

EXPLORING FUNCTION IN PEOPLE WITH  
CHRONIC LIVER DISEASE

Christine Susan Elliott

A thesis submitted to the  
Graduate School, Faculty of Medical Sciences, Newcastle University,  
in candidacy for the degree of Doctor of Philosophy,  
April 2012

NEWCASTLE UNIVERSITY LIBRARY

-----  
210 26637 2  
-----

MED THESIS L10270

## CONTENTS

Dedication .....	1
Acknowledgements .....	2
Abstract Exploring Functional Difficulty in People with Chronic Liver Disease .....	3
Associated Peer Reviewed Published Abstracts .....	7
Aims .....	8
Chapter 1 Introduction .....	10
1.1 Chronic liver disease; mortality and morbidity .....	10
1.1.1 The Liver diseases .....	11
1.1.1.1 Alcoholic Liver Disease. ....	12
1.1.1.2 NAFLD.....	12
1.1.1.3 Primary Biliary Cirrhosis (PBC).....	13
1.1.1.4 Primary sclerosing cholangitis (PSC).....	13
1.2 Chronic liver disease; worldwide recommendations and UK national guidelines. ....	13
1.3 Occupational Therapy; definitions and core skills .....	15
1.4 Chronic liver disease and quality of life .....	16
1.5 The current role of occupational therapy in chronic liver disease .....	17
1.6 Occupational therapy in other chronic conditions .....	20
1.7 Treating the disease or treating the person .....	20
1.8 The need for further occupational therapy research in CLD .....	21
Chapter 2 Methods.....	23
2.1 Environment.....	23
2.2 Methodology.....	25
2.3 Study Design.....	28
2.3.1 Phase One (a): Defining whether function is a problem for people with chronic liver disease.....	28
2.3.2 Phase One (b). Determining whether function for people with CLD alters over time.....	29
2.3.3 Phase One (c). Defining whether function is a problem for people following liver transplantation .....	29

2.3.4	Phase Two: The participant perspective .....	29
2.4	The participants.....	30
2.4.1	Non Alcoholic Fatty Liver Disease (NAFLD).....	31
2.4.2	Alcoholic Liver Disease (ALD).....	32
2.4.3	Primary Biliary Cirrhosis (PBC).....	32
2.4.4	Primary Sclerosing Cholangitis (PSC).....	32
2.4.5	Post Liver Transplant (LT).....	33
2.4.6	Comparators – community-dwelling comparator group .....	33
2.5	Recruitment of study Participants.....	33
2.5.1	Recruiting participants for Phase One.....	33
2.5.2	Recruiting of participants for Phase Two.....	35
2.6	Ethics .....	36
2.6.1	Ethical consideration.....	36
2.6.1.1	Independent review .....	36
2.6.1.2	Informed consent.....	36
2.6.1.3	Anonymity and confidentiality.....	37
2.6.1.4	Consensus, dissent and disclosure.....	37
2.6.2	Ethical Approval .....	37
2.6.2.1	Ethical approval for Phase One .....	37
2.6.3	Ethical approval for Phase Two .....	38
2.7	Measuring function and the aims of the study.....	38
2.7.1	Measuring function in CLD: Phase One .....	38
2.7.1.1	The assessment tools used in the patient group ‘questionnaire pack’ ...	39
2.7.2	The liver patient group; measuring their responses .....	44
2.7.3	The patient group’s responses.....	44
2.7.4	The assessment tools used in this study.....	46
2.8	Describing the biochemical and histological results used in this study.....	49
2.8.1	Alanine transaminase (ALT).....	49
2.8.2	Alkaline phosphatase (ALP) .....	50
2.8.3	Albumin (ALB).....	50
2.8.4	Bilirubin .....	50

2.8.5	Cirrhotic and pre cirrhotic .....	50
2.9	Measuring function in people with CLD over time .....	50
2.10	Exploring function in ALD and NAFLD; a qualitative study .....	51
2.11	Data Analysis .....	51
2.11.1	Phase One analysis .....	51
2.11.2	Phase Two analysis .....	52
Chapter 3	Results 1: Defining the Functional Difficulty Experienced by People with Chronic Liver Disease .....	53
3.1	Aims .....	53
3.2	Comparing overall functional difficulty experienced by the CLD and comparator groups; the PHAQ total scores .....	55
3.3	Comparing overall functional difficulty experienced by the CLD and comparator groups; the PHAQ WD total scores .....	56
3.4	Describing and comparing as whole groups, the functional difficulty of participants with CLD and comparator participants using domains of function; the PHAQ Domain scores .....	57
3.5	Describing and comparing the functional difficulty of those participants with CLD and comparator participants experiencing difficulty using domains of function; the PHAQ WD Domain scores .....	61
3.5.1	Percentage of participants experiencing difficulty in each group .....	61
3.5.2	The level of difficulty experienced by participants in each group .....	63
3.6	Exploring the relationship between function and liver disease severity for those with CLD .....	65
3.7	Exploring the relationship between function and the symptoms experienced by those with CLD .....	68
3.8	Determining independent associations of functional difficulty .....	71
3.9	Summary .....	72
Chapter 4	Results 2: Defining Functional Difficulty in CLD; a Comparison of Chronic Liver Diseases .....	73
4.1	Aims .....	74
4.1.1	Describing the liver diseases in terms of gender and age .....	75
4.2	Age .....	76
4.2.1	Chi squared analysis of percentage of experienced functional difficulty .....	79

4.3	Summary.....	79
4.4	Comparing the chronic liver diseases' functional domain scores.....	80
4.4.1	Dressing .....	83
4.4.1.1	Comparing the chronic liver diseases' dressing domain scores: Specifically, using questions 1 and 2 of the PHAQ; to get dressed including ability to fasten buttons and tie shoelaces and the ability to shampoo your own hair. ....	83
4.4.1.2	Proportion of participants experiencing difficulty in the dressing domain .....	84
4.4.2	Arising.....	86
4.4.2.1	Comparing the chronic liver diseases' arising domain scores: Specifically using PHAQ questions 3 and 4; to stand straight from an armless chair and to get in and out of bed.....	86
4.4.2.2	Comparing the proportion of participants experiencing difficulty in the arising domain.....	88
4.4.3	Eating .....	90
4.4.3.1	Comparing the chronic liver diseases' eating domain scores: Specifically using PHAQ questions 5, 6 and 7; to cut food using utensils, lift a full glass to your mouth and open a milk carton.....	90
4.4.3.2	Comparing the proportion of participants experiencing difficulty in the eating domain.....	91
4.4.4	Walking.....	93
4.4.4.1	Comparing the chronic liver diseases' walking domain scores: Specifically using PHAQ questions 8 and 9; to walk to the end of your road on the flat and climb five steps. ....	93
4.4.4.2	Comparing the proportion of participants experiencing difficulty in the walking domain.....	94
4.4.5	Hygiene .....	96
4.4.5.1	Comparing the chronic liver diseases' hygiene domain scores: Specifically, using questions 9, 10 and 11 of the PHAQ; to get in and out the bath, off and on the toilet and to dry your body.....	96
4.4.5.2	Comparing the proportion of participant's functional difficulty in the hygiene domain.....	97
4.4.6	Reach.....	99
4.4.6.1	Comparing the chronic liver diseases' reach domain scores: Specifically, using questions 13 and 14 of the PHAQ; to reach and retrieve a 5lb object from above you head and to bend down to pick clothes from the floor....	99
4.4.6.2	Comparing the proportion of participant's functional difficulty in the reach domain.....	100
4.4.7	Grip .....	102

4.4.7.1	Comparing the chronic liver diseases' grip domain scores: Specifically, using questions 16 and 17 of the PHAQ; to open previously opened jars, turn taps on and off and open car doors.....	102
4.4.7.2	Comparing the proportion of participants functional difficulty in the grip domain .....	103
4.4.8	Activity.....	105
4.4.8.1	Comparing the chronic liver diseases' activity domain scores: Specifically, using questions 18, 19 and 20 of the PHAQ to get in and out of a car, go shopping; do the gardening and the vacuuming.....	105
4.4.8.2	Comparing the proportion of participant's functional difficulty in the activity domain.....	107
4.5	Summary.....	109
4.6	Describing each liver disease group; function, liver disease markers and symptoms .....	111
4.6.1	Alcoholic liver disease .....	111
4.6.2	Non alcoholic fatty liver disease .....	114
4.6.3	Primary biliary cirrhosis.....	118
4.6.4	Primary sclerosing cholangitis .....	121
4.7	Summary.....	124
Chapter 5	Results 3: Does function alter over time? A three year follow up study of functional difficulty in NAFLD and ALD. ....	126
5.1	Aims.....	126
5.2	Comparing the participant's data; 2008 to 2011.....	127
5.3	Describing the PHAQ and PHAQ WD total data scores; comparison over time .....	130
5.3.1	Comparing change in function of NAFLD participants over time .....	131
5.3.2	Comparing change in function of ALD participants over time.....	133
5.4	Summary.....	134
Chapter 6	Results 4: Defining the functional ability of participants following liver transplantation. ....	135
6.1	Aims.....	135
6.2	Describing the demographics and function of post liver transplant and comparator participants .....	136
6.2.1	The PHAQ Totals of LT and Comparator participants.....	138

6.2.2	The PHAQ WD totals of LT and comparator participants .....	138
6.3	Describing and comparing function using the domain data of LT and comparator participants.....	140
6.3.1	Percentage of participants experiencing difficulty in each group.....	143
6.3.2	Comparing the level of difficulty experienced by those participants with difficulty in each domain. ....	144
6.4	Summary.....	145
6.5	Exploring the relationship between function and liver disease severity in liver transplant recipients .....	146
6.6	Exploring the relationship between participants’ function following liver transplant and symptoms associated with liver disease. ....	147
6.7	Determining independent associations of functional difficulty.....	148
6.8	Describing and comparing the function of post liver transplant participants with matched disease groups.....	150
6.9	Summary.....	152
Chapter 7	Results 5: A Qualitative Topical Survey to Explore People with ALD and NAFLD’s Experience of Living with CLD. ....	153
7.1	Aims.....	154
7.2	Discussing the experience of functional difficulty for people with ALD and NAFLD in in the context of the performance areas of Productivity, Self-care and leisure .....	155
7.2.1	Productivity.....	156
7.2.2	Self-care .....	158
7.2.3	Leisure.....	159
7.3	Summary.....	161
7.4	Exploring the issues affecting functional performance .....	161
7.4.1	Alcohol.....	163
7.4.2	The use of alcohol .....	163
7.4.3	Detox .....	164
7.4.4	Respect .....	165
7.4.5	Anxiety.....	167
7.4.6	Liver disease.....	168
7.4.7	Understanding .....	169

7.4.8	Exercise and weight .....	170
7.4.9	Pain and Fatigue.....	171
7.4.10	Sleep.....	172
7.4.11	Memory and Concentration.....	173
7.5	Summary .....	174
Chapter 8	Discussion .....	175
8.1	Predicting mortality in CLD .....	176
8.2	The significant difficulty people with CLD are experiencing with hygiene and arising .....	177
8.3	The significance of liver disease severity and poor function.....	179
8.4	The significance of symptom burden and poor function .....	179
8.5	The significance of age and poor function.....	180
8.6	The significance of day time somnolence and poor function .....	180
8.7	The significance of fatigue and poor function .....	181
8.8	The significance of cognition and poor function.....	182
8.9	The significance of orthostatic symptoms and poor function.....	183
8.10	Functional difficulty and symptom burden in people post liver transplant.	183
8.11	The impact of anxiety on function.....	184
Chapter 9	Conclusion .....	186
9.1	Limitations .....	186
9.1.1	The database.....	186
9.1.2	The participants.....	187
9.1.3	Data collection .....	188
9.1.4	Biochemical parameters .....	189
9.1.5	Analysis.....	189
9.1.6	Questionnaires.....	190
9.2	Future Work.....	190
9.2.1	Developing results from this study .....	190
9.2.2	In other liver diseases.....	190
9.2.3	An In service development.....	190



9.2.4	In Occupational Therapy.....	191
9.2.5	In public awareness .....	191
9.2.6	In liver transplantation .....	192
	References .....	193
Appendix 1	Patient Information Sheet.....	208
Appendix 2	Ethics approval.....	215
Appendix 3	R & D approval .....	218
Appendix 4	Qualitative interview topic guide.....	220
Appendix 5	HAD .....	221
Appendix 6	Cognitive Failure Questionnaire .....	222
Appendix 7	Canadian Occupational Performance Measure .....	224
Appendix 8	PHAQ.....	226
Appendix 9	NAFLD ALT and PHAQ Correlation.....	228

## List of Figures

Figure 1. The Newcastle NIHR Biomedical Research Centre in Ageing detailing the seven themes of research, the research infrastructure and in the centre, the cross cutting themes. ....	24
Figure 2. The hierarchical structure of the multidisciplinary team members of the BRC in Ageing Liver Theme. ....	24
Figure 3 Chronological order of studies within this thesis .....	27
Figure 4. The Newcastle Upon Tyne NHS Foundation Trusts CLD database numbers, percentage of those consenting to further research and percentage of participants who returned the questionnaires for this study as a whole .....	34
Figure 5. The proportion of each liver disease making up the CLD group .....	35
Figure 6. The patient groups response to the PRO functional measurement tools; per cent of patient group's opinion of easiest to complete, most difficult to complete and most relevant to their CLD.....	45
Figure 7. The range and p value statistical comparison of functional difficulty between CLD participants and comparator participants using their PHAQ total scores. ....	55
Figure 8. The range and p value statistical comparison of functional difficulty as measured by their PHAQ WD scores, between CLD participants and comparator participants. ....	57
Figure 9a (CLD) and 8b (comparator) showing the PHAQ domain mean scores in each cohort.....	60
Figure 10. The age spread between the chronic liver disease groups. ....	76
Figure 11. Scatter plots describing the significant difference between the CLD cohorts using their PHAQ totals. ....	78
Figure 12. Scatter plots describing the significant difference between the CLD cohorts using their PHAQ WD totals. ....	78
Figure 13. The significant difference between the liver disease groups in the dressing domain using PHAQ domain median and range scores.....	83
Figure 14. The percentage of participants in each chronic liver disease experiencing difficulty with dressing. ....	84
Figure 15. The significant difference between the liver disease groups in the arising domain using the PHAQ domain median and range scores. ....	86
Figure 16. The significant difference of between the liver disease groups in the arising domain using the PHAQ WD domain median and range scores. ....	87
Figure 17. The percentage of difficulty with arising experienced by the liver disease cohorts. ....	88

Figure 18. The significant difference of the liver disease groups in the eating domain using the PHAQ domain median and range scores.....	90
Figure 19. The percentage of difficulty with eating experienced by the liver disease cohorts.....	91
Figure 20. The significant difference between the liver disease groups in the walking domain using the PHAQ domain median and range scores.....	93
Figure 21. The percentage of difficulty with walking experienced by the liver disease cohorts.....	94
Figure 22. The significant difference of between the liver disease groups in the hygiene domain using the PHAQ domain median and range scores.....	96
Figure 23. The percentage of difficulty with hygiene experienced by the liver disease cohorts.....	97
Figure 24. The significant difference between the liver disease groups in the reach domain using the PHAQ domain median and range scores.....	99
Figure 25. The percentage of difficulty with reach experienced by the liver disease cohorts.....	100
Figure 26. The significant differences between the liver disease groups in the grip domain using the PHAQ domain median and range scores.....	102
Figure 27. The percentage of difficulty with grip experienced by the liver disease cohorts.....	103
Figure 28. The significant difference between the liver disease groups in the activity domain using the PHAQ domain median and range scores.....	105
Figure 29. The significant difference between the liver disease groups in the activity domain using the PHAQ WD domain median and range scores.....	106
Figure 30. The percentage of difficulty with activity experienced by the liver disease cohorts.....	107
Figure 31. The number of participants who returned or did not return the PHAQ in 2011.....	128
Figure 32. Comparing the paired PHAQ and PHAQ WD median and range scores of the combined NAFLD and ALD group over a three year follow up study.....	131
Figure 33. The comparison of returned NAFLD PHAQ totals n=162 (paired) 2008 [10.9 (0-93.75)] and 2011 [13.6 (0-90.63)]. No significant difference found.....	132
Figure 34. The comparison of returned ALD PHAQ totals n=69 (paired) 2008 [28.13 (0-93.6)] to 2011 [32.82 (0-90.60)]. No significant difference was found.....	133
Figure 35. The age spread of LT and comparator participants.....	136
Figure 36. The comparison of LT and comparator participants PHAQ Total median and range scores.....	138

Figure 37. The comparison of LT and comparator participants PHAQ WD Total median and range scores .....	139
Figure 38 a (LT) and 37b (comparator) showing the PHAQ domain mean scores, visually demonstrating the functional difficulty in the two participant groups .....	142
Figure 39. The functional difficulty reported by the NAFLD, ALD and ALD AB participants using the occupational performance areas of productivity, self-care and leisure. ....	155
Figure 40. The issues affecting ability to be productive as described by the NAFLD and ALD and ALD AB participants. ....	162

## List of Tables

Table 1 Describing the Type 1 and Type 2 errors and their potential importance.....	52
Table 2. The age, gender and functional difficulty (PHAQ totals of whole groups and PHAQ WD totals of those within each group experiencing difficulty) of participants from the CLD and comparator groups. ....	54
Table 3. The p value statistical comparison of CLD and comparator domain data in the PHAQ Domains; presented as median and range. ....	59
Table 4. The percentage of participants in each group experiencing difficulty with function; the chi squared results and p value showing the significance of that difference. ....	62
Table 5. The comparison between the PHAQ WD domain scores of participants with CLD and the comparator group, using median and range. ....	63
Table 6. The participants with CLD's PHAQ totals, their age and their LFT results.....	65
Table 7. The significant associations between CLD participants' LFT and PHAQ Total scores.....	66
Table 8. The PHAQ Total scores [median and (range)] and p value statistic of those participants with CLD who are pre cirrhotic or cirrhotic.....	66
Table 9. The participants with CLD's symptoms associated with liver disease scores and age (mean and $\pm$ SD).....	68
Table 10. The significant associations between the participants with CLD's PHAQ total scores and their symptom tool results. ....	70
Table 11. The regression analysis of the significant correlations in CLD participants PHAQ total scores and their histological results, symptom tool scores and their age....	71
Table 12. The number of participants per disease group and the female participant percentage. ....	75
Table 13. The PHAQ and PHAQ WD totals of each chronic liver disease group.....	77
Table 14. The significant difference between those experiencing and those not experiencing difficulty in the chronic liver disease groups .....	79
Table 15. The PHAQ domain scores in each liver disease cohort demonstrated as median (range) .....	81
Table 16. The PHAQ WD domain scores [median and (range)] of participants in each liver disease and the [number of] and percentage of participants in each disease experiencing difficulty. ....	82
Table 17. The percentage, Chi squared value and p value of participants in each group experiencing difficulty and no difficulty with dressing. ....	85
Table 18. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with arising.....	89

Table 19. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with eating.....	92
Table 20. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with walking.....	94
Table 21. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with hygiene.....	98
Table 22. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with reach.....	101
Table 23The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with grip.....	104
Table 24. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with activity. ....	108
Table 25. Ranking the liver disease groups function using the mean value of the PHAQ WD domain scores. ....	109
Table 26. Ranking the liver disease groups proportion of participants experiencing difficulty.....	109
Table 27. The significant associations between the ALD Participants PHAQ totals and their LFT results and symptoms tools scores.....	112
Table 28. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic ALD participants.....	112
Table 29. The regression analysis of the significant correlations in ALD participants between their PHAQ total scores and symptom tool scores. ....	113
Table 30. The significant associations between the NAFLD Participants PHAQ totals and their LFT results and symptoms tools scores.....	115
Table 31. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic NAFLD participants.....	116
Table 32. The regression analysis of the significant correlations in NAFLD participants between their PHAQ total scores and their histological results, symptom tool scores and their age.....	117
Table 33. The significant associations between the PBC Participants' PHAQ totals and their LFT results and symptoms tools scores.....	119
Table 34. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic PBC participants.....	119
Table 35. The regression analysis of the significant correlations in PBC participants between their PHAQ total scores and their symptom tool scores.....	120
Table 36. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic PSC participants.....	121

Table 37. The significant associations between the PSC Participants' PHAQ totals and their LFT results and symptoms tools scores.....	122
Table 38. The regression analysis of the significant correlations in ALD participants between their PHAQ total scores, their FIS symptom tool scores and their age. ....	123
Table 39. The LFT results and symptom tools which correlated with PHAQ totals (✓) and those independently associated with the PHAQ Totals (★) in each disease group. ....	124
Table 40. The PHAQ and PHAQ WD 2008 scores of participants who returned, did not return, or could not return, their PHAQ questionnaires in 2011.....	129
Table 41. The age, gender, PHAQ and PHAQ WD of returning NAFLD and ALD participants. ....	130
Table 42. Comparing the NAFLD PHAQ total results from 2008 and 2011. ....	132
Table 43. Comparing the ALD PHAQ total results from 2008 and 2011. ....	133
Table 44. The demographic data and PHAQ and PHAQ WD results of LT and comparator data. ....	137
Table 45. The p value statistical differences between the PHAQ domain (median and range) scores of the LT and comparator groups.....	141
Table 46. The chi squared significant difference between the proportion of participants from the LT and comparator groups who are, and are not, experiencing difficulty with function. ....	143
Table 47. The PHAQ WD domain scores of LT and comparator participants and the p value of significant difference in functional difficulty. Median and (range.).....	144
Table 48. The biochemical results, time since transplant and immunosuppressant therapy dosage of participants in the LT cohort.....	146
Table 49. The relationships between poor function in LT participants and their symptom assessment tool scores.....	148
Table 50. The regression analysis between LT participants function with age, LFT's, time since transplant and symptoms. ....	149
Table 51. The comparable LFT results and symptom assessment tool scores between the LT participants and their matched CLD participants.....	151

## Dedication

This thesis is dedicated to my beautiful daughters

Maya and Hope.

You amaze me. I adore you. I love you more.

In loving memory of

Agnes W. Telfer. 1920-2009



## Acknowledgements

*“I’m playing all the right notes, but not necessarily in the right order”*

*Eric Morecambe*

My overwhelming thanks go to Professor Julia Newton. This has been an incredible journey made possible purely by your limitless support and encouragement. The understanding you have of your students makes you an amazing and unique supervisor. You have unlocked a potential long thought lost. To you I dedicate ‘The climb’ by Miley Cyrus.

To my wonderful BRC MDT team Lisa Robinson and James Frith, I thank you for a great 4 years together. To you I dedicate Temper Traps’ ‘Sweet Disposition’. For Ruthie I dedicate Lily Allen’s ‘The Fear’.

Dr Jimjams, you get an extra special dedication of Kings of Leon ‘Sex on fire’. Your unbelievable patience and graciously given help has been instrumental in my research success. Thank you.

Linda Jobling you have been heaven sent. The qualitative transcription and the building of the Ultimate Analysis database would have been impossible if not for your relentless help and good cheer. I dedicate to you everything by Keane. Forever.

My great thanks go to the participants in this study who took the time and effort to share their experience of chronic liver disease. A huge thank you to Tilly Hale and the LIVErNORTH patient group, Elsbeth Henderson, and the library staff of Newcastle University Walton Library, and the RVI Peacock Hall library, for their kindness and help. A special thanks to Sue Vecsey and Lin James for their patience, help and advice.

Grannie Annie and Papa John and Acky, I give you my love and offer my thanks for your support.

*“Behind every great man is a great woman and behind every great woman is her mother.”*

*Anon*

# Abstract      Exploring Functional Difficulty in People with Chronic Liver Disease

## Introduction

Chronic liver disease (CLD) is a real and ever growing problem which has significant morbidity and mortality. It is one of the most prevalent diseases in the world and its rate is rising.

CLD remains the only one of the top 5 UK killers to be on the increase; and it is the only one of these diseases to be without official guidelines or good practice documentation in the UK. A dearth of literature is available to inform clinicians of the functional ability and empirical experience of people with CLD, or of those having undergone a liver transplant. This study aims to address this much needed shortfall in the literature.

## Methods

This is a mixed methods study. The quantitative study explores the functional difficulty and symptom burden experienced by people with CLD. Here standardised functional assessment and symptom burden measurement tools were completed by people with CLD (n=468). Specifically those with alcoholic liver disease (n=107), non-alcoholic fatty liver disease (n=224), primary biliary cirrhosis (n=90), Primary sclerosing cholangitis (n=47). The scores were analysed using Prism 0.3 and SPSS version 19. A nested qualitative study (n=12) was used to add narrative depth to the quantitative results giving insight of the empirical issues of CLD. The qualitative study took the form of semi structured interviews' of participants, specifically those with ALD (n=8) and NAFLD (n=4). The interviews used an occupational therapy model [Canadian Occupational Performance Model (COPM)] as their topic guide.

## Results

Functional difficulty is great in people with CLD and significantly more people with CLD are experiencing worse functional difficulty than comparator groups. In particular, people with CLD experience high levels of functional difficulty in the areas of hygiene and arising. This is an incredibly important finding for this patient group and for the profession of Occupational therapy. Here CLD is placed within the context of its impact rather than its physical/medical presentation. Furthermore, functional difficulty does not

associate with liver disease severity but does associate with symptom burden. This again reiterates the importance of assessing the person rather than their condition. In particular, orthostatic and autonomic problems and cognitive difficulty have independent associations with worsening function. These are areas of disease management where occupational therapists are well placed to deliver expert intervention.

Functional difficulty increases over time but not significantly so; although this increase in functional difficulty may have clinical implications. This reinforces the need for an occupational therapy strong CLD service that delivers intervention promoting symptom management and functional independence. People living with ALD and NAFLD are at most risk of functional difficulty and symptom burden and are disengaging with daily activity due to the constellation of functional difficulty, symptom burden, and impact of lifestyle.

Functional difficulty is significant in people having undergone a liver transplant, and the number of those experiencing functional difficulty is significantly greater, than participants in comparator groups. Those having undergone a liver transplant were experiencing functional difficulty to the same degree as those with CLD. Symptom burden is important in the worsening of function for those in the LT cohort, with increased fatigue independently associating with increased functional difficulty. These findings are of great importance as for the first time, the notion of 'cure' for liver disease realises that functional difficulty and symptom burden remain significant for those transplanted. Occupational therapy could lead a major change in the service delivery currently given to those pre and post transplantation to address this shortfall.

## Conclusion

People with CLD, and those following liver transplant, are experiencing significant functional difficulty which to date has not been recognised, and as a consequence, not treated. The increasing number of people with CLD combined with the significant functional difficulty they experience is set to impact heavily on health resources both globally and in the UK. The development of an occupational therapy strong CLD service, which addresses specifically the holistic impact of the functional difficulty and symptom burden experienced by this patient group, is needed urgently to address the rising demand. An occupational therapy strong service is necessary to complement

established liver services. This will address specifically of the under recognised and under treated management of daily activity and symptom burden for people with CLD; areas currently lacking in liver service provision and in which Occupational Therapists are expert .

## Associated Peer Reviewed Publications

Elliott C, Frith J, Pairman J, Jones DEJ, Newton JL (2011). Reduction in functional ability is significant post liver transplantation compared with matched liver disease and community dwelling comparators. *Transplant International*, 24(6): 588-595.

Elliott C, Frith J, Newton J, (2010). Occupational therapy in chronic liver disease: a preliminary study to explore the views of occupational therapists and physicians working in the acute medical setting. *British Journal of Occupational Therapy*, 73(3): 116-120.

Elliott C, Newton J. (2009). Occupational therapy in chronic liver disease: A gap in service delivery. *British Journal of Occupational Therapy*, 72 (3):133-136.

Newton JL, Elliott C, Frith J, Ghazala C, Pairman J, Jones DEJ (2011). Functional capacity is significantly impaired in primary biliary cirrhosis and is related to orthostatic symptoms. *European Journal of Gastroenterology and Hepatology*, 23(7): 566-572.

Frith J, Day C, Robinson L, Elliott C, Jones D, Newton J.(2011) Potential strategies to improve uptake of exercise interventions in non-alcoholic fatty liver disease. *Journal of Hepatology*, 52(1): 112-116.

Costigan A, Elliott C, McDonald C, Newton J, (2010). Orthostatic symptoms predict functional capacity in chronic fatigue syndrome: Implications for management. *QJM*, 103(8): 589-595.

Frith J, Day C, Robinson L, Elliott C, Jones D, Newton J (2010). Potential strategies to improve uptake of exercise interventions in non-alcoholic fatty liver disease. *Journal of Hepatology*, 52(1): 112-116.

Frith J, Kerr S, Elliott C, Robinson L, et al (2010). Primary Biliary Cirrhosis is associated with falls and significant fall related injury. *QJM*, 103:153-161.

Newton J, Elliott C, Frith J, Robinson L, Jungerius D, Jones D, Day C (2008). Appreciation of the benefits of exercise programmes in non-alcoholic fatty liver disease- implications of fatigue and impact upon activities of daily living. *Hepatology*; 48:1136.

## Associated Peer Reviewed Published Abstracts

Elliott C, Frith J, Newton JL, (2011). Functional Impairment is significant in Chronic Liver Disease. *College of Occupational Therapists' Annual Conference*. Brighton.

Elliott C, Newton J, Jones D (2010). Functional difficulty is significant for people with chronic liver disease. *NIHR Experimental Medicine UK summer school* (awarded highly commended prize).

Elliott C, Frith J, Robinson L, Newton J, Jones D (2010). Functional impairment is significant in chronic liver disease. *British Geriatric Society*. Winter Conference. (Nominated for award)

Elliott C, Frith J, Robinson L, Newton J (2009). Patient Reported Activity in Liver Disease and Implications for Service Delivery. *American Association for the Study of Liver Disease*. San Francisco.

Elliott C, Frith J, Robinson L, Newton J (2008). Patient Reported Activity in Liver Disease and Implications for Service Delivery. *Society for Social Medicine*

Frith J, Elliott C, Pairman J, Patanwala I, Jones DE, Newton JL (2010). Liver transplantation is not associated with significant improvement in functional ability or symptoms. *In: 61st Annual Meeting of the American Association for the Study of Liver Diseases*. Boston, MA: *Hepatology: Wiley-Blackwell*.

Newton JL, Elliott C, Frith J, Robinson L, Jungerius D, Jones DE, Day CP (2008). Appreciation of the benefits of exercise programmes in non-alcoholic liver disease: implications of fatigue and impact upon activities of daily living. *In: 59th Annual Meeting of the American Association for the Study of Liver Diseases*. San Francisco, CA, USA: *Hepatology: John Wiley & Sons*.

## Aims

The broad aims of this thesis are to determine the functional difficulty experienced by people with chronic liver disease (CLD); specifically those with alcoholic liver disease (ALD), non alcoholic fatty liver disease (NAFLD), primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC). The study proposes to achieve this aim by:

- Quantifying CLD participants' function using a self reported, functional assessment outcome measure, and comparing scores to those of a community dwelling comparator group.
- Exploring the association between functional ability in the CLD participants' biochemical and histological markers, to determine the impact of liver disease severity on function.
- Examining the relationship between functional ability, and other frequently reported symptoms in CLD, to determine the impact upon function, of those symptoms associated with liver disease e.g. fatigue, day time somnolence, memory and concentration difficulty and orthostatic symptom.

The study also aims to determine if function changes in participants with CLD over time by conducting a three year follow up study of participants' self-reported functional difficulty.

To determine if functional difficulty improves after liver transplantation, functional difficulty will be quantified using the self-reported functional assessment outcome measure tool, in a cohort who has undergone a liver transplant (LT), and the scores compared to:

- The self reported, functional assessment outcome measure tool scores of community dwelling community comparator group.
- The LT participants' biochemical data to determine liver function and its association with functional difficulty in those having undergone transplantation.
- The LT participants' symptom assessment tools scores to determine the impact upon function of those symptoms associated with liver disease e.g. fatigue, day time somnolence, memory and concentration difficulty and orthostatic symptom
- The self reported, functional assessment outcome measure tool scores of people with who have their matched (pre transplant) CLD.

The LT participants will also have their biochemical, and their symptom assessment tool scores, compared to those with matched (pre transplant) CLD participants, to determine relationships therein.

To describe the empirical living experience of people with CLD; specifically NAFLD and ALD, a qualitative topical survey will be carried out using semi structured interviews, during which the participants will be asked to describe their daily activities, and the functional difficulties they experience.



## Chapter 1 Introduction

Chronic Liver Disease (CLD) is an umbrella term used to describe a range of chronic liver conditions including the diseases investigated in this study; non alcoholic fatty liver disease (NAFLD), alcoholic liver disease (ALD), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC).

### 1.1 Chronic liver disease; mortality and morbidity

CLD has significant morbidity and mortality and is considered to be one of the most prevalent chronic diseases in the world (Frith et al, 2008). Although ranking mortality and morbidity is difficult due to influencing factors such as age, sex and location (Griffiths et al, 2005; Elliott and Newton, 2009), CLD remains not only in the top 5 UK killers along with ischaemic heart disease, stroke, respiratory disease and cancer, but is the only one of these diseases to be on the increase (Roderick et al, 2002; Elliott et al, 2009).

Increasingly, CLD is being recognised as a serious public health problem globally, encompassing not only physical and psychological morbidity and mortality, but also incurring significant societal costs. A report by Roderick et al (2002) for the British Liver Trust stated that hospital episode statistics in the UK for 2000/01 showed over 15,000 admissions for alcoholic liver disease accounting for 129,000 bed days and almost 4000 admissions of people with fibrosis and cirrhosis of the liver accounting for 25,000 bed days. The mean length of stay for patients with cirrhosis/fibrosis was 12 days and for those with alcoholic liver disease 14 days. Recent figures show that liver disease could overtake stroke and coronary heart disease in 10 to 20 years (Day, British Liver Trust, 2012).

Alcohol accounts for 80% of deaths from liver disease, with 8,664 alcohol-related deaths recorded in 2009, more than double the 4,023 recorded during 1992; and has been likened to a death toll equivalent to a passenger filled Jumbo jet crashing every 17 days (Day, British Liver Trust, 2012).

