 0.46 | 4 |
| | PF | -2.79 | 31.62 | -0.09 | |
| | RE | -3.73 | 49.01 | -0.08 | |
| | RP | 11.25 | 44.56 | 0.25 | 7 |
| | SF | -0.60 | 33.32 | -0.02 | |
| | VT | 10.93 | 31.25 | 0.35 | 5 |
| | MCS | 3.27 | 10.72 | 0.31 | 6 |
| | PCS | 0.91 | 13.94 | 0.07 | 8 |
| | | | | | |
| EQ5D | EQ5D VAS | 13.23 | 22.62 | 0.58 | 1 |
| | | | | | |
| GHQ | GHQ1 | -6.69 | 11.89 | -0.56 | |
| | GHQ2 | -1.63 | 6.18 | -0.26 | |
| | | | | | |
| Laboratory Indices | AST | -51.30 | 56.20 | -0.91 | |
| | ALT | -33.09 | 90.53 | -0.37 | |
| | ALP | -49.11 | 127.37 | -0.39 | |
| | ALB | 6.70 | 12.52 | 0.54 | 2 |
| | INR | -0.35 | 0.37 | -0.94 | |
| | PT | -1.97 | 1.95 | -1.01 | |
| | PTT | -8.71 | 7.78 | -1.12 | |
| | TB | -27.90 | 34.25 | -0.81 | |

$$SRM = Mean\ \Delta\ /\ SD_{change\ scores}$$

**Table 10: HRQL Change and Relative Efficiencies for its Detection, by Assessment Method**

| Test | Subtest | Mean | SD | T Statistics | Relative Efficiency | Ranking |
|---|---|---|---|---|---|---|
| SF 36 | BP | 0.57 | 38.08 | 0.10 | 0.001 | 19 |
| (reference standard) | GH | 16.02 | 33.52 | 3.06 | 1.00 | **2** |
| | MH | 9.98 | 21.78 | 3.04 | 0.99 | **3** |
| | PF | -2.79 | 31.62 | -0.57 | 0.035 | 16 |
| | RE | -3.73 | 49.01 | -0.48 | 0.025 | 17 |
| | RP | 11.25 | 44.56 | 1.60 | 0.27 | 12 |
| | SF | -0.60 | 33.32 | -0.12 | 0.001 | 19 |
| | VT | 10.93 | 31.25 | 2.32 | 0.57 | 8 |
| | MCS | 3.27 | 10.72 | 2.02 | 0.44 | 10 |
| | PCS | 0.91 | 13.94 | 0.43 | 0.02 | 18 |
| EQ5D | EQ5D VAS | 13.23 | 22.62 | 3.20 | 1.10 | **1** |
| GHQ | GHQ1 | -6.69 | 11.89 | -2.25 | 0.54 | 9 |
| | GHQ2 | -1.63 | 6.18 | -1.05 | 0.12 | 15 |
| Laboratory Indices | AST | -51.30 | 56.20 | -2.89 | 0.89 | **4** |
| | ALT | -33.09 | 90.53 | -1.21 | 0.16 | 13 |
| | ALP | -49.11 | 127.37 | -1.16 | 0.14 | 14 |
| | ALB | 6.70 | 12.52 | 1.69 | 0.31 | 11 |
| | INR | -0.35 | 0.37 | -2.65 | 0.75 | 6 |
| | PT | -1.97 | 1.95 | -2.68 | 0.76 | **5** |
| | TB | -27.90 | 34.24 | -2.58 | 0.71 | 7 |

**Relative Efficiency = (t statistic$_{(test\ 1)}$ / t statistic$_{(test\ 2)}$)$^2$**

### 3.8 Comparison of Patient Groups and Generalization of Results

This analysis focused on the "matched" group of 44 patients with pre- and post-OLT data. From those patients that completed at least one HRQL measure, 22 had filled out surveys up to the time of OLT (pre-transplant only) and 150 patients had started completing surveys only after surgery (post-transplant only). Baseline demographics, HRQL scores and laboratory indices were shown in Tables 2 and 3. Table 11 shows an analysis of selected variables to see if there were significant differences between the 3 groups (pre-transplant only, post-transplant only, and the matched group with pre- and post-transplant data). Although age, Child-Pugh Class and proportion of Anglophones were not significantly different between groups, Ethnicity and Gender were different. Therefore, the generalization of these results needs to be verified by further study.

**Table 11: Tests of Significance of Selected Demographic Variables Between Patients Who Have Matched (Pre & Post), Pre-Transplant Only and Post-Transplant Only**

| Variable | Chi-Square (*p* value) | Fisher's Exact Test | ANOVA |
|---|---|---|---|
| % Anglophone | $\chi^2$ 2.58, p = 0.28 | --- | --- |
| % Males* | $\chi^2$ 11.19, p = 0.0037 | --- | --- |
| Child-Pugh Class | --- | p = 0.095 | --- |
| Ethnicity* | --- | p = 0.013 | --- |
| Age | --- | --- | p = 0.94 |

*significant difference between groups

# CHAPTER IV: DISCUSSION

## 4.1 Discussion of Results

Outcomes in liver transplantation have often focused on "length of life" as a measure of success, rather than "quality of life", with the patient's perception often in contrast to that of the physician's. Doctors are accustomed to using traditional clinical measures to estimate changes in patient health status. These biologic indices assess function in concrete terms (i.e. albumin in g/L, or bilirubin in μmol/L), with an established, population-based "normal range" to interpret abnormal clinical outcomes (refer to Appendix 6.6).

HRQL measurement is based on "constructs", that is, "domains of content"[85], that are not traditionally used in medicine. HRQL scales present change in units that have no direct biologic meaning (i.e. mobility, or anxiety). Although a physician may believe an important clinical change has occurred with normalization of lab values in response to a therapy, patients may instead feel the reduction in their symptoms or improved function to be most relevant. As well, although two patients may have similar clinical or physiological status, they could conceivably place a different value on the same aspects of HRQL.

Although disease specific HRQL measures exist, such as the LDQOL[33] and CLDQ[34], these instruments were created and validated in the literature after the data collection period began at the MUHC in 1997. It would be interesting to see how these newer, disease-specific measurement tools compare to established, well-validated generic measures such as the SF-36, EQ-5D and GHQ-30.

The SF-36 has been used in evaluation of musculoskeletal disorders[86], the frail elderly[87], patients with total hip arthroplasty[88] with varying degrees of responsiveness. Beaton et al[86] found that the SF-36 was the most responsive measurement tool in workers with musculoskeletal disorders, when compared to the Nottingham Health Profile, Health Status Section of the Ontario Health Survey (OHS), Duke Health Profile, and the Sickness Impact Profile. This is in contrast to Stadnyk et al[87] who found the SF-36 reliable and valid, but it had marginal responsiveness in the frail elderly population. Blanchard et al[88] found the SF-36 ranked behind disease specific measures for responsiveness in their group of hip arthroplasty patients, but was still responsive to changes and provided additional meaningful information.

Wright et al[89] and Guyatt et al[90] have found that disease-specific measures tend to be more responsive vs. generic ones likely because disease-specific measures generally explore a domain in greater depth than the corresponding domain of a generic tool, and sub-domains of generic instruments often have a broader focus than that of the matching disease-specific measure. Liver disease specific measures for HRQL were limited in 1997, with most of the currently available measures being non-existent or in the development phase. It would be a logical next step to compare the SF-36 and EQ-5D to a liver disease specific instrument in future studies.

Three of four physical health scales (BP, PF, RP) of the SF-36 were highly correlated with the EQ-5D VAS, as well as three of four mental health scales (MH, RE, and SF). The mental health and physical health summary scores were also highly correlated with the EQ-5D VAS. This provides evidence that both instruments are measuring similar constructs (convergent validity). Although the GHQ-30 was not as

strongly correlated with either scale, it tended to have better agreement with mental health scales (RE, SF, MCS), over physical health (RP) which is consistent with its principal function, detecting psychological stress. In our patient population, preoperative scores were poor with significant correlations between subcomponents of the SF-36 and between the EQ-5D VAS and GHQ-30 (refer to Tables 3 - 7).