There is no evidence to date that the diseases PBC and PSC both chronic cholestatic diseases causing fibrosis and cirrhosis of the liver, are increasing at the same rate, rather any escalation in incidence is thought to be due to longer survival and earlier, and better, diagnosis (James et al, 1999). Importantly improved management of people with

PBC has resulted in a plateau of hospital stays which means that people in this disease population are largely managed in the community via liver clinics rather than requiring admission to hospital. PBC research in particular has been very important contributing substantially to the understanding of the diversity, medical management and symptom burden in chronic liver disease and the complexity of service delivery required to address patient needs.

Recent statistics in NAFLD show it to now be the leading cause of liver dysfunction in the west; more worryingly, a recent prospective study from the USA confirmed that 46% of the population were living with NAFLD as well as 12% of the population having steatohepatitis, the results of which came from an asymptomatic cohort (Williams et al., 2011). In England, government statistics from 2005 indicate that up to 2 million people are living with CLD, many of whom remain unaware of their illness and as the prevalence of liver disease increases, so will the worrying number of people not yet diagnosed.; statistics also showed a worrying 12% increase in liver disease related deaths between 2005 and 2008 (Mortality rates in Liver disease: UK statistics.gov, 2009). In the UK, the high occurrence of obesity in 22% of men and 24% of women aged 16 years or older (Claridge, 2011; NHS Information Centre, 2012) is undoubtedly a contributing factor, but recent research is now showing that a ‘double whammy’ effect of obesity and alcohol consumption will increase the incidence of liver disease further (Claridge, 2011).

### *1.1.1 The Liver diseases*

CLD is an umbrella term used to describe a range of chronic liver conditions. The conventional view of symptoms experienced by people with CLD is that they are related to advanced stages of the underlying liver disease. The symptoms seen in people with even milder forms of liver disease include; joint pain, abdominal pain, muscle cramps, depression and anxiety, loss of appetite, decreased sexual interest/activity and problems with memory and concentration (Gutteling 2007, Blackburn 2007; Frith and Newton, 2008).

Participants with the liver diseases, alcoholic liver disease (ALD), non-alcoholic liver disease (NAFLD), Primary Biliary Cirrhosis (PBC) and Primary sclerosing cholangitis (PSC) are included in this study and described below.

#### 1.1.1.1 Alcoholic Liver Disease.

Alcoholic liver disease (ALD) is caused by consuming excessive alcohol. People with ALD can develop symptoms such as jaundice, weight loss, swelling of legs and ankles, ascites and nausea. The early stages of ALD are alcoholic fatty liver disease. Here, a build up of fatty acids cause distress to the liver that can be reversed with abstinence from alcohol in a relatively short period of time (NHS Choices 2012). Alcohol related hepatitis presents as inflammation of the liver and usually occurs following years of alcohol misuse. Increasing incidence is however being recognised in binge drinkers (O'shea et al 2009). Improvement in liver function for those with alcohol related hepatitis requires months if not years of abstinence from alcohol. Cirrhosis is the final phase of alcoholic liver disease and this scarring of the liver can be life threatening (Friedman and Brandt, 2006; NHS Choices 2012).

Although ALD usually occurs after years of excessive drinking, not every chronic heavy drinker will develop the disease (O'Shea et al 2010). According to UK government statistics women are considered to be more at risk of developing ALD than men however, the death rate for men with ALD has almost doubled in recent years ([www.statistics.gov.uk](http://www.statistics.gov.uk)). An increase in younger people presenting with ALD and alcohol related problems has also been recognised in recent years. Strategies including raising the price of alcohol per unit to tackle this growing epidemic are currently being trialed (Alcohol (minimum pricing) (Scotland) 2012).

#### 1.1.1.1.1.2 NAFLD.

Non alcoholic fatty liver disease (NAFLD) includes those histological changes to the liver which mirror liver disease typically found in people with ALD; inflammation, fibrosis, scarring and cirrhosis. Importantly people with NAFLD have negligible alcohol intake, reporting the consumption of <20g alcohol a day for women and <30g alcohol a day for men (Jorgensen, 2003; Anstee et al, 2011).

NAFLD is considered a condition caused by lifestyle. The constellation of increased calorie intake and sedentary lifestyle has led to increased incidence of obesity and diabetes in Western countries. In turn, NAFLD has become a growing problem as in simple terms, fat infiltrates and then damages the liver. NAFLD is often asymptomatic and is often first discovered during routine blood tests (Harrison and Day, 2007;

Cobbold et al, 2010; Ratzui et al 2008). The recommended treatment for NAFLD is weight loss in conjunction with increased exercise (Chalasani et al, 2012).

#### 1.1.1.2 1.1.1.3 Primary Biliary Cirrhosis (*PBC*).

Unlike ALD and NAFLD which are considered to be liver diseases associated with lifestyle, Primary biliary cirrhosis (PBC), is an autoimmune disease. PBC is a chronic cholestatic liver disease caused by slow progressive destruction of the small bile ducts within the liver. When these ducts are damaged, bile builds up in the liver causing cholestasis and over time damages the tissue. This damage leads to scarring; fibrosis and cirrhosis. PBC was previously thought to be a rare disease, but more recent studies have shown that it may affect up to 1 in 3–4,000 people. The disease predominantly affects women who are aged over 50 years. (Clavien et al 2006; Blackburn et al 2007; Frith and Newton, 2008

#### 1.1.1.3 1.1.1.4 Primary sclerosing cholangitis (*PSC*)

Primary sclerosing cholangitis (PSC) is a chronic liver disease also considered to be an autoimmune disease, which like PBC results in cholestasis. It is caused by progressive inflammation and scarring of the bile ducts of the liver. This inflammation obstructs the flow of bile to the gut. In time, this leads to fibrosis, cirrhosis, liver failure and a possibility liver cancer (Charatcharoenwitthaya and Lindor, 2006; Field and Heathcote, 2003). Prevalence of PSC in the UK was calculated by Card (2008) in 2001 at 3.85 per 100,000 people. Card's study showed a 40 fold increased risk of those with PSC developing primary liver cancer. PSC has also been shown to have strong associations with bowel disease (Jørgensen et al 2012).

## 1.2 Chronic liver disease; worldwide recommendations and UK national guidelines.

According to the World Health Survey around 785 million (15.6%) of adults worldwide live with a disability, while the WHO Global Burden of Disease estimates a figure of around 975 million (19.4%) people. Of these, the World Health Survey estimates that 110 million people (2.2%) have very significant difficulties in functioning; this is in part because populations are ageing and because of the global increase in chronic health conditions associated with disability, such as diabetes and cardiovascular diseases. Patterns of disability are influenced by trends in health conditions including the

detrimental effects of diet and substance abuse. Some studies have also indicated that people with disabilities have higher rates of risky behaviours such as smoking, poor diet and physical inactivity; In addition, the World Health Organization ascribed in 2004 a disability-adjusted life year (DALY) estimate of 37,760 years lost due to ill health, disability or early death per 100,000 individuals suffering from chronic liver disease (WHO, 2004). The recommendations made by the WHO report on disability (2011) are to improve rehabilitation and participation of people with disability associated with chronic disease, but as yet no definitive policy has been established for this in the UK.

Although national guidelines for chronic conditions exist, CLD remains the only one of the top 5 diseases to be without a specific National Service Framework (NSF) in the U.K. The same is also true of good practice documents with NICE guideline publications only available for heart disease, chronic respiratory disease, cancers and stroke. A new public health report by the Department of Health (DOH), NHS Outcomes Framework 2012-13 may be partway to addressing this shortfall, as for the first time the importance of addressing the premature mortality from major causes of death includes liver disease (section 1.3); and improving functional ability in people with long term conditions (section 2.2); and information and service development may also improve as the government calls upon the Office for National Statistics to provide a list of all conditions considered amenable to healthcare for 2012/13 (DOH, 2012).

Importantly for occupational therapy, is the inclusion and emphasis in the NSF for long term conditions and in new legislation and policy of the NHS Outcomes Framework, of specialised units and/or multidisciplinary teams (MDT) to be used in conjunction with medical intervention. Occupational therapists are the ideal professional group to take forward initiatives in this growing epidemic, especially in light of the WHO's global disability report which as stated, recommends the rehabilitation and participation of those with significant functional difficulty; areas of skill in which occupational therapists are highly experienced. This study aims to determine if people with liver CLD are disabled by significant functional difficulty and in doing so, demonstrate the necessity for occupational therapy in meeting the needs of the people living with liver disease.

### 1.3 Occupational Therapy; definitions and core skills

Occupational therapy is a complex, broadly based profession whose focus is on the use of activity; both as an explanation of a person's function and as a therapeutic tool where the treatment of the whole person is through their active participation in occupations. The purpose of occupational therapy defined by the College of Occupational Therapists (2009; 2011) is "to enable people to fulfil, or to work towards fulfilling, their potential as occupational beings. Occupational therapists promote function, quality of life and the realisation of potential in people who are experiencing occupational deprivation, imbalance or alienation. They believe that activity can be an effective medium for remediating dysfunction, facilitating adaptation and recreating identity". Much has been written about defining occupational therapy, but it is largely accepted that by definition, 'occupations' are an accumulation of activities which are formed from tasks, and are described as, everything we do to look after ourselves, enjoy ourselves and participate in society. Occupational therapy enables people to achieve health, well-being and life satisfaction through participation in occupation (COT, 2004).

Activity analysis, graded activity and use of activity in therapy are recognised core skills of the occupational therapist, with the therapist working with their client to facilitate best possible function, from basic motor functions, to complex self-management strategies, using different approaches to prevent permanent loss of function. The International Classification of Function (ICF) defines functional limitations as the result of the interaction between an individual with a health condition, and that individual's contextual factors; environmental and personal factors (WHO, 2011). In other words, function is not only limited by physical disability or illness, but by the impact on an individual of concerns such as housing, lifestyle, education, social structures and cultural issues.

The aim of occupational therapy is to prevent people from "activity alienation caused by feelings of powerlessness, or prolonged occupation preclusion due to geographic isolation, incarceration or disability" (Hagedorn, 1997, Christiansen and Townsend, 2004, in ENOTHE cited in COT code of Ethics 2010). As literature in CLD has already highlighted that fatigue associates with liver disease (specifically people with PBC) this study aims to see if this symptom, and others, has an impact on function, contributing to

the ‘disabling’ of this growing disease population and their decreasing quality of life (Mahmood et al, 2008).

#### 1.4 Chronic liver disease and quality of life

Improvements in the management of chronic disease has increased life expectancy (Peterson, 2005). However, the importance of addressing quality of life in people living with chronic diseases such as liver disease is becoming appreciated in both the commissioning of services and in clinical practise, The patient support group, The Dutch Liver Patient Association, states that people with CLD are still “fighting for recognition of the disease related physical, mental and social problems of chronically ill (liver) patients” (Simone, 2007). Understanding these specific problems and symptoms and their consequent impact upon meaningful activities of daily living will result in an important service development that as stated, occupational therapists are ideally placed to drive forward.

Over recent years, qualitative and quantitative research has suggested that CLD is a systemic disease, the symptom burden of which significantly impacts upon a person’s quality of life (Cauch-Dudek 1998; Newton 2006a, Newton 2006b, Newton 2008; Mahmood 2008). Cognitive difficulty has long been recognised as a systemic symptom in people with chronic liver disease (Hilsabeck, 2003; Collie 2003; Withers, 2005) and recent studies have confirmed that quality of life is impaired in people with PBC, and that this is frequently related to the debilitating symptoms of fatigue and excessive day time sleepiness. Importantly, these symptoms have been shown to be unrelated to the severity of the underlying liver disease, and in terms of developing effective interventions will therefore not necessarily improve if the liver disease is treated. Furthermore, fatigue in CLD has been found to lead to reduced physical activity (Cauch-Dudek 1998; Newton 2006a; Newton 2008) and several studies have confirmed that it is independent of the presence of depression (Jacoby 2005; Gutteling 2006; Blackburn 2007). A study by Blackburn (2007) has also shown that a positive multidisciplinary approach to quality of life management in PBC leads to an improvement in quality of life, underlining the potential that an appropriate holistic intervention package could have for people living with CLD.

The constellation of symptoms of fatigue, reduced and impaired activity and excessive sleepiness are frequently seen and addressed by occupational therapists in many clinical

areas; but what impact these symptoms have upon a person with CLD, their ability to function and the potential for occupational therapists to influence these significant symptoms in this increasing client group, requires further study.

The philosophy of occupational therapy is considered to be congruent with the concept of quality of life (Liddle 2000). As such a hypothesis can be formed that raising awareness of the prevalence of symptoms and their functional impact for people with CLD among clinicians and occupational therapists, will improve quality of life for people with CLD as well as produce improvements in patient care. More simply, as all those involved in 'managing' CLD become better informed to the symptom burden and its empirical consequence, an improvement in patient service and experience will follow. The central core skills of occupational therapy applied to symptom prevalence and management in CLD will lead to a greater understanding, and as a consequence, improvement in quality of life as any functional difficulty established in people with CLD fuels the need for improved service provision. These would focus upon an understanding of the impact of symptoms on daily living, the use of activity, and the belief that interventions should be client-centered, holistic and evidence based. Leonardi et al (2006) argues that quality of life data that includes wellbeing and satisfaction are useful for health policy planning, but may not be predictors of the presence or extent of disability. It is vital that this is considered in the context of UK legislation calling for the provision of high quality services that reflect client satisfaction ('Health, our care, our say: a new direction for community services', 2006); but more importantly, it is essential to appreciate clients' perspective and opinion of their daily experience of liver disease, and their goals of intervention, if we are to engage people in new services which confront their diet, exercise and lifestyle choices.

### 1.5 The current role of occupational therapy in chronic liver disease

A literature search using AHMED, CINAHL, OT Seeker, NHS Trust and COT library services including a range of liver disease descriptions (liver, liver disease, CLD, alcohol, ALD, NAFLD, PBC and PSC) and occupational therapy derivatives (occupational therapy, occupational therapist, OT, occupational science) resulted in no combined hits in February 2008. [A repeat search carried out in March 2012 retrieved 2 hits which are available as a result of this study (Elliott et al 2009, et al 2010)]. Literature is available to support brief occupational therapy intervention in the hospital



setting e.g. alcohol misuse (McQueen et al, 2009) but literature is not comprehensive, nor is any information available describing the current practice of occupational therapists in the acute NHS setting. This lack of evidence underlines the fact that although there appears to be a role for occupational therapy intervention with people who have CLD, no disease specific research or best practice documentation currently exists, mirroring the lack of national guidelines and recommendations. It may be possible that knowledge from other chronic conditions whose symptoms mirror those associated with CLD can inform future clinical practise, and details of this are given on pg. 16; however obtaining a clear understanding of current practise in the acute NHS setting of occupational therapy with people who have chronic liver disease was necessary.

A survey was therefore carried out by Elliott and Newton (2010) of occupational therapists and physicians who work with liver patients on acute wards, in 13 Trusts across the north east of England and Scottish Borders; its broad aim was to elicit trends in current referral rates and reasons for referral to occupational therapy for people with CLD. The opinion of physicians' perceptions of occupational therapy with patients who have CLD was also sought to explore physicians' knowledge of what OT's do and to provide insight into whether occupational therapists were being referred to appropriately.

The results showed that safe discharge home from hospital was the predominant reason for referral to occupational therapy, indicating a homogeneous approach to the intervention of those with CLD comprising of, initial contact, functional assessment focusing on physical need, probable home visit and possible follow up visit for equipment. This expedient intervention approach is still perceived to be the means by which successful discharge can be secured in the interests of the acute care setting, with care being transferred onto community providers (Hospital Discharge Workbook, 1994; Mountain and Pighills, 2003).

For people living with CLD the problems with this reductionist approach to intervention is the need people with CLD have for therapeutic symptom management in the acute setting, and the insufficiency of symptom management resources available to people with CLD in the community.

The prevalence of referral to occupational therapy for equipment provision described in the survey reinforced this reductionist approach in current intervention. Findings from published studies show short-term focus on equipment provision combined with limited post discharge intervention may not meet patient and carer expectations or concerns with longer-term issues (Chamberlain et al, 1981; Kraskowsky and Finlayson, 2001; Welch and Lowes, 2005). Williams (2004) conducted a study of chronically ill patients and their reflections of acute care, the findings of which have relevance to the potential treatment of people with CLD. The main themes were the beliefs of the patients that their co morbidities were poorly managed during their stay; that the health staff lacked insight into the impact the hospital stay had on their normal healing process; that all the participants experienced fatigue post discharge; and that the patients wanted improved comprehensive discharge planning with ongoing health maintenance. The discrepancy within the survey by Elliott and Newton which highlighted the therapists' knowledge of occurrence of symptoms but described their practice only in the terms of discharge planning and equipment provision is further highlighted here.

It could be argued that, certainly in the acute setting, there is a perception that the occupational therapists' role is that of discharge facilitators (Lane, 2000; Griffin and McConnell, 2001). This limited scope of assessment evidence consequently provides only a 'snap shot' of a client's circumstance and ability at discharge (Barras, 2005); the dilemma for occupational therapists being that this excludes many of the skills and knowledge they use which holistically assesses and identifies long term needs, goals and outcomes for their clients (Lane, 2001; Korner-Bitensky et al 2008). For Occupational Therapists working with those with CLD, this limited exploration of discharge from the hospital setting underestimates the needs of clients with CLD and undervalues the complex assessment and skills used by the occupational therapist.

The limited role of occupational therapy with this client group may help clarify why the physicians in the Elliott and Newton survey who referred to occupational therapy had difficulty describing why they referred or what interventions were carried out; the physicians also had difficulty in reporting the symptom experience of people with CLD in their care. This difference can not be explained without further study, however to state that the physicians are unaware of the associated symptoms of CLD seems unlikely. One explanation may be that physicians do not recognise the ability occupational therapists have in managing these symptoms and so have not listed them in

the context of the survey. It has been noted before that occupational therapists are good at knowing intrinsically and instinctively their practice, but lack depth in describing it or in documenting it fully (Mattingly 1991; Lundgren, 2001). This may contribute to occupational therapists not being credited, in this instance of CLD, with the depth of knowledge and skill they possess.

#### 1.6 Occupational therapy in other chronic conditions

There is comprehensive literature relating to a number of chronic conditions (e.g. chronic fatigue syndrome (CFS), malignancy and rheumatoid arthritis) from which important information on universal symptoms e.g. fatigue and cognitive dysfunction, could be extrapolated. This would potentially aid understanding, and direct management, of the symptom complex experienced by people with CLD. Occupational therapists have extensive experience working in the area of fatigue and activity management in chronic diseases including CFS (Cox 1994; 1998; 2004). This naturally raises the question considering the prevalence of fatigue in CLD, whether the same, or similar, management could be successfully applied in the clinical setting of symptom management for people with CLD.

The NICE guidelines for chronic fatigue syndrome/myalgic encephalomyelitis (2007) recommend that a successful client centred intervention should include; sleep management (1.4.2.1), rest periods (1.4.2.4.), relaxation (1.4.2.7), pacing (1.4.2.7) and use of equipment (1.4.4) (NICE 2007). Gray and Fossey (2002) comment that such an approach may allow clients with CFS to re-engage in meaningful occupations. Symptom parallels have been noted between CFS and the autoimmune liver disease, PBC (Blackburn et al 2007). Blackburn et al's (2007) study also suggested that the development and evaluation of intervention strategies are required, using a multidisciplinary approach, to include occupational therapy, using a model of service delivery currently established in other chronic conditions.

#### 1.7 Treating the disease or treating the person

One important question is whether service delivery can be disease specific or if the constellation of symptom burden requires a tailored intervention. In other words, is it correct to presume that interventions are disease specific rather than symptom specific? It appears that the literature may be contradictory in this area when we consider examples of skills central to occupational therapy. Studies examining energy

conservation techniques in the management of fatigue in cancer patients have shown only minimal improvements in perceived fatigue despite changes in activity behaviours (Barsevick et al 2005; Ip et al 2006). This suggests that energy conservation, a technique used widely by occupational therapists may not be universally useful in the management of fatigue in all chronic conditions and its value in the management of CLD should be specifically evaluated.

Increasing exercise tolerance has been another method used generically to improve fatigue where conflicting outcomes have been reported. Recent studies examining the effect of aerobic exercise in clients with cancer demonstrate improvements in fatigue in addition to global health and well-being (McKneely et al 2006; Kirschbaum, 2007; Mitchell et al 2007). The NICE guidelines also recommend exercise for clients with CFS. However, a recent study (Nijs et al 2008) concludes that even with exercise limits, short term post exercise malaise can be a significant problem in CFS. It has also been noted that in CFS exercise goals may take weeks, months and even years for this client group to achieve, and that, unsupervised exercise may even worsen symptoms (NICE 2007).

The suggestion therefore is that generic management strategies for symptoms such as fatigue and impaired activity are not necessarily appropriate in CLD and that disease specific interventions are required. In addition a growing body of research suggests that diagnostic information alone may not adequately reflect an individual's health condition and that medically-diagnosed diseases or impairments may manifest differently across individuals; similar functioning does not imply similar diagnosis, nor does disease severity reflect symptom burden (Newton et al, 2008; Peterson et al, 2010.). As client centred practitioners the importance of distinguishing between objective descriptions of the 'disability experience' and the individual's satisfaction of that experience become apparent.

#### 1.8 The need for further occupational therapy research in CLD

Clinically there is a need to investigate, and address, the functional issues affected by the symptoms of the disease and the impact this has on an individual's ability to carry out the activities of daily life which have meaning and purpose to them. The appreciation of function is critical for people with CLD in light of the prevalence of physical dysfunction, cognitive difficulty and fatigue in this client group. Recent studies

observing fatigue, daytime somnolence, and impairment of daily activities in people with CLD (Newton et al., 2006a, 2006b, 2008; Elliott et al, 2011) are providing a clearer picture of what affects people living with CLD and are indicating the role that occupational therapists, who are considered to be experts in activity could have with people with CLD.

Comprehensive research that better understands the living experience of people with CLD; their functional difficulty, symptom burden, and occupational priority, is urgently needed and occupational therapists have a real opportunity to address and fulfill this need.

This study therefore aims to determine the functional difficulty experienced by people with CLD in the context of their daily activities. Participants with CLD; specifically ALD, NAFLD, PBC and PSC who agree to partake in the study will be asked to complete self-reported questionnaires on their ability to carry out daily activities and of the symptom burden they experience.

Their biochemistry and histology results will be used along with the functional and symptom assessment tool scores to look for correlations and associations lending valuable insight into the holistic impact of CLD.

Qualitative interviews will be used to elicit the life experience of these functional difficulties and symptom burdens with a view to better understanding of people with CLD and in turn developing appropriate management strategies and quality service provision.

## Chapter 2 Methods

### 2.1 Environment

The National Institute for Health Research Biomedical Centre in Newcastle was formed in 2007 as collaboration between Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University. It was one of 12 Biomedical Research Centres (BRC) in the UK and was specifically designated as the UK's BRC in Ageing and Age related disorders.

The mission statement of this Centre is:

*“We aim to translate basic biomedical research into excellent clinical research for the benefit of patients, focusing on ageing and age-related diseases”*

The Liver Theme from which the data presented in this thesis has been collected forms one of the seven themes within the BRC in Ageing (Figure 1).

A principal aim of the Liver Disease in Ageing theme was to define the impact of liver disease and establish therapeutic needs of benefit to patients. This study addresses this aim by focussing on the daily functioning of people with chronic liver disease.

In order to achieve that aim, the BRC funded a multidisciplinary team (Figure 2) who set out to explore different domains of the impact of CLD. This thesis will focus upon the work performed within the team by the author, an advanced Occupational Therapist.

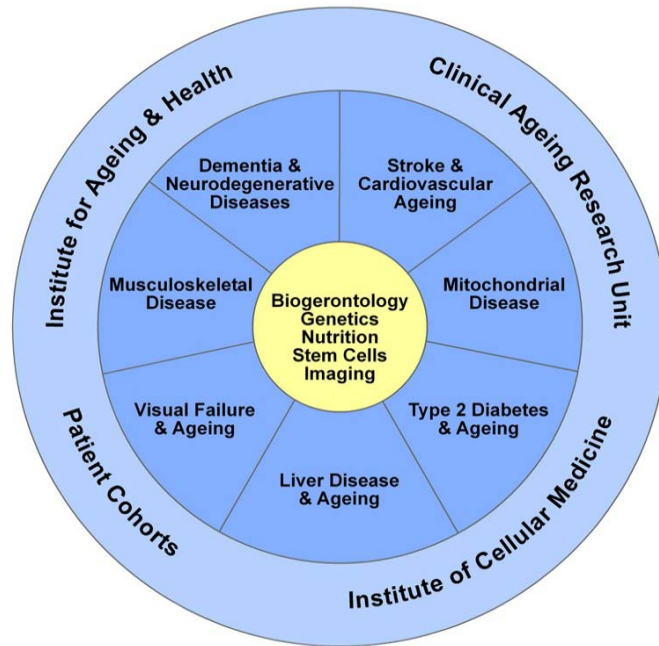


Figure 1. The Newcastle NIHR Biomedical Research Centre in Ageing detailing the seven themes of research, the research infrastructure and in the centre, the cross cutting themes.

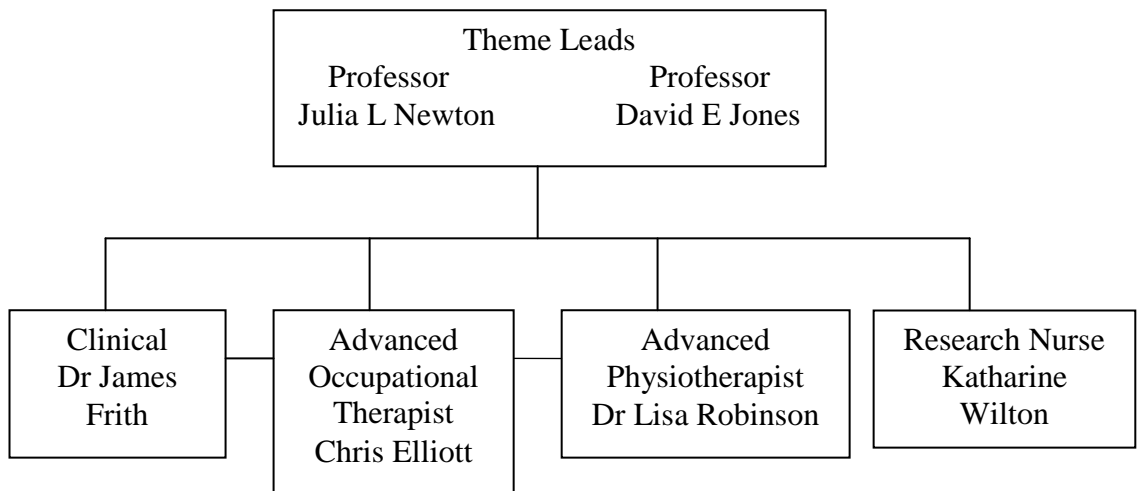


Figure 2. The hierarchical structure of the multidisciplinary team members of the BRC in Ageing Liver Theme.

## 2.2 Methodology

This is an exploratory mixed methods study that incorporates a nested qualitative element into a quantitative cross-sectional cohort study of people with CLD.

All forms of research inquiry are “formed, in the simplest of terms, from a desire to understand the world around us” (Bryman, 2007). To an Occupational Therapist concerned with ensuring client-centred holistic research, using a mixed methods approach to gathering information seems apt. However methodology literature typically continues to class quantitative and qualitative approaches as separate paradigms (Bergman 2011).

Quantitative approaches that incorporate standardised assessment tools such as PHAQ and are analysed using statistical techniques are typically linked with the positivist paradigm. Positivism is based on the philosophy that a person’s preconception is set aside in order to identify objective facts based on empirical observations (Robson 2002). In the context of this study a purposive sample of people with CLD was used to explore function using a closed-response questionnaire (McEvoy and Richards, 2006). A hypothesis that people with CLD have functional difficulty was established; this was tested and the findings generalised to a wider population (Bergman 2011).

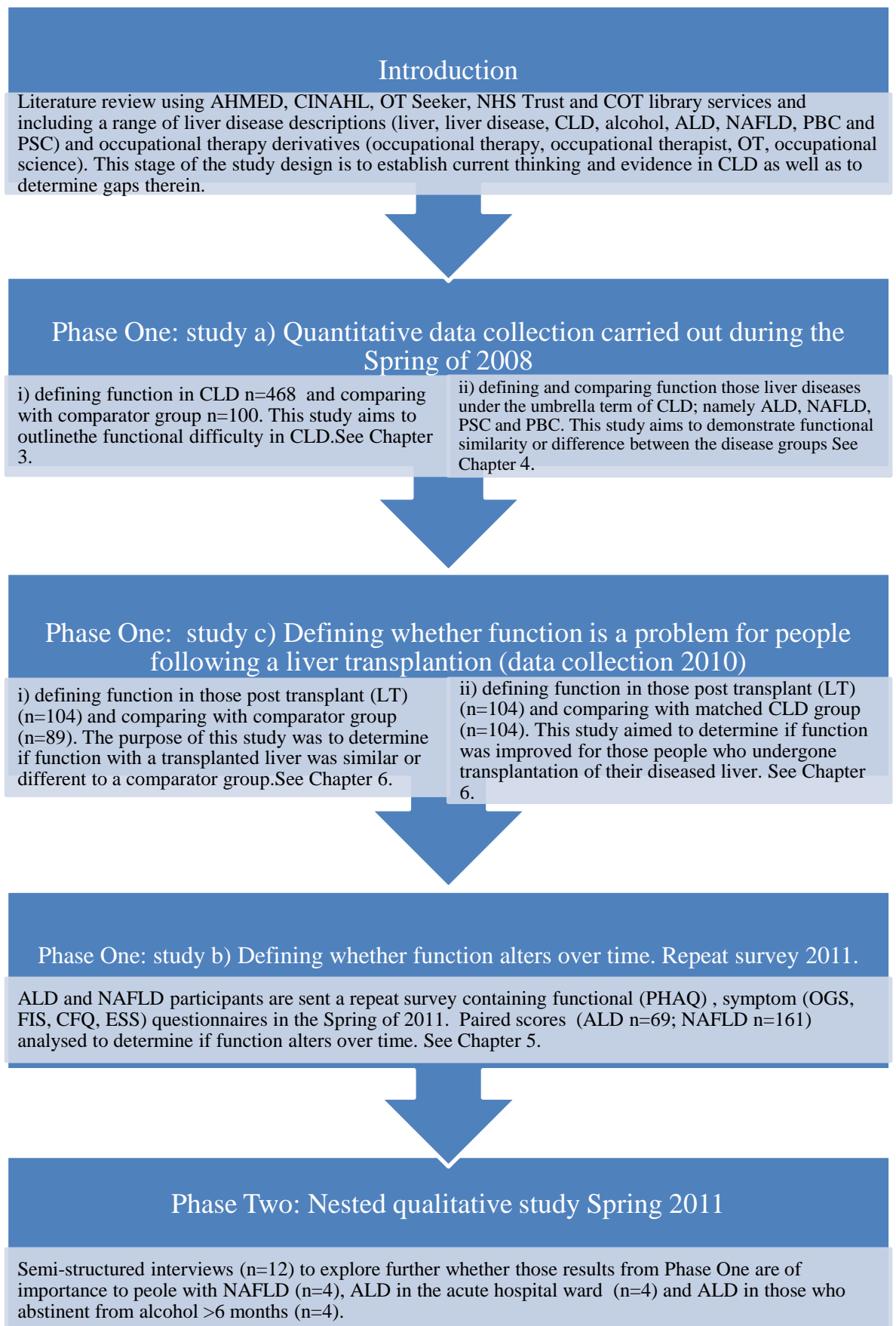
In contrast qualitative approaches, based on non-numeric narratives are commonly associated with the interpretivist paradigm. In simple terms, the interpretivist paradigm allows for the *meaning* of the data to be given. In the context of this study, the quantitative data showed that problem areas in functional difficulty exist, but was unable to tell us if this was a problematic for those concerned. Using an interpretivist approach allowed the researcher to demonstrate (by use of narrative) just how those functional difficulties affect the daily lives of people with CLD. In this study, the recruitment of a small sample of participants useful for their likelihood to be able to answer the questions raised by phase one of the study (Kitzinger 2006; Bergman 2011), were sought to add depth to the findings of that quantitative data.

These conflicting theories of knowledge are assumed to create ‘dissonant data’ (Perlesz and Lindsay, 2003; Johnstone, 2004); in other words they generate data sets that show different and possibly incompatible results. Critical realists however argue that research methods should be dictated by the nature of the research problem and suggest that an



effective tactic is to combine qualitative and quantitative approaches; the importance being in *how* they are used (Modell, 2009). In this study, the integration of quantitative and qualitative data was used to strengthen the ‘theory generation’ (McEvoy and Richards 2006) that people with CLD are experiencing functional difficulty and that occupational therapy intervention is the appropriate service to address their need.

This thesis presents a research strategy of a pre-determined series of studies that aims to explore function in people with CLD clarifying difference in disease type, disease severity, symptom burden and impact. An over view is given in Fig. 3.



*Figure 3. Chronological order of studies within this thesis*

## 2.3 Study Design

### 2.3.1 *Phase One (a): Defining whether function is a problem for people with chronic liver disease.*

To determine whether a problem with function existed for those participants in our study with chronic liver disease (CLD) and to define the extent of any problems found, a cross-sectional approach was undertaken. The CLD population was identified from the comprehensive databases held by the Newcastle upon Tyne NHS Foundation Trust (as described in Participants pg. 24). This method of data collection is relatively large, and although clinic cohorts do not define a disease population, it is useful in describing the breadth of living experience for people with a range of liver diseases.

To define if a problem existed within our CLD population, data describing the function of people with CLD was compared to a community dwelling comparator group who were matched group wise by age and gender.

A North East liver patient group, LIVERNORTH was instrumental in the choosing of a tool which best captured their functional difficulty. The tool that best described the patients' functional difficulty experience and that was appropriate for a postal survey was the PROMIS Health Assessment Questionnaire (PHAQ). The process of choosing the tool with the patient group is described in 'Measuring function and the aims of the study' (pg. 31-38) along with a description of PHAQ.

The participants' PHAQ scores were also compared between the disease cohorts, namely non alcoholic fatty liver disease (NAFLD), alcoholic liver disease (ALD), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) and associations explored by way of correlation, with age, biochemical disease markers alanine transaminase (ALT), alkaline phosphatase (ALP), albumin ALB, bilirubin (described in: Describing the biochemical and histological markers used in this study pg.41-42), and the symptom assessment tools; cognitive failure questionnaire (CFQ), fatigue impact scale (FIS), orthostatic grading scale (OGS) and the Epworth somnolence scale (ESS) (described in: The symptom assessment tools used in this study, pg.39-41).

It is important to note here that not all the data compared in this study was collected at the same time. The first round of data collection of the PHAQ was the spring of 2008.

The biochemical and histological data was then sourced from the Newcastle upon Tyne NHS Foundation Trust liver database (described in: Participants pg. 24) that was accessed on March 3rd 2008. The data base comprises both incident cases, and review patients, with chronic liver disease and as such the data is continuously updated. The biochemical and histological results accessed were those most recent to the receipt of the participants' completed PHAQ, and in a minority of cases these results were over 2 years old.

### *2.3.2 Phase One (b). Determining whether function for people with CLD alters over time*

To determine if function worsened over time and if biochemical and histological markers of disease severity influenced change in function, NAFLD participants' and ALD participants' PHAQ data were compared over time. The symptom assessment tools completed in 2008 were sent again to participants in 2011. Results of this comparison were compared with the results from their LFT results and symptom assessment tools data to determine whether worsening function could be predicted.

### *2.3.3 Phase One (c). Defining whether function is a problem for people following liver transplantation*

The post-transplant group were not included in the CLD whole group and their data and findings were compared and described separately. The community-dwelling comparator group (comparator group) and post-transplant cohort were matched group wise for age and gender. The comparator participants for this part of the study were drawn from the total group used throughout the study; however fewer comparator participants were included in the comparison with LT participants in order to achieve the best possible group wise match. The post-transplant cohort was also compared with a non-transplanted chronic liver disease comparator group from the Newcastle upon Tyne NHS Foundation Trust. Here, each transplanted participant was matched on a case-by-case basis with a CLD participant of the same aetiology, age and gender, in a blinded manner. In order to achieve the best possible group wise match, fewer LT participants were included.

### *2.3.4 Phase Two: The participant perspective*

Once the scale of the problem was identified and comparisons and correlations made, a small purposively sampled, nested qualitative 'topical survey' of people living with

ALD and NAFLD was carried out to explore in further detail the implications of impaired function in CLD and the patient experience. Participants were recruited via an out-patient liver clinic by a specialist nurse at the Newcastle upon Tyne NHS Foundation Trust outpatient liver clinic or in-patient liver ward in accordance with local research ethics approval request that a professional independent of the research team approach and recruit suitable participants, over a three month period.

The first four participants to agree to an interview in each category were accepted for the study. This approach to recruitment may have affected the power of the study as well as bias the results (discussed in Limitations pg. 186/7) as those who participated may have held strong or outlying opinions. The concluded number of participants was based on the nested nature of the qualitative study and time constraints.

Gender and age were not criteria priorities at this pilot stage, but the information was collected for consideration.

Participants recruited were from NAFLD and ALD cohorts and were required to meet the following criteria to form 3 informant groups:

NAFLD: Confirmed diagnosis of NAFLD

ALD: Confirmed diagnosis of ALD

ALD abstinent (ALD AB): Confirmed diagnosis of ALD, abstinent from alcohol >6 months.

The interviews were conducted in an environment chosen by the participant and lasted no longer than 90 minutes, as requested by the ethics panel. The interviews were audio recorded and transcribed verbatim.

Semi-structured interviews were carried out with participants in a place of their choosing and following completion of an informed consent document, in accordance with the ethical considerations and principles described in Ethics, pg. 30-31).

#### 2.4 The participants

The participants of this study were recruited from existing databases held by the Newcastle upon Tyne NHS Foundation Trust.

Patients who met the diagnostic criteria and who provided fully informed consent for their data to be stored and used for research (including contact for future research) were included. Data stored on the databases includes contact details, date of birth, gender, medical history, drug history and results of investigations, including liver blood tests and details of liver histology where available. The data bases are held on the Newcastle upon Tyne NHS Foundation Trust website server and access is severely restricted, limited only to one research nurse, Elsbeth Henderson. Access was permitted at the Freeman hospital in March 3rd 2008, when the databases were interrogated. The database represented patients attending liver clinics between the years of 2005 to 2008; and represents both newly diagnosed, and review patients with CLD. Caldicott and data protection permission is in place for the databases. The uploading of data onto a spread sheet is only provided by Mrs Henderson and quality comparator assured by double entry and rigorous checking of 10% of the patients.

#### *2.4.1 Non Alcoholic Fatty Liver Disease (NAFLD)*

All patients who attended the outpatient clinic between 2005 and 2008 who met the inclusion criteria were included in the database used for this study. Diagnosis of NAFLD is determined with

1. Elevated aminotransferases (either ALT or AST)
2. A liver biopsy showing a minimum 10% steatosed hepatocytes
3. Exclusion of other liver disease with clinical, biochemical, radiological or histological data
4. Weekly alcohol intake of <140g (female) and <210g (male) (self-reported, relatives/carer reported or measurement of random serum alcohol level).

The NAFLD database also includes patient information detailing weight and height (BMI), insulin resistance level [graded by the homeostasis assessment index (HOMA) (Matthews, 1985).], lipids and disease severity (steatosis, NASH or cirrhosis) and the liver function test (LFT) results ALT, ALP, ALB and bilirubin (described on pg.42-43). In 2007/2008 the symptom assessment tools orthostatic grading scale (OGS), cognitive failures questionnaire (CFQ), the fatigue impact scale (FIS) and the Epworth sleepiness scale (ESS) were sent out to all the people on the database and the scores were then added to the database.

#### 2.4.2 *Alcoholic Liver Disease (ALD)*

All eligible and consenting patients attending the outpatient liver clinic were included in this database. Eligibility is established if the patient has consumed >80g of alcohol per day for the previous 10 years and has had other causes of liver disease excluded (using clinical, biochemical, radiological or histological data). Diagnosis was confirmed in all patients histologically. The database included details of age, gender, histology biochemical markers (LFT's) and symptom assessment tools OGS, CFQ, ESS and FIS.

#### 2.4.3 *Primary Biliary Cirrhosis (PBC)*

The existing database for people with PBC is comprised of people who meet the inclusion criteria who were living within the NE1-NE25 postal code area. This geographical cohort rather than a clinic cohort, and thus allows for descriptions based on a 'well' defined population irrespective of hospital admission/attendance which better reflects this population. The database included details of age, gender, histology biochemical markers (LFT's) and symptom assessment tools OGS, CFQ, ESS and FIS.

The inclusion criteria to the database are to meet two of the following:

- a) Evidence of a serum anti-mitochondrial antibody or PBC specific anti-nuclear antibody
- b) A cholestatic abnormality of LFT's
- c) Compatible liver histology

(Prince, 2000; Goldblatt, 2002)

#### 2.4.4 *Primary Sclerosing Cholangitis (PSC)*

The existing database of PSC patients is comprised of people on the Newcastle Upon Tyne NHS Foundation Hospitals patient database who met the inclusion criteria of having a confirmed diagnosis of PSC following a magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography and liver biopsy. The information on the database included histological and biochemical (LFT) results, and the symptom assessment tool scores, OGS, CFQ, FIS and ESS.

#### 2.4.5 *Post Liver Transplant (LT)*

The existing database of post transplant patients is comprised of people who have received their liver transplant in Newcastle upon Tyne NHS Trusts in the previous 5 years. For this study those five years are 2005 to 2010. The people on the database may be from any part of the UK and have any condition requiring transplantation. The database included details of age, gender, histology biochemical markers (LFT's) and symptom assessment tools OGS, CFQ, ESS and FIS.

#### 2.4.6 *Comparators – community-dwelling comparator group*

Comparator data was collected specifically for this study. Comparator participants were recruited anonymously using the following approaches:

- i) Best friend approaches where participants from the conditions cohorts were asked to have a friend or family member also complete a questionnaire.
- ii) Anonymous completion of questionnaires detailing age and gender by relatives or carers of people who attended outpatient liver clinics at Newcastle upon Tyne NHS Foundation Trust.

The comparator group was databased chronologically and was deemed complete when group wise age and gender matched without significant differences.

### 2.5 Recruitment of study Participants

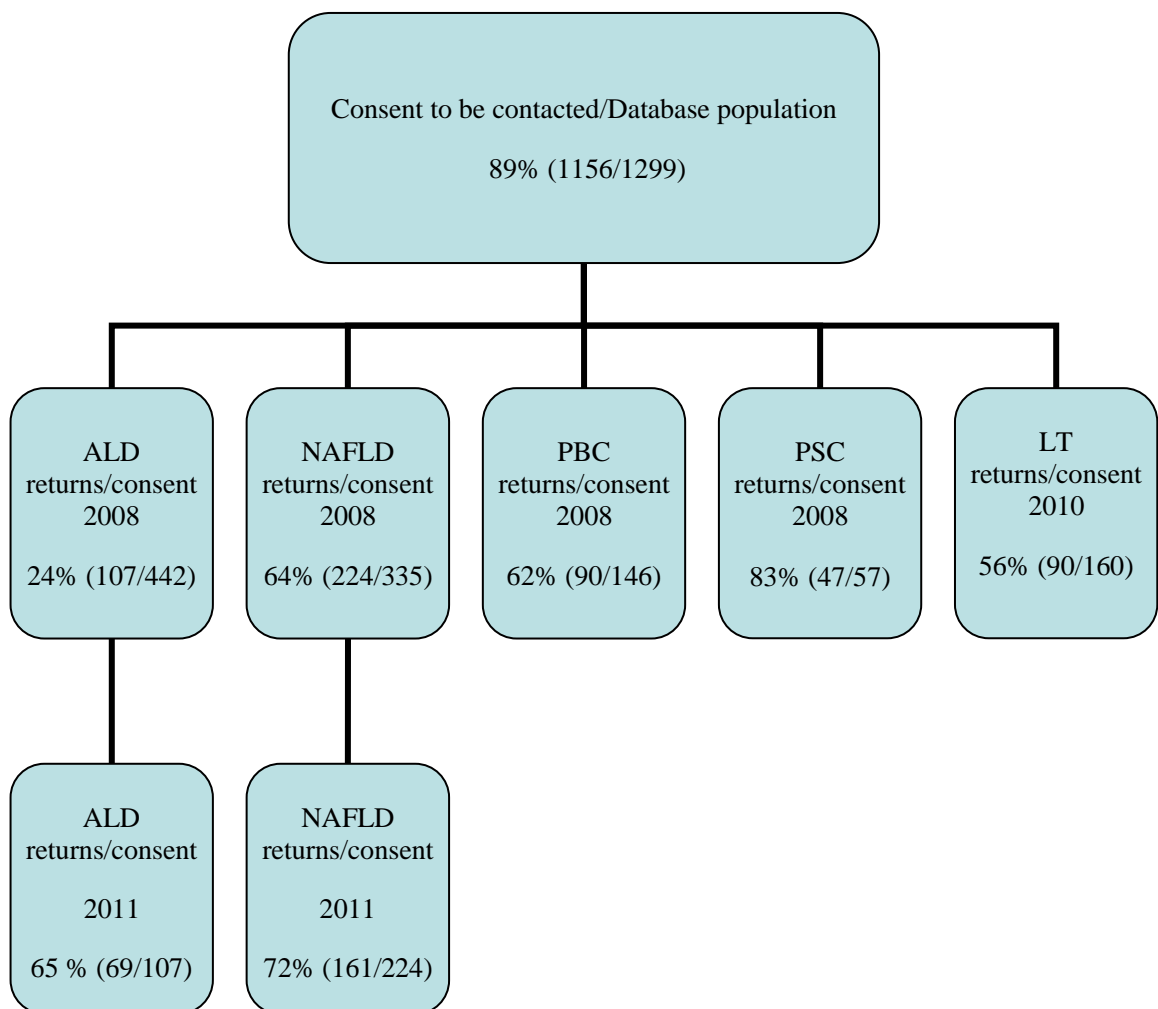
#### 2.5.1 *Recruiting participants for Phase One*

Details of participants in Phase One were all accessed from the Newcastle upon Tyne NHS Foundation Trust liver database by the research nurse Elsbeth Henderson on one particular time point, March 3<sup>rd</sup> 2008, and subsequently approached via post to take part in the study by completing and returning the functional measurement assessment tools. The numbers of participants are described in Figure 3 below. A number of individuals had previously requested not to be contacted for research purposes; service evaluation or teaching and so were excluded. This exclusion was also honoured when considering change over time in NAFLD and ALD survey in 2011 if a participant had returned questionnaires in 2008 but had requested not to be contacted again. LT participants were considered separately from the CLD group, as by virtue of their transplant they are no longer deemed to have diseased livers. This cohort was approached via the transplant

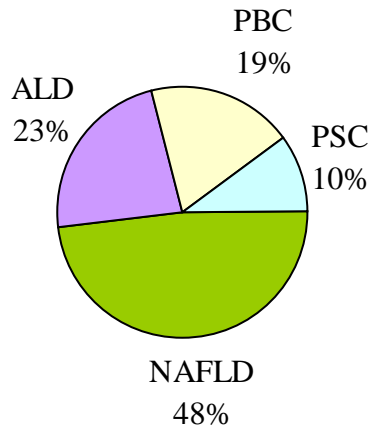


co-ordinator and the symptom assessment tools sent to them in the post. Response rates are shown in Figure 4.

Community dwelling comparator participants were approached either by post in conjunction with CLD participants (as described earlier) on a voluntary basis by completing the questionnaires in the waiting areas of the Newcastle upon Tyne NHS Foundation Trust liver clinics. Anonymity was ensured by the use of a sealed questionnaire deposit box and anonymous completion of the questionnaires.



*Figure 4. The Newcastle Upon Tyne NHS Foundation Trusts CLD database numbers, percentage of those consenting to further research and percentage of participants who returned the questionnaires for this study as a whole*



*Figure 5. The proportion of each liver disease making up the CLD group*

#### *2.5.2 Recruiting of participants for Phase Two*

NAFLD and ALD AB participants for the semi structured interviews were approached by the specialist liver nurse when attending out-patient liver clinic appointments and handed a patient information sheet detailing the study and the participant requirements (Appendix 1). Interested parties informed the nurse of either their willingness to participate verbally or using the ‘interested in further information’ return slip. The nurse then contacted the researcher to provide participant contact details.

The specialist liver nurse approached ALD participants during an acute in-patient hospital stay and gave them a participant information sheet. Similarly, the interested participants informed the nurse of their willingness to be interviewed and their names and preferred time of contact were given to the researcher.

## 2.6 Ethics

### 2.6.1 *Ethical consideration*

Health service research is said to benefit from a clear appreciation of ethics and methodology (Shaw, 2003). Lincoln and Guba (1989) are quoted as saying that ‘conventional (positivist) science has failed ethically’, however to state that only qualitative study is ‘ethically privileged’ (Shaw, 2003) undermines the importance that quantitative data can add to a study.

More over, certain ethical issues are important to consider when designing a research study. Outlined below are those issues encountered during the design and execution of this study.

#### 2.6.1.1 *Independent review*

This study received ethical approval as detailed below in section 2.6.2. Ethical approval. Independent review ensures that individuals not affiliated with the research project evaluate the proposal to ensure that ethical and scientific standards are met (Khanlou and Peter, 2005). Care must be given to emerging ethical considerations throughout a study and caution given at ‘addressing and neatly tidying away’ initial ethical issues. (Shaw, 2003). In the context of this study, specific ethical approval was sought and granted for the nested qualitative component of the study after the quantitative element of the study had begun. This was to address those issues raised in recruiting participants to interview.

#### 2.6.1.2 *Informed consent*

Participants from the Phase One studies had agreed previously to part-take in future studies. Their consent had therefore been taken at an earlier date. Participants for the Phase Two study were required to provide written consent in accordance with the Ethical Approval (see section 2.6.2).

Voluntary participation may be motivated by a want to ‘give back’ or to please the researcher (Blackmer, 2003; Shaw, 2003). To limit perceived coercion in this study, participants were given a participant information sheet (see appendix 1) and asked to return an expression of interest form. In the case of those participants in the acute setting, those participants wanting to be involved in the interviews were asked to

express their interest to a third party blinded to the study (i.e. a ward staff nurse). Individuals were reassured that participation was voluntary and that it would not affect their quality of care. In practitioner-researcher projects, it is likely that the researcher is aiming to change or enhance practice (Costley and Gibbs, 2006) and it was with this ethos that this study was undertaken.

#### *2.6.1.3 Anonymity and confidentiality*

Whilst this study maintained confidentiality and anonymity in strict accordance with both the ethical guidelines and Trust and University policy, it is said that true anonymity and confidentiality can not be fully guaranteed in research (Kruegar and Casey, 2009). In this study, the use of a pre-existing group who are largely PBC participants may have raised ethical issues with regard to anonymity (Barbour, 2007; Williams and Posser, 2002)

#### *2.6.1.4 Consensus, dissent and disclosure.*

All qualitative researchers need to consider how the participants perceive them and what effect characteristics such as class, race and gender will have on the data obtained (Barbour 2006). These characteristics are said to be emphasised if the researcher is perceived to be a medical or health care professional (Britten, 1995). The impact of this is the 'social desirability effect' which occurs when participants respond or act in a way that they feel the researcher would like (Kruegar and Casey, 2009). The researcher in this study is a highly experienced occupational therapist with vast experience in formally and informally 'interviewing' people. It is the skill of the researcher in this context that will have helped to reduce the social desirability effect.

### *2.6.2 Ethical Approval*

#### *2.6.2.1 Ethical approval for Phase One*

Each of the CLD databases has approval from the Newcastle upon Tyne NHS Foundation Trust Caldicott Guardian. The Caldicott principals were reviewed at the outset of the study and strictly adhered to for its duration. The databases were interrogated for patient identifiables only when deemed absolutely necessary and on a strictly need-to-know basis. All participants in the study had provided prior, fully informed consent to be contacted regarding audit, service evaluation and research purposes.

The community-dwelling comparator group (comparators) contained no identifiable data. The permission for obtaining this data was granted by the chairman of the ethics committee who first approved the BRC project, and considered it Service Development. The principles of service development/evaluation allow the collection of data from individuals who would typically benefit from the existing service, where the service is typical and unchanged from usual service delivery. Data collected from patients and in the case of comparators, friends, carers or relatives of patients could, ethically, be used as long as the data analysis could not be used to identify individuals and the results could not cause harm or distress.

The project was carried out with participants predominately in the north east of England between February 2008 and July 2011. The exception to the geographical status was that of the post liver transplant patients, who by virtue of the service may have been nationwide.

### *2.6.3 Ethical approval for Phase Two*

The study design was submitted to the Sunderland Research Ethics Committee REC reference 10/H0904/51 for consideration. A favourable ethical opinion was granted on November 8<sup>th</sup> 2010 (Appendix 2).

This study was submitted to the Newcastle Upon Tyne NHS Hospitals Foundation Trust Research and Development Department, Project number 5427. The study was approved by the department on 20<sup>th</sup> January 2011 (Appendix 3).

All ethical guidelines were strictly adhered to throughout the study. Anonymity was upheld and all participants provided fully informed consent to the interview process and its future dissemination.

The study was carried out between April 2011 and July 2011.

## *2.7 Measuring function and the aims of the study*

### *2.7.1 Measuring function in CLD: Phase One*

Utilising the most appropriate tool was essential to measure what, if any, daily activities are affected by CLD. An extensive literature search using AHMED, CINAHL, OT Seeker, NHS Trust and COT library services including a range of liver disease

descriptions (liver, liver disease, CLD, alcohol, ALD, NAFLD, PBC and PSC) occupational therapy derivatives (occupational therapy, occupational therapist, OT, occupational science) and functional terms [function, activities of daily living (ADL), activity] demonstrated that no studies used any activity or function specific data collection method with people who have CLD.

The internet, NHS, Newcastle University and COT libraries, as well as departmental resources, were searched for functional assessment tools that measured ability to carry out activities of daily living. Of these, those questionnaires that were patient reported outcome tools (PRO's) were considered. Using PRO measures was important as it enabled the questionnaire to be completed without the researchers' presence thus a) lessening the influence of the researcher on the research participant and b) the questionnaire could be completed by the participant and returned by post.

To incorporate client centred participation to the study, a local patient group were asked to complete a workbook of the considered questionnaires and give their opinion of the tool's value in measuring their function as people with CLD, in their daily activities.

The considered questionnaires were Patient Recorded Outcome Measure Information System Health Assessment Questionnaire (PHAQ), the EuroQol EQ-5D, The International Physical Activity Questionnaire (IPAQ) (short form), The Measure Yourself Medical Outcome Measure (MYMOP), Functional Assessment Status Questionnaire (FAS) and the Mayers Lifestyle Questionnaire (described below). The tools were collected into a pack along with a grading sheet of each tool that asked the patient group mark its ease of use and its relevance to their experience of living with CLD.

#### *2.7.1.1 The assessment tools used in the patient group 'questionnaire pack'*

##### *PHAQ*

The Patient Recorded Outcome Measure Information System Health Assessment Questionnaire (PHAQ) was derived from the Health Assessment Questionnaire Disability Index (HAQ-DI) developed by the Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS) group at Stanford University during the early 2000's (PROMIS 2008). The HAQ-DI has been widely used for research purposes in hundreds of studies. Initially developed as a tool to measure functional difficulty for

people with rheumatism (Hurst, 1997; Bruce and Fries 2003), it has been shown to be useful in a wide range of chronic conditions including HIV/AIDS (O'Brien, 2010), lupus (Hyphantis et al, 2011), normal ageing populations (Bruce and Fries, 2003) and nutritional studies (Hubert 1993; Bruce and Fries 2003). It has been repeatedly shown to be reliable and valid in different languages and contexts with consensus that it possesses face and content validity. The construct/convergent validity, predictive validity and sensitivity to change have also been established in numerous observational studies and clinical in trials; as well as convergent validity based on the pattern of correlations with other clinical and laboratory measures (Fries, 1982, 1983; Bruce and Fries 2003,). The PHAQ items have been demonstrated as 'clearer, simpler, more clearly understood, assessed more quickly, have less floor and ceiling effects, have greater information content, smaller measurement errors, and are more reliable with better face and content validity and better responsiveness than their HAQ-DI counterparts' (Fries et al, 2005, 2006).

PHAQ consists of 20 questions that ask patients to rate their ability to carry out daily activities on a five-point scale of 0 'without any difficulty' to 4 'unable to do'. The 20 questions are divided into 8 domains of physical function: dressing, arising, eating, walking, hygiene, reach, grip and activity.

The highest scoring question in each domain is used as the PHAQ domain score. All 8 domain scores can be added together, divided by 8 and multiplied by 25 to calculate a PHAQ total score. The range of scores is 0 – 100 and higher scores indicate worse functional ability and therefore greater functional impairment.

In this study the term 'PHAQ Total' scores is where the data represents all the participants in a group and is the total of all the questions in the functional assessment tool. Similarly where the term 'PHAQ domain' is used, the data represents all the participants of a group and the questions in the PHAQ questionnaire within the stated domain; e.g. Dressing domain: Questions 1 and 2; Are you able to get dressed including fastening buttons and tying shoelaces and can you manage to shampoo your own hair?

The term 'PHAQ WD' (PHAQ with difficulty) is used to describe the data sets where all those participants in a group scoring zero i.e. those without functional difficulty in each of the 20 questions, have been removed. The advantage of this is in determining a) the proportion of people in each group experiencing difficulty and b) comparing the

actual level of difficulty experienced in each group. As such, 'PHAQ WD total' represents all 20 questions in the functional assessment tool and 'PHAQ WD domain score' represents those questions in the tool within the stated domain.

### *EQ 5D*

The EuroQol (EQ-5D) is a self-reported questionnaire with observer, proxy and telephone versions available in over 50 languages. It is a reliable and validated tool developed by the EuroQol group in 1987 to provide a simple descriptive profile and a single index value for health status.

The EQ-5D consists of 5 domains; mobility, self-care, usual activity, pain, anxiety/depression and has 3 response options per domain question and a VAS general health scale.

Scores are given 1-3; 1 'no problems', 2 'moderate problems', 3 'extreme problems' to create a profile of ability, health or pain status. The EQ VAS records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints 100 represents 'Best imaginable health state' and 0 represents 'Worst imaginable health state'.

Data collected using EQ-5D can be presented in various ways.

1. Presenting results from the descriptive system as a health profile
2. Presenting results of the EQ VAS as a measure of overall self-rated health status
3. Presenting results from the descriptive system as a weighted index

EQ-5D has been demonstrated as being valid, reliable and responsive in numerous studies and in a wide range of conditions including chronic obstructive pulmonary disease, orthopaedics, depression and type 2 diabetes, (Hurst et al 1997, Schrag et al, 2000, Cleland et al 2007)



### *IPAQ (short form)*

The International Physical Activity Questionnaire (IPAQ) is a telephone administered or self-reported questionnaire developed in Geneva in 1998 as an instrument for cross-national monitoring of physical activity and inactivity. It is available in long and short forms. The IPAQ consists of 4 domains: leisure time physical activities, domestic and gardening activities, work-related physical activity and transport related activity. The IPAQ short form asks the client about walking, moderate-intensity activities and vigorous-intensity activities in each domain.

Computation of the total scores requires the summation of the duration and frequency of the activities. Continuous variable indicators are presented as median MET-minutes/week (METS are multiples of the resting metabolic rate, MET-minutes, the multiple of the MET score of an activity by the minutes performed). Categorical variables are presented as Low, moderate and high.

The IPAQ's validity, reliability and responsiveness were demonstrated in a 12 country reliability study which measured the physical activity among 18 to 65 year old adults in diverse settings (Booth, 2000; Craig et al, 2003).

### *MYMOP*

The Measure Yourself Medical Outcome Measure (MYMOP) was developed by Charlotte Paterson in the mid 1990's as a self-reported questionnaire for use in general practice. The approximate time given for completion is 10 minutes. The MYMOP consists of four items, each scored by the client on a seven point scale 1 is 'as good as it could be' and 7 is 'as bad as it could be'.

The first two scales ask the client to describe the two symptoms that they specify as of most importance to them. The third scale describes the activity of daily living that is being disrupted or prevented by the client's condition. The fourth asks the client to rate their general feeling of wellbeing. All ratings are for the previous week. Second and subsequent questionnaires are used to measure change. The wording of the previously chosen items remains unchanged and an optional fifth item is allowed if a new symptom is present. The profile score is calculated as the mean of the scored items.

Construct validity was demonstrated by the correlation between perceived change in condition and MYMOP score and criterion validity by comparison with SF-36 scores (Paterson 1996). Paterson describes the property of responsiveness as including the concept of reproducibility and for evaluative instruments; responsiveness replaces the concept of reliability (Guyatt et al, 1987; Paterson, 1996).

### *FAS*

The Functional Assessment Status Questionnaire (FAS) is an outcome measure developed by the Texas Back Institute in the U.S.A which asks clients their ability to carry out activities of daily living in relation to their pain.

The questionnaire consists of 24 questions based on activities of daily living e.g. personal and domestic activities, transfers and roles. It is scored on a five point scale; No Problems Occasionally a Problem, Frequently a Problem, Constantly a Problem, Can not Perform.

FAS is a tool created for clinical use by therapists in the Texas Back Institute as part of a patient pack, and has no literature available demonstrating validity or reliability (texasback.com, 2008).

### *Mayers' lifestyle Questionnaire*

The Mayers' Lifestyle Questionnaire is a person centred instrument which enables people with problems related to physical disability (version 1) enduring mental health problems (version 2) older people (version 3) to state their quality of life priorities at the beginning of occupational therapy intervention. It was developed by Professor Chris Mayers of York University U.K. in the 1990's and has been translated into Norwegian, Greek, French and German. (Mayers 1995, 1998).

The questionnaire consists of 8 domains addressing issues of independence, daily activity, environment, role, spirituality, occupations and activity, and is scored by clients responding with two or three point scale options.

Clinical utility and face validity have been explored by Mayers, with occupational therapists claiming it a good tool with 70% stating it will be useful with a the majority

of clients. 89.3% of clients stated it included all the areas of their life that are of importance to them (Mayers, 2003).

### *2.7.2 The liver patient group; measuring their responses*

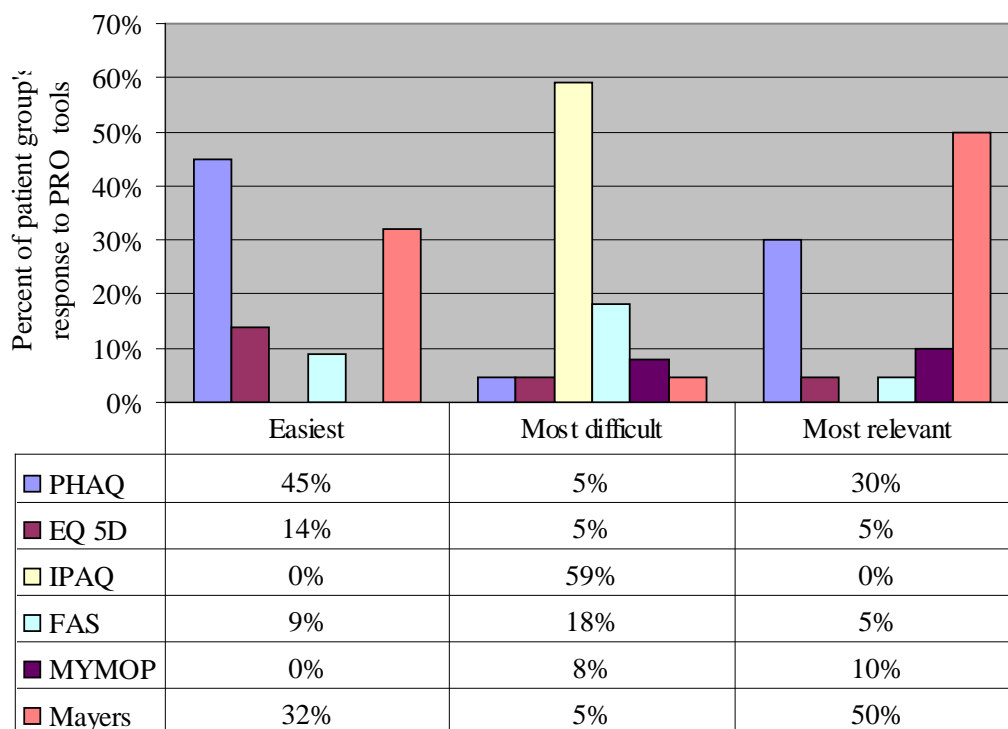
22 participants from a local patient group, LIVErNORTH, who volunteered to give their opinion of the PRO functional assessment tools were asked to mark each questionnaire then answer the following question; 'The questionnaire asked 'all, most, some, not enough, not any' of the questions I wanted it to about my liver disease and my ability to carry out activities.'

Once all the questionnaires were completed the clients were also asked to choose which tool was the 'easiest, most difficult and most relevant' to the question of how chronic liver disease impacted on their function.

The participants were also given the opportunity to add any further comments they had about each questionnaire including what was good about it and what improvements they would make to it.

### *2.7.3 The patient group's responses*

The results demonstrated that the participants found the PHAQ the easiest to complete and the Mayers' Lifestyle questionnaire the most relevant at addressing the question about their ability to carry out the activities which are of importance to them (Figure 6).



*Figure 6. The patient groups response to the PRO functional measurement tools; per cent of patient group's opinion of easiest to complete, most difficult to complete and most relevant to their CLD.*

The qualitative responses further enriched the informing process by giving the researcher insight into the experience of using the tools and of completing the questionnaire pack.

Three themes emerged from these responses.

- 1) The tools do not account for fluctuations in the condition, namely the variability of fatigue.
- 2) Space is needed by the answers to explain responses (especially in light of the variability of their symptoms).
- 3) The process of completing the questionnaires was exhausting both mentally and physically.

The Mayers' lifestyle questionnaire, although chosen as the most relevant by the clients, was also the longest tool in the questionnaire pack. In addition, although comprising a baseline and outcome measure, it is not a quantitative tool. It was for these reasons deemed unsuitable for a postal questionnaire, but useful for future consideration when measuring the impact of occupational therapy intervention in CLD.

The PHAQ was therefore chosen for the postal questionnaire as the second most relevant, but easiest to fill in questionnaire. To address the issues of variability of symptom due to fatigue, a VAS scale asking 'how tired or fatigued have you been in the last week' was added, along with a box providing responses to the following statement 'please tell us anything else about how your condition affects you'.

#### *2.7.4 The assessment tools used in this study*

As a result the PHAQ was the central tool in this study and was used to quantify the function of participants with CLD and participants in the comparator group. In order to determine whether function associated with symptoms commonly found in CLD, PHAQ scores were correlated with the CLD participants' self-reported fatigue measured using FIS, daytime somnolence measured using ESS, concentration and memory measured using CFQ and autonomic dysfunction symptoms i.e. dizziness measured using OGS (described below). The FIS, CFQ, OGS and ESS have been used in several studies with CLD as these symptoms have been shown in previous studies to be commonly seen in those with CLD participants and were therefore chosen for use in this study.

### *FIS*

Fatigue Impact Scale (FIS) measures fatigue experienced by patients, and how the fatigue functionally limits them in their lives and activities. FIS assesses patients' perception of how fatigue affects their cognitive, physical and psychosocial functions. This includes the impact of fatigue on their work, family and financial responsibilities, their mood, their reliance on others, their social activities, and on their quality of life. It is made up of 40 items and subjects must rate how badly affected these items are due to fatigue on a 5-point scale ranging from 0 (no problem) to 4 (extreme problem). The total FIS score is calculated by adding all answers from the 40 questions together. Higher scores indicate greater impact of fatigue (Fisk 1994).