There is no consensus as to what constitutes a "meaningful" change in health status. Interpretation of a 2-point change on a health scale would also likely vary between clinicians. What is "meaningful" pertains strictly to the patient, is detectable by them or content referenced, norm referenced or criterion referenced[91]. After all, not all changes that are "statistically significant" are relevant clinically, and not all clinically relevant issues are statistically significant.

The use of effect sizes allows a benchmark for interpretation of health status changes. Effect sizes have been used in social and behavioral sciences[92], and increasingly in clinical medicine[93]. An effect size is a standardized measure of change in a group or a difference in changes between two groups, by taking the mean difference and dividing it by the standard deviation of that variable. The SD at baseline is used in the calculation, to allow a comparison of the magnitude or size of change, as opposed to statistical significance. As units of measurement are removed with ES, direct comparisons of magnitude between traditional clinical tools (blood work) and health status measures[85] is possible. The calculated effect size of a new intervention can be compared to an effect size of a well-proven therapy, perhaps previously published in the literature, without having been utilized simultaneously in the same study.

In this study, albumin had the greatest effect size, followed by the EQ-5D and then the GH (General Health perception) subcomponent of the SF-36. It is interesting that its dominance was not reflected in the SRM or RE. The large effect size may be an artifact from the use of albumin infusions post-operatively to assist in fluid management. Therefore, the EQ-5D VAS had the highest SRM and relative efficiency in assessing HRQL change. It surpassed all subcomponents of the SF-36 including the mental and physical summary scores, and the GHQ. It also had the most consistently strong correlations across the board for the subcomponents of the SF-36.

## 4.2 Limitations and Challenges to This Study

There were challenges in performing this study. Liver failure patients are often quite unwell, and keeping regularly scheduled appointments is sometimes difficult with clinical deterioration. It was not uncommon for patients to either miss appointments entirely or arrive a few weeks before or after their scheduled appointment. This made it difficult to establish a common reference time point for follow-ups (i.e. 1, 6 months).

Within Quebec, there exist 2 liver transplantation programs: the MUHC (McGill University Health Centre) and the CHUM (Centre Hospitalier de l'Université de Montréal). Patient preference for referral to a particular program may result in selection bias, as patients who are predominantly non-Francophone will more likely be transplanted at the MUHC, and the spectrum of liver disease may be different (i.e. Hepatitis B infection in Chinese patients, who tend to be Anglophone). Other potential sources of selection bias include exclusion of patients with fulminant liver failure, who often reflect specific types of liver disease (i.e. drug overdoses, ± mental health issues)

and those with language barriers (i.e. non-English or French speaking). However, hospital referral and language biases should be minimized with our use of bilingual staff and validated English/French translated questionnaires. But for those whose primary language is neither English nor French, responses may be overestimated or underestimated if filled out by a family member. And unfortunately, response rates, reasons for non-response or participation were not recorded in the database. It is unknown if they were too ill, or if cultural issues were present (i.e. Asian patients tend to be "silent" and not voice concerns).

The Child-Pugh Score is a commonly used clinical classification system for liver disease patients with cirrhosis, and utilizes both liver function tests (albumin, INR and bilirubin) as well as clinical indicators of disease (presence of encephalopathy and ascites). Unfortunately, it was only available pre-transplant, and this variable could not assessed for responsiveness. But it may be argued that post-transplant, the use of this classification system is inappropriate, for ascites may be iatrogenic from post-operative edema, and not reflect liver dysfunction in patients have a new, non-cirrhotic liver.

It was discovered during the analysis that the 3 measures were stapled together and administered in a single package always in the same order: SF-36, EQ-5D and GHQ-30. Understandably, patients who are debilitated by liver failure would find difficulty in completing all 3 measures, which can be time-consuming. This had a negative impact on response rates for the latter surveys and is another source of selection bias. For future studies, by providing the surveys in random order at adhered-to time points in the future would remove this systematic error, and subsequent bias.

Use of English-only versions of the GHQ-30 was another source of selection bias. Our study coordinator was unable to obtain a copy of the French translation for use, and this may have potentially affected the response from Francophone patients, although 86.4% of respondents listed English as their primary language of communication. A memorandum from our study nurse was provided on each GHQ survey, offering translation support if needed, but it is possible this language barrier affected the response rates.

Finally, this analysis had problems with small sample size. Out of 219 patients who responded, only 44 (20%) had pre- and post-transplant QOL HRQL measures. However, while it is true that small sample sizes affect the precision and confidence of study estimates, this was offset by the use of the REff index, which uses a ratio of t-tests. As t-statistics include a sample-size factor, missing data is accounted for, and the instrument with the highest REff should give the best trade-off between sample size and statistical power to detect HRQL change.

## 4.3 Conclusions

As a measurement tool, the EQ-5D is a well-validated measure in several different patient populations, and is easy and quick to administer. The "thermometer" appearance of the VAS was easily understood by patients to gauge their HRQL. In this study, the EQ-5D VAS was found to be superior to the other measurement tools for SRM and relative efficiency, and its addition to a patient's routine follow-up in liver transplant clinic may give a more complete view of patient perceptions of health.

HRQL measurement is complementary to traditional clinical assessments, and may give a more global view of a patient's health status. The results of this study suggest that HRQL measurement tools compare favorably to traditional "liver function tests", and are responsive and efficient in evaluating patient health status. The addition of the EQ-5D to a patient's routine follow-up in liver transplant clinics can provide valuable insight into patient perceptions of health.

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# CHAPTER VI: APPENDICES

## 6.1: Child-Pugh Score

| Variable | Points Scored: | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| Bilirubin (μmol/L) | <36 | 36-54 | >54 |
| Albumin (g/L) | >35 | 28-35 | <28 |
| PT (sec) [INR equivalent] | 1-3 [<1.65] | 4-6 [1.65-2.3] | >6 [>2.3] |
| Ascites | nil | slight - moderate | large - tense |
| Hepatic Encephalopathy | nil | stages 1-2 | stages 3-4 |

| Total Score: | 5-6 | 7-9 | 10-15 |
|---|---|---|---|
| Child's Cirrhosis Grade: | A | B | C |

PT = Prothrombin time prolongation, INR = International Normalized Ratio

## 6.2 Study Consent Form: English

Quality of Life Questionnaire

# QUALITY OF LIFE IN

# LIVER TRANSPLANTATION RECIPIENTS

## PATIENT CONSENT FORM

You are invited to voluntarily answer Quality-of-Life questionnaires, because you are a candidate for, or a recipient of, a liver transplantation.

The results of liver transplantation nowadays, in terms of survival, are very good. Eighty-five to ninety percent of our patients live one year or more following liver transplantation. We are thus now turning our attention to the issue of the quality of life of our patients before and after liver transplantation.

In order to monitor your quality of life, we will ask you to answer 4 questionnaires that have been standardized and validated internationally. The names of these questionnaires are:

1) The Short-Form 36
2) EuroQol
3) The Basic Northern Sleep Questionnaire
4) The General Health Questionnaire-30.

We are asking you to answer these questionnaires once before the liver transplantation, every month during the first six months after the liver transplantation, then every 3 months during the rest of the first year, and yearly afterward.

Answering all these questionnaires by yourself will require 30 or 40 minutes of your time.

Although you may not directly benefit from answering these questionnaires, your participation can contribute to our further understanding of the evolution of the quality of life recipients of a liver transplantation, which, hopefully in the future, will allow us to develop ways to improve it.

If the results of the Quality of Life measures are to be reported in Medical Journals or at meetings, the identity of the participants will be withheld.

## Quality of Life Questionnaire

### Patient Statement

I have had ample time to read and consider all the information in the consent form. I voluntarily consent to fill out the questionnaires and I understand that refusal to fill-out the questionnaires will involve no penalty or lost of benefits. I also understand that if I decide not to fill out the questionnaires in the future, I can do so at any time without penalty and without prejudice to future or alternative medical treatment at this institution.

Any questions regarding these questionnaires may be addressed any time to Ms. Myriam Fernandez at 842-1231 Ext. 6881 or through locating Ext. 6111, to Dr. M. Deschênes at 843-1616, or Dr. J. Barkun at 843-1231 Ext. 5964.