### *CFQ*

The Cognitive Failures Questionnaire (CFQ), a fully validated measure which assesses level of cognitive ability. The CFQ assesses the prevalence of cognitive symptoms, by measuring the frequency of cognitive slips or failures occurring in everyday life. The cognitive abilities assessed in the CFQ include memory, attention, concentration, forgetfulness, word-finding abilities and confusion. The questionnaire consists of 25 items covering failures in perception, memory and motor function and asks patients to rate how often these failures occur, on a 5-point Likert scale of 0 to 4 (0=never, 4=very often). The responses for the 25 questions are added together to obtain the total CFQ score. The higher the score, the greater the cognitive impairment (Broadbent et al, 1982; Wagle et al, 1999; Rast et al, 2009).

### *ESS*

The Epworth Sleepiness Scale (ESS) is a short questionnaire used to quantify people's day time somnolence. The questionnaire asks participants to rate their probability of falling asleep on a scale of 0 to 3 for eight different situations. The scores for the eight questions are added together to obtain a single number. A number in the 0–9 range is considered to be normal while a number in the 10–24 range indicates that expert

medical advice should be sought (Johns, 1991). The tool has been validated in studies researching sleep apnoea (Hardinge et al, 1995).

### *OGS*

The Orthostatic Grading Scale (OGS) is a self-report assessment tool consisting of 5 items which assess the frequency of orthostatic symptoms, severity of orthostatic symptoms, conditions under which orthostatic symptoms occur, activities of daily living and standing time. Patients are asked to grade each item on a scale of 0 to 4, 0 being the lowest and 4 the highest. The total OGS score is calculated from adding up the scores from each item. Higher scores indicate greater severity of autonomic dysfunction (Schrezenmaier et al, 2005).

### *HADS*

Hospital anxiety and Depression Scale (HADS) is a short questionnaire designed to describe affective disorder where participants are asked to complete a questionnaire composed of statements relevant to either generalised anxiety or 'depression'.

Each question is answered on four point (0–3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression.; a score of 0 to 7 for either subscale could be regarded as being in the normal range, a score of 11 or higher indicating probable presence of the mood disorder and a score of 8 to 10 being just suggestive of the presence of the respective state.

The questionnaire is commonplace and there are over 700 studies demonstrating its validity and reliability (Herrman, 1997; Bjelland, 2002; Snaith 2003).

The HAD assessment tool was used in this study to inform the topic guide used when interviewing the participants in Phase two of the study. As such, no HAD data is presented in this study.

## *COPM.*

The Canadian Occupational Performance Measure (COPM) is a standardized PRO measure designed for use by occupational therapists to identify change function over time. The COPM focuses on the three areas of function; self-care, productivity and leisure central to the Canadian Model of Occupational Performance (CMOP) and asks the participant to rate activities of importance to them and to rate the satisfaction with which they can perform them. The measure is repeated over time following Occupational Therapy intervention (Canadian Association of Occupational therapists, 2012).

The COPM is designed for use with people with a variety of disabilities and across all developmental stages. It has been used in many studies with a variety of conditions such as fibromyalgia (Bailey et al, 1999), spinal cord injury (Barclay, 2002) mental health and neurorehabilitation (Chen et al 2002).

People following stroke, those with ankylosing spondylitis and children with disabilities are some of the studies in which the reliability and validity of COPM has been shown (Cup et al , 2003; Cusick et al, 2006; Spadaro et al 2011).

In this study the COPM tool was used as a template to inform and structure the topic guide used when interviewing the participants in Phase two of the study. It was also used to categorise the qualitative data that emerged from the transcripts generated by the interviews namely the performance areas; productivity, self-care and leisure.

## 2.8 Describing the biochemical and histological results used in this study.

In order to explore whether functional ability associated with markers of liver disease severity PHAQ scores were correlated with histological and the biochemical markers, ALT, ALP, ALB, and bilirubin (described below).

### 2.8.1 Alanine transaminase (ALT)

Alanine transaminase (ALT) (biomarker) is an enzyme present in liver cells (hepatocytes). When the hepatocyte is damaged the enzyme leaks into the blood stream



where it can be measured. A high ALT result is therefore suggestive of liver cell damage or disease.

#### 2.8.2 *Alkaline phosphatase (ALP)*

Alkaline phosphatase (ALP) is an enzyme present in cells which line the bile ducts. Like ALT, when these cells are damaged, the enzyme is leaked into the blood stream where it can be measured. High levels of ALP suggest obstructive biliary problems or cholestasis.

#### 2.8.3 *Albumin (ALB)*

Albumin (ALB) is a protein made by the liver. Low levels can indicate reduced synthetic liver function i.e. reduced ability of the liver to synthesis problems including albumin.

#### 2.8.4 *Bilirubin*

Bilirubin is a breakdown product of Haeme (haemoglobin) and is usually carried away in bile. High levels of bilirubin denote problems with liver function.

#### 2.8.5 *Cirrhotic and pre cirrhotic*

Cirrhotic and pre cirrhotic participants were determined by liver biopsy in those participants with PSC, ALD and NAFLD. Not all the participants with PBC had undergone a liver biopsy, and therefore where liver biopsy data was unavailable, differentiation between early and advanced disease was made using a clinical risk predictor (Patanwala et al, 2010)

### 2.9 Measuring function in people with CLD over time

The change in function of the NAFLD and ALD cohorts was measured over time, between 2008 and 2011, to determine if

- a) The function of returning participants had worsened over time
- b) There were any differences in the function of those participants in 2008 who either did or did not return their questionnaire in 2011, or who had died following the survey in 2008.
- c) If liver disease severity factors influenced worsening function over time.

## 2.10 Exploring function in ALD and NAFLD; a qualitative study

Semi-structured interviews were carried out with n=4 ALD, n=4 ALD in alcohol recovery (ALD AB) and n=4 NAFLD participants. The rationale to interview both inpatient ALD and abstinent ALD was to determine similarities and differences in function between those people with ALD who were consuming alcohol and those who had not consumed alcohol during the previous 6 months.. The interviews were semi structured and used elements from PHAQ, HAD, CFQ and COPM to inform the topic guide (Appendix 4). The purpose of the topic guide was to create discussion around those functions highlighted in Phase One as problematic, but also to leave the interview questions broad and open enough to elicit from the participants their living experience of CLD.

## 2.11 Data Analysis

A mixed methods approach was used in this study to both quantify and define the functional difficulties experienced by people with CLD. Phase one used subjective functional measurement tools to demonstrate the significance and prevalence of functional difficulty for people with CLD, followed in phase two by qualitative data that expressed the empirical living experience of people with ALD and NAFLD.

### *2.11.1 Phase One analysis*

The data analysis was performed using Prism Graph pad version 3.0. and SPSS version 19. To classify distribution of data, normal or non-parametric histograms were plotted and interpreted alongside the Kruskal-Wallis Gaussian approximation test. Where data was considered normally distributed, it is summarised with mean and standard deviation (SD). Non-parametric data is described as median with minimum and maximum range.

Because of the non-parametrically distributed nature of the PHAQ data and with cohort numbers exceeding 25 in most categories, the Mann-Whitney test was used in all compared column tests and comparisons are presented as p values. Where multiple comparisons were made, the Kruskal-Wallis test was used and the data presented as p values. The Spearman rho was used to describe data associations alongside the p value.

Contingency tables were used to describe the proportion of participants experiencing functional difficulty and are presented as chi squared ( $\chi^2$ ) and p values. A threshold of

p<0.05 was used to signify statistical significance. Type 1 and Type 2 errors and their potential importance in this study are given in Table 1.

*Table 1 Describing the Type 1 and Type 2 errors and their potential importance.*

	<u>Null hypothesis (<math>H_0</math>) is true:</u> People with CLD <b>do not</b> have functional difficulty	<u>Null hypothesis (<math>H_0</math>) is false</u> People with CLD have functional difficulty
Reject null hypothesis	<b>Type I error</b> False positive  <i>Results show people with CLD have functional difficulty when they don't (causing them worry)</i>	Correct outcome True positive  <i>Results show people with CLD have functional difficulty</i>
Fail to reject null hypothesis	Correct outcome True negative  <i>Results show people with CLD don't have functional difficulty when they do</i>	<b>Type II error</b> False negative  <i>Results show people with CLD don't have functional difficulty</i>

Regression was performed where correlations were made and independent associations were sought. Transformation of the data was required in order to perform linear regression and this achieved using a regression stepwise model. These independent associations are presented as p values.

### *2.11.2 Phase Two analysis*

The data was analysed using 'broad brush' thematic analysis and was carried out manually. This method is useful when analysing data for a nested 'topical survey' qualitative study as it collects all the data together (broad brush) and divides it into categories (Barbour, 2008). This is important when looking at data to give an overview of an issue rather than searching for data saturation (Sandelowski, 1995; Barbour 2008). Priori codes were used to reflect themes pertinent to occupational therapy, namely the performance areas in COPM; productivity, self-care and leisure as well as describing emerging themes, from the transcribed data. A constant comparative method was used to extract rich descriptive data reflecting the daily living experience of people with liver disease, thus creating further codes and sub codes.

## Chapter 3 Results 1: Defining the Functional Difficulty Experienced by People with Chronic Liver Disease

This chapter explores the functional difficulty experienced by people with CLD. It considered the participants with chronic liver disease (CLD) as a whole population in order to ascertain if overall, people with CLD experience worse function in their daily activities than populations without liver disease.

As well as describing the prevalence of functional difficulty experienced by participants with CLD this chapter explores function in terms of overall self-reported ability, and then self-reported ability in the specific domains of dressing, arising, eating, walking, hygiene, reach grip and general activity.

Comparison is made in this chapter between the functional difficulty experienced by those participants with CLD and the age and gender matched comparator group, to define the overall difficulty with function that participants with CLD are experiencing.

### 3.1 Aims

- To establish if people with CLD are experiencing differing function to that of a comparator population
- To explore if people with CLD are experiencing differing difficulty with function to that of a comparator populations because of the symptoms they experience
- To determine whether those participants with CLD with more advanced liver disease stages experience worse function

Table 2 demonstrates the comparability of the CLD group to the comparator group in terms of demographic data. The table also describes the groups in terms of their self-reported ability to function in daily activities using the PHAQ total and PHAQ WD total (participants *with difficulty*, as explained in methods pg. 33) where all those participants who are not experiencing difficulty were removed from the data totals. The purpose of using both the PHAQ and the PHAQ WD data allows for comparison of the level of

difficulty experienced by each group as well as the proportion of participants experiencing difficulty in each group.

The age of the participants at the time of sampling in 2008 with CLD ranged from 20 to 97 years with a mean of 62 years. The age of the participants from the comparator group ranged from 18 to 87 years with a mean of 61 years. No significant difference was found between the groups' ages.

There were 211 female participants in the CLD group which represented 45% of the overall group. There were 48 female participants in the comparator group representing 48% of the participants.

	CLD	Comparators
N=	468	100
Age mean $\pm$ SD	62 $\pm$ 12.7	61 $\pm$ 13.8
% Female	45 (211/469)	48 (48/100)
PHAQ median (range)	12.5 (0-100)	0 (0-93.8)
N of cohort with difficulty (%)	372/469 (79%)	39/100 (39%)
PHAQ WD median (range)	31.3 (3.13-100)	6.3 (3.13-93.8)

*Table 2. The age, gender and functional difficulty (PHAQ totals of whole groups and PHAQ WD totals of those within each group experiencing difficulty) of participants from the CLD and comparator groups.*

### 3.2 Comparing overall functional difficulty experienced by the CLD and comparator groups; the PHAQ total scores

The PHAQ totals were compared to the matched comparator population using a Mann-Whitney test. The total scores of participants with CLD ranged from 0 which represents no functional difficulty to 100 which represents ‘completely unable to do’ (functional tasks). The median score for participants with CLD was 12.5. Overall the CLD participants PHAQ totals data showed significantly worse function than that of the comparator participants ( $p < 0.0001$ ) who’s difficulty, whilst ranging from 0 to 93.8 had a median score of 0 (Figure 7).

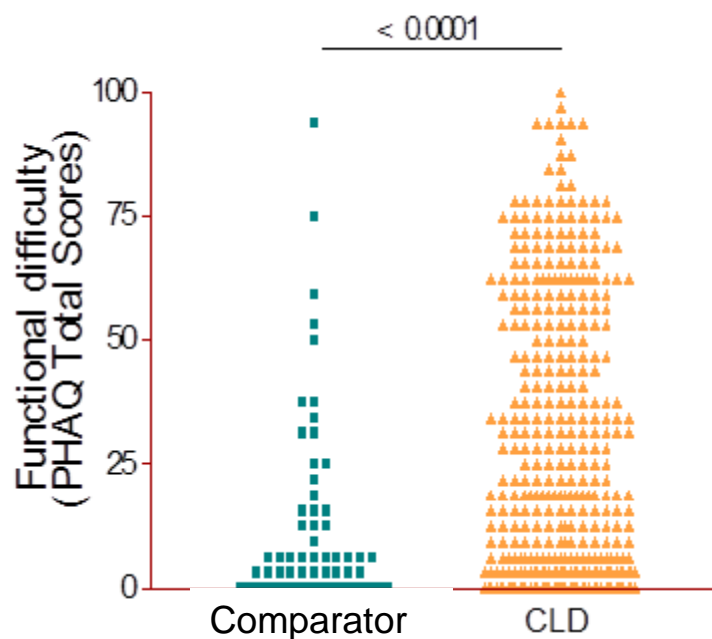


Figure 7. The range and  $p$  value statistical comparison of functional difficulty between CLD participants and comparator participants using their PHAQ total scores.

To determine if those participants who were completely able to function and who reported having no difficulty influenced the PHAQ total findings, all participants in both cohorts scoring zero for all questions in the PHAQ were removed. This created a second data set describing participants whose self-reported scores were therefore PHAQ *with difficulty* (PHAQ WD). This gave insight into, where present, the amount of functional difficulty the participants were experiencing in each group; it also allowed for comparison between the groups and any differences therein without the influence from those participants able to carry out their activities without difficulty.

### 3.3 Comparing overall functional difficulty experienced by the CLD and comparator groups; the PHAQ WD total scores

The same Mann-Whitney analysis used with the PHAQ totals data was carried out using the data where all the participants not experiencing difficulty were removed, leaving only those with difficulty in each cohort (PHAQ WD). This allowed a comparison of the level of difficulty experienced by the two groups. The use of the PHAQ WD data also allowed for comparison of the proportion in each group of people experiencing difficulty.

372 participants with CLD reported difficulty with function representing (372/468) 80% of the CLD group. The difficulty in function of participants with CLD, where they had some difficulty, ranged from 3.13 to 100 and with a median score of 31.3.

39 participants from the comparator group reported experiencing difficulty with function representing (39/100) 39% of the comparator population. The difficulty in function of the comparator group, where they had some difficulty, ranged from 3.125 to 93.8 with a median score of 6.3.

Analysis of the proportion of difficulty in the two groups using Chi Square test showed that there were significantly more participants with difficulty in the CLD cohort [73.91(1)  $p < 0.0001$ ].

Again participants with CLD demonstrated significantly worse function than those participants in the comparator group ( $p < 0.01$ ) when comparing the PHAQ WD total scores (shown visually in Figure 8).

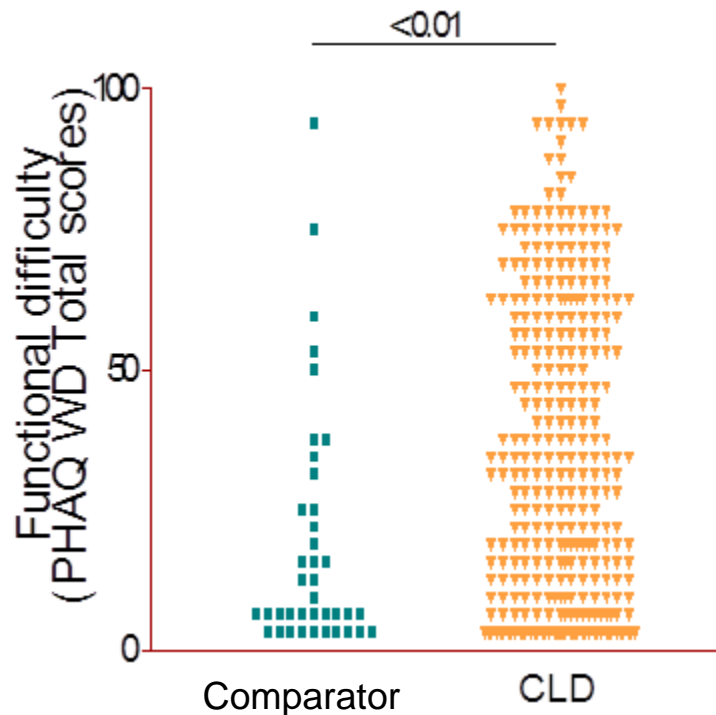


Figure 8. The range and *p* value statistical comparison of functional difficulty as measured by their PHAQ WD scores, between CLD participants and comparator participants.

### 3.4 Describing and comparing as whole groups, the functional difficulty of participants with CLD and comparator participants using domains of function; the PHAQ Domain scores

Within PHAQ there are 8 function domains (as described in methods, pg. 32) namely dressing, arising, eating, walking, hygiene, reach, grip and activity. As significant differences were found between the levels of difficulty experienced between participants with, and without, liver disease in the overall totals, the next step was to consider where across the different domains these difficulties may lie.

Comparisons were therefore made between the CLD participants and comparator group participants using their PHAQ domain scores.

Table 3 describes the median score and range of each group of participants in each of the 8 functional domains. The data is also presented graphically in, 8a) the CLD group; and 8b) the comparator group, to give a visual representation of the data. In the domains of dressing, arising eating, hygiene, reach and activity, the comparator group had participants scoring '0' indicating no difficulty at all and '4' which represents unable to



do. In the domains of walking and grip the range of score was from '0' to '3'. The median value in each of the comparator group domains was '0'.

The participants in the CLD group reported PHAQ domain scores ranging from '0' to '4' in every domain. The median score of the CLD participants was '0' in the domains of dressing, eating, walking, hygiene, reach and grip but reported a median score of '1', indicating that overall there was a little difficulty, in the domains of arising and activity.

Kruskall-Wallis analysis of the data demonstrated that participants with CLD have significantly worse functional difficulty in each of the 8 domains than the matched comparator group when comparing PHAQ domain totals; namely dressing ( $p < 0.0001$ ), arising ( $p < 0.0001$ ), eating ( $p = 0.0010$ ), walking ( $p < 0.0001$ ), hygiene ( $p < 0.0001$ ), reach ( $p < 0.0001$ ), grip ( $p = 0.004$ ), activity ( $p < 0.001$ ) (Table 3).

<i>PHAQ Domains</i>	CLD n=468	comparators n=100	P Value
Dressing median (range)	0 (0-4)	0 (0-4)	<0.0001
Arising median (range)	1 (0-4)	0 (0-4)	<0.0001
Eating median (range)	0 (0-4)	0 (0-4)	0.0010
Walking median (range)	0 (0-4)	0 (0-3)	<0.0001
Hygiene median (range)	0 (0-4)	0 (0-4)	<0.0001
Reach median (range)	0 (0-4)	0 (0-4)	<0.0001
Grip median (range)	0 (0-4)	0 (0-3)	0.0004
Activity median (range)	1 (0-4)	0 (0-4)	<0.0001

*Table 3. The p value statistical comparison of CLD and comparator domain data in the PHAQ Domains; presented as median and range.*

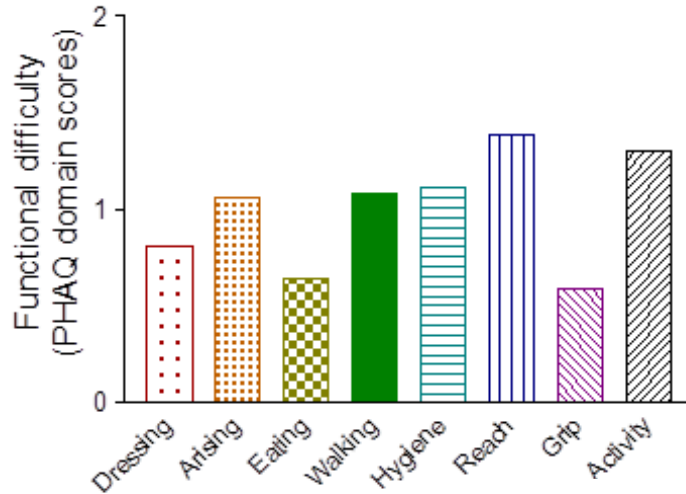


Figure 9a, the CLD group

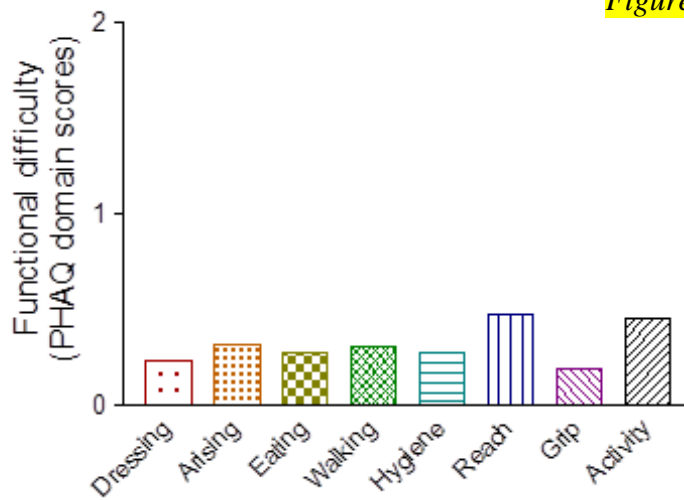


Figure 9b, the comparator group

Figure 9a (CLD) and 8b (comparator) showing the PHAQ domain mean scores in each cohort.

These results demonstrated that as whole populations, people with CLD are experiencing greater functional difficulty in those areas of daily living represented by each PHAQ domain, than the comparator population. What proportion of each population was experiencing functional difficulty and to what level those people were experiencing difficulty required comparison of the domain data where the influence of those participants not experiencing difficulty to be removed, to allow for analysis of the groups where the participants have difficulty; the (PHAQ WD) domain scores.

### 3.5 Describing and comparing the functional difficulty of those participants with CLD and comparator participants experiencing difficulty using domains of function; the PHAQ WD Domain scores

Comparison was then made using the data where all the participants not experiencing difficulty were removed, leaving only those with difficulty in each cohort (PHAQ WD domain scores). This allowed measurement of the proportion in each group of people experiencing difficulty as well as comparison of their level of difficulty in each domain.

#### *3.5.1 Percentage of participants experiencing difficulty in each group*

Table 4 describes the number and percentages of participants in each group who were and who were not experiencing difficulty in each of the 8 domains.

Using contingency tables (Chi squared test) for each domain to compare the numbers of participants experiencing and not experiencing difficulty with function showed that significantly less participants in the comparator group were experiencing difficulty with function in each of the domains ( $p < 0.0001$ ) in all domains except eating where  $p = 0.0002$ ) (Table 3). This indicates that both the incidence of functional difficulty and the level of functional difficulty experienced by participants with CLD are worse than that of the comparator population.

<i>PHAQ WD Domains</i>	CLD N=/469 (% with difficulty)	CLD N=/469 number and ( % with NO difficulty)	Ctrl N=/100 (% with difficulty)	Ctrl N=/100 (% with NO difficulty)	Chi Squared of % experienci g difficulty	P value of % experienci ng difficulty
Dressing	183 (39%)	285 (61%)	12 (12%)	78 (78%)	21.9 (1)	<0.0001
Arising	246 (52.6%)	222 (47.4%)	23 (23%)	77 (77 %)	28.7 (1)	<0.0001
Eating	176 (37.5%)	292 (62.4%)	18 (18%)	82 (82%)	13.99 (1)	0.0002
Walking	208 (44.2%)	260 (55.7%)	14 (14%)	86 (86%)	31.9 (1)	<0.0001
Hygiene	207 (44.2%)	261 (55.8%)	15 (15%)	85 (85%)	29.4 (1)	<0.0001
Reach	270 (57.7%)	198 (42.3%)	24 (24%)	76 (76%)	37.2 (1)	<0.0001
Grip	157 (33.5%)	311 (66.5%)	12 (12%)	88 (88%)	18.2 (1)	<0.0001
Activity	256 (54.7%)	212 (45.3%)	21 (21%)	79 (79%)	37.2 (1)	<0.0001

*Table 4. The percentage of participants in each group experiencing difficulty with function; the chi squared results and p value showing the significance of that difference.*

### 3.5.2 The level of difficulty experienced by participants in each group

The level of functional difficulty experienced by those participants with difficulty (PHAQ WD) in each group, in each domain, was then compared; this was to determine if there was a difference in the levels of difficulty experienced by the participants in each group once the influence of those not having any difficulty were removed. The results are described in Table 5 and show that of those experiencing difficulty, participants with CLD have significantly worse function in the domains of arising ( $p=0.01$ ), and hygiene ( $p=0.04$ ).

<i>PHAQ WD Domains</i>	CLD n=468 experiencing difficulty	comparators n=100 experiencing difficulty	P Value
Dressing median (range)	2 (1-4)	1.5 (1-4)	ns
Arising median (range)	2 (1-4)	1 (1-4)	0.01
Eating median (range)	1 (1-4)	1 (1-4)	ns
Walking median (range)	3 (1-4)	2 (1-3)	ns
Hygiene median (range)	3 (1-4)	1 (1-4)	0.04
Reach median (range)	3 (1-4)	2 (1-4)	ns
Grip median (range)	1 (1-4)	1 (1-3)	ns
Activity median (range)	2 (1-4)	2 (1-4)	ns

*Table 5. The comparison between the PHAQ WD domain scores of participants with CLD and the comparator group, using median and range.*

As shown in Table 4, significantly more participants with CLD are experiencing functional difficulty in each domain when comparing the numbers of participants with difficulty; but this greater incidence of functional difficulty did not result in a globally greater difficulty with function in every domain as it did when comparing the CLD and the comparators as whole groups. Rather, the results showed significantly worse

functional ability of the CLD participants with difficulty to comparator participants with difficulty in the domains of arising ( $p=0.01$ ) and hygiene ( $p=0.04$ ) (Table 5).

In other words, although significantly more participants with CLD are having functional difficulty with the activities represented by the domain categories than the participants in the comparator group, the level of difficulty they are experiencing in the areas of dressing, eating, walking, grip, reach and activity is to the same degree. The exceptions are getting up and down from, or in and out of, chairs, beds (arising) toilets and baths (hygiene) where participants with CLD have significantly more difficulty.

### 3.6 Exploring the relationship between function and liver disease severity for those with CLD

To determine if the participants with CLD's function was related to the severity of their liver disease, the participants PHAQ totals were correlated with their liver function test (LFT) results; namely ALT, ALP, ALB, and bilirubin (described in Methods pg. 41-42) and with cirrhotic and pre cirrhotic disease data.

Details of the participants' age and biochemical markers are given in Table 6.

CLD cohort	
N=	468
Mean Age SD	61.53 ±12.67
PHAQ median (range)	12.5 (0-100)
ALT mean ±SD iu/L	47.6 ± 38.6
ALP mean ±SD iu/L	125.8 ± 117.1
Bilirubin mean ±SD µmol/L	13.1 ± 15.2
ALB mean ±SD iu/L	43.0 ±5.4

*Table 6. The participants with CLD's PHAQ totals, their age and their LFT results.*

No relationship was found between ALP and function for the participants with CLD. This suggests that although these enzymes produced in the liver which in large quantities denotes poor liver function, higher levels of this particular enzyme did not associate with poorer function.

Interestingly however, a low ALB, a raised bilirubin and a raised ALT result did significantly associate with function in those with CLD. Here, a contradiction is present as a low albumin score (suggestive of worse liver disease) correlated with poorer function ( $p=0.007$ ,  $r= -0.13$ ), whereas higher bilirubin ( $p=0.002$ ,  $r= -0.15$ ) and ALT



LFT and PHAQ Total scores ( $p=0.001$ ,  $r= -0.15$ ) scores, also suggestive of worse liver disease, correlated with better function (see Table 7).

CLD PHAQ Totals v LFT results			
	N=	P Value	r
ALB	430	0.007	-0.13
Bilirubin	429	0.002	-0.15
ALP	431	ns	0.04
ALT	431	0.001	-0.15

Table 7. The significant associations between CLD participants' LFT and PHAQ Total scores.

In order to consider liver disease severity in more detail we then went on to explore PHAQ scores in those with cirrhosis compared to those without cirrhosis (Table 8).

CLD $n=397$	Cirrhotic	Pre Cirrhotic	p value
n= (%)	98 (25%)	299 (75%)	
PHAQ Total median (range)	25 (0-93.8)	15.6 (0-100)	0.23 ns

Table 8. The PHAQ Total scores [median and (range)] and p value statistic of those participants with CLD who are pre cirrhotic or cirrhotic.

The disassociation between the biochemical data and its relationship with function may be caused by the grouping together of the liver diseases' data. As such, further exploration of associations between the LFT scores and disease specific PHAQ totals seems prudent. Importantly however, the lack of significant difference in function found when comparing the PHAQ Total scores between those participants who are cirrhotic and those who are pre cirrhotic suggests that disease severity itself does not imply functional difficulty (Table 8).

### 3.7 Exploring the relationship between function and the symptoms experienced by those with CLD

To determine if the participants with CLD's function related to those symptoms previously shown to be associated with liver disease; namely fatigue, day time somnolence, cognitive problems and orthostatic symptoms, participants' PHAQ totals were correlated with the symptom assessment tools, The Fatigue Impact Scale (FIS) to quantify fatigue, the Cognitive Failure Questionnaire (CFQ) to quantify memory and concentration difficulties, the Epworth Somnolence Scale (ESS) to quantify day time somnolence and the Orthostatic Grading Scale (OGS) which quantifies autonomic nervous system symptom burden.

Table 9 describes the age and symptom assessment tool scores of participants with CLD; Table 10 shows the correlation between the CLD participants PHAQ Total score and the age and symptoms assessment tools scores.

CLD cohort	
N=	468
FIS mean $\pm$ SD	50.6 $\pm$ 41.5
CFQ mean $\pm$ SD	65.6 $\pm$ 30.2
ESS mean $\pm$ SD	8.6 $\pm$ 9.2
OGS mean $\pm$ SD	3.6 $\pm$ 4.2
Age mean $\pm$ SD	61.53 $\pm$ 12.67

*Table 9. The participants with CLD's symptoms associated with liver disease scores and age (mean and  $\pm$ SD).*

The data demonstrated that, unsurprisingly, increasing age associated with worsening function ( $p < 0.0001$ ,  $r = 0.19$ ) (Table 10), i.e. the older the participant, the worse their function.

The results also established that the more fatigue the participants were experiencing (quantified using FIS) the worse their function ( $p=0.0001$ ,  $r=0.46$ ). Increasing day-time somnolence quantified using the ESS tool, associated with poor function ( $p<0.0001$ ,  $r=0.29$ ) demonstrating that either sleepiness was affecting the participants ability to function, or that the stress of daily activities was exhausting.

Increased dizziness measured using the Orthostatic Grading Scale (OGS) associated with worsening function ( $p<0.0001$ ,  $r=0.52$ ) suggesting that dizziness is impacting on the participants ability to carry out their activities. This may in part explain why the domains of arising and hygiene, the two domains requiring the greatest sit to stand transfer were the domains where the participants with CLD experienced their most significant difficulty.

Poor memory and concentration, as measured by the CFQ ( $p<0.0001$ ,  $r=0.38$ ) also correlated significantly with greater difficulty in function (Table 10). As the questions within the PHAQ require physical ability, the question of how worsening cognition relates to worsening function may require further investigation.

Chronic Liver Disease PHAQ Totals v Symptoms			
	N=	P Value	r
OGS	361	<0.0001	0.52
CFQ	421	<0.0001	0.38
FIS	367	0.0001	0.5
ESS	240	<0.0001	0.29
AGE	468	<0.0001	0.19

*Table 10. The significant associations between the participants with CLD's PHAQ total scores and their symptom tool results.*

To summarise, this data has shown that those symptoms frequently seen in liver disease; increased fatigue, poor cognition, dizziness and day time somnolence, as well as age, all impact upon people with CLD's ability to function.

The question remained as to which if any of the symptoms or histological data independently associated with function.

### 3.8 Determining independent associations of functional difficulty

Multi linear regression of the PHAQ totals with biochemical results and symptom assessment tool scores was performed to analyse the data in order to distinguish which, if any of the LFT's or symptoms were independently associated with functional difficulty for those participants with CLD; the results of which are given in Table 11.

Adjusted R= 0.233, Model F (5) 16.209, p <0.001					95% Confidence intervals	
	Coefficient	Standard error	t statistic	p	Lower	Upper
Constant	17.418	7.372	2.363	0.019	2.931	31.906
ALT	-0.073	0.042	-1.74	0.08	-0.6	0.009
Bilirubin	-0.158	0.159	-0.99	0.3	-0.5	0.16
ALB	-0.053	0.101	-0.53	0.6	-0.25	0.15
CFQ	0.418	0.059	7.10	<0.0001	0.303	0.534
Age	-0.118	0.092	-1.28	0.2	-0.299	0.063
FIS	0.065	0.035	1.88	0.06	-0.0003	0.133
ESS	-0.187	0.235	-0.79	0.43	-0.649	0.276
OGS	1.519	0.392	8.879	<0.0001	0.749	2.289

*Table 11. The regression analysis of the significant correlations in CLD participants PHAQ total scores and their histological results, symptom tool scores and their age.*

The regression analysis showed that PHAQ was independently associated with CFQ ( $p < 0.001$ ) and OGS ( $p < 0.001$ ), therefore poor concentration or memory difficulties and orthostatic symptoms are indicative of poor function for people with CLD.

### 3.9 Summary

This chapter has shown that people with CLD have significantly worse functional ability than people in comparator groups. There is a greater proportion of people experiencing functional difficulty within the CLD population than in the comparator population and the activities captured in the domains of arising and hygiene are significantly more difficult for people with CLD to perform.

Correlations performed between PHAQ totals and biochemical markers of liver disease and assessment tool scores results of those symptoms frequently seen in people with CLD showed significant relationships with function; worsening cognition and worsening autonomic symptoms being directly and independently linked to poorer function.

What isn't yet clear is the influence each individual disease may have on the collective CLD scores. Further insight into the specific disease cohorts would be beneficial for both highlighting and comparing disease specific functional problems and in investigating the relationship that function has with the symptoms typical to liver disease.

By separating the CLD group into disease specific cohorts, light may also be shed on the disassociated findings of worsening function and the ALT, bilirubin and ALB correlations when compared as a collective CLD group.

## Chapter 4 Results 2: Defining Functional Difficulty in CLD; a Comparison of Chronic Liver Diseases

The previous chapter established that participants with CLD have significantly more difficulty with function than community comparator populations, and that the difficulty is greatest in the domains of arising and hygiene. The previous chapter also demonstrated the significant association of function with those symptoms associated with liver disease; specifically fatigue, cognitive problems, day time somnolence and orthostatic symptoms.

In essence, we now know that people with CLD experience greater difficulty with function than comparator populations, especially with activities that require the gross motor movement needed in the arising and hygiene domains and we can only surmise that this is at least in part, occurring because of the impact of autonomic symptom burden and fatigue. The independent association of autonomic symptom burden with function adds weight to this hypothesis but it remains unclear as to why there is an independent association of poor cognition and increased functional difficulty.

In addition, further information is required to explore whether the functional difficulties experienced by people with CLD are specific to a particular disease or are generic liver disease problems.

This chapter compares functional difficulty across the spectrum of liver diseases within the CLD group previously described, namely; NAFLD, ALD, PBC and PSC to explore whether by separating the data according to specific disease groups, better insight into why those activities in the arising and hygiene domains are of particular difficulty; and whether it is a generic liver disease problem or a disease specific one.

The chapter first describes the cohorts as whole groups using their PHAQ totals and then as groups where those not experiencing any difficulty are removed, leaving only those experiencing difficulty, therefore using the PHAQ WD (*with difficulty*) totals. It then contextualises function in each domain; dressing, arising, eating, walking, hygiene, reach, grip and activity by describing the comparisons between the liver disease groups.



Each liver disease group is then discussed individually describing participants' function and its relationship with their liver disease severity, and their function and its relationship with the data collected for those symptoms typically associated with liver disease.

#### 4.1 Aims

- To describe each disease cohort in terms of gender and age.
- To describe and compare the PHAQ totals of each disease cohort and the PHAQ WD totals of each disease cohort.
- To describe and compare each domain of function using the PHAQ domain scores and the PHAQ WD domain scores of each disease cohort.
- To describe the participants in each disease cohort, comparing function, associations with function and their histological results and associations with function and symptoms typically experienced by those with CLD.

#### 4.1.1 Describing the liver diseases in terms of gender and age

Details regarding age, gender, numbers and disease cohorts are shown in Table 12.

	CLD	NAFLD	ALD	PBC	PSC	CTRL
N=	468	224	107	90	47	100
Age mean ±SD	61.5±12.7	59.3 ±12.8	60.2±9.6	70.0 ±11.6	59.9 ±14.3	60.6 ±13.8
% Female	(211/469) 45	(92/224) 45	(32/107) 30	(84/90) 93	(15/47) 32	(48/100) 48

*Table 12. The number of participants per disease group and the female participant percentage.*

As expected considering the demographics of the PBC, this group had the highest percentage of female participants (93%) as it is typically a disease associated with women over the age of 50 years.

There were 44% of participants in the NAFLD group who were female and 40% in the PSC group. The ALD cohort had the lowest percentage of female participants at 30%.

The comparator group were 48% female.

## 4.2 Age

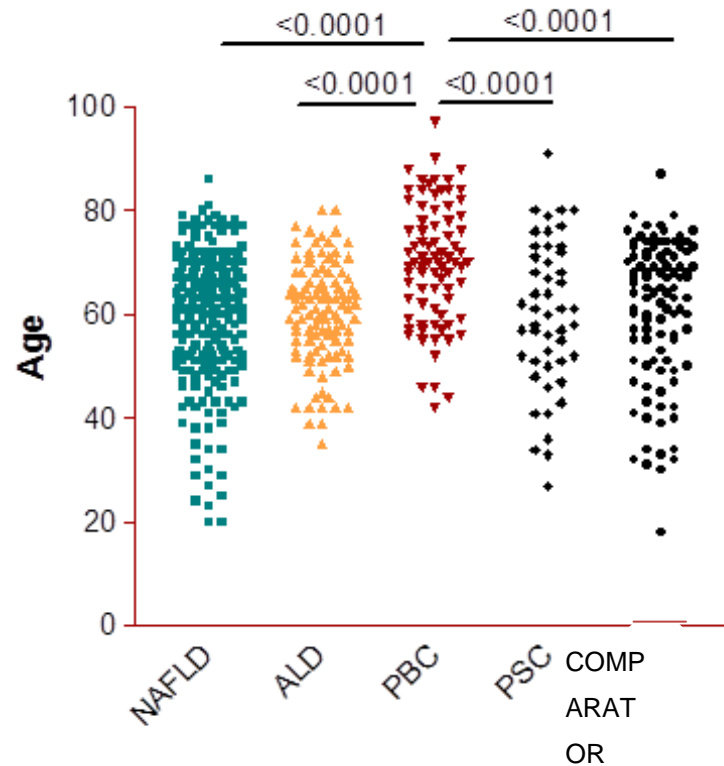


Figure 10. The age spread between the chronic liver disease groups.

Participants with PBC were significantly older than NAFLD, ALD, PSC and comparators ( $P < 0.0001$ ). Ages ranged from 20 years to 86 years in NAFLD, 35 years to 80 years in ALD, 42 years to 97 years in PBC and 21 years to 91 years in PSC (shown visually in Figure 10)

Describing and comparing functional difficulty in each chronic liver disease group

Table 12 describes the functional difficulty experienced by each disease cohort, specifically NAFLD, ALD, PBC and PSC. The community comparator data is also described to provide a comparator.

The results are described as both complete disease groups' functional ability totals (PHAQ) and as disease groups with those participants experiencing difficulty (PHAQ WD).

	NAFLD n=224	ALD n=107	PBC n=90	PSC n=47	comparator n=100
PHAQ Median (range)	12.5 (0-100)	28.1 (0-93.8)	18.6 (0-93.8)	0 (0-75)	0 (0-93.8)
PHAQ WD Median (range)	31.3 (3.13-100)	43.8 (3.13-93.8)	23.4 (3.13-93.8)	15.6 (3.13-8)	6.3 (3.13-93.8)

Table 13. The PHAQ and PHAQ WD totals of each chronic liver disease group.

The participants with ALD had the highest median score of difficulty with function 28.1 (0-93.8). One participant from the NAFLD cohort reported a score of 100 which describes them as being completely unable to function, and each group had participants who reported no difficulty with function. Both the PSC participants and the comparator group had a median score of 0 which represents no difficulty with function. Scatter plots (Figure 11) visually demonstrate the large spread of participants' reported function as whole groups (PHAQ Totals) and as groups where the participants are experiencing difficulty (PHAQ WD Totals) (Figure 12).

Comparisons were analysed using one way ANOVA Kruskal-Wallis test with Dunn's multiple comparison and are presented in Figures 11 and 12.

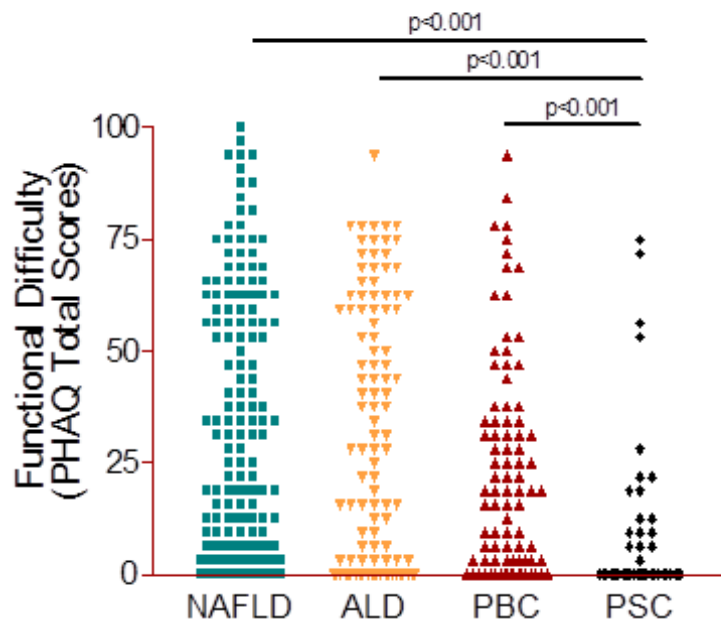


Figure 11. Scatter plots describing the significant difference between the CLD cohorts using their PHAQ totals.

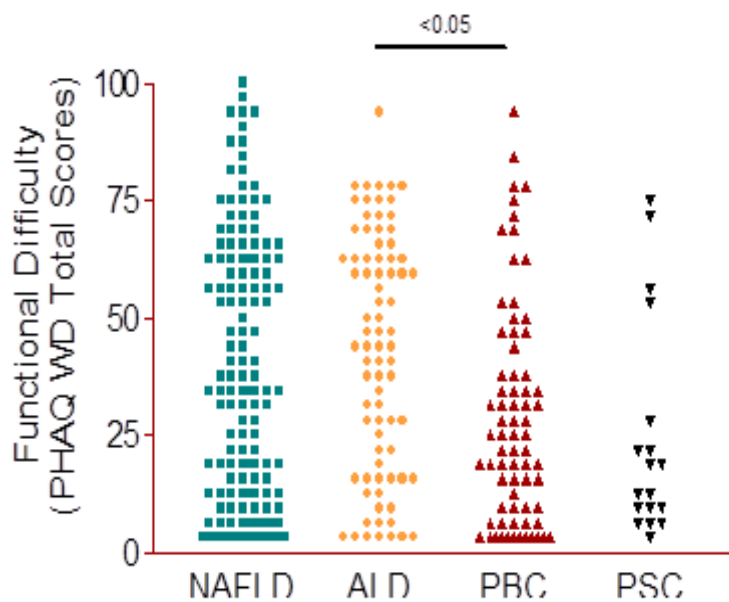


Figure 12. Scatter plots describing the significant difference between the CLD cohorts using their PHAQ WD totals.

NAFLD, ALD and PBC all demonstrated significantly worse function than PSC ( $P < 0.001$ ) when the PHAQ total scores were compared (see Figure 10). When all those participants who reported having no difficulty were removed, leaving only those with difficulty, the comparison of their PHAQ WD totals confirmed that ALD participants

have significantly more difficulty ( $p < 0.05$ ) with function than participants with PBC (Figure 12).

#### 4.2.1 Chi squared analysis of percentage of experienced functional difficulty

A contingency table was used to analyse the percentage of participants in each group experiencing difficulty with function to determine if there was an even spread of difficulty in each disease group.

	NAFLD	ALD	PBC	PSC	chi squared	p value
PHAQ No Diff	(67/224) 30%	(27/107) 25%	(18/90) 20%	(29/47) 62%	27.9 (3)	<0.0001
PHAQ WD <i>n=%</i>	(157/224) 70%	(80/107) 75%	(72/90) 80%	(18/47) 38%		

Table 14. The significant difference between those experiencing and those not experiencing difficulty in the chronic liver disease groups

The chi squared results demonstrated a significant difference in the proportion of participants experiencing difficulty between the liver disease groups [ $\chi^2$  27.9 (3), ( $p < 0.0001$ )] (Table 14), indicating significantly less participants with PSC experience difficulty with function than those with PBC, ALD, or NAFLD.

#### 4.3 Summary

As whole groups, ALD, NAFLD and PBC participants have significantly worse function than those participants with PSC. However, there are significantly less participants with PSC experiencing difficulty with their function. When comparing those participants experiencing difficulty, NAFLD, PBC and PSC are experiencing difficulty to the same degree. Those participants with ALD who have functional difficulty are however, experiencing greater levels of difficulty with their daily function than those with PBC.

This functional difference between those participants with ALD and PBC is interesting as the PBC cohort is significantly older than the ALD cohort, and is predominantly female. In other words, the data tentatively suggests that the older females of the PBC cohort are functioning better than the younger males of the ALD cohort.

#### 4.4 Comparing the chronic liver diseases' functional domain scores

Comparisons were then made between each disease cohort using the PHAQ functional domains of dressing, arising, eating, walking, hygiene, reach, grip and activity.

The data tables describing the PHAQ domain functional difficulty scores are presented for an over view in Table 15 and the percentage of participants with difficulty and their PHAQ WD domain scores are presented in Table 16.

<b><i>PHAQ Domain Scores</i></b>	NAFLD (n=224)	ALD (n=107)	PBC (n=90)	PSC (n=47)	comparator (n=100)
Dressing median (range)	0 (0-4)	1 (0-4)	0 (0-4)	0 (0-3)	0 (0-4)
Arising median (range)	1 (0-4)	1 (0-4)	1 (0-4)	0 (0-4)	0 (0-4)
Eating median (range)	0 (0-4)	0 (0-4)	0 (0-4)	0 (0-2)	0 (0-4)
Walking median (range)	0 (0-4)	1 (0-4)	0 (0-4)	0 (0-4)	0 (0-3)
Hygiene median (range)	0 (0-4)	1 (0-4)	0 (0-4)	0 (0-4)	0 (0-4)
Reach median (range)	1 (0-4)	2 (0-4)	1 (0-4)	1 (0-4)	0 (0-4)
Grip median (range)	0 (0-4)	0 (0-4)	0 (0-4)	0 (0-2)	0 (0-3)
Activity median (range)	1 (0-4)	1 (0-4)	1 (0-4)	0 (0-4)	0 (0-4)

*Table 15. The PHAQ domain scores in each liver disease cohort demonstrated as median (range)*



<b>PHAQ WD Domain Scores</b>	NAFLD [n=%/224]	ALD [n=%/107]	PBC [n=%/90]	PSC [n=%/47]	comparator [n=%/100]
Dressing median (range)	[94] 42% 2 (1-4)	[54] 50.5% 2 (1-4)	[29] 32.2 % 2 (1-4)	[6] 12.8% 1.5 (1-3)	[12] 12% 1 (1-4)
Arising median (range)	[117] 52.2% 2 (1-4)	[67] 62.6% 1 (0-4)	[51] 56.7% 1 (0-4)	[11] 23.4% 0 (0-4)	[23] 23% 0 (0-4)
Eating median (range)	[84] 37.5% 0 (0-4)	[47] 43.9% 0 (0-4)	[39] 43.3% 0 (0-4)	[6] 12.8% 0 (0-2)	[18] 18% 0 (0-4)
Walking median (range)	[96] 42.9% 0 (0-4)	[61] 57% 1 (0-4)	[39] 43.3% 0 (0-4)	[12] 25.5% 0 (0-4)	[14] 14% 0 (0-3)
Hygiene median (range)	[99] 44.2% 0 (0-4)	[58] 54.2% 1 (0-4)	[42] 46.7% 0 (0-4)	[8] 17.02% 0 (0-4)	[15] 15% 0 (0-4)
Reach median (range)	[130] 58% 1 (0-4)	[72] 67.3% 2 (0-4)	[55] 61.1% 1 (0-4)	[13] 27.7% 1 (0-4)	[24] 24% 0 (0-4)
Grip median (range)	[94] 42% 0 (0-4)	[41] 38.3% 0 (0-4)	[35] 38.9% 0 (0-4)	[5] 10.6% 0 (0-2)	[12] 12% 0 (0-3)
Activity median (range)	[113] 50.4% 1 (0-4)	[71] 66.4% 1 (0-4)	[58] 64.4% 1 (0-4)	[14] 29.8 0 (0-4)	[12] 12% 0 (0-4)

*Table 16. The PHAQ WD domain scores [median and (range)] of participants in each liver disease and the [number of] and percentage of participants in each disease experiencing difficulty.*

Each disease group is described and compared in the context of each domain using the domain scores of participants as whole disease groups (PHAQ domain scores) and in each domain where only those experiencing difficulty are included (PHAQ WD domain scores).

Comparison is made using the participants' median and range scores and was analysed using Kruskal-Wallis and Dunn's multiple comparison post test as the data was not normally distributed.

#### 4.4.1 Dressing

4.4.1.1 Comparing the chronic liver diseases' dressing domain scores: Specifically, using questions 1 and 2 of the PHAQ; to get dressed including ability to fasten buttons and tie shoelaces and the ability to shampoo your own hair.

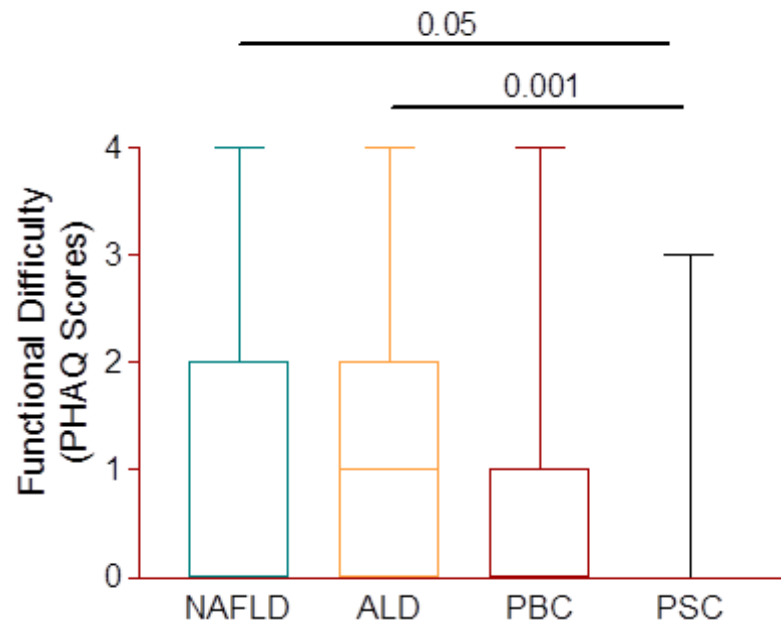


Figure 13. The significant difference between the liver disease groups in the dressing domain using PHAQ domain median and range scores.

Both NAFLD [2 (0-4),  $p < 0.05$ ] and ALD [1 (0-4),  $p < 0.001$ ] participants reported significantly more difficulty with dressing than PSC [0 (0-3)] participants when comparing each disease group overall as shown in Figure 13 above.

This did not remain significantly worse compared to the other disease cohorts when comparing the PHAQ WD domains scores. Indeed, there were no significant differences in function between the disease groups once those not experiencing difficulty were removed.

#### 4.4.1.2 Proportion of participants experiencing difficulty in the dressing domain

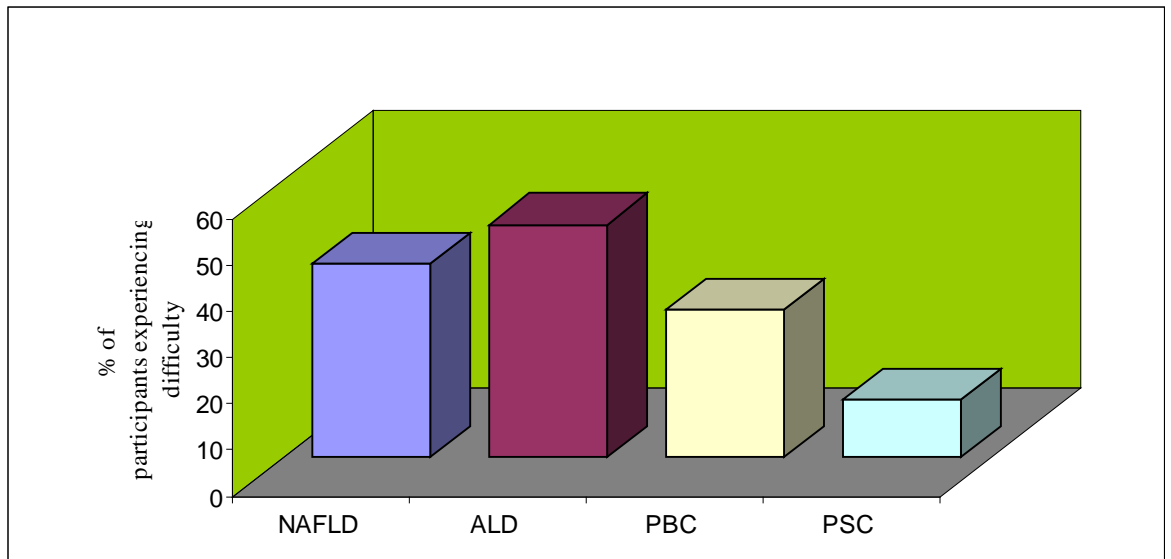


Figure 14. The percentage of participants in each chronic liver disease experiencing difficulty with dressing.

By removing those participants who were not experiencing any difficulty with dressing, comparison could be made between the groups as to the proportion of participants experiencing difficulty in each disease group. NAFLD [94/224 (42%)] and ALD [54/107 (50.5%)] had the highest percentage of participants experiencing difficulty with dressing (Figure 14). Chi squared analysis demonstrated a significant difference in the percentages of experienced difficulty in dressing [ $\chi^2$  15.72 (3),  $p=0.0013$ ] indicating that there are significantly less participants with PSC experiencing difficulty in dressing than in the other liver disease groups (Table 17).

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(94/224) 42%	(54/107) 50.5%	(29/90) 32.2%	(6/47) 12.8%	15.72 (3)	0.0013
NO difficulty	(130/224) 58%	(80/107) 75%	(61/90) 67.8%	(41/47) 87.2%		

*Table 17. The percentage, Chi squared value and p value of participants in each group experiencing difficulty and no difficulty with dressing.*

This demonstrates that although participants with ALD and NAFLD have the largest proportion of participants experiencing difficulty with dressing, their difficulty is to the same degree as that of the participants in the other conditions. PSC participants have significantly less participants experiencing difficulty with the activities in the dressing domain than those in with ALD, NAFLD and PBC, but those who are having difficulty are having it to the same degree.

#### 4.4.2 Arising

##### 4.4.2.1 Comparing the chronic liver diseases' arising domain scores: Specifically using PHAQ questions 3 and 4; to stand straight from an armless chair and to get in and out of bed.

NAFLD [1 (0-4),  $p < 0.01$ ] and ALD [1 (0-4),  $p < 0.001$ ] participants reported significantly more difficulty than participants from the PSC [0 (0-4)] cohort with arising when comparing the overall groups (Figure 15).

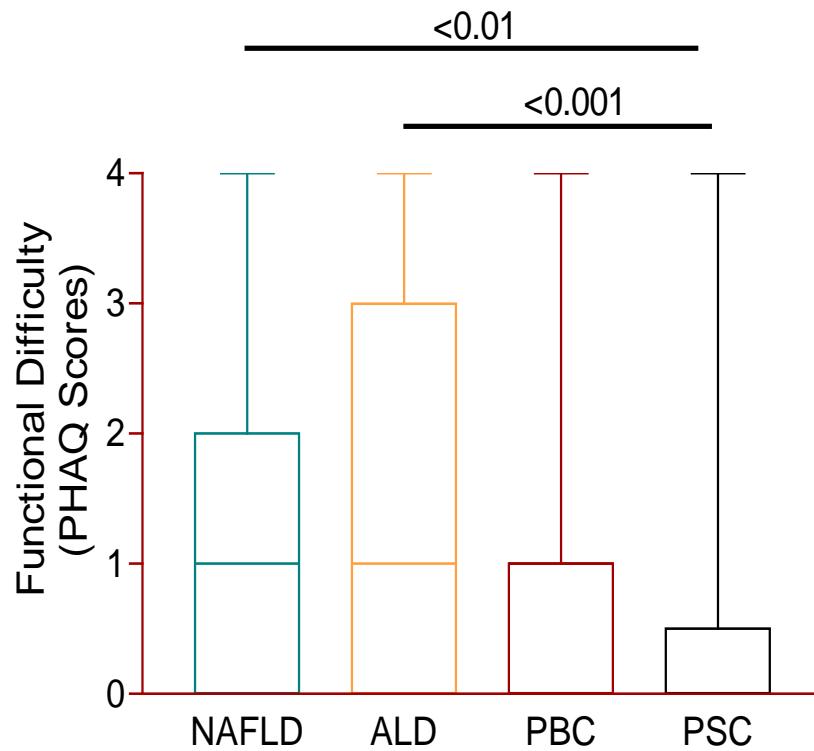
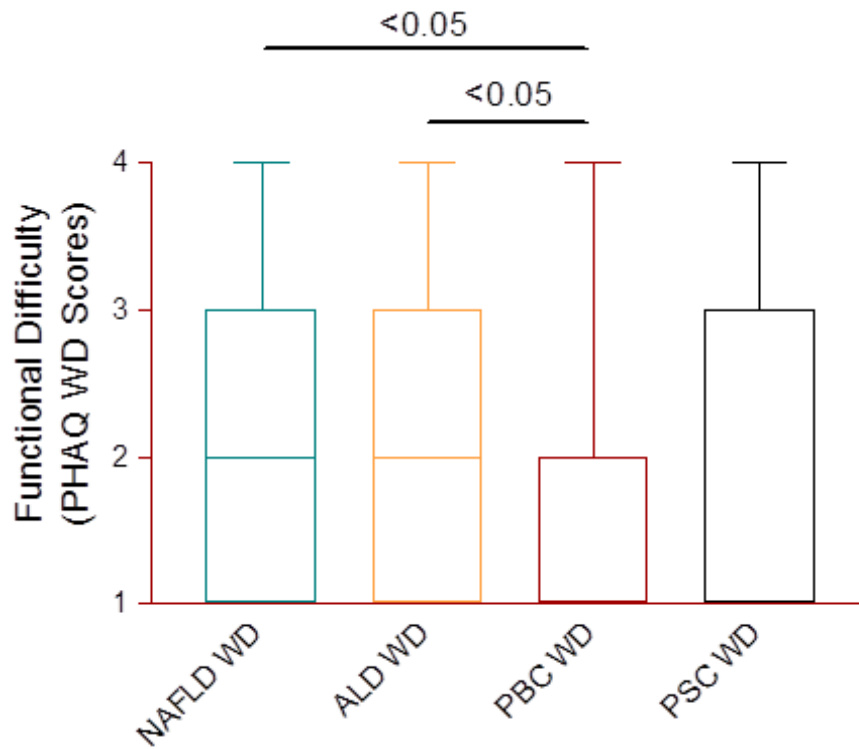


Figure 15. The significant difference between the liver disease groups in the arising domain using the PHAQ domain median and range scores.

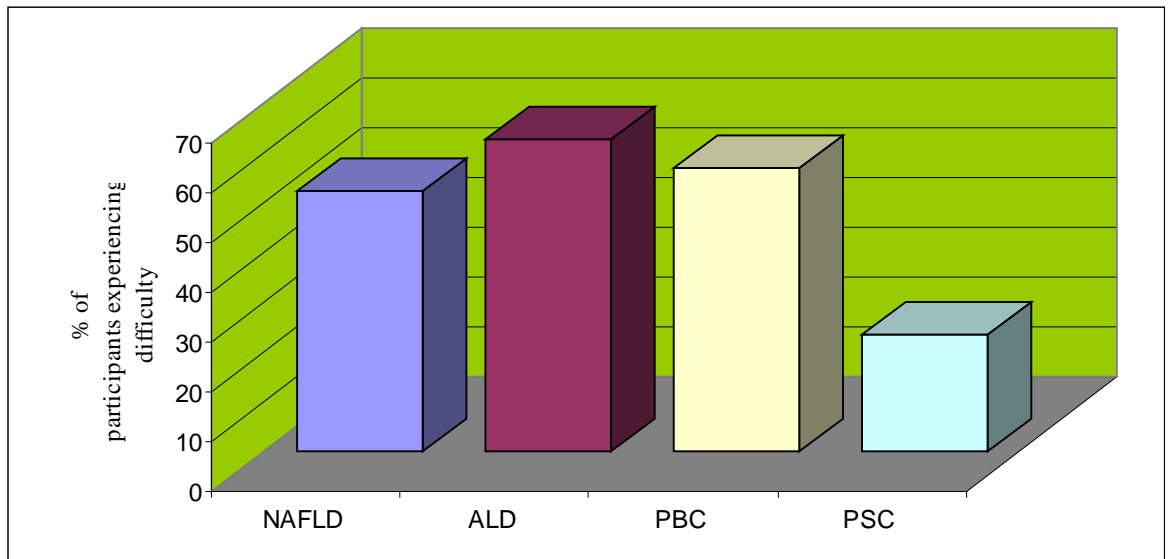


*Figure 16. The significant difference of between the liver disease groups in the arising domain using the PHAQ WD domain median and range scores.*

However, of those participants reporting difficulty with arising, there was a significant difference between the NAFLD ( $p < 0.05$ ) and ALD ( $p < 0.05$ ) participants and those with PBC, but no longer with participants with PSC (Figure 16).

4.4.2.2 *Comparing the proportion of participants experiencing difficulty in the arising domain*

More than half of NAFLD [117/224 (52.2%)], ALD [67/107 (62.6%)] and PBC [51/90 (56.7%)] participants reported having difficulty with arising (Figure 17) compared to only (11/47) 23.4 % of participants with PSC;



*Figure 17. The percentage of difficulty with arising experienced by the liver disease cohorts.*

Chi squared analysis demonstrated a significant difference in the percentages of experienced difficulty in arising [ $\chi^2$  20.98 (3),  $p < 0.001$ ] indicating that there are significantly less participants with PSC experiencing difficulty in arising than the in the other liver disease groups (Table 18).

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(117/224) 52.2%	(67/107) 62.6%	(51/90) 56.7%	(11/47) 23.4%	20.98 (3)	<0.0001
NO difficulty	(107/224) 47.8%	(40/107) 37.4%	(39/90) 43.3%	(36/47) 76.6%		

*Table 18. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with arising.*

The results demonstrate that whilst there are more participants experiencing difficulty with arising in the NAFLD, ALD and PBC groups than those in the PSC group, the difficulty experienced by participants with PSC is to the same degree as those with NAFLD and ALD, both of which are experiencing more difficulty with the activities in the arising domain; getting in and out of bed, standing up and down from chairs, than those participants with PBC.



### 4.4.3 Eating

#### 4.4.3.1 Comparing the chronic liver diseases' eating domain scores: Specifically using PHAQ questions 5, 6 and 7; to cut food using utensils, lift a full glass to your mouth and open a milk carton

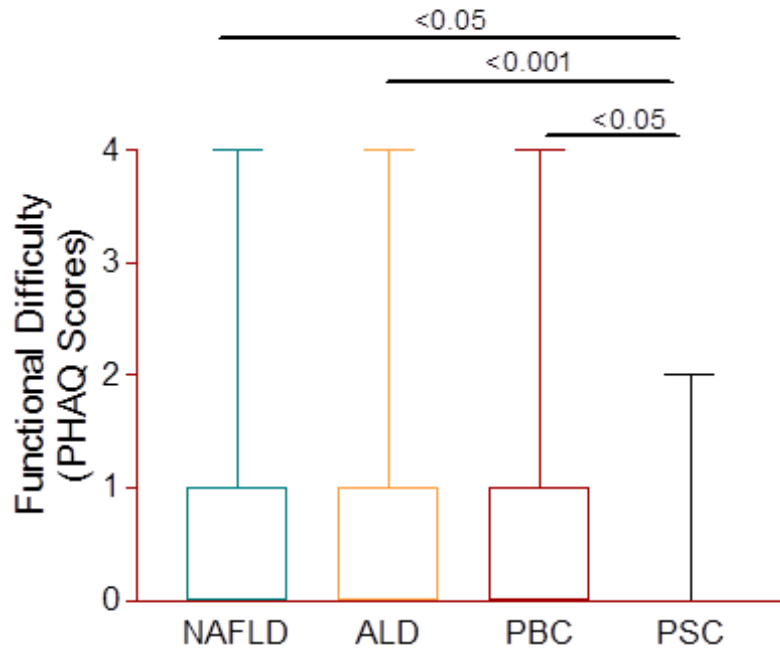


Figure 18. The significant difference of the liver disease groups in the eating domain using the PHAQ domain median and range scores.

NAFLD [0 (0-4), p<0.05], ALD [0 (0-4), p<0.01] and PBC [0 (0-4), p<0.05] all reported experiencing significantly more difficulty with the activities in the eating domain than PSC when groups were compared overall (Figure 18). No significant difference was found between the other groups.

There were no significant differences found between any disease groups when comparing the PHAQ WD eating domain scores.

4.4.3.2 Comparing the proportion of participants experiencing difficulty in the eating domain

ALD [67/107 (43.9%)] and PBC [39/90 (43.3%)] had the highest percentage of participants experiencing difficulty with the activities in the eating domain (Figure 18).

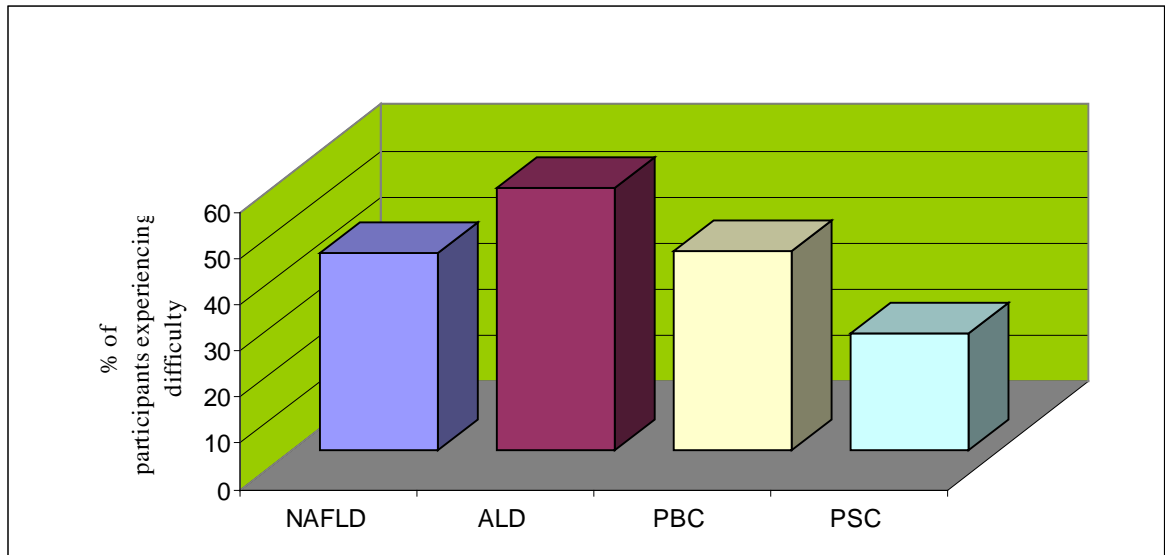


Figure 19. The percentage of difficulty with eating experienced by the liver disease cohorts.