Should you have any questions about your rights you can please call the patient representative at 842-1231 Ext. 5655.

| | |
|---|---|
| Patient's Name (printed) | Date |
| Patient's Signature | Date |

## 6.2 Study Consent Form: French

### FORMULE DE CONSENTEMENT

**Nom de l'étude:**
**ÉTUDE DE LA QUALITÉ DE VIE POUR LES PATIENTS EN TRANSPLANTATION DU FOIE.**

Vous êtes invités à répondre volontairement à un questionnaire sur la qualité de vie, puisque vous êtes un patient qui recevra ou qui a déjà reçu une transplantation de foie. Les résultats d'une transplantation de foie, de nos jours, en terme de survie sont très bons. De 85 % à 90 % des patients vivent plus d'un an et encore plus.

Nous en sommes maintenant, a nous retourner vers la qualité de vie nos patients avant et après la transplantation.

Afin de bien évaluer la qualité de votre vie, nous vous demanderons de répondre à 4 questionnaires qui ont été standardisés et validés internationalement. Les noms de ces questionnaires sont:

1) Etat de santé SF-36
2) EuroQol (EQ-5D)
3) Questionnaire sur le sommeil
4) Questionnaire général de la santé (GHQ)

On vous demande de les remplir une fois avant la transplantation, à tous les mois durant six mois , tous les trois mois pour la première année et à chaque année ensuite.

Pour répondre à toutes les questions cela vous demandera environ de 30 à 40 minutes de votre temps.

Toutefois vous ne bénificierez peut-être pas directement des résultats mais votre participation peut contribuer grandement à la compréhension et l'évolution de la qualité de vie des patients ayant reçu une transplantation de foie. Ce qui dans le futur nous permettra de l'améliorer.

Les données obtenues dans cette étude pourraient être publiées dans des articles médicaux ou des réunions, mais l'information concernant votre participation restera confidentielle. Tout document vous identifiant ne pourra être utilisé sans une permission spéciale de votre part et de celle de votre médecin, tel que stipulé par la loi.

## 10. DÉCLARATION DU PATIENT ET SIGNATURE

J'ai lu les renseignements ci-dessus et je comprends le but de l'étude. On a répondu à toutes mes questions.

La participation à cette étude est entièrement volontaire. Vous pouvez refuser d'y participer ou pouvez vous en retirer en tout temps sans pénalité ni perte des avantages auxquels vous auriez droit.

Si vous avez des questions au sujet du questionnaire vous pouvez rejoindre Myriam Fernandez au 842-1231 ext:6111, Dr. Marc Deschênes au 843-1616 ou Dr. Jeffrey Barkun au 842-1231 ext:5964.

Si vous avez des questions concernant vos droits en tant que participant à cette étude clinique, vous pouvez aussi communiquer avec un tierce parti impartial; le Représentant des patients, au 842-1231, poste 5655.

_____Date:_____

Signature

_____

Nom en lettres moulées

# SF-36 HEALTH STATUS SURVEY / CANADA

## Questionnaire (APPENDIX 6.3)

Name: _____ Date: _____

Hospital: _____

**INSTRUCTIONS:** This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent . . . . . 1

Very good . . . . . 2

Good . . . . . 3

Fair . . . . . 4

Poor . . . . . 5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago . . . . . 1

Somewhat better now than one year ago . . . . . 2

About the same as one year ago . . . . . 3

Somewhat worse now than one year ago . . . . . 4

Much worse now than one year ago . . . . . 5

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

| ACTIVITIES | Yes, Limited A Lot | Yes, Limited A Little | No, Not Limited At All |
|---|---|---|---|
| a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports | 1 | 2 | 3 |
| b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf | 1 | 2 | 3 |
| c. Lifting or carrying groceries | 1 | 2 | 3 |
| d. Climbing **several** flights of stairs | 1 | 2 | 3 |
| e. Climbing **one** flight of stairs | 1 | 2 | 3 |
| f. Bending, kneeling, or stooping | 1 | 2 | 3 |
| g. Walking **more than a kilometre** | 1 | 2 | 3 |
| h. Walking **several blocks** | 1 | 2 | 3 |
| i. Walking **one block** | 1 | 2 | 3 |
| j. Bathing or dressing yourself | 1 | 2 | 3 |

4. During the past 4 weeks have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

| | YES | NO |
|---|---|---|
| a. Cut down the **amount of time** you spent on work or other activities | 1 | 2 |
| b. **Accomplished less** than you would like | 1 | 2 |
| c. Were limited in the **kind** of work or other activities | 1 | 2 |
| d. Had **difficulty** performing the work or other activities (for example, it took extra effort) | 1 | 2 |

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

| | YES | NO |
|---|---|---|
| a. Cut down the **amount of time** you spent on work or other activities | 1 | 2 |
| b. **Accomplished less** than you would like | 1 | 2 |
| c. Didn't do work or other activities as **carefully** as usual | 1 | 2 |

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one)

Not at all . . . . . 1

Slightly . . . . . 2

Moderately . . . . . 3

Quite a bit . . . . . 4

Extremely . . . . . 5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None . . . . . 1

Very mild . . . . . 2

Mild . . . . . 3

Moderate . . . . . 4

Severe . . . . . 5

Very severe . . . . . 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

| | |
|---|---|
| Not at all | 1 |
| A little bit | 2 |
| Moderately | 3 |
| Quite a bit | 4 |
| Extremely | 5 |

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks

(circle one number on each line)

| | **All of the Time** | **Most of the Time** | **A Good Bit of the Time** | **Some of the Time** | **A Little of the Time** | **None of the Time** |
|---|---|---|---|---|---|---|
| a. Did you feel full of pep? | 1 | 2 | 3 | 4 | 5 | 6 |
| b. Have you been a very nervous person? | 1 | 2 | 3 | 4 | 5 | 6 |
| c. Have you felt so down in the dumps that nothing could cheer you up? | 1 | 2 | 3 | 4 | 5 | 6 |
| d. Have you felt calm and peaceful? | 1 | 2 | 3 | 4 | 5 | 6 |
| e. Did you have a lot of energy? | 1 | 2 | 3 | 4 | 5 | 6 |
| f. Have you felt downhearted and blue? | 1 | 2 | 3 | 4 | 5 | 6 |
| g. Did you feel worn out? | 1 | 2 | 3 | 4 | 5 | 6 |
| h. Have you been a happy person? | 1 | 2 | 3 | 4 | 5 | 6 |
| i. Did you feel tired? | 1 | 2 | 3 | 4 | 5 | 6 |

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

All of the time . . . . . 1

Most of the time . . . . . 2

Some of the time . . . . . 3

A little of the time . . . . . 4

None of the time . . . . . 5

11. How **TRUE** or **FALSE** is each of the following statements for you?

(circle one number on each line)

| | **Definitely True** | **Mostly True** | **Don't Know** | **Mostly False** | **Definitely False** |
|---|---|---|---|---|---|
| a. I seem to get sick a little easier than other people | 1 | 2 | 3 | 4 | 5 |
| b. I am as healthy as anybody I know | 1 | 2 | 3 | 4 | 5 |
| c. I expect my health to get worse | 1 | 2 | 3 | 4 | 5 |
| d. My health is excellent | 1 | 2 | 3 | 4 | 5 |

# QUESTIONNAIRE SUR L'ÉTAT DE SANTÉ SF-36

**(APPENDIX 6.3)**

Nom: _____ Date: _____

Hôpital: _____

**DIRECTIVES:** Les questions qui suivent portent sur votre santé, telle que vous la percevez. Vos réponses permettront de suivre l'évolution de votre état de santé et de savoir dans quelle mesure vous pouvez accomplir vos activités courantes.

Répondez à toutes les questions en suivant les indications qui vous sont données. En cas de doute, répondez de votre mieux.