Chi squared analysis showed a significant difference in the percentages of experienced difficulty in dressing [ $\chi^2$  15.44 (3),  $p=0.002$ ] indicating that there are significantly less participants with PSC experiencing difficulty in eating for those in the other liver disease groups (Table 19).

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(84/224) 37.5%	(47/107) 43.9%	(39/90) 43.3%	(6/47) 12.8%	15.44 (3)	0.002
NO difficulty	(140/224) 62.5%	(60/107) 55.1%	(51/90) 66.7%	(41/47) 87.2%		

*Table 19. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with eating.*

This demonstrates that although NAFLD, ALD and PBC participants have a greater proportion of participants experiencing functional difficulty than PSC in the eating domain, the difficulty the participants are experiencing regardless of their disease grouping is to the same degree.

#### 4.4.4 Walking

##### 4.4.4.1 Comparing the chronic liver diseases' walking domain scores: Specifically using PHAQ questions 8 and 9; to walk to the end of your road on the flat and climb five steps.

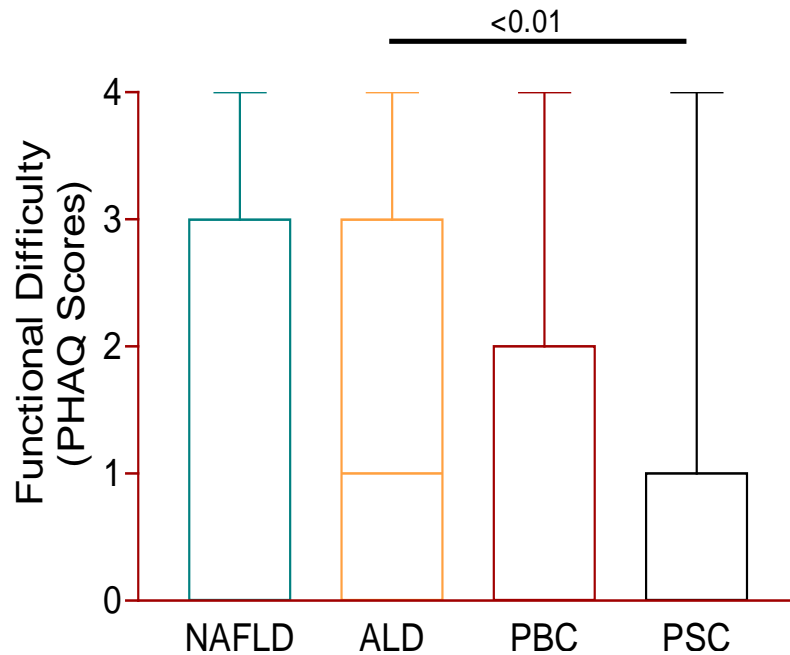


Figure 20. The significant difference between the liver disease groups in the walking domain using the PHAQ domain median and range scores.

ALD [1 (0-4)] participants reported experiencing significantly more difficulty with the activities in the walking domain than PSC [0 (0-4),  $p < 0.001$ ] (Figure 20). No other significant differences were found when comparing the groups overall.

No significant differences were found when comparing the PHAQ WD domain scores.

4.4.4.2 Comparing the proportion of participants experiencing difficulty in the walking domain

The highest percentages of participants experiencing difficulty with the activities in the walking domain were ALD at (61/107) 57% (Figure 21)

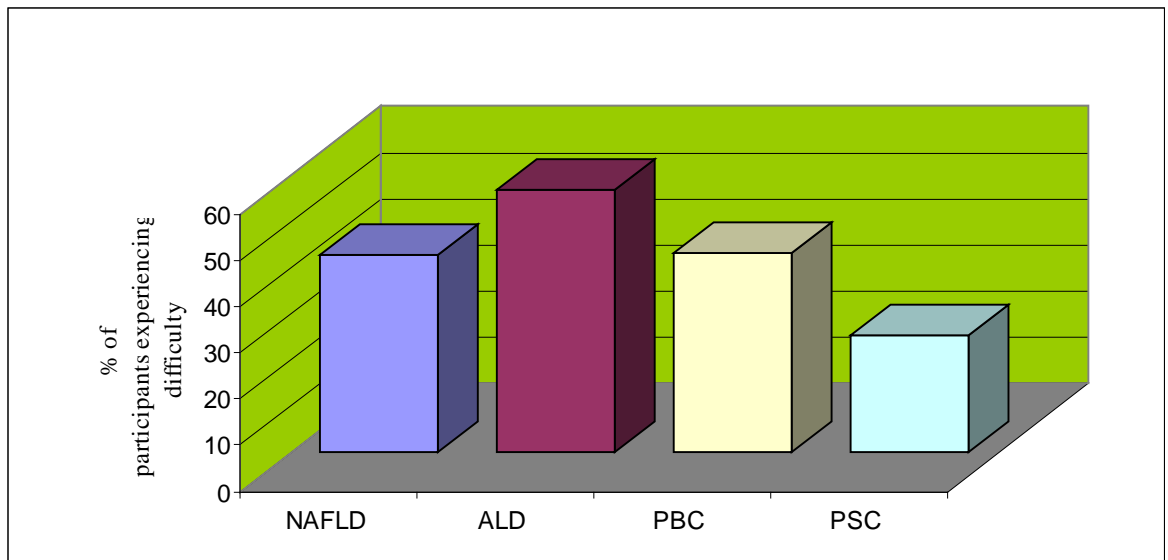


Figure 21. The percentage of difficulty with walking experienced by the liver disease cohorts.

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(96/224) 42.9%	(61/107) 57.0%	(39/90) 43.3%	(12/47) 25.5%	13.92(3)	0.003
NO difficulty	(128/224) 57.1%	(46/107) 43.0%	(51/90) 46.7%	(35/47) 74.5%		

Table 20. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with walking.

Chi squared analysis showed a significant difference in the percentages of experienced difficulty in walking [ $\chi^2$  13.92 (3),  $p=0.003$ ] indicates that there are significantly less participants with PSC experiencing difficulty in walking for those in the other liver disease groups (Table 20).

This demonstrates that although more participants in the ALD cohort are experiencing difficulty with the activities in the walking domain; walking to the end of their road or climbing 5 steps, the level of difficulty experienced is to the same degree in all the disease cohorts. In other words, many more people with ALD are experiencing difficulty with getting around their external environment, but the amount of difficulty is the same for all the participants with liver disease.

#### 4.4.5 Hygiene

4.4.5.1 Comparing the chronic liver diseases' hygiene domain scores: Specifically, using questions 9, 10 and 11 of the PHAQ; to get in and out the bath, off and on the toilet and to dry your body.

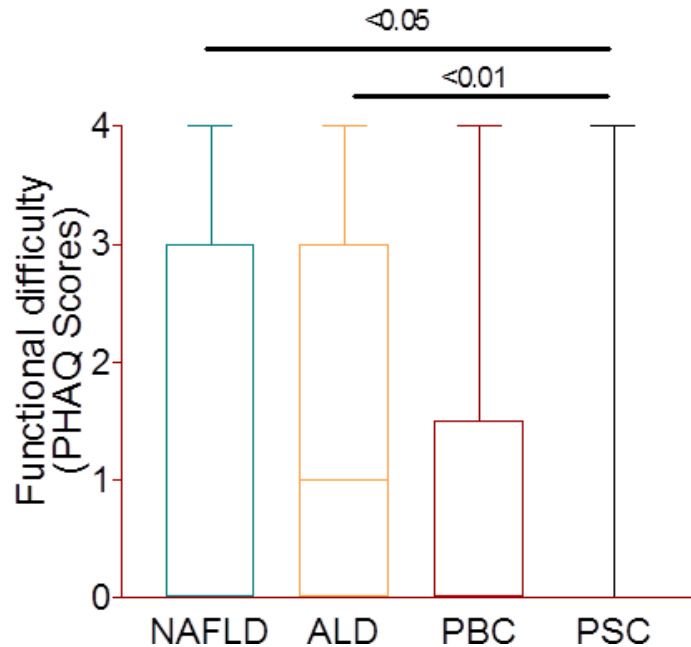


Figure 22. The significant difference of between the liver disease groups in the hygiene domain using the PHAQ domain median and range scores.

NAFLD [0 (0-4),  $p < 0.05$ ] and ALD [1 (0-4),  $p < 0.001$ ] reported experiencing significantly more difficulty with the activities in the hygiene domain than those participants with PSC [0 (0-4)] (Figure 22).

No significant differences were found between the disease cohorts when comparing the PHAQ WD hygiene domain scores.

4.4.5.2 Comparing the proportion of participant's functional difficulty in the hygiene domain

(58/107) 54.2% of ALD participants experienced difficulty with the activities in the hygiene domain compared to (99/224) 44.2% NAFLD, (42/90) 46.7% PBC and (8/47) 12% PSC (Figure 23).

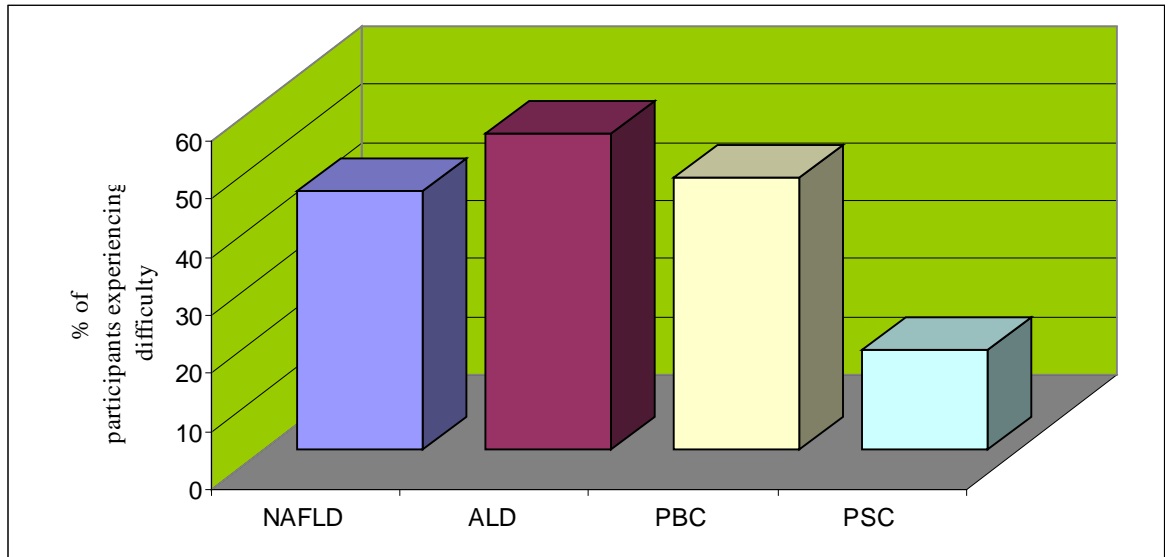


Figure 23. The percentage of difficulty with hygiene experienced by the liver disease cohorts.



CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(99/224) 44.2%	(58/107) 54.2%	(42/90) 46.7%	(8/47) 17.0%	18.64 (3)	0.0003
NO difficulty	(125/224) 55.8%	(49/107) 45.8%	(48/90) 53.3%	(39/47) 83%		

*Table 21. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with hygiene.*

Chi squared analysis showed a significant difference in the percentages of experienced difficulty in hygiene [ $\chi^2$  18.64 (3),  $p=0.0003$ ] and indicates that there are significantly less participants with PSC experiencing difficulty in hygiene than for those in the other liver disease groups (Table 21).

The data demonstrates that more participants with NAFLD and ALD are experiencing problems with hygiene than in the other liver disease groups, however, those participants with liver disease who are experiencing difficulty with the activities in the hygiene domain; getting up and down from the toilet, in and out of the bath and drying their bodies, are experiencing it to the same degree.

#### 4.4.6 Reach

4.4.6.1 Comparing the chronic liver diseases' reach domain scores: Specifically, using questions 13 and 14 of the PHAQ; to reach and retrieve a 5lb object from above you head and to bend down to pick clothes from the floor.

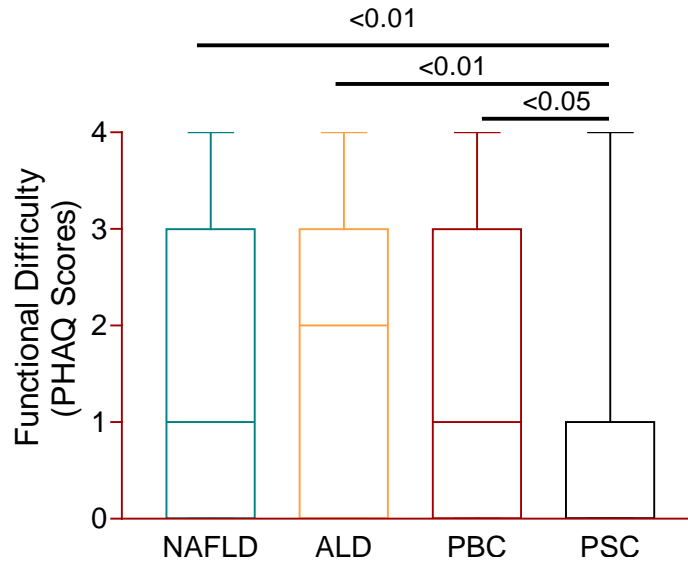


Figure 24. The significant difference between the liver disease groups in the reach domain using the PHAQ domain median and range scores.

NAFLD [1 (0-4),  $p < 0.01$ ], ALD [2 (0-4),  $p < 0.01$ ] and PBC [1 (0-4),  $p < 0.05$ ] participants all reported significantly more difficulty with the activities in the reach domain than PSC (Figure 24).

No significant differences were found between the disease cohorts when comparing the PHAQ WD reach domain scores.

#### 4.4.6.2 Comparing the proportion of participant's functional difficulty in the reach domain

Reach was the domain for both ALD and NAFLD [130/224 (58%)] where the most participants had difficulty in comparison to the other domains.

ALD [72/107 (67.3%)] and PBC [55/90 (61.1%)] experienced the most difficulty with the activities in the reach domain (Figure 25).

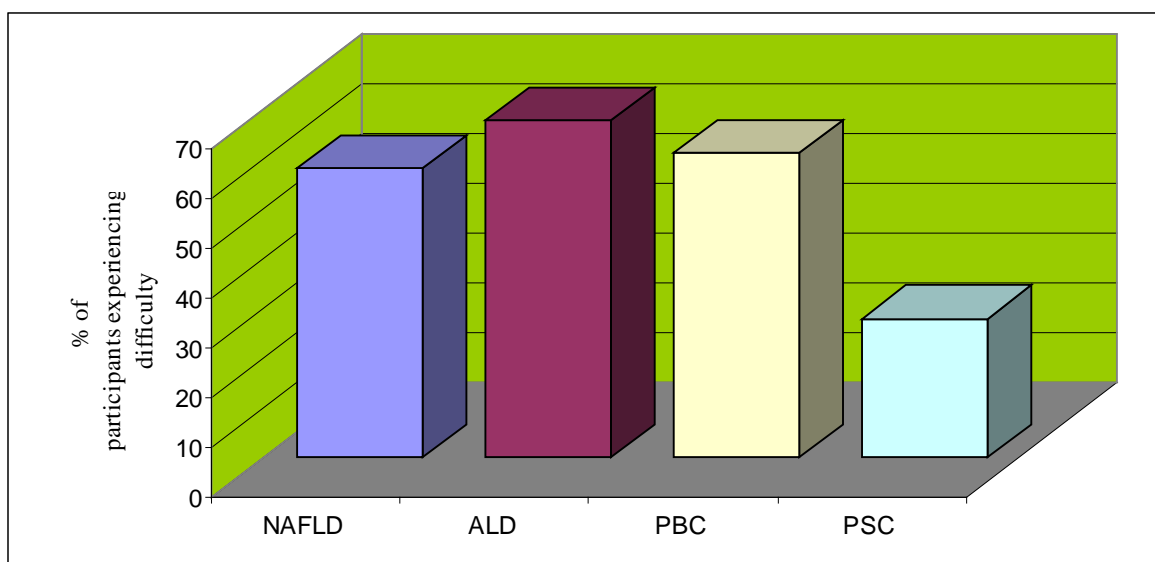


Figure 25. The percentage of difficulty with reach experienced by the liver disease cohorts.

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(130/224) 58%	(72/107) 67.2%	(55/90) 61.1%	(13/47) 27.7%	21.85 (3)	<0.0001
NO difficulty	(94/224) 42%	(35/107) 32.8%	(35/90) 38.9%	(34/47) 72.3%		

*Table 22. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with reach.*

A Chi squared analysis showed a significant difference in the percentages of experienced difficulty in reach [ $\chi^2$  21.85 (3),  $p < 0.0001$ ] indicating that there are significantly less participants with PSC experiencing difficulty in reach for those in the other liver disease groups (Table 22).

The data demonstrates that although more participants with NAFLD, ALD and PBC are experiencing difficulty with reach, the level of difficulty is to the same degree between all the disease cohorts.

#### 4.4.7 Grip

4.4.7.1 Comparing the chronic liver diseases' grip domain scores: Specifically, using questions 16 and 17 of the PHAQ; to open previously opened jars, turn taps on and off and open car doors.

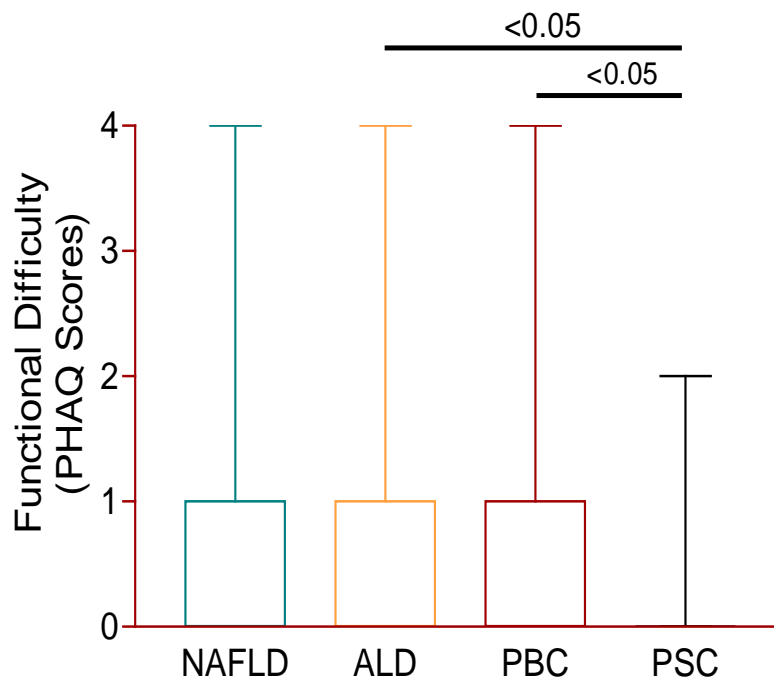


Figure 26. The significant differences between the liver disease groups in the grip domain using the PHAQ domain median and range scores.

ALD [0 (0-4),  $p < 0.05$ ] and PBC [0 (0-4),  $p < 0.05$ ] participants reported experiencing significantly more difficulty with the activities in the grip domain than those participants with PSC [0 (0-2)] (Figure 26).

No significant difference was found when comparing each cohorts PHAQ WD grip domain scores.

#### 4.4.7.2 Comparing the proportion of participants functional difficulty in the grip domain

NAFLD [94/224 (42%)] had the greatest percentage of participants experiencing difficulty with turning taps, opening previously opened jars and opening car doors. ALD [41/107 (38.3%)] and PBC [35/90 (38.9%)] had similar amounts of participants experiencing difficulty and PSC (5/47)10.63% (Figure 27).

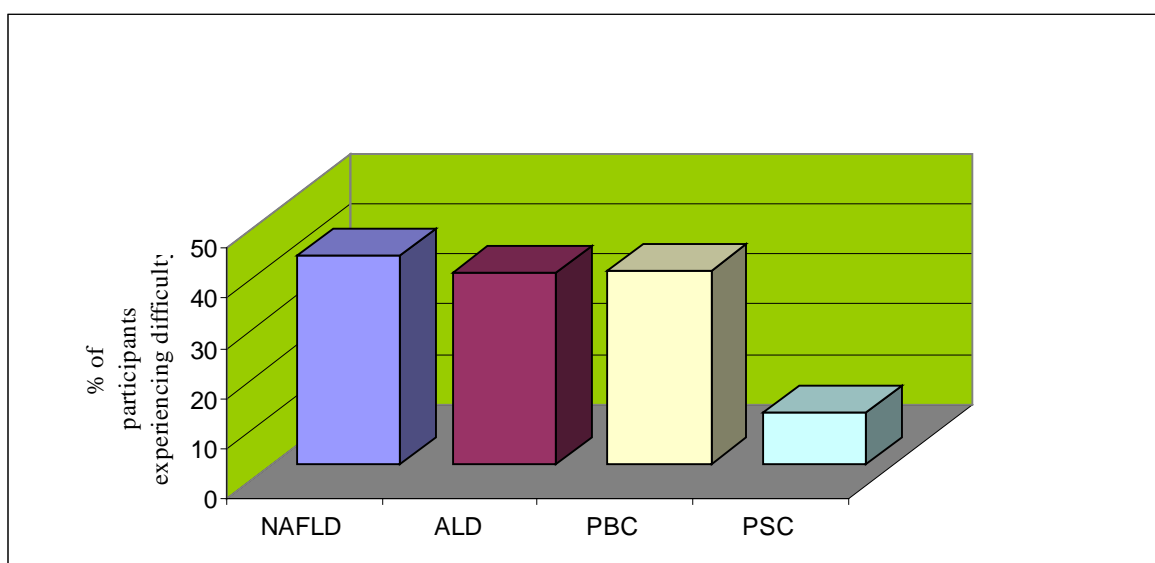


Figure 27. The percentage of difficulty with grip experienced by the liver disease cohorts.

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(94/224) 42.0%	(41/107) 38.3%	(35/90) 38.9%	(5/47) 10.6%	14.39 (3)	0.0024
NO difficulty	(130/224) 58%	(66/107) 61.7%	(55/90) 61.1%	(42/47) 89.4%		

*Table 23 The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with grip.*

Chi squared analysis showed a significant difference in the percentages of experienced difficulty in grip [ $\chi^2$  14.39 (3),  $p=0.002$ ] indicating that there are significantly less participants with PSC experiencing difficulty in grip for those in the other liver disease groups (Table 23).

This demonstrates that although there is greater percentage of ALD, NAFLD and PBC participants experiencing difficulty than those with PSC in the activities of the grip domain, the level of difficulty experienced is to the same degree for all the disease cohorts.

#### 4.4.8 Activity

4.4.8.1 Comparing the chronic liver diseases' activity domain scores: Specifically, using questions 18, 19 and 20 of the PHAQ to get in and out of a car, go shopping; do the gardening and the vacuuming.

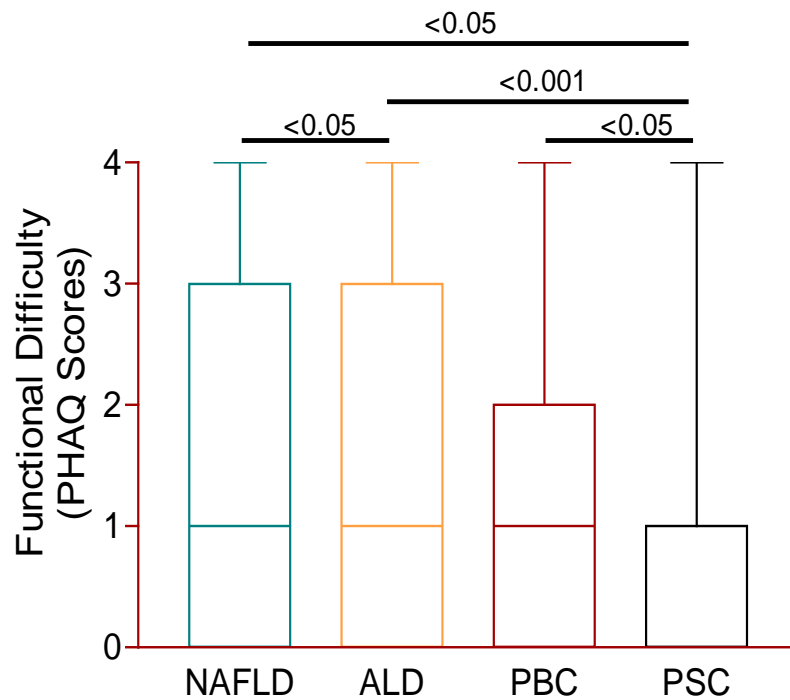
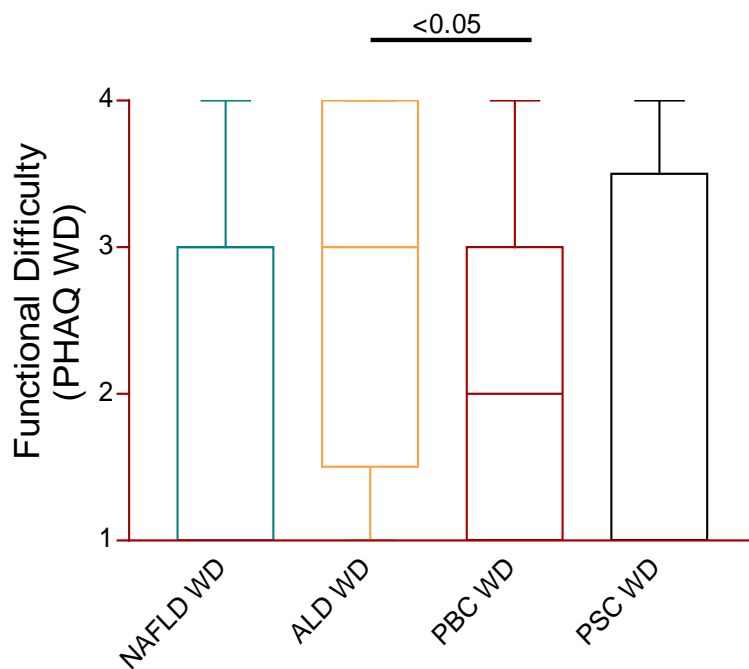


Figure 28. The significant difference between the liver disease groups in the activity domain using the PHAQ domain median and range scores.

ALD [1 (0-4),  $p < 0.001$ ], NAFLD [1 (0-4),  $p < 0.05$ ] and PBC [1 (0-4),  $p < 0.05$ ] participants reported experiencing significantly more difficulty with the tasks in the activity domain than PSC [0 (0-4)] participants (Figure 28). Those with ALD were also found to have significantly more difficulty than those with NAFLD ( $P < 0.05$ ) (Figure 28).





*Figure 29. The significant difference between the liver disease groups in the activity domain using the PHAQ WD domain median and range scores.*

When comparing the activity PHAQ WD domain scores a significant difference was found only between ALD and PBC ( $p < 0.05$ ) (Figure 29).

#### 4.4.8.2 Comparing the proportion of participant's functional difficulty in the activity domain

Activity was the domain for both PBC [58/90 (64.4%)] and PSC [14/47 (29.8%)] where the most participants had difficulty in comparison to the other domains.

ALD [71/107 (66.4%)] participants had the greatest percentage of participants experiencing difficulty with tasks in the activity domain (Figure 30) when compared to the other disease groups.

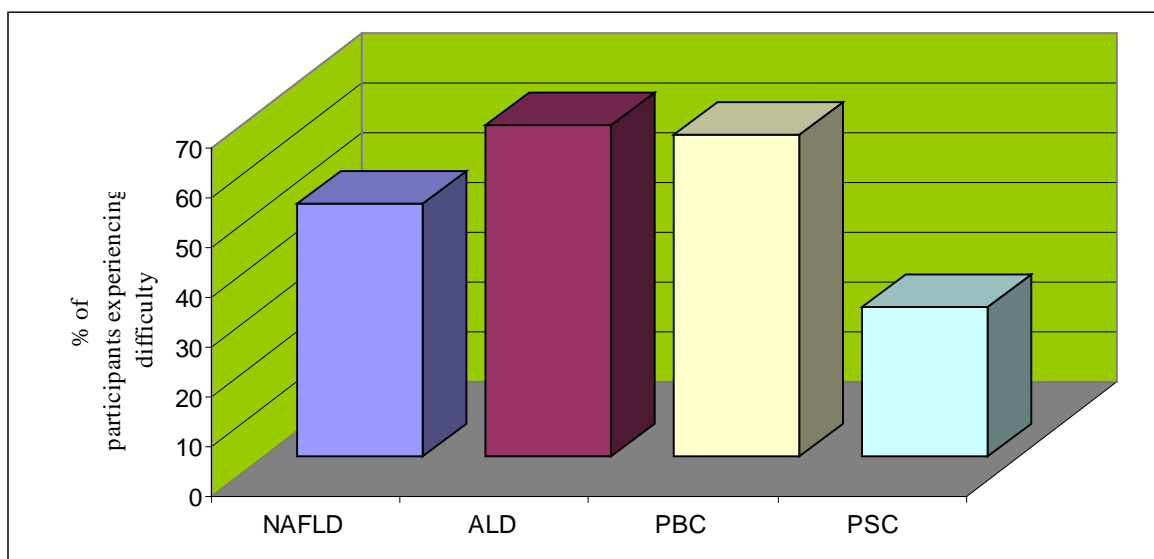


Figure 30. The percentage of difficulty with activity experienced by the liver disease cohorts.

CLD participants	NAFLD	ALD	PBC	PSC	chi squared	p value
WITH difficulty	(113/224) 50.5%	(71/107) 66.4%	(58/90) 64.4%	(14/47) 29.8%	22.72 (3)	<0.0001
NO difficulty	(111/224) 49.5%	(36/107) 33.6%	(32/90) 35.6%	(33/47) 70.2%		

*Table 24. The percentage, Chi squared and p value of participants in each group experiencing difficulty and no difficulty with activity.*

Chi squared analysis showed a significant difference in the percentages of experienced difficulty in activity [ $\chi^2$  22.72 (3),  $p < 0.0001$ ] and indicates that there are significantly less participants with PSC experiencing difficulty in activity for those in the other liver disease groups (Table 24).

ALD, NAFLD and PBC participants had more participants with functional difficulty with the tasks in the activity domain, the level of difficulty between NAFLD, PBC and PSC participants is to the same degree.

Those participants with ALD however have significantly more difficulty with the tasks in the activity domain; shopping, gardening, vacuuming and getting in and out of cars than participants with PBC, even though this is the domain in which the highest percentages of participants with PBC have difficulty (compared to PBC participants' experience in the other domains).

#### 4.5 Summary

	Dressing	Arising	Eating	Walking	Hygiene	Reach	Grip	Activity
Worst function ↓ Best function	NAFLD	ALD	ALD	NAFLD	NAFLD	ALD	NAFLD	ALD
	ALD	NAFLD	NAFLD	ALD	ALD	NAFLD	ALD	NAFLD
	PBC	PSC	PBC	PBC	PSC	PBC	PBC	PBC
	PSC	PBC	PSC	PSC	PBC	PSC	PSC	PSC

Table 25. Ranking the liver disease groups function using the mean value of the PHAQ WD domain scores.

	Dressing	Arising	Eating	Walking	Hygiene	Reach	Grip	Activity
Most % ↓ Least %	ALD	ALD	ALD	ALD	ALD	ALD	NAFLD	ALD
	NAFLD	PBC	PBC	PBC	PBC	PBC	PBC	PBC
	PBC	NAFLD	NAFLD	NAFLD	NAFLD	NAFLD	ALD	NAFLD
	PSC	PSC	PSC	PSC	PSC	PSC	PSC	PSC

Table 26. Ranking the liver disease groups proportion of participants experiencing difficulty

Tables 25 and 26 give an overview of the liver disease groups; the difficulty they are experiencing and the proportion of participants experiencing those functional difficulties. In simple terms participants with ALD have the largest proportion of participants experiencing functional difficulty, demonstrated by their being top of the % leader board in 7 of the 8 domains. Of the ‘worst difficulty’ table, participants with ALD experience the most functional difficulty in 4 out of the 8 domains (arising, eating, reach and activity).

NAFLD participants match the ALD participants when ranked by terms of the level functional difficulty they are experiencing the most difficulty in 4 of the 8 domains (dressing, walking, hygiene and grip), but PBC participants are the liver disease group second to ALD participants when considering the proportion of participants with functional difficulty.

To in part answer the question relating to the domain of hygiene, there are differences in the prevalence of difficulty between the disease cohorts, but the actual difficulty experienced by the participants is to the same degree and is worse, as previously demonstrated in chapter 1, than comparator groups. In other words, all the participants with CLD, regardless of what liver disease they have, are experiencing more difficulty with hygiene than comparator populations. If the participants have NAFLD or ALD, they are more likely to experience that difficulty than if they have PSC. This observation is interesting as both NAFLD and ALD are considered diseases of lifestyle and as such modifiable.

The domain of arising is slightly different. Although established that participants with CLD are experiencing greater prevalence and degree of difficulty than those participants from the comparator group, there is a difference between the liver disease cohorts.

The data shows that if you have PSC you are less likely to have problems with arising than if you have ALD or NAFLD, but if you do have difficulty, it will be to the same degree.

If you have PBC, you are just as likely to have difficulty with arising as those with ALD and NAFLD, but to a lesser degree of difficulty.

Just why those activities are more difficult for participants with CLD required examination of the impact of disease markers and the symptoms associated with liver disease upon function; importantly though, is the recognition that functional problems are not necessarily CLD specific, but that there are significant problems with function for people with CLD across a range of CLD aetiologies.

#### 4.6 Describing each liver disease group; function, liver disease markers and symptoms

##### 4.6.1 *Alcoholic liver disease*

People with ALD had the greatest functional difficulty of the four groups at 28.13 (0-93.75) with 75% (80/107) of participants reporting having 'a little difficulty' or above, taking their median value to 43.75 (3.125-93.75).