1. En général, diriez-vous que votre santé est:

(encerclez une seule réponse)

| | |
|---|---|
| Excellente | 1 |
| Très bonne | 2 |
| Bonne | 3 |
| Passable | 4 |
| Mauvaise | 5 |

2. Par comparaison à l'an dernier, comment évaluez-vous, maintenant, votre santé générale?

(encerclez une seule réponse)

| | |
|---|---|
| Bien meilleure maintenant que l'an dernier | 1 |
| Un peu meilleure maintenant que l'an dernier | 2 |
| À peu près la même que l'an dernier | 3 |
| Un peu moins bonne maintenant que l'an dernier | 4 |
| Bien moins bonne maintenant que l'an dernier | 5 |

3. Les questions suivantes portent sur les activités que vous pourriez avoir à faire au cours d'une journée normale. Votre état de santé actuel vous limite-t-il dans ces activités? Si oui, dans quelle mesure?

(encerclez un seul chiffre par ligne

| ACTIVITÉS | Mon état de santé me limite beaucoup | Mon état de santé me limite un peu | Mon état de santé ne me limite pas du tout |
|---|---|---|---|
| a. Dans les activités exigeant un effort physique important comme courir, soulever des objets lourds, pratiquer des sports violents | 1 | 2 | 3 |
| b. Dans les activités modérées comme déplacer une table, passer l'aspirateur, jouer aux quilles ou au golf | 1 | 2 | 3 |
| c. Pour soulever ou transporter des sacs d'épicerie | 1 | 2 | 3 |
| d. Pour monter plusieurs étages à pied | 1 | 2 | 3 |
| e. Pour monter un seul étage à pied | 1 | 2 | 3 |
| f. Pour me pencher, me mettre à genoux ou m'accroupir | 1 | 2 | 3 |
| g. Pour faire plus d'un kilomètre à pied | 1 | 2 | 3 |
| h. Pour faire plusieurs coins de rue à pied | 1 | 2 | 3 |
| i. Pour marcher d'un coin de rue à l'autre | 1 | 2 | 3 |
| j. Pour prendre un bain ou m'habiller | 1 | 2 | 3 |

4. Au cours des quatre dernières semaines, avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de votre état de santé physique?

(encerclez un seul chiffre par ligne)

| | OUI | NON |
|---|---|---|
| a. Avez-vous dû consacrer **moins de temps** à votre travail ou à d'autres activités? | 1 | 2 |
| b. **Avez-vous accompli moins** de choses que vous l'auriez voulu? | 1 | 2 |
| c. Avez-vous été limité(e) dans la **nature** de vos tâches ou de vos autres activités? | 1 | 2 |
| d. Avez-vous eu **du mal** à accomplir votre travail ou vos autres activités (par exemple vous a-t-il fallu fournir un effort supplémentaire)? | 1 | 2 |

5. Au cours des quatre dernières semaines, avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de l'état de votre moral (comme le fait de vous sentir déprimé(e) ou anxieux(se))?

(encerclez un seul chiffre par ligne)

| | OUI | NON |
|---|---|---|
| a. Avez-vous dû consacrer **moins de temps** à votre travail ou à d'autres activités? | 1 | 2 |
| b. Avez-vous **acccompli moins** de choses que vous l'auriez voulu? | 1 | 2 |
| c. Avez-vous fait votre travail ou vos autres activités avec moins de soin qu'à l'habitude? | 1 | 2 |

6. Au cours des quatre dernières semains, dans quelle mesure votre état physiques ou moral a-t-il nui à vos activités sociales habituelles (famille, amis, voisins ou autres groupes)?

(encerclez une seule réponse)

Pas du tout . . . . . 1

Un peu . . . . . 2

Moyennement . . . . . 3

Beaucoup . . . . . 4

Enormément . . . . . 5

7. Au cours des quatre dernières semaines, avez-vous éprouvé des douleurs physique?

(encerclez une seule réponse)

Aucune douleur . . . . . 1

Douleurs très légères . . . . . 2

Douleurs légères . . . . . 3

Douleurs moyennes . . . . . 4

Douleurs intenses . . . . . 5

Douleurs très intenses . . . . . 6

8. Au cours des quatre dernières semaines, dans quelle mesure la douleur a-t-elle nui à vos activités habituelles (au travail comme à la maison)?

(encerclez une seule réponse)

Pas du tout . . . . . 1

Un peu . . . . . 2

Moyennement . . . . . 3

Beaucoup . . . . . 4

Enormément . . . . . 5

9. Ces questions portent sur les quatre dernières semaines. Pour chacune des questions suivantes, donné la réponse qui s'approche le plus de la façon dont vous vous êtes senti(e). Au cours des quatre dernières semaines, combien de fois:

(encerclez un seul chiffre par ligne)

| | **Tout le temps** | **La plupart du temps** | **Souvent** | **Quel-que-fois** | **Rare-ment** | **Jamais** |
|---|---|---|---|---|---|---|
| a. Vous êtes-vous senti(e) plein(e) d'entrain (de pep)? | 1 | 2 | 3 | 4 | 5 | 6 |
| b. Avez-vous été très nerveux(se)? | 1 | 2 | 3 | 4 | 5 | 6 |
| c. Vous êtes-vous senti(e) si déprimé(e) que rien ne pouvait vous remonter le moral? | 1 | 2 | 3 | 4 | 5 | 6 |
| d. Vous êtes-vous senti(e) calme et serein(e)? | 1 | 2 | 3 | 4 | 5 | 6 |
| e. Avez-vous eu beaucoup d'énergie? | 1 | 2 | 3 | 4 | 5 | 6 |
| f. Vous êtes-vous senti(e) triste et abattu(e)? | 1 | 2 | 3 | 4 | 5 | 6 |
| g. Vous êtes-vous senti(e) épuisé(e) et vidé(e)? | 1 | 2 | 3 | 4 | 5 | 6 |
| h. Vous êtes-vous senti(e) heureux(se)? | 1 | 2 | 3 | 4 | 5 | 6 |
| i. Vous êtes-vous, senti(e) fatigué(e)? | 1 | 2 | 3 | 4 | 5 | 6 |

10. Au cours des quatre dernières semaines, combien de fois votre état physique ou moral a-t-il nui à vos activité sociales (comme visiter des amis, des parents, etc.)?

(encerclez une seule reponse)

Tout le temps . . . . . 1

La plupart du temps . . . . . 2

Parfois . . . . . 3

Rarement . . . . . 4

Jamais . . . . . 5

11. Dans quelle mesure chacun des énoncés suivants est-il VRAI ou FAUX dans votre cas?

(encerclez un seul chiffre par ligne)

| | **Tout à fait vrai** | **Plutôt vrai** | **Ne sais pas** | **Plutôt faux** | **Tout à fait faux** |
|---|---|---|---|---|---|
| a. Il me semble que je tombe malade un peu plus facilement que les autres | 1 | 2 | 3 | 4 | 5 |
| b. Je suis aussi en santé que les gens que je connais | 1 | 2 | 3 | 4 | 5 |
| c. Je m'attends à ce que ma santé se détériore | 1 | 2 | 3 | 4 | 5 |
| d. Ma santé est excellente | 1 | 2 | 3 | 4 | 5 |

# EURO-QOL (EQ) - 5D (APPENDIX 6.4)

## Questionnaire

Name: _____ Date: _____

Hospital: _____

Please indicate which statement best describes your own health state today. Do not tick more than one box in each group.

**Mobility**

I have no problems in walking about ☐
I have some problems in walking about ☐
I am confined to bed ☐

**Self-Care**

I have no problems with self-care ☐
I have some problems washing or dressing myself ☐
I am unable to wash or dress myself ☐

**Usual Activities** (*e.g. work, study, housework, family or leisure activities*)

I have no problems with performing my usual activities ☐
I have some problems with performing my usual activities ☐
I am unable to perform my usual activities ☐

**Pain / Discomfort**

I have no pain or discomfort ☐
I have moderate pain or discomfort ☐
I have extreme pain or discomfort ☐

**Anxiety / Depression**

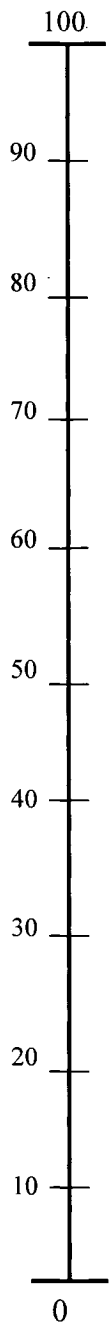
I am not anxious or depressed ☐
I am moderately anxious or depressed ☐
I am extremely anxious or depressed ☐

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your current health state is.

**Your own health state today**

**Best imaginable health state**




**Worst imaginable health state**

Because all replies are anonymous, it will help us to understand your answers better if we have a little background data from everyone, as covered in the following questions.

1. **What is your age in years?**

   _____

2. **Are you:**
   - ☐ Male
   - ☐ female

3. **Are you:**
   - ☐ a current smoker
   - ☐ an ex-smoker
   - ☐ a never smoker

4. **Which of the following categories best describes your usual daily activity?**
   *(choose only one)*
   - ☐ full or part-time paid work
   - ☐ volunteer work
   - ☐ housework or family care
   - ☐ student
   - ☐ retired
   - ☐ on disability or sick leave
   - ☐ unemployed

5. **Have you completed high school?**
   - ☐ yes
   - ☐ no

6. **Do you have a university degree or equivalent professional qualification?**
   - ☐ yes
   - ☐ no

7(a). **Do you suffer from a chronic health condition?**
   - ☐ yes

   If yes, what is the condition?

   _____

   - ☐ no

   **(b) Are you currently under medical care for this condition?**
   - ☐ yes
   - ☐ no

8. **Compared to other persons of your age, how would you rate your health?**
   - ☐ excellent
   - ☐ very good
   - ☐ good
   - ☐ fair
   - ☐ poor

9. **Compared to your health in the past, is your health today:**
   - ☐ better than usual
   - ☐ about the same as usual
   - ☐ worse than usual

   If worse, why? _____

   _____

# EUROQOL (EQ) - 5D (APPENDIX 6.4)

## Questionnaire

Nom: _____ Date: _____

Hôpital: _____

Indiquer, pour chaque catégorie, l'énoncé décrivant l'état présent de votre santé. Cochez une seule case par catégorie.

**Mobilité**
Je n'ai aucune difficulté à marcher ☐
J'ai de la difficulté à marcher ☐
Je suis obligé(e) de rester alité(e) ☐

**Soins autonomes**
Je n'ai aucune difficulté à prendre soin de moi ☐
J'ai des difficulté à me laver et à m'habiller seul(e) ☐
Je suis incapable de me laver et m'habiller seul(e) ☐

**Activités habituelles** (*ex. travail, études, ménage, activités familiales ou loisirs*)
Je n'ai aucune difficulté à faire mes activités habituelles ☐
J'ai des difficulté à faire mes activités habituelles ☐
Je suis incapable à faire mes activités habituelles ☐

**Douleurs / Malaises**
Je ne ressens aucune douleur ou malaise ☐
Je ressens des douleurs ou des malaises légers ☐
Je ressens des douleurs ou des malaises intenses ☐

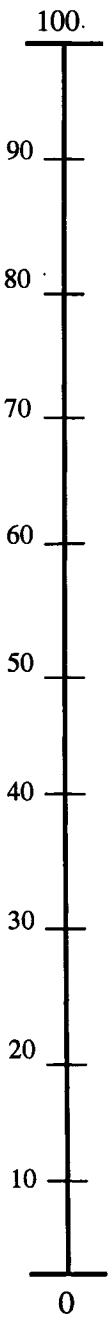
**Inquiétude / Dépression**
Je ne suis pas inquiet(e) ni déprimé(e) ☐
Je suis légèrement inquiet(e) et déprimé(e) ☐
Je suis très inquiet(e) et déprimé(e) ☐

Pour vous aider à exprimer votre état de santé, nous vous dressé une échelle (qui ressemble à un thermomètre) sur laquelle le meilleur état de santé que vous pouvez imaginer correspond à la graduation 100 et le pire état de santé que vous pouvez imaginer correspond à la graduation 0.

Nous aimerions que vous indiquiez sur cette échelle comment vous vous sentez aujourd'hui, a votre avis. Pour cela, nous vousdemandons de bien vouloir tirer une ligne à partir de la case ci-dessous jusqu'à la graduation qui correspond le mieux à votre état de santé actuel

**Votre propre état de santé aujourd'hui**

**Meilleur état de santé imaginable**




**Pire état de santé imaginable**

Comme les réponses sont anonymes, il serait très utile que vous répondiez aux questions qui suivent afin de nous aider à mieux comprendre vos réponses.

1. **Quel est votre âge?**

   _____

2. **Êtes-vous:**
   - ☐ un homme
   - ☐ une femme

3. **Êtes-vous:**
   - ☐ un fumeur
   - ☐ un ancien fumeur
   - ☐ vous n'avez jamais fumé

4. **Laquelle de ces catégories suivantes Décrit le mieux vos activités habituelles?** *(cochez une seule case)*
   - ☐ Travail rémunéré à temps plein ou à temps partiel
   - ☐ bénévolat
   - ☐ entretien de la maison
   - ☐ étudiant(e)
   - ☐ retraité(e)
   - ☐ en accident de travail ou en congé de maladie
   - ☐ sans emploi

5. **Avez vous terminé votre secondaire?**
   - ☐ oui
   - ☐ non

6. **Avez-vous un diplôme universitaire ou une qualification professionnelle équivalente?**
   - ☐ oui
   - ☐ non

7(a). **Souffrez-vous d'un problème de santé chronique?**
   - ☐ oui

   Si oui, quel est-il?

   _____
   - ☐ non

**(b) Êtes-vous présentementsuivi(e) par un médecin pour ce problème?**
   - ☐ oui
   - ☐ non

8. **Si vous comparez votre état de santé avec celui des autres personnes de votre âge, comment le qualifiez-vous?**
   - ☐ excellent
   - ☐ very good
   - ☐ good
   - ☐ fair
   - ☐ poor

9. **Si vous comparez votre état de santé d'aujourd'hui avec le mois dernier, est-il:**
   - ☐ meilleur que d'habitude
   - ☐ à peu près le même
   - ☐ moins bon que d'habitude

   Si moins bon, pourquoi?

   _____

   _____

# GENERAL HEALTH QUESTIONNAIRE


**Please read this carefully:** * DESOLÉ IL N'Y A PAS DE TRADUCTION DE CE QUESTIONNAIRE.

We should like to know if you have had any medical complaints, and how your health has been in general, *over the past few weeks.* Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those you had in the past. It is important that you try to answer ALL the questions.

VOUS N'ÊTES PAS OBLIGÉ D'Y RÉPONDRE SI VOUS NE LE COMPRENEZ PAS.

Thank you very much for your co-operation.

**HAVE YOU RECENTLY:**

| | | | | |
|---|---|---|---|---|
| 1 – **been able to concentrate on whatever you're doing?** | Better than usual | Same as usual | Less than usual | Much less than usual |
| 2 – **lost much sleep over worry?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 3 – **been having restless, disturbed nights?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 4 – **been managing to keep yourself busy and occupied?** | More so than usual | Same as usual | Rather less than usual | Much less than usual |
| 5 – **been getting out of the house as much as usual?** | More so than usual | Same as usual | Less than usual | Much less than usual |
| 6 – **been managing as well as most people would in your shoes?** | Better than most | About the same | Rather less well | Much less well |
| 7 – **felt on the whole you were doing things well?** | Better than usual | About the same | Less well than usual | Much less well |
| 8 – **been satisfied with the way you've carried out your task?** | More satisfied | About same as usual | Less satisfied than usual | Much less satisfied |
| 9 – **been able to feel warmth and affection for those near to you?** | Better than usual | About same as usual | Less well than usual | Much less well |
| 10 – **been finding it easy to get on with other people?** | Better than usual | About same as usual | Less well than usual | Much less well |
| 11 – **spent much time chatting with people?** | More time than usual | About same as usual | Less time than usual | Much less than usual |
| 12 – **felt that you are playing a useful part in things?** | More so than usual | Same as usual | Less useful than usual | Much less useful |
| 13 – **felt capable of making decisions about things?** | More so than usual | Same as usual | Less so than usual | Much less capable |