The ALD cohort distribution tended towards higher scores in all the domains compared to the other conditions and was significantly higher than PSC in all domains.

ALD participants had significantly worse function than PSC ( $P < 0.0001$ ) in PHAQ total scores but not in PHAQ WD totals.

ALD participants had significantly worse overall function than PBC ( $P < 0.05$ ) when comparing those participants with difficulty (PHAQ WD total).

Correlations between the ALD PHAQ totals and the participant's biochemical data showed no association with ALT, Bilirubin or ALB, therefore these disease severity tests are not a marker of function for people with ALD.

ALP however, was found to have a significant correlation with the PHAQ total for participants with ALD suggesting that the ALD participants with more severe liver damage have worse function ( $P = 0.0431$   $r = 0.2$ ) (Table 27). This is not a strong association and no statistically significant difference was found between the functional difficulty of pre cirrhotic and cirrhotic participants with ALD (Table 28) indicating again that liver disease severity is not an indicator of functional difficulty.

Correlations with the PHAQ totals of participants with ALD and their fatigue, measured using FIS ( $r = 0.4$ ,  $p = 0.0006$ ) their autonomic symptoms measured by OGS ( $r = 0.4$ ,  $p < 0.0001$ ) and their cognitive symptoms measured by CFQ ( $r = 0.4$ ,  $p < 0.0001$ ) scores demonstrated an association between increasing symptom burden and worsening function (Table 27). Interestingly the association with ESS showed that participants with ALD have better function the more day time sleepiness they experience ( $r = -0.25$ ,  $p = 0.003$ ). The age of ALD participants did not associate with PHAQ totals.

ALD PHAQ Totals and their association with LFT's			
	N=	P Value	r
ALT	105	ns	0.025
ALP	105	0.04	0.2
BILIRUBIN	104	ns	-0.004
ALB	105	ns	-0.14
ALD PHAQ Totals and their association with symptoms			
FIS	75	0.0006	0.39
CFQ	104	<0.0001	0.38
ESS	75	0.003	-0.25
OGS	50	<0.0001	0.41
AGE	105	ns	-0.09

*Table 27. The significant associations between the ALD Participants PHAQ totals and their LFT results and symptoms tools scores.*

In order to consider liver disease severity in more detail PHAQ scores in those with cirrhosis were compared to those without cirrhosis (Table 28).

ALD	Cirrhotic	Pre Cirrhotic	p value
n= (%)	62 (65.3%)	33 (34.7%)	
PHAQ Total median (range)	29.7 (0-93.8)	37.5 (0-78.1)	0.96 ns

*Table 28. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic ALD participants.*

The biochemical results and symptom tools results that had correlated significantly with the PHAQ totals were then analysed using a regression model to determine any independent associations.

Adjusted R= 0.19., Model F (4) 7.15, p <0.001 ALD					95% Confidence intervals	
	Coefficient	Standard error	t statistic	p	Lower	Upper
Constant	9.5	5.7	1.7	0.1	-1.8	20.8
CFQ	0.3	0.1	2.3	0.02	0.15	0.6
OGS	1.5	0.7	2.1	0.04	0.16	3.0
ESS	0.7	0.4	1.8	0.68	-0.1	1.4
FIS	0.1	0.1	1.5	0.1	-0.02	0.2

*Table 29. The regression analysis of the significant correlations in ALD participants between their PHAQ total scores and symptom tool scores.*

Of those, higher orthostatic symptoms [OGS (p=0.04)] and cognitive symptoms [CFQ (p=0.02)] were independently associated with higher PHAQ total scores in ALD participants’.



#### 4.6.2 *Non alcoholic fatty liver disease*

Participants with NAFLD demonstrated significantly worse function than those with PSC in all domains except grip, where no significance was noted as previously mentioned.

The participants with NAFLD scored as having worse function than ALD and PBC as whole groups, but were second to ALD once those without difficulty (30% 67/224) had been removed from the data.

NAFLD demonstrated significantly less difficulty with in the activity domain than ALD.

NAFLD participants were the only condition where function correlated significantly with decreased ALT ( $P < 0.0006$ ,  $r = -0.23$ ) and low bilirubin ( $P = 0.04$ ,  $r = -0.14$ ) (Table 29). The bilirubin scores surprisingly suggest that the more liver damage the participant has, the better their function becomes, mirroring the unusual findings when the CLD group as a whole were correlated with their LFT and PHAQ totals. It is important to note however that  $r = -0.14$  is a weak correlation and the results may have been influenced by outlying data. In addition, the significant level of  $p < 0.04$  may have risen due to chance alone.

A scatter plot (Appendix 5) of the ALT correlation demonstrates that whilst some outlying scores may have impacted on the overall correlation result, ALT decreases in line with increased functional difficulty. This can be explained by the tendency for ALT levels to fall in those patients with NAFLD whose disease has progressed to fibrosis.

Again, there was no significant difference in the function of NAFLD participants who were cirrhotic and pre cirrhotic (Table 31), indicating that disease severity does not predict functional difficulty. Further investigation into the participant's histological data would be interesting in explaining these findings.

Lower ALB scores correlated with worsening function ( $P = 0.0059$ ,  $r = -0.1840$ ) showing that poorer liver synthetic function leads to worsening function (Table 30) but as with ALT and bilirubin, this is a weak association and suggest that liver disease markers do not determine worsening function.

Correlations with the PHAQ totals of participants with NAFLD and their FIS ( $r= 0.5$ ,  $p<0.0001$ ) OGS ( $r= 0.5$ ,  $p<0.0001$ ) and CFQ ( $r= 0.4$ ,  $p<0.0001$ ) scores and age ( $r= 0.3$ ,  $p<0.0001$ ) demonstrated an association between increasing symptom burden and age and worsening function (Table 30). Daytime somnolence measured with ESS was not found to correlate significantly with their PHAQ totals.

NAFLD PHAQ Totals and their association with LFT's			
	N=	P Value	r
ALT	223	0.0006	-0.23
ALP	223	ns	0.07
BILI	222	0.0391	-0.14
ALB	223	0.0059	-0.18
NAFLD PHAQ Totals and their association with symptoms			
FIS	172	<0.0001	0.50
CFQ	222	<0.0001	0.43
ESS	81	Ns	0.22
OGS	162	<0.0001	0.46
AGE	224	<0.0001	0.31

*Table 30. The significant associations between the NAFLD Participants PHAQ totals and their LFT results and symptoms tools scores.*

In order to consider liver disease severity in more detail PHAQ scores in those with cirrhosis were compared to those without cirrhosis (Table 30).

<i>NAFLD</i>	Cirrhotic	Pre Cirrhotic	p value
n= (%)	15 (7.9%)	175 (92.1%)	
PHAQ Total median (range)	18.75 (0-75)	12.5 (0-100)	0.31 ns

*Table 31. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic NAFLD participants.*

The LFT results and symptom assessment tools scores that had correlated significantly with the PHAQ totals were then analysed using a regression model to determine any independent associations.

Adjusted to r 0.232., Model $F(6) 16.209, p < 0.001$ NAFLD					95% Confidence intervals	
	Coefficient	Standard error	$t$ statistic	$p$	Lower	Upper
Constant	24.7	23.7	1.0	0.3	-21.98	71.5
CFQ	0.5	0.1	5.4	<0.0001	0.3	0.7
Age	0.14	0.2	3.4	0.001	0.2	0.74
FIS	0.05	0.1	2.6	0.01	0.03	0.2
ALB	0.44	0.4	-2.4	0.02	-1.9	-0.2
BILIRUBIN	0.23	0.3	-2.1	0.04	-1.2	-0.02
OGS	0.54	0.5	1.6	0.1	-0.2	-1.9

*Table 32. The regression analysis of the significant correlations in NAFLD participants between their PHAQ total scores and their histological results, symptom tool scores and their age.*

Of those correlating results, increased cognitive difficulty measured by CFQ ( $p < 0.0001$ ), increasing age ( $p = 0.001$ ), increase fatigue measured by FIS ( $p = 0.01$ ), lower ALB ( $p = 0.02$ ), and lower bilirubin ( $p = 0.04$ ) were independently associated with NAFLD participants' increased PHAQ total scores (Table 32).

#### 4.6.3 *Primary biliary cirrhosis*

Participants with PBC had significantly more difficulty with function than those with PSC ( $P < 0.001$ ) when compared using PHAQ totals but not when comparing PHAQ WD totals; and their difficulty was significantly less than those with ALD when comparing PHAQ WD totals ( $P < 0.05$ ).

PBC demonstrated significantly worse function in the domains of eating, reach, grip ( $P < 0.05$ ) and activity ( $P < 0.05$ ) than PSC, and no significant differences between ALD and NAFLD when comparing PHAQ domain scores. PBC participants had significantly better function ( $p < 0.05$ ) in the domain of arising than ALD participants when comparing PHAQ WD domain scores.

No significant correlations were found between function and LFT's in the PBC cohort. Nor was function influenced by age. No significant difference was found between the functional difficulty of cirrhotic and pre cirrhotic participants (Table 33).

Significant correlations were found however between participants FIS, CFQ and OGS and increased PHAQ scores. This demonstrates that liver disease markers and therefore disease status do not determine the difficulty of function that people with PBC experience. Increased fatigue, poorer cognition and orthostatic symptoms do contribute to those people with PBC's worsening function (Table 33).

PBC PHAQ Totals and their association with LFT's			
	N=	P Value	r
ALT	60	ns	-0.19
ALP	60	ns	-0.15
BILI	60	ns	-0.14
ALB	59	ns	0.06
PBC PHAQ Totals and their association with symptoms			
FIS	74	0.0011	0.37
CFQ	81	<0.0001	0.42
ESS	63	0.008	0.33
OGS	82	<0.0001	0.54
AGE	90	ns	0.21

*Table 33. The significant associations between the PBC Participants' PHAQ totals and their LFT results and symptoms tools scores.*

In order to consider liver disease severity in more detail PHAQ scores in those with cirrhosis were compared to those without cirrhosis (Table 34).

<i>PBC</i>	Cirrhotic	Pre Cirrhotic	p value
n= (%)	16 (26.9%)	49 (73.1%)	
PHAQ Total median (range)	9.34 (0-53.1)	18.6 (0-93.8)	0.5 ns

*Table 34. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic PBC participants.*

The symptom tools that correlated significantly with the PHAQ totals for participants with PBC were then analysed using a regression model to determine if any associated independently.

Adjusted R= 0.36., Model $F(4)$ 13.23, $p < 0.001$ PBC					95% Confidence intervals	
	Coefficient	Standard error	$t$ statistic	$p$	Lower	Upper
Constant	3.4	4.8	0.7	0.5	-6.1	12.8
OGS	3.6	0.7	5.0	<0.0001	2.2	5.0
ESS	-1.7	0.6	-2.7	0.008	-2.9	-0.4
CFQ	0.3	0.1	2.1	0.04	0.01	0.5
FIS	0.1	0.06	1.6	0.1	-0.02	0.2

*Table 35. The regression analysis of the significant correlations in PBC participants between their PHAQ total scores and their symptom tool scores.*

Of those correlating results, CFQ ( $p=0.04$ ), ESS ( $p=0.008$ ), OGS ( $p<0.0001$ ), were independently associated with PBC participants' PHAQ total scores (Table 35). Therefore poorer memory and concentration, daytime somnolence and orthostatic symptoms can all be used as indicators for functional difficulty in people with PBC.

#### 4.6.4 Primary sclerosing cholangitis

Participants with PSC functioned significantly better than those with NAFLD, ALD and PBC as previously mentioned and no significant differences were found in the function of those with PSC and comparators. This is an interesting finding which warrants further study. Possible explanations may be that those with PSC do not have the additional comorbidity of those with NAFLD and ALD through differing lifestyle choice. In the instance of PBC, it may be that those with PSC do not have those comorbidities associated with age.

Significant correlations were found with participants as worsening function was influenced by increased fatigue ( $p < 0.0001$ ) as measured using FIS, poorer cognition ( $p = 0.0003$ ) measured using CFQ and increased orthostatic symptoms ( $p = 0.0001$ ) measured using OGS. Increased age also significantly associated with worsening function.

Participants with PSC's LFT scores were not found to have a significant correlation with increased PHAQ totals, nor was there a significant difference in the function of those participants who were cirrhotic with those pre cirrhotic (Table 36), suggesting that the disease severity does not determine ability to function; but fatigue, orthostatic symptoms and poorer memory and concentration are all indicators of worsening function (Table 37).

<i>PSC</i>	Cirrhotic	Pre Cirrhotic	p value
n= (%)	5	42	
PHAQ Total median (range)	12.5 (0-71.9)	0 (0-100)	0.34 ns

*Table 36. The number, percentage and PHAQ totals scores [median and (range)] of cirrhotic and pre cirrhotic PSC participants.*



PSC PHAQ Totals and their association with LFT's			
	N=	P Value	r
ALT	43	ns	-0.12
ALP	43	ns	0.07
BILI	43	ns	-0.25
ALB	43	ns	-0.12
PSC PHAQ Totals and their association with symptoms			
FIS	46	<0.0001	0.55
CFQ	46	0.0003	0.51
ESS	46	ns	0,25
OGS	47	<0.0001	0.53
AGE	47	0.0237	0.33

*Table 37. The significant associations between the PSC Participants' PHAQ totals and their LFT results and symptoms tools scores.*

The symptom tools that correlated significantly with the PHAQ totals were then analysed using a regression model to determine if any associated independently.

Adjusted R=0.36, Model $F(2) 13.7, p < 0.001$ PSC					95% Confidence intervals	
	Coefficient	Standard error	$t$ statistic	$p$	Lower	Upper
Constant	-18.506	9.7	-1.9	0.06	-37.99	1.0
FIS	0.4	0.1	4.8	<0.0001	0.3	0.6
Age	0.3	0.2	1.9	0.7	-0.02	0.6

*Table 38. The regression analysis of the significant correlations in ALD participants between their PHAQ total scores, their FIS symptom tool scores and their age.*

The regression analysis showed only fatigue, measured by FIS ( $p < 0.0001$ ) independently associated with PSC participants' PHAQ total scores (Table 38).

#### 4.7 Summary

Table 39 summarises the correlating and independently associating LFT results and symptom measurement tool scores with the PHAQ totals in each liver disease group.

	ALD	NAFLD	PBC	PSC
ALT		✓		
ALP	✓			
Bilirubin		✓★		
ALB		✓★		
FIS	✓	✓★	✓	✓★
CFQ	✓★	✓★	✓★	✓
ESS	✓		✓★	
OGS	✓★	✓	✓★	✓
Age		✓		✓

*Table 39. The LFT results and symptom tools which correlated with PHAQ totals (✓) and those independently associated with the PHAQ Totals (★) in each disease group.*

Although some associations were present between participants LFT results and their PHAQ total scores in ALD and NAFLD, the absence of significant differences between the cirrhotic and pre cirrhotic participants in each disease group shows that disease severity can not determine functional difficulty in people with CLD. The independent associations of low bilirubin and low ALB with worsening function in the NAFLD participant group requires further investigation.

There are significant correlations with the symptoms associated with liver disease. In each disease group functional difficulty relates to poorer memory and concentration, increased fatigue and increased orthostatic symptoms. Increasing age correlates with functional difficulty for both NAFLD and PSC participants. Interestingly, day time somnolence associates with poorer functioning in PBC participants and improved function in ALD participants.

Cognition independently associates with worsening function for participants with ALD, NAFLD and PBC. Fatigue independently associates with worsening function in participants with NAFLD and PSC. Increased orthostatic symptoms independently associates with worsening function in ALD and PBC.

So, participants with ALD have a greater likelihood of experiencing difficulty with their function than the other liver disease groups and this is due to the combined impact of their ALP markers, increased fatigue, cognitive difficulty and increased orthostatic symptoms. High scores from either the OGS or CFQ would indicate poor function for people with ALD.

NAFLD participants are experiencing increased difficulty with their function due in part to the combined effects of low bilirubin and low ALB markers, increased fatigue, increased cognitive difficulty, increased orthostatic symptoms and increasing age. The independent use of participants ALB and Bilirubin results, and high CFQ and FIS scores would indicate poor function in people with NAFLD.

Fatigue, poor cognitive function, day time somnolence and increased orthostatic symptoms are related to the increased difficulty in function of people with PBC. Of those, fatigue as measured by FIS is the only symptom tool not to associate independently with poor function. A high score in OGS, CFQ and ESS would all indicate poor function in people with PBC.

Fatigue measured by FIS was the only independent indicator of increased functional difficulty for people with PSC. Other association which when combined play a role in functional difficulty for people with PSC are worsening cognition, increased orthostatic symptoms and increasing age.

## Chapter 5 Results 3: Does function alter over time? A three year follow up study of functional difficulty in NAFLD and ALD.

The findings from the previous results chapters 1 and 2 demonstrated that participants with CLD experience more difficulty with function than comparator groups, particularly in gross motor transfers; that ALD and NAFLD participants reported greater levels of functional difficulty than participants with PBC and PSC, and that a greater proportion of ALD and PBC participants experience functional difficulty than NAFLD and PSC participants.

In view of these findings, the question was raised as to whether the participants' with the greatest levels of functional difficulty, specifically participants with NAFLD and those with ALD's ability to function alters over time, and if the proportion of participants experiencing functional difficulty in those disease groups increases over time.

This chapter explores those changes by comparing the PHAQ scores of participants with NAFLD and ALD over a three year period. To do this a repeat PHAQ functional assessment tool was sent out by post in 2011 to all those participants who responded in 2008.

### 5.1 Aims

- To describe the participants functional data from 2008 and 2011
- To compare the participants functional data from 2008 and 2011
- To describe and compare data over time for participants with ALD
- To describe and compare data over time for participants with NAFLD

## 5.2 Comparing the participant's data; 2008 to 2011

Comparisons were firstly made between those participants who had returned the PHAQ questionnaire in 2011 and those who had not, to determine

- i) If there were differences in the groups which may suggest reasons for not returning the questionnaire
- ii) If those returning participants were different to, or representative of, the 2008 participants as a whole

231 of the 331 (69.8%) participants who took part in 2008 returned a PHAQ questionnaire in 2011. Of these, 162 were participants with NAFLD. This represented (162/224) 72.3% of the NAFLD participants from 2008. 69 participants with ALD returned the tools in 2011 which represented (69/107) 64.5% of the participants with ALD from 2008.

20 participants had died since 2008, 7 (7/224, 3%) NAFLD participants and 12 (12/107, 12.2%) participants with ALD (Figure 30).

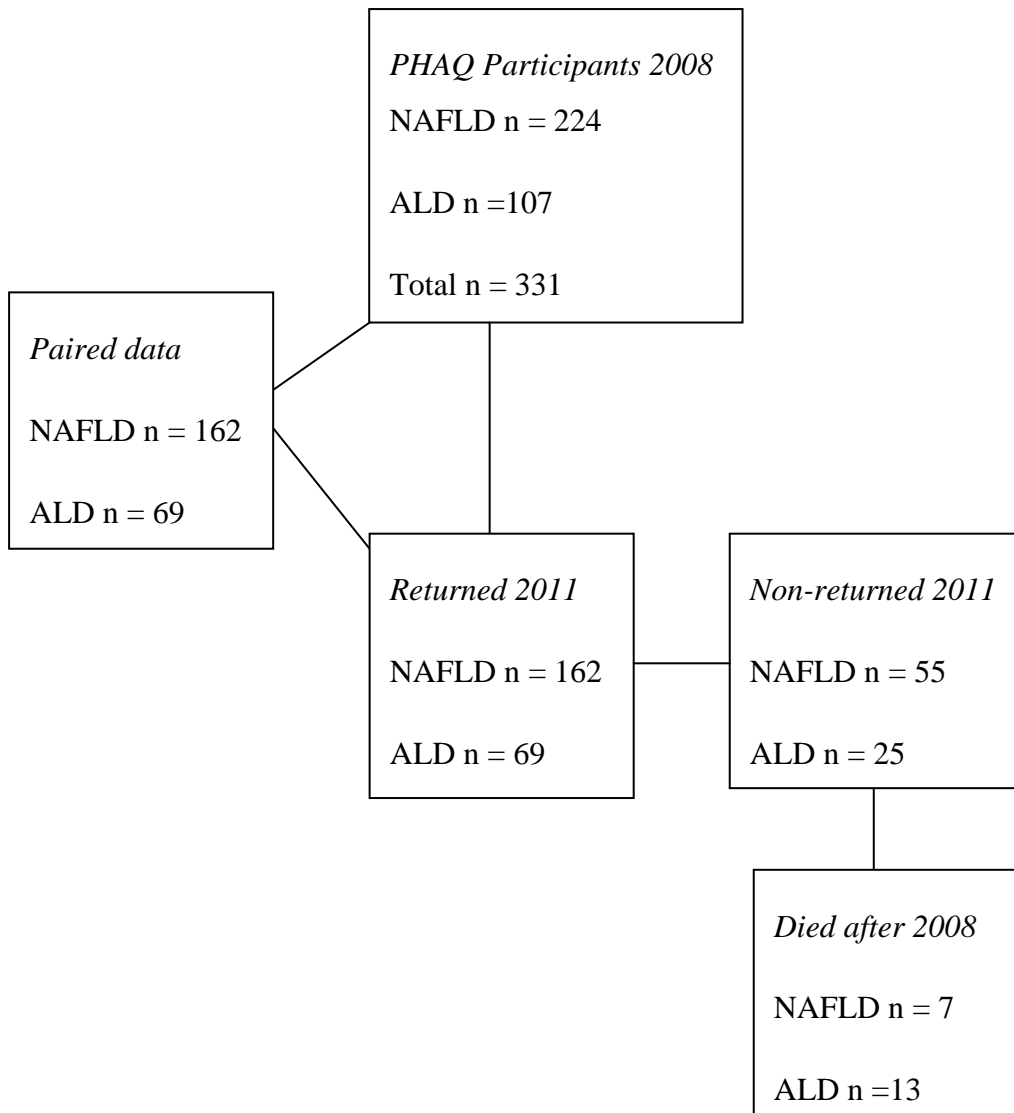


Figure 31. The number of participants who returned or did not return the PHAQ in 2011.

	NAFLD and ALD participant results from 2008 who returned PHAQ in 2011	NAFLD and ALD participant results from 2008 who did not return PHAQ in 2011	NAFLD and ALD participants who returned PHAQ in 2008 but who had died by 2011
N=	231	80	20
Age mean $\pm$ SD	60 $\pm$ 11.79	59 $\pm$ 10.56	66 $\pm$ 11.78
PHAQ Total median (range)	15.6 (0-93.8)	14.06 (0-96.9)	40.6 (0-100)
N=% PHAQ WD	70.1 (162/231)	75.7 (53/80)	95 (19/20)
PHAQ WD Total median (range)	34.4 (3.1-93.6)	46.9 (3.1-96.9)	43.75 (93.1-100)
% female	36 (84/231)	42 (34/80)	35 (7/20)

*Table 40. The PHAQ and PHAQ WD 2008 scores of participants who returned, did not return, or could not return, their PHAQ questionnaires in 2011.*

The data from the NAFLD and ALD group combined was analysed using a t-test to determine any differences between those participants who did and who did not return their questionnaires in 2011. No significant differences were found between the 2008 PHAQ totals of participants who returned their questionnaire [15.6 (0-93.8)] in 2011 and participants who did not return their questionnaires in 2011 [14.06 (0-96.9)] (Table 39). This demonstrates that the participants who returned their questionnaires in 2011 are representative of the CLD group as a whole.

A significant difference ( $p=0.02$ ) occurred when comparing the functional difficulty of NAFLD and ALD combined, with those participants who are alive [15.6 (0-96.9)] and those who died [40.6 (0-100)] following investigation in 2008 (Table 40). This demonstrated that those people who died had worse functioning than their disease peers when invited to complete the PHAQ in 2008.



5.3 Describing the PHAQ and PHAQ WD total data scores; comparison over time

The PHAQ data collected from the 2011 investigation was scored and matched person to person with the PHAQ data of 2008. The demographic details of those participants whose data was paired is presented in Table 41 along with their PHAQ and PHAQ WD total scores from 2008 and 2011.

<i>Paired NAFLD and ALD participant scores 2008 and 2011</i>	NAFLD and ALD participant results from 2008	NAFLD and ALD participant results from 2011
N=	231	231
Age mean $\pm$ SD	60 $\pm$ 11.79	63 $\pm$ 11.78
PHAQ Total median (range)	15.63 (0-93.8)	18.75 (0-90.6)
N=% PHAQ WD	70.1% (162/231)	71.9% (166/231)
median (range)	34.4 (3.1-93.6)	37.5 (3.1-90.6)
% female	36 (84/231)	36 (84/231)

*Table 41. The age, gender, PHAQ and PHAQ WD of returning NAFLD and ALD participants.*

To determine if function altered over time for those participants who returned their PHAQ questionnaires in both 2008 and 2011, a paired t-test was carried out on the combined NAFLD and ALD cohorts using the PHAQ totals. Although scores had increased over the 3 year period by 21% (3.2/15.6) [15.6 (0-93.8)] in 2008 to 18.75 (0-90.6) 2011, no statistically significant differences were found (Figure 32).

Those participants not experiencing any difficulty and who had scored zero on all their PHAQ questions were then removed from the data, leaving only those experiencing difficulty with function (PHAQ WD). The PHAQ WD totals were compared to explore if those participants experiencing difficulty were experiencing increased difficulty. PHAQ WD scores had increased over time by 9% (3.1/34.4) from 34.4 (3.1-93.6) in 2008 to 37.5 (3.1-90.6) in 2011 (Table 41) but this was not significant.

The proportion of participants experiencing difficulty rose by 2.6% from 70.1% in 2008 to 71.9% in 2011

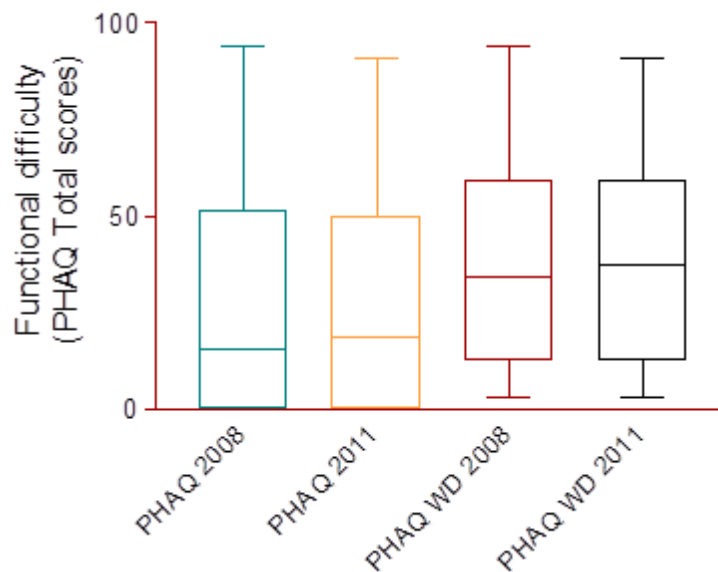


Figure 32. Comparing the paired PHAQ and PHAQ WD median and range scores of the combined NAFLD and ALD group over a three year follow up study.

### 5.3.1 Comparing change in function of NAFLD participants over time

Comparisons were then made between the PHAQ totals of the two disease cohorts over time to determine if any differences were apparent once the disease groups were separated.

There was a 20% (2.7/10.9) increase in the scores of the NAFLD participants over time from 10.9 (0-93.75) in 2008 to 13.6 (0-90.63) (Table 42) however, the difference was not significant (Figure 33).

NAFLD	N= Returned 2008	N=Returned 2011	PHAQ totals 2008 Median (range)	PHAQ totals 2011 Median (range)
	224	162 (72.3%)	10.9 (0-93.75)	13.6 (0-90.6)

Table 42. Comparing the NAFLD PHAQ total results from 2008 and 2011.

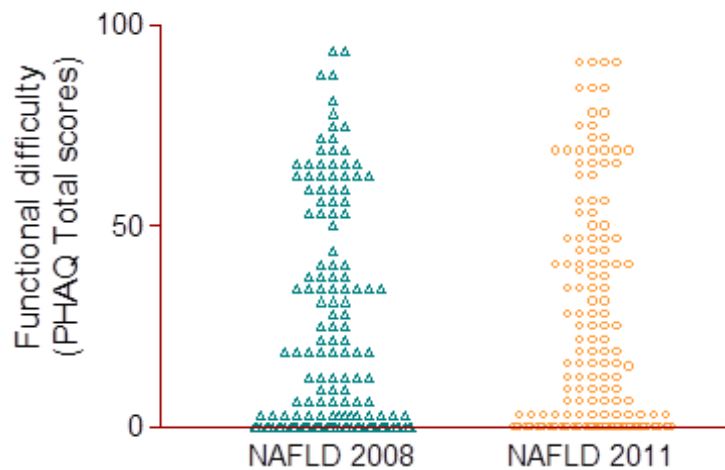


Figure 33. The comparison of returned NAFLD PHAQ totals n=162 (paired) 2008 [10.9 (0-93.75)] and 2011 [13.6 (0-90.63)]. No significant difference found.

### 5.3.2 Comparing change in function of ALD participants over time

There was a 17% (4.7/28.1) increase in the functional difficulty experienced by participants with ALD from 28.13 (0-93.6) in 2008 to 32.82 (0-90.6)] (Table 43) but this increase was not significant.

ALD	N= Returned 2008	N=Returned 2011	PHAQ totals 2008 Median (range)	PHAQ totals 2011 Median (range)
	107	69 (64.5%)	28.1 (0-93.6)	32.8 (0-90.6)

Table 43. Comparing the ALD PHAQ total results from 2008 and 2011.

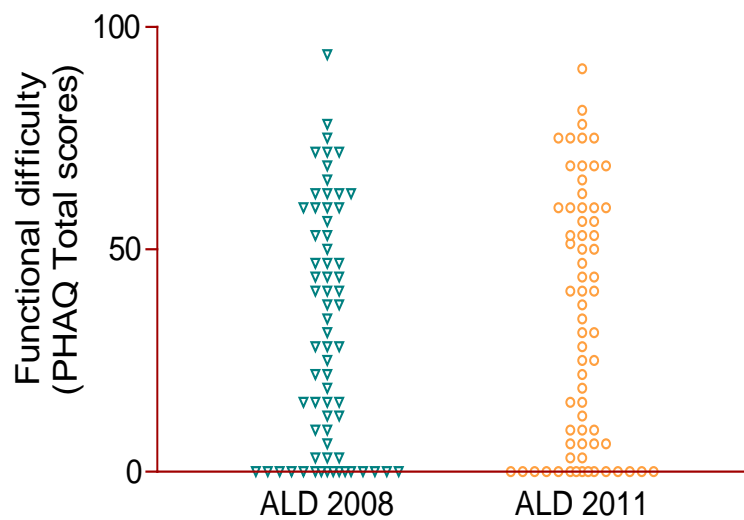


Figure 34. The comparison of returned ALD PHAQ totals n=69 (paired) 2008 [28.13 (0-93.6)] to 2011 [32.82 (0-90.60)]. No significant difference was found.

#### 5.4 Summary

In summary, those participants who had died during follow up were found to have significantly worse function than those who were still alive who returned the PHAQ questionnaire in 2008.

Of those participants who returned their assessment tool in 2011, an increase was noted in their PHAQ scores over the three years, but it was not statistically significant. It may be however that the increase demonstrated is clinically relevant and so should not at this stage be dismissed. In addition is the small but present 2.6% increase over time of the proportion of participant's now experiencing difficulty and the implication this may have on service demands in years to come.

The value in establishing a statistical plateau of functional difficulty for these participants over a three year period means that the PHAQ data taken in 2008 can be compared and correlated reliably with all other data in this study. In other words, where data has been sourced from temporal medical records, the participants PHAQ score is comparable even if not measured at the same time.

For the participants themselves, the results show that their function is significantly impaired in comparison to community dwelling comparator groups and that it will remain significantly impaired. This suggests that further follow up studies are needed to monitor what if any changes in function happen over longer periods of time; more importantly, these results raise further questions as to the experience of living with such unchanging long term difficulties are and the impact this has for people with CLD.

## Chapter 6 Results 4: Defining the functional ability of participants following liver transplantation.

Over the last decade, improving liver transplant survival rates have established liver transplantation surgery as a durable therapy that prolongs life for most forms of end-stage liver disease and for some malignant conditions.

Historically, the perception of most clinicians has been that liver transplantation is a procedure that affects a cure for their underlying liver disease thus eliminating associated symptoms, lengthening life expectancy and improving function.

As the previous chapters have established that participants with CLD have significantly worse function than matched comparator populations and the preconception is that transplantation will reverse liver disease, this chapter aims to define the functional ability of participants following a liver transplant (LT) to determine if a difference between their function and that of comparator populations occurs. This chapter also aims to determine if a difference occurs between the function of LT participants and that of disease, gender and age matched CLD participants.

### 6.1 Aims

- To describe the function of participants following liver transplantation
- To compare LT participants with matched age and gender comparator populations
- To compare LT participants with matched age, gender and disease specific CLD participants

## 6.2 Describing the demographics and function of post liver transplant and comparator participants

The LT group was made up of 104 participants, all of whom had received a donor liver in the 5 years previous to this study, namely 2005 to 2010. Demographic data is described in table 43; the mean age of the LT participants was 58 years and age ranged from 28 years to 80 years. The LT group was (n=42/104) 40% female.

The LT participants were age and gender matched group wise to comparator participants also described in Table 44. The mean age of the comparator group was 59 years their age range being 18 years to 89 years. The comparator group was (n=36/89) 40% female (Figure 35).