**PLEASE TURN OVER**

**HAVE YOU RECENTLY:**

| | | | | |
|---|---|---|---|---|
| 14 – **felt constantly under strain?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 15 – **felt you couldn't overcome your difficulties?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 16 – **been finding life a struggle all the time?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 17 – **been able to enjoy your normal day-to-day activities?** | More so than usual | Same as usual | Less so than usual | Much less than usual |
| 18 – **been taking things hard?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 19 – **been getting scared or panicky for no good reason?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 20 – **been able to face up to your problems?** | More so than usual | Same as usual | Less able than usual | Much less able |
| 21 – **found everything getting on top of you?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 22 – **been feeling unhappy and depressed?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 23 – **been losing confidence in yourself?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 24 – **been thinking of yourself as a worthless person?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 25 – **felt that life is entirely hopeless?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 26 – **been feeling hopeful about your own future?** | More so than usual | About same as usual | Less so than usual | Much less hopeful |
| 27 – **been feeling reasonably happy, all things considered?** | More so than usual | About same as usual | Less so than usual | Much less than usual |
| 28 – **been feeling nervous and strung-up all the time?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 29 – **felt that life isn't worth living?** | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 30 – **found at times you couldn't do anything because your nerves were too bad?** | Not at all | No more than usual | Rather more than usual | Much more than usual |

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## 6.6: Normal Reference Ranges for Liver Biochemistries

| | |
|---|---|
| **ALB** | 38-50 g/L |
| **ALT** | 6-45 U/L |
| **ALP** | 25-115 U/L |
| **AST** | 6-35 U/L |
| **INR** | 0.8-1.2 |
| **PT** | 11.2-15.7 s |
| **TB** | 1.7-18.9 umol/L |

# Pearson Correlations (APPENDIX 6.7)

matched data n=44

The CORR Procedure

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 21 With Variables: | PF | RP | BP | GH | VT | SF | RE |
| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | |
| | ALB | TB | ALP | ALT | AST | INR | PT |
| | PTT | | | | | | |
| 21 Variables: | PF | RP | BP | GH | VT | SF | RE |
| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | |
| | ALB | TB | ALP | ALT | AST | INR | PT |
| | PTT | | | | | | |

The CORR Procedure

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

| | PF | RP | BP | GH | VT | SF | RE |
|---|---|---|---|---|---|---|---|
| PF | 1.00000 | 0.54820 | 0.48299 | 0.33598 | 0.46560 | 0.77819 | 0.37395 |
| PF | | 0.0002 | 0.0009 | 0.0296 | 0.0014 | <.0001 | 0.0147 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |
| RP | 0.54820 | 1.00000 | 0.35947 | 0.21707 | 0.24911 | 0.51294 | 0.33528 |
| RP | 0.0002 | | 0.0194 | 0.1785 | 0.1116 | 0.0005 | 0.0321 |
| | 42 | 42 | 42 | 40 | 42 | 42 | 41 |
| BP | 0.48299 | 0.35947 | 1.00000 | 0.29730 | 0.28210 | 0.55246 | 0.24965 |
| BP | 0.0009 | 0.0194 | | 0.0559 | 0.0636 | 0.0001 | 0.1108 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |
| GH | 0.33598 | 0.21707 | 0.29730 | 1.00000 | 0.54043 | 0.30202 | 0.33127 |
| GH | 0.0296 | 0.1785 | 0.0559 | | 0.0002 | 0.0519 | 0.0368 |
| | 42 | 40 | 42 | 42 | 42 | 42 | 40 |
| VT | 0.46560 | 0.24911 | 0.28210 | 0.54043 | 1.00000 | 0.31584 | 0.38308 |
| VT | 0.0014 | 0.1116 | 0.0636 | 0.0002 | | 0.0367 | 0.0123 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |

| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | ALB |
|---|---|---|---|---|---|---|---|
| PF | 0.33240 | 0.80176 | 0.36707 | 0.63516 | -0.25233 | -0.35593 | 0.38741 |
| PF | 0.0275 | <.0001 | 0.0142 | <.0001 | 0.2454 | 0.0955 | 0.1382 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |

# Pearson Correlations (APPENDIX 6.7)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| RP | 0.15438 | 0.66118 | 0.19298 | 0.50176 | -0.52812 | -0.57935 | 0.07180 |
| RP | 0.3290 | <.0001 | 0.2208 | 0.0034 | 0.0096 | 0.0038 | 0.7993 |
| | 42 | 42 | 42 | 32 | 23 | 23 | 15 |
| BP | 0.23826 | 0.70442 | 0.19537 | 0.65454 | -0.40762 | -0.33395 | 0.12590 |
| BP | 0.1194 | <.0001 | 0.2037 | <.0001 | 0.0535 | 0.1194 | 0.6422 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |
| GH | 0.39097 | 0.54991 | 0.45905 | 0.07478 | -0.27180 | -0.43060 | -0.50503 |
| GH | 0.0105 | 0.0002 | 0.0022 | 0.6945 | 0.2333 | 0.0513 | 0.0655 |
| | 42 | 42 | 42 | 30 | 21 | 21 | 14 |
| VT | 0.52022 | 0.38187 | 0.61841 | 0.21422 | -0.34225 | -0.50071 | -0.17167 |
| VT | 0.0003 | 0.0105 | <.0001 | 0.2391 | 0.1099 | 0.0150 | 0.5250 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |

# Pearson Correlations (APPENDIX 6.7)

| | TB | ALP | ALT | AST | INR | PT | PTT |
|---|---|---|---|---|---|---|---|
| PF | -0.35781 | -0.33100 | -0.27319 | -0.18456 | 0.02428 | -0.06081 | 0.08650 |
| PF | 0.1449 | 0.1944 | 0.2578 | 0.4782 | 0.9238 | 0.8295 | 0.7329 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| RP | -0.15060 | -0.33411 | -0.33852 | -0.25363 | 0.13900 | 0.12337 | -0.13016 |
| RP | 0.5640 | 0.1900 | 0.1694 | 0.3432 | 0.5947 | 0.6614 | 0.6067 |
| | 17 | 17 | 18 | 16 | 17 | 15 | 18 |
| BP | -0.03266 | -0.12938 | -0.14174 | 0.10435 | 0.43136 | 0.43102 | 0.13321 |
| BP | 0.8976 | 0.6207 | 0.5627 | 0.6902 | 0.0739 | 0.1087 | 0.5982 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| GH | -0.15289 | -0.16220 | -0.14054 | -0.28100 | -0.09963 | -0.39676 | -0.28394 |
| GH | 0.5719 | 0.5636 | 0.5906 | 0.3103 | 0.7135 | 0.1795 | 0.2865 |
| | 16 | 15 | 17 | 15 | 16 | 13 | 16 |
| VT | -0.00395 | 0.22109 | -0.02239 | -0.21562 | -0.48216 | -0.70871 | -0.44308 |
| VT | 0.9876 | 0.3938 | 0.9275 | 0.4059 | 0.0427 | 0.0031 | 0.0655 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |

| | PF | RP | BP | GH | VT | SF | RE |
|---|---|---|---|---|---|---|---|
| SF | 0.77819 | 0.51294 | 0.55246 | 0.30202 | 0.31584 | 1.00000 | 0.30458 |
| SF | <.0001 | 0.0005 | 0.0001 | 0.0519 | 0.0367 | | 0.0499 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |
| RE | 0.37395 | 0.33528 | 0.24965 | 0.33127 | 0.38308 | 0.30458 | 1.00000 |
| RE | 0.0147 | 0.0321 | 0.1108 | 0.0368 | 0.0123 | 0.0499 | |
| | 42 | 41 | 42 | 40 | 42 | 42 | 42 |
| MH | 0.33240 | 0.15438 | 0.23826 | 0.39097 | 0.52022 | 0.29995 | 0.54325 |
| MH | 0.0275 | 0.3290 | 0.1194 | 0.0105 | 0.0003 | 0.0479 | 0.0002 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |
| PCS | 0.80176 | 0.66118 | 0.70442 | 0.54991 | 0.38187 | 0.69243 | 0.12685 |
| PCS | <.0001 | <.0001 | <.0001 | 0.0002 | 0.0105 | <.0001 | 0.4234 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |
| MCS | 0.36707 | 0.19298 | 0.19537 | 0.45905 | 0.61841 | 0.41646 | 0.81395 |
| MCS | 0.0142 | 0.2208 | 0.2037 | 0.0022 | <.0001 | 0.0049 | <.0001 |
| | 44 | 42 | 44 | 42 | 44 | 44 | 42 |

| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | ALB |
|---|---|---|---|---|---|---|---|
| SF | 0.29995 | 0.69243 | 0.41646 | 0.73319 | -0.52244 | -0.36298 | 0.29728 |

# Pearson Correlations (APPENDIX 6.7)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| SF | 0.0479 | <.0001 | 0.0049 | <.0001 | 0.0105 | 0.0887 | 0.2635 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |
| RE | 0.54325 | 0.12685 | 0.81395 | 0.36001 | -0.52637 | -0.67193 | 0.01765 |
| RE | 0.0002 | 0.4234 | <.0001 | 0.0467 | 0.0119 | 0.0006 | 0.9483 |
| | 42 | 42 | 42 | 31 | 22 | 22 | 16 |
| MH | 1.00000 | 0.06581 | 0.85130 | 0.38717 | -0.22286 | -0.32853 | 0.19182 |
| MH | | 0.6712 | <.0001 | 0.0286 | 0.3067 | 0.1259 | 0.4767 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |
| PCS | 0.06581 | 1.00000 | 0.06383 | 0.50973 | -0.29453 | -0.35488 | 0.04853 |
| PCS | 0.6712 | | 0.6806 | 0.0029 | 0.1725 | 0.0966 | 0.8583 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |
| MCS | 0.85130 | 0.06383 | 1.00000 | 0.42113 | -0.45709 | -0.52589 | 0.06810 |
| MCS | <.0001 | 0.6806 | | 0.0164 | 0.0283 | 0.0100 | 0.8021 |
| | 44 | 44 | 44 | 32 | 23 | 23 | 16 |

| | TB | ALP | ALT | AST | INR | PT | PTT |
|---|---|---|---|---|---|---|---|
| SF | 0.07861 | -0.32524 | -0.28169 | -0.02932 | 0.36538 | 0.34478 | 0.38615 |
| SF | 0.7565 | 0.2027 | 0.2427 | 0.9110 | 0.1360 | 0.2082 | 0.1135 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| RE | 0.18899 | -0.31555 | -0.45417 | -0.19532 | -0.07669 | -0.33725 | -0.12573 |
| RE | 0.4526 | 0.2173 | 0.0508 | 0.4525 | 0.7623 | 0.2190 | 0.6191 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| MH | 0.24003 | 0.21467 | -0.13054 | 0.05014 | -0.60854 | -0.32685 | -0.40577 |
| MH | 0.3374 | 0.4080 | 0.5943 | 0.8484 | 0.0074 | 0.2344 | 0.0948 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| PCS | -0.49061 | -0.39326 | -0.21314 | -0.21628 | 0.31243 | 0.17064 | 0.02003 |
| PCS | 0.0387 | 0.1184 | 0.3810 | 0.4044 | 0.2069 | 0.5432 | 0.9371 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |
| MCS | 0.39276 | 0.00820 | -0.27824 | -0.04535 | -0.38512 | -0.37174 | -0.21919 |
| MCS | 0.1069 | 0.9751 | 0.2487 | 0.8628 | 0.1145 | 0.1725 | 0.3822 |
| | 18 | 17 | 19 | 17 | 18 | 15 | 18 |

| | PF | RP | BP | GH | VT | SF | RE |
|---|---|---|---|---|---|---|---|
| EQ_5D | 0.63516 | 0.50176 | 0.65454 | 0.07478 | 0.21422 | 0.73319 | 0.36001 |
| EQ_5D | <.0001 | 0.0034 | <.0001 | 0.6945 | 0.2391 | <.0001 | 0.0467 |
| | 32 | 32 | 32 | 30 | 32 | 32 | 31 |

# Pearson Correlations (APPENDIX 6.7)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| GHQ1 | -0.25233 | -0.52812 | -0.40762 | -0.27180 | -0.34225 | -0.52244 | -0.52637 |
| GHQ1 | 0.2454 | 0.0096 | 0.0535 | 0.2333 | 0.1099 | 0.0105 | 0.0119 |
| | 23 | 23 | 23 | 21 | 23 | 23 | 22 |
| GHQ2 | -0.35593 | -0.57935 | -0.33395 | -0.43060 | -0.50071 | -0.36298 | -0.67193 |
| GHQ2 | 0.0955 | 0.0038 | 0.1194 | 0.0513 | 0.0150 | 0.0887 | 0.0006 |
| | 23 | 23 | 23 | 21 | 23 | 23 | 22 |
| ALB | 0.38741 | 0.07180 | 0.12590 | -0.50503 | -0.17167 | 0.29728 | 0.01765 |
| ALB | 0.1382 | 0.7993 | 0.6422 | 0.0655 | 0.5250 | 0.2635 | 0.9483 |
| | 16 | 15 | 16 | 14 | 16 | 16 | 16 |
| TB | -0.35781 | -0.15060 | -0.03266 | -0.15289 | -0.00395 | 0.07861 | 0.18899 |
| TB | 0.1449 | 0.5640 | 0.8976 | 0.5719 | 0.9876 | 0.7565 | 0.4526 |
| | 18 | 17 | 18 | 16 | 18 | 18 | 18 |

| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | ALB |
|---|---|---|---|---|---|---|---|
| EQ_5D | 0.38717 | 0.50973 | 0.42113 | 1.00000 | -0.66912 | -0.56296 | 0.29112 |
| EQ_5D | 0.0286 | 0.0029 | 0.0164 | | 0.0007 | 0.0064 | 0.3126 |
| | 32 | 32 | 32 | 32 | 22 | 22 | 14 |
| GHQ1 | -0.22286 | -0.29453 | -0.45709 | -0.66912 | 1.00000 | 0.88552 | 0.27214 |
| GHQ1 | 0.3067 | 0.1725 | 0.0283 | 0.0007 | | <.0001 | 0.4469 |
| | 23 | 23 | 23 | 22 | 23 | 23 | 10 |
| GHQ2 | -0.32853 | -0.35488 | -0.52589 | -0.56296 | 0.88552 | 1.00000 | 0.18703 |
| GHQ2 | 0.1259 | 0.0966 | 0.0100 | 0.0064 | <.0001 | | 0.6049 |
| | 23 | 23 | 23 | 22 | 23 | 23 | 10 |
| ALB | 0.19182 | 0.04853 | 0.06810 | 0.29112 | 0.27214 | 0.18703 | 1.00000 |
| ALB | 0.4767 | 0.8583 | 0.8021 | 0.3126 | 0.4469 | 0.6049 | |
| | 16 | 16 | 16 | 14 | 10 | 10 | 16 |
| TB | 0.24003 | -0.49061 | 0.39276 | 0.41053 | -0.16753 | -0.02944 | -0.12853 |
| TB | 0.3374 | 0.0387 | 0.1069 | 0.1285 | 0.6436 | 0.9357 | 0.6352 |
| | 18 | 18 | 18 | 15 | 10 | 10 | 16 |

# Pearson Correlations (APPENDIX 6.7)

| | TB | ALP | ALT | AST | INR | PT | PTT |
|---|---|---|---|---|---|---|---|
| EQ_5D | 0.41053 | 0.04607 | -0.09214 | 0.26117 | 0.10255 | 0.10510 | 0.31005 |
| EQ_5D | 0.1285 | 0.8655 | 0.7343 | 0.3671 | 0.7055 | 0.7093 | 0.2258 |
| | 15 | 16 | 16 | 14 | 16 | 15 | 17 |
| GHQ1 | -0.16753 | 0.06637 | 0.27421 | 0.28763 | -0.15218 | 0.35810 | -0.09037 |
| GHQ1 | 0.6436 | 0.8463 | 0.4145 | 0.4203 | 0.6551 | 0.3440 | 0.7800 |
| | 10 | 11 | 11 | 10 | 11 | 9 | 12 |
| GHQ2 | -0.02944 | 0.13384 | 0.27687 | 0.31510 | 0.06143 | 0.49837 | 0.13398 |
| GHQ2 | 0.9357 | 0.6948 | 0.4098 | 0.3752 | 0.8576 | 0.1721 | 0.6780 |
| | 10 | 11 | 11 | 10 | 11 | 9 | 12 |
| ALB | -0.12853 | 0.15347 | -0.16670 | -0.01555 | -0.30400 | -0.16173 | -0.20032 |
| ALB | 0.6352 | 0.5850 | 0.5372 | 0.9544 | 0.2523 | 0.5807 | 0.4741 |
| | 16 | 15 | 16 | 16 | 16 | 14 | 15 |
| TB | 1.00000 | 0.43718 | 0.27233 | 0.58723 | 0.22509 | 0.36467 | 0.54358 |
| TB | | 0.0904 | 0.2903 | 0.0132 | 0.3851 | 0.1814 | 0.0295 |
| | 18 | 16 | 17 | 17 | 17 | 15 | 16 |

| | PF | RP | BP | GH | VT | SF | RE |
|---|---|---|---|---|---|---|---|
| ALP | -0.33100 | -0.33411 | -0.12938 | -0.16220 | 0.22109 | -0.32524 | -0.31555 |
| ALP | 0.1944 | 0.1900 | 0.6207 | 0.5636 | 0.3938 | 0.2027 | 0.2173 |
| | 17 | 17 | 17 | 15 | 17 | 17 | 17 |
| ALT | -0.27319 | -0.33852 | -0.14174 | -0.14054 | -0.02239 | -0.28169 | -0.45417 |
| ALT | 0.2578 | 0.1694 | 0.5627 | 0.5906 | 0.9275 | 0.2427 | 0.0508 |
| | 19 | 18 | 19 | 17 | 19 | 19 | 19 |
| AST | -0.18456 | -0.25363 | 0.10435 | -0.28100 | -0.21562 | -0.02932 | -0.19532 |
| AST | 0.4782 | 0.3432 | 0.6902 | 0.3103 | 0.4059 | 0.9110 | 0.4525 |
| | 17 | 16 | 17 | 15 | 17 | 17 | 17 |
| INR | 0.02428 | 0.13900 | 0.43136 | -0.09963 | -0.48216 | 0.36538 | -0.07669 |
| INR | 0.9238 | 0.5947 | 0.0739 | 0.7135 | 0.0427 | 0.1360 | 0.7623 |
| | 18 | 17 | 18 | 16 | 18 | 18 | 18 |
| PT | -0.06081 | 0.12337 | 0.43102 | -0.39676 | -0.70871 | 0.34478 | -0.33725 |
| PT | 0.8295 | 0.6614 | 0.1087 | 0.1795 | 0.0031 | 0.2082 | 0.2190 |
| | 15 | 15 | 15 | 13 | 15 | 15 | 15 |

# Pearson Correlations (APPENDIX 6.7)

| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | ALB |
|---|---|---|---|---|---|---|---|
| ALP | 0.21467 | -0.39326 | 0.00820 | 0.04607 | 0.06637 | 0.13384 | 0.15347 |
| ALP | 0.4080 | 0.1184 | 0.9751 | 0.8655 | 0.8463 | 0.6948 | 0.5850 |
| | 17 | 17 | 17 | 16 | 11 | 11 | 15 |
| ALT | -0.13054 | -0.21314 | -0.27824 | -0.09214 | 0.27421 | 0.27687 | -0.16670 |
| ALT | 0.5943 | 0.3810 | 0.2487 | 0.7343 | 0.4145 | 0.4098 | 0.5372 |
| | 19 | 19 | 19 | 16 | 11 | 11 | 16 |
| AST | 0.05014 | -0.21628 | -0.04535 | 0.26117 | 0.28763 | 0.31510 | -0.01555 |
| AST | 0.8484 | 0.4044 | 0.8628 | 0.3671 | 0.4203 | 0.3752 | 0.9544 |
| | 17 | 17 | 17 | 14 | 10 | 10 | 16 |
| INR | -0.60854 | 0.31243 | -0.38512 | 0.10255 | -0.15218 | 0.06143 | -0.30400 |
| INR | 0.0074 | 0.2069 | 0.1145 | 0.7055 | 0.6551 | 0.8576 | 0.2523 |
| | 18 | 18 | 18 | 16 | 11 | 11 | 16 |
| PT | -0.32685 | 0.17064 | -0.37174 | 0.10510 | 0.35810 | 0.49837 | -0.16173 |
| PT | 0.2344 | 0.5432 | 0.1725 | 0.7093 | 0.3440 | 0.1721 | 0.5807 |
| | 15 | 15 | 15 | 15 | 9 | 9 | 14 |

| | TB | ALP | ALT | AST | INR | PT | PTT |
|---|---|---|---|---|---|---|---|
| ALP | 0.43718 | 1.00000 | 0.54832 | 0.48152 | -0.39230 | -0.13304 | -0.01899 |
| ALP | 0.0904 | | 0.0279 | 0.0692 | 0.1329 | 0.6364 | 0.9423 |
| | 16 | 17 | 16 | 15 | 16 | 15 | 17 |
| ALT | 0.27233 | 0.54832 | 1.00000 | 0.81319 | -0.30135 | 0.01615 | 0.13586 |
| ALT | 0.2903 | 0.0279 | | 0.0001 | 0.2243 | 0.9545 | 0.6031 |
| | 17 | 16 | 19 | 16 | 18 | 15 | 17 |
| AST | 0.58723 | 0.48152 | 0.81319 | 1.00000 | -0.06201 | 0.37961 | 0.36503 |
| AST | 0.0132 | 0.0692 | 0.0001 | | 0.8195 | 0.1807 | 0.1809 |
| | 17 | 15 | 16 | 17 | 16 | 14 | 15 |
| INR | 0.22509 | -0.39230 | -0.30135 | -0.06201 | 1.00000 | 0.79197 | 0.62415 |
| INR | 0.3851 | 0.1329 | 0.2243 | 0.8195 | | 0.0004 | 0.0074 |
| | 17 | 16 | 18 | 16 | 18 | 15 | 17 |
| PT | 0.36467 | -0.13304 | 0.01615 | 0.37961 | 0.79197 | 1.00000 | 0.54094 |
| PT | 0.1814 | 0.6364 | 0.9545 | 0.1807 | 0.0004 | | 0.0373 |
| | 15 | 15 | 15 | 14 | 15 | 15 | 15 |

| | PF | RP | BP | GH | VT | SF | RE |
|---|---|---|---|---|---|---|---|

# Pearson Correlations (APPENDIX 6.7)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| PTT | 0.08650 | -0.13016 | 0.13321 | -0.28394 | -0.44308 | 0.38615 | -0.12573 |
| PTT | 0.7329 | 0.6067 | 0.5982 | 0.2865 | 0.0655 | 0.1135 | 0.6191 |
| | 18 | 18 | 18 | 16 | 18 | 18 | 18 |

| | MH | PCS | MCS | EQ_5D | GHQ1 | GHQ2 | ALB |
|---|---|---|---|---|---|---|---|
| PTT | -0.40577 | 0.02003 | -0.21919 | 0.31005 | -0.09037 | 0.13398 | -0.20032 |
| PTT | 0.0948 | 0.9371 | 0.3822 | 0.2258 | 0.7800 | 0.6780 | 0.4741 |
| | 18 | 18 | 18 | 17 | 12 | 12 | 15 |

| | TB | ALP | ALT | AST | INR | PT | PTT |
|---|---|---|---|---|---|---|---|
| PTT | 0.54358 | -0.01899 | 0.13586 | 0.36503 | 0.62415 | 0.54094 | 1.00000 |
| PTT | 0.0295 | 0.9423 | 0.6031 | 0.1809 | 0.0074 | 0.0373 | |
| | 16 | 17 | 17 | 15 | 17 | 15 | 18 |