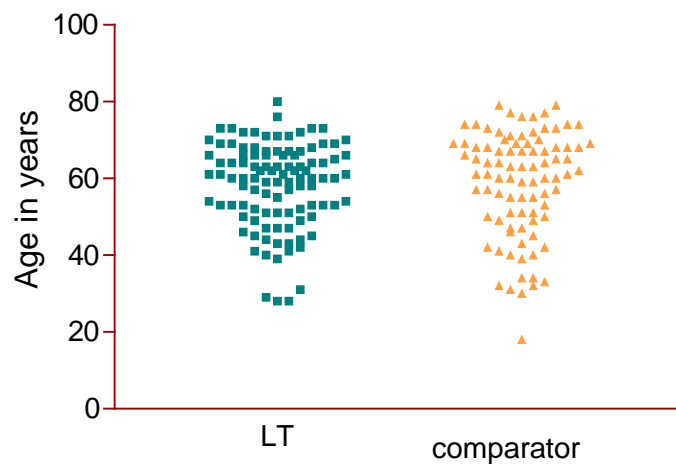


Figure 35. The age spread of LT and comparator participants.

	LT	comparator
<i>n</i>	104	89
<i>Age Years, Mean ± SD</i>	59 ± 11	59 ± 14
<i>Females (%)</i>	42 (40.38)	36 (40.44)
<i>PHAQ Totals Median (range)</i>	28.1 (0-93.8)	0 (0-59.4)
<i>PHAQ WD Totals Median (range)</i>	39.1 (3.1-93.8)	7.8 (3.1-59.4)

*Table 44. The demographic data and PHAQ and PHAQ WD results of LT and comparator data.*



### 6.2.1 The PHAQ Totals of LT and comparator participants

The PHAQ totals described in Table 44 from the LT participants and the comparator participants were compared using the Mann-Whitney as the scores were not normally distributed. The results showed LT participants had significantly worse function [28.1 (0-93.75)] than their age and sex matched community comparator group [0 (0-59.38)] ( $p < 0.0001$ ) (Figure 36).

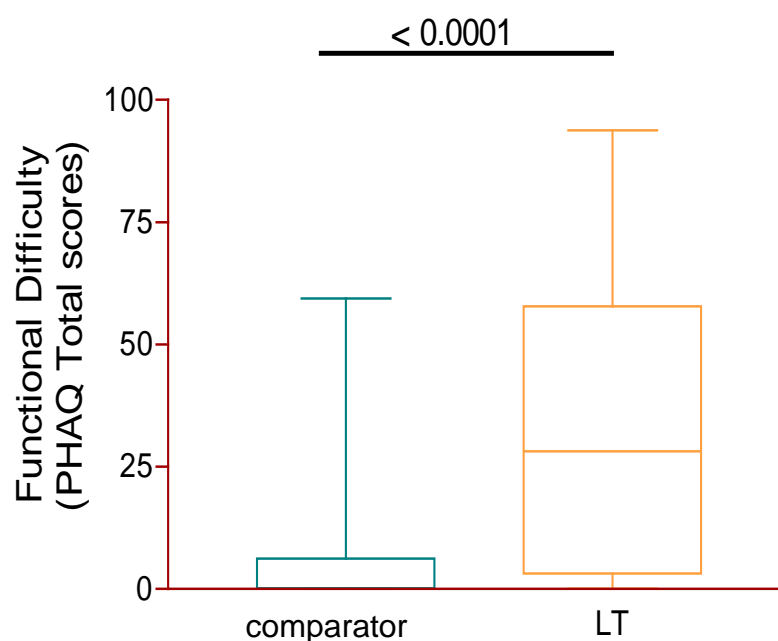


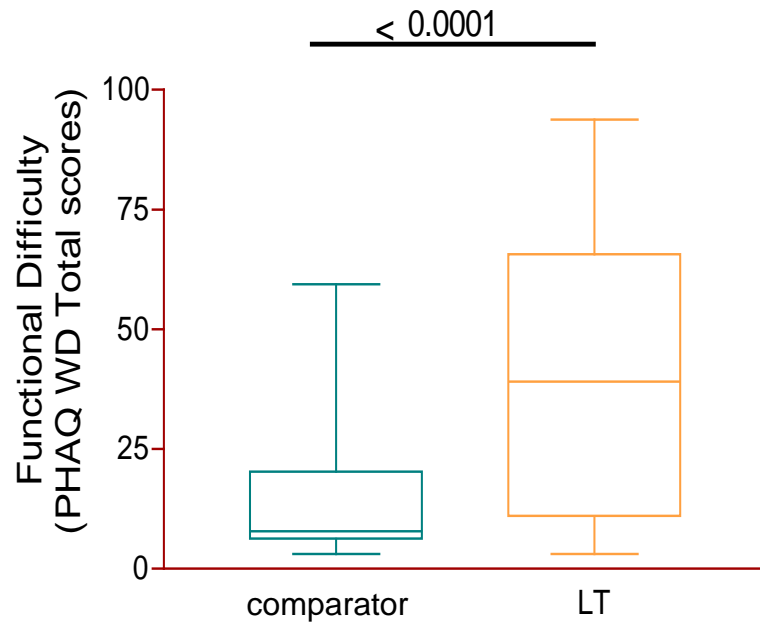
Figure 36. The comparison of LT and comparator participants PHAQ Total median and range scores

### 6.2.2 The PHAQ WD totals of LT and comparator participants

All those respondents who reported having no difficulty were then removed from the data in each group, creating PHAQ with difficulty data sets (PHAQ WD) to determine prevalence of difficulty and level of difficulty, in each group.

The results showed that 36% (32/89) of the participants from the comparator group were experiencing difficulty with function as were 75% (80/104) of the LT participants. A difference remained between the two groups with LT participants [39.07 (3.13-93.75)] experiencing significantly more difficulty ( $p < 0.0001$ ) with function than the comparator participants [7.81 (3.13-59.38)] (Figure 37). Chi squared analysis of those

participants with and without difficulty in each group reached significance ( $\chi^2 35.05 (3)$ ,  $p < 0.0001$ ) indicating that significantly more participants in the LT group are experiencing functional difficulty.



*Figure 37. The comparison of LT and comparator participants PHAQ WD Total median and range scores*

### 6.3 Describing and comparing function using the domain data of LT and Comparator participants

Within the scoring system of the PHAQ are 8 function domains (as described in Methods pg. 32); namely dressing, arising, eating, walking, hygiene, reach, grip and activity. As significant differences were found between the difficulty and the amount of difficulty experienced between LT and comparator group participants disease in the overall totals, consideration was given to where these difficulties may lie.

Comparisons were therefore made between the LT participants and comparator group participants using their PHAQ domain scores.

Table 45 describes the median score and range of each group of participants in each of the 8 functional domains. The data is presented by each domain using graphs to give a visual representation of the data (Figures 37a and 37b).

In each of the domains the comparator group scored a median of '0' indicating no difficulty with function. The comparator participants difficulty ranged from '0' no difficulty in all the domains to '2' some difficulty in the arising domain, to '3' much difficulty in the dressing, eating, walking and grip domains, and '4' unable to do in the hygiene reach and activity domains.

The LT participants PHAQ domain scores ranged from '0' no difficulty to '4' unable to do in each of the domains. LT participants had a median score of '0' no difficulty in the domains of dressing, eating and grip; '1' a little difficulty in arising, walking, hygiene and reach; and '2' some difficulty in the activity domain.

The comparison of the data using Mann-Whitney demonstrates that the participants following liver transplant have significantly worse functional difficulty in each of the 8 domains compared to the matched comparator group when comparing PHAQ domain totals; namely dressing ( $p<0.0001$ ), arising ( $p<0.0001$ ), eating ( $p=0.0099$ ), walking ( $p<0.0001$ ), hygiene ( $p<0.0001$ ), reach ( $p<0.0001$ ), grip ( $p=0.0001$ ), activity ( $p<0.0001$ ) (Table 45).

PHAQ Domains	comparator	LT	p
Dressing	0 (0-3)	0 (0-4)	<0.0001
Arising	0 (0-2)	1 (0-4)	<0.0001
Eating	0 (0-3)	0 (0-4)	0.0099
Walking	0 (0-3)	1 (0-4)	<0.0001
Hygiene	0 (0-4)	1 (0-4)	<0.0001
Reach	0 (0-4)	1 (0-4)	<0.0001
Grip	0 (0-3)	0 (0-4)	<0.0001
Activity	0 (0-4)	2 (0 -4)	<0.0001

*Table 45. The p value statistical differences between the PHAQ domain (median and range) scores of the LT and comparator groups*

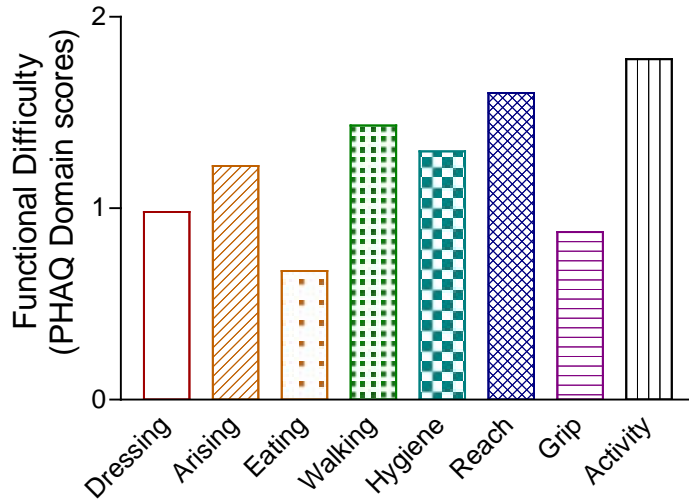


Figure 38a; LT participants

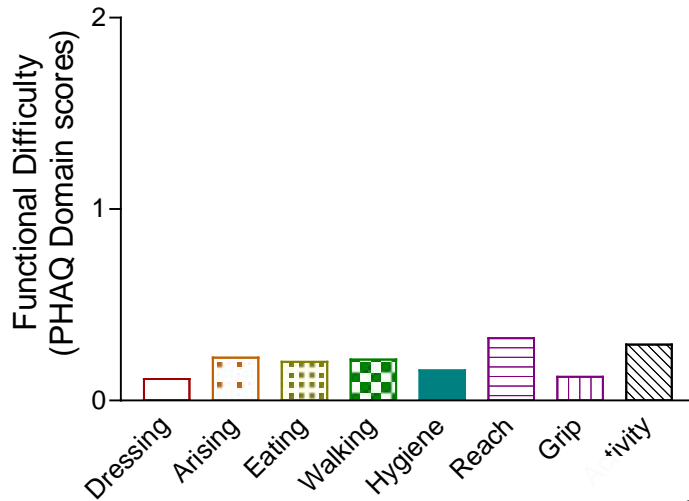


Figure 38b; comparator participants

Figure 38 a (LT) and 37b (comparator) showing the PHAQ domain mean scores, visually demonstrating the functional difficulty in the two participant groups

This means that as whole participant groups, people with CLD are experiencing greater functional difficulty within each area of daily activities than the comparator population. What percentage of those participants in each group are experiencing difficulty, and how great that amount of functional difficulty is, required comparison of the domain data minus those participants reporting they experienced no difficulty.

### 6.3.1 Percentage of participants experiencing difficulty in each group

<i>PHAQ WD Domains</i>	LT % with difficulty (n/104)	LT % with NO difficulty (n/104)	comparator % with difficulty (n/89)	comparator % with NO difficulty (n/89)	Chi Squared of %	P value of %
Dressing	(47) 45.2%	(57) 54.8%	(7) 7.9%	(82) 92.1%	33.2(1)	<0.0001
Arising	(60) 57.7%	(44) 42.3%	(18) 20.2%	(71)% 79.8	27.7 (1)	<0.0001
Eating	(36) 34.6%	(68) 65.4%	(14) 13.5%	(75) 86.6%	8.9 (1)	0.003
Walking	(58) 55.8%	(46) 44.2%	(9) 10.1%	(80) 89.9%	44.1 (1)	<0.0001
Hygiene	(54) 51.9%	(50) 48.1%	(10) 11.2%	(79) 88.8%	35.8 (1)	<0.0001
Reach	(67) 64.4%	(37) 35.6%	(18) 20.2%	(71) 79.8%	38.0 (1)	<0.0001
Grip	(44) 42.3%	(60) 67.7%	(8) 8.99%	(81) 91.01%	27.1 (1)	<0.0001
Activity	(71) 68.3%	(33) 31.7%	(13) 14.6%	(74) 85.4%	56.2 (1)	<0.0001

*Table 46. The chi squared significant difference between the proportion of participants from the LT and comparator groups who are, and are not, experiencing difficulty with function.*

Comparing the proportion of participants experiencing difficulty in each domain using Chi squared test showed that significantly less participants in the comparator group were experiencing difficulty with function in each of the domains (Table 46). This indicates that both the incidence of functional difficulty and the amount of functional difficulty experienced by participants following liver transplantation is worse than that of the comparator population.

*6.3.2 Comparing the level of difficulty experienced by those participants with difficulty in each domain.*

PHAQ WD domain scores were then compared between the LT and comparator participants. The results of which are described in Table 47.

<i>PHAQ WD Domains</i>	comparator experiencing difficulty	LT experiencing difficulty	p value
Dressing Median (range)	1 (1-3)	2 (1-4)	ns
Arising Median (range)	1 (1-2)	2 (1-4)	0.0002
Eating Median (range)	1 (1-3)	2 (1-4)	0.0312
Walking Median (range)	3 (1-3)	3 (1-4)	ns
Hygiene Median (range)	1 (1-4)	3 (1-4)	0.004
Reach Median (range)	1 (1-4)	3 (1-4)	0.004
Grip Median (range)	1 (1-3)	2 (1-3)	ns
Activity Median (range)	1 (1-4)	3 (1-4)	ns

*Table 47. The PHAQ WD domain scores of LT and comparator participants and the p value of significant difference in functional difficulty. Median and (range.)*

As described in Table 47, participants with following liver transplant had greater percentage of participant difficulty in each domain when comparing the PHAQ WD domain data; but this greater incidence did not result in a globally greater difficulty with function in every domain as it did when comparing LT and comparators as whole groups. Rather, the results showed a significantly worse functional ability of the LT participants to comparator participants only in the domains of arising ( $p=0.0002$ ), eating ( $p=0.0312$ ), hygiene ( $p=0.004$ ) and reach ( $p=0.004$ ).

#### 6.4 Summary

To summarise, significantly more participants in the LT cohort are having difficulty with functions than those in the comparator group and with significantly greater difficulty.

The difficulty experienced between the LT participants and comparators in the domains of dressing, walking, grip and activity is to a the same degree, however those participants who have received a liver transplant are experiencing significantly more difficulty than comparators in getting up and down from, or in and out of, chairs, beds (arising) toilets and baths (hygiene); in bending to pick object from the floor or lift down object weighing more than 5lbs (reach) and in cutting up their food, opening cartons and lifting full cups to their mouths (eating).



### 6.5 Exploring the relationship between function and liver disease severity in liver transplant recipients

To determine if the participants function following liver transplant was related to their liver disease markers, PHAQ totals were correlated with liver function test (LFT) results; namely ALT, ALP, ALB, and bilirubin (described in Methods pg. 41-42). All the LT participants were under long-term follow-up by the Newcastle Liver Unit and were subject to regular renal and liver serum biochemical assessment for clinical management reasons. The participants LFT data were directly related in time to their functional and symptom assessments.

Biochemical results, time since transplant and immunosuppressant dosages were compared, details of which are in given in Table 48.

LT Participants PHAQ Total and LFT's (n=104)	
ALB iu/L	43 ± 3.8
Bilirubin µmol/L	11 ± 7.1
ALP iu/L	137 ± 103
ALT iu/L	37 ± 34
Time since transplant (months) median and range	40 (2-155)
Tacrolimus Therapy (%) Mean level	82 (3.3 ± 2.5)

*Table 48. The biochemical results, time since transplant and immunosuppressant therapy dosage of participants in the LT cohort.*

Spearman r was used to correlate the participants PHAQ Total scores with their age, LFT results and time since transplant to determine if any relationships existed which would influence function. No significant associations were present. In other words, although this participant cohort is functioning significantly worse than their matched comparator group, it does not appear to be related to their liver function, their age or to the length of time since transplant.

This raised further questions therefore in explaining the significantly worse function experienced by the LT participants. As the use of immuno-suppressive drug therapy is known to cause side effects for patients following transplant, exploration of the relationship between their use and participants' functional difficulty seemed prudent. The LT participants tacrolimus dosage was therefore correlated with the participants PHAQ total scores. Again, no significance was present indicating that the answer to the LT's functional difficulty did not lie in their post transplant drug therapy.

#### 6.6 Exploring the relationship between participants' function following liver transplant and symptoms associated with liver disease.

As liver function, age, time since transplant or immuno-suppressive drug therapy did not associate with the poorer function experienced by the LT participants, the symptoms associated with liver disease were correlated with the LT participants PHAQ Total scores to determine if those could be predictors of functional difficulty. PHAQ totals were correlated with the following symptom assessment tools; FIS to measure fatigue, CFQ to measure memory and concentration difficulties, ESS to measure day time somnolence and OGS which measures orthostatic symptoms. Analysis was performed using Spearman r test.

The participants' symptoms scores and correlation with their PHAQ totals are presented in Table 49.

LT participants symptom scores and the correlation with their PHAQ Totals			
	Symptom scores	P Value	r
<i>FIS</i>	54.5 ± 42	<0.0001	0.7
<i>CFQ</i>	38 ± 25.2	<0.0001	0.3
<i>ESS</i>	8.7 ± 6	<0.0001	0.4
<i>OGS</i>	4.5 ± 5.0	<0.0001	0.3

Table 49. The relationships between poor function in LT participants and their symptom assessment tool scores.

The results showed strong correlations with all the symptoms; increased orthostatic symptoms ( $p < 0.0001$ ,  $r = 0.3$ ), increased memory and concentration difficulties ( $p < 0.0001$ ,  $r = 0.3$ ), increased day time somnolence ( $p < 0.0001$ ,  $r = 0.4$ ) and increased fatigue ( $p < 0.0001$ ,  $r = 0.7$ ). This suggests that those symptoms associated with liver disease in post liver transplant patients are still impacting upon the LT participants' ability to function.

### 6.7 Determining independent associations of functional difficulty

Multi linear regression was performed to analyse the data in order to distinguish which, if any of the LFT's or symptoms associated with liver disease independently associated with functional difficulty for those participants following liver transplant. All the results were considered, even where no significant relationship had been found, and so the regression model included age, months since transplant, liver function tests (ALP, ALT, Bilirubin, ALB), symptoms tools scores (FIS, OGS, CFQ, ESS).

The results of which are shown in Table 50.

Multi linear regression LT						95.0% Confidence Interval for B	
		Coefficient	Std. Error	Beta	p	Lower	Upper
1	(Constant)	9.094	35.857		.801	-62.891	81.080
	Age	0.035	0.288	.012	.903	-.543	.613
	Albumin	-0.273	0.703	-0.037	.700	-1.685	1.139
	Bilirubin	0.068	0.356	0.018	0.849	-0.647	0.783
	ALP	0.006	0.026	0.025	0.802	-0.045	0.058
	ALT	-0.117	0.083	-0.140	0.167	-0.283	0.050
	FIS	0.496	0.095	0.727	<b>0.000</b>	0.304	0.688
	OGS	0.602	0.657	0.107	0.365	-0.718	1.921
	CFQ	-0.050	0.157	-0.043	0.751	-0.365	0.265
	Months since LT	-0.066	0.090	-0.069	0.463	-0.247	0.114

*Table 50. The regression analysis between LT participants function with age, LFT's, time since transplant and symptoms.*

The symptom of fatigue was the only factor that independently associated with increased difficulty of function, as quantified by FIS ( $p < 0.0001$ ).

## 6.8 Describing and comparing the function of post liver transplant participants with matched disease groups.

To further explore if there was a difference between the function of participants following liver transplant, comparison was made between LT participants and participants from the CLD group who matched the LT participants in age, gender and (pre transplant) disease. In order to achieve the best possible group wise match, fewer LT participants were included than when comparing function between the LT and community comparator groups (methods pg.23); the details of which are presented in Table 51.

The mean age of the LT group was 59 years with ages ranging from 28 years to 79 years. The matched disease group's mean age was 60 years and ranged from 28 years to 80 years. Both groups were 40% female (27/67). There was no significant difference in age or gender between the LT and the CLD groups.

Paired T-test analysis was performed to ascertain differences between the liver function test results, the symptom assessment tools FIS and CFQ and the functional assessment tool PHAQ between the LT group and the CLD group (Table 51).

	LT	Matched CLD	p
N	67	67	
Age	59 ± 10	60 ± 10	ns (0.2)
Female n= (%)	27 (40)	27 (40)	ns
ALD (%)	34 (50)	34 (50)	ns
PSC (%)	15 (22)	15 (22)	
PBC (%)	13 (19)	13 (19)	
NAFLD (%)	5 (7)	5 (7)	
PHAQ	7.5 (0-85)	7.5 (0-85)	ns (0.9)
FIS	57 ± 44	62 ± 45	ns (0.12)
CFQ	40 ± 27	41 ± 25	ns (1.0)
BILIRUBIN	10.3 ± 6.2	17 ± 15.6	0.0021
ALB	43 ± 3.8	42 ± 5.3	0.05

*Table 51. The comparable LFT results and symptom assessment tool scores between the LT participants and their matched CLD participants.*

Unsurprisingly, significant differences were found between the participant' ALB (p=0.05) and Bilirubin (p=0.002) results demonstrating improvement in liver function for the post liver transplant participants.

There were no significant differences however in the symptoms tool scores. In other words LT participants are experiencing as much fatigue as measured by comparing FIS, as much cognitive difficulty as measured by CFQ and as much functional difficulty as measured using PHAQ total scores as the participants from the CLD group with the same aetiology who had not undergone transplantation (Table 51).

## 6.9 Summary

This chapter has shown that people following liver transplant have significantly worse functional ability than people in comparator groups. There is a greater prevalence of functional difficulty experienced within the LT population than in the comparator population and the activities captured in the domains of arising, eating, hygiene and reach are significantly more difficult for people who have undergone a transplant to perform.

The impact of fatigue, concentration and memory difficulties, day time somnolence and orthostatic symptoms have a combined affect on people following transplants ability to function; and fatigue as measured with the symptom assessment tool FIS can be used independently in his participant group to determine function.

This chapter has also demonstrated that although liver function improves significantly following a liver transplant when compared to people living with a matched liver disease, function and symptom experience do not. In other words, people following a liver transplant are still experiencing difficulty with function and the impact of symptoms to the same degree as people living with CLD.

## Chapter 7 Results 5: A Qualitative Topical Survey to Explore People with ALD and NAFLD's Experience of Living with CLD.

The previous chapters have demonstrated that people with CLD experience significantly more functional difficulty at a significantly greater level than community dwelling comparator groups and that over time this functional difficulty persists. In particular the activities captured in the domains of arising and hygiene are significantly more difficult to carry out for people with CLD and are impacted upon by a combined effect of increased fatigue, poorer cognition and increased orthostatic symptoms.

Participants with ALD and NAFLD reported the highest levels of difficulty with function equally, with the ALD group having the greatest proportion of participants experiencing difficulty [as measured by the functional assessment tool PROMIS HAQ (PHAQ)] in all domains except grip, where NAFLD participants had the greater incidence. The purpose of this chapter is to explore in more detail, the experience of living with CLD, and as the ALD and NAFLD participants experience the poorest function, these two participant groups were chosen for further investigation.

Four people with NAFLD, four people with ALD and four people with ALD who were abstinent from drinking alcohol for 6 months or more were invited to take part in semi-structured interviews (outlined in Study design, pg. 24) in order to discuss their daily experience of CLD. The Canadian Occupational Performance Model (COPM) was used alongside the questions from PHAQ to structure the topic guide (described in Methods, pg. 40) and elements from the measurement tools Hospital anxiety and Depression scale (HADS) the Cognitive Failures Questionnaire (CFQ) utilised to elicit rich data. These tools were not used to quantify responses but to guide the semi-structured interview (described in Methods pg. 40) and the responses given are those of the participants' perception of activity and difficulty with function.



## 7.1 Aims

- To describe the daily experience of living with CLD in the context of the performance areas, productivity, self-care and leisure.
- to describe the issues reported by participants with ALD and NAFLD's and how they impact on their ability to engage in activity
- To explore disease specific difficulties in activities or in engaging with activity.

7.2 Discussing the experience of functional difficulty for people with ALD and NAFLD in in the context of the performance areas of Productivity, Self-care and leisure

Figure 39 summarises the collective responses from the participants when asked to describe their usual day; the participants were asked to describe any difficulties they were experiencing with their activities. The responses were categorised by the theoretical framework of COPM, namely the functional performance areas; productivity, self-care and leisure.

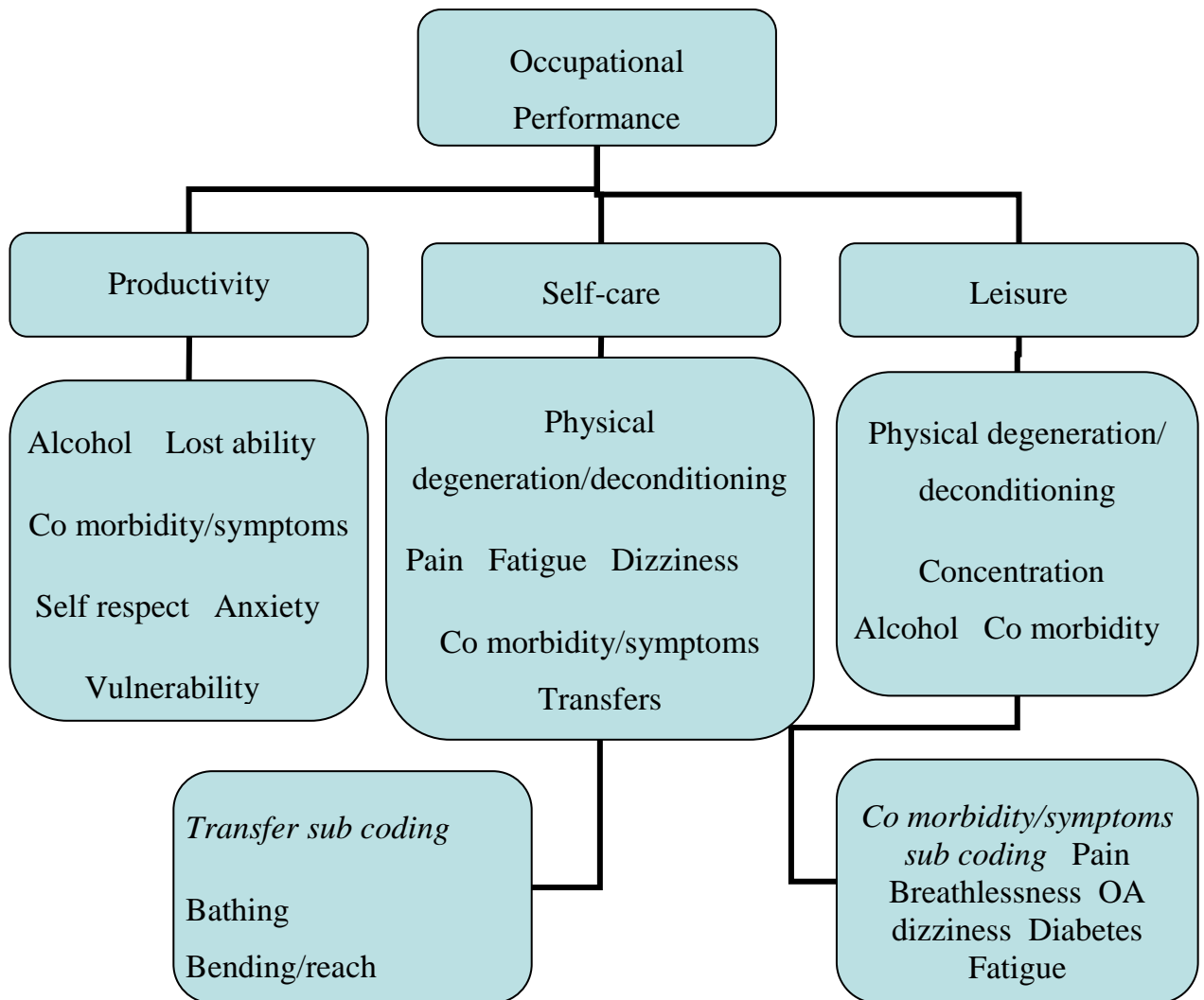


Figure 39. The functional difficulty reported by the NAFLD, ALD and ALD AB participants using the occupational performance areas of productivity, self-care and leisure.

### 7.2.1 Productivity

All the participants with ALD reported an inability to be productive, including the participant who described himself as a 'functioning alcoholic'. The unanimous reason was that their dependence on alcohol and the effect of alcohol was greater than their need to be productive:

*"You'd think a bit of dusting was nothing but I can't even be bothered to get up and go and get a duster even though it desperately needs doing. I could go to sleep on a night time, whether I was in a proper sleep or a drowsy sleep and I would think 'right, in the morning I'm going to Hoover those crumbs up', and I would be thinking about it, and yet when I woke up I couldn't be bothered even to get out of bed and I thought 'well that was just all a load of rubbish. It was the drink'."*

ALD 1

With this inability came a sense of loss. All the participants with ALD described their earlier lives and occupations, their interests and their roles:

*"I love doing work if I'm alright. I worked for the same company for 20 years. It was hard graft. You don't do something like that if you don't like work. I was carrying flagstones around, bags of sand, gravel, plaster – full bags. I felt as fit as a lop, I was happy, I was useful."*

ALD 3

Only 2 of the 4 ALD participants reported a sense of wanting to regain the previous productivity. Reasons for regaining productivity centred on self-respect and a sense of self and identity. The respondents also reported anxiety at the prospect of becoming productive again:

*"If I can do voluntary work and prove to future employers that I used to be an alcoholic but I am clean now, after 3 or 4 months I can start applying for jobs and just be honest with them, fingers crossed, and get them to trust me. That is my biggest fear, 'I'm not employing an ex-alcoholic'."*

ALD 5

The ALD AB participants were, in the main, describing high levels of function and productivity. Interestingly, it was the participant at 6 month sobriety who described poor productivity. Those ALD AB who were abstinent for 2 years or more were reporting fulfilling levels of productivity, marred only by co-morbid problems [in all cases it was osteo arthritis (OA)].

The ALD AB participants who were productive lent valuable insight into the downward spiral of the use of alcohol and its impact on productivity:

*“It was easy getting a sick note from the doctor because of my health. ‘I can’t handle this doctor’ – I pulled the wool over his eyes, which was wrong, but I did it. So they were paying me even though I wasn’t working”*

ALD AB 4

For the participants remaining unproductive concerns of anxiety and vulnerability prevailed. When asked if they were able to function in order to get alcohol one participant stated:

*“I would rather other people go for it and I am counting the seconds while they are away.”*

ALD 3

Social vulnerabilities were further identified when problems surrounding assistance with productivity and self-care were described:

*“I spoke to my mate; I told you he’s my carer. He doesn’t really like to do any caring like; he just does it to get the money. Basically, I’ve given him a place to live because he has nowhere to go. When you were asking before about general housework, I can’t get any out of him.”*

ALD 3

3 out of the 4 participants with NAFLD described great problems with productivity due to physical limitations, all of which were explained by co-morbid functional difficulties. These included diabetes, hernias, chronic obstructive pulmonary disease (COPD) and orthopaedic abnormalities; the participants reported their symptoms as breathlessness, fatigue, pain and poor mobility:

*“If I could find someone like my cleaning lady who could come and keep my garden under comparator that would be good. I would probably have done a bit more in the way of decorating and projects around the house which involve a bit more physical strength and endurance. I can’t summon up so much of that at the moment.”*

NAFLD 1

### 7.2.2 Self-care

Ability to self-care was a problem described by respondents in each of the three conditions; however, whilst all those with ALD reported difficulty, along with 3 of the 4 of NAFLD, only 1 of the 4 of ALD AB raised self caring as a problem due to his painful knee, causing difficulties with bath transfers. This participant had previously refused the provision of any adaptive or physical assistance:

*“I lie in the bath and sort myself out. I don’t worry about things like that. I’m not going to have somebody in. I’m alright. I don’t give in, see. If someone gives me I walking stick I would give them it back. I am not going to use a walking stick, I’ve got the bike.”*

ALD AB 2

Bathing and dressing were the predominant examples of difficulty with self-care given by the ALD and NAFLD participants, the reason given being; difficulty with the bath transfer, with the fine motor movement required for buttons and shoelaces and with the bending down to put shoes on.

*“It’s only a button for God’s sake, just fasten it, and I go back 5 or 6 times, and eventually I do it, and then I feel alright, but there are lots of things I still can’t do.”*

ALD 1

The issue of bending down to reach shoelaces was noted in both groups; in NAFLD bending was difficult due to the physical restraint of the size of their abdomens, breathlessness and pain. In ALD the issue of dizziness when bending, along with tremor, prevented participants from reaching down,

*“When I first came in I couldn’t pull my pants up because if I bent down I used to go dizzy, spin, like you know when I used to get in the bath. That’s why I’m frightened to get in the bath at home, with me being on my own. It’s not so much getting in, it’s getting back out, I’m frightened in case I slip and I will be there for I don’t know how long.”*

ALD 3

and the mixed effect of alcohol on confidence and ability was demonstrated,

*“Yes, because I haven’t the confidence to do it (bathing and dressing), unless I have had a drink like.”*

ALD 3

Pride and appearance featured in both ALD and NAFLD and was affected by the participants' ability to self-care satisfactorily,

*“Well all I can tell you is how I feel. I often walk around in the same clothes that I slept in, because I know I am not going to get changed properly. I have problems with cleanliness and hygiene because of that. So like I say, I do things as and when I can.”*

NAFLD 2

*“I'm not bothered about dressing; I used to take pride in my dressing at one time. I'm lucky to get a pair of pants and a top on now.”*

ALD 3

### 7.2.3 Leisure

Physical degeneration and ageing were the main reasons for participants not engaging with leisure pursuits, along with alcohol for each of the participants in the ALD group.

The four participants with NAFLD described deriving enjoyment from reading, soap operas and pets.

*“Yes, all my soaps. But since we got the allotment isn't it, we go up there on an afternoon.”*

*(Husband) – “Oh we've got a massive greenhouse, but when I say it gets her out of the house and doing things, that doesn't mean she does gardening or carry water, stuff like that, it's just basically giving her something to do in the garden like feeding the ducks, feeding the chickens.”*

NAFLD 4

They reported being prevented from physically demanding leisure pursuits previously enjoyed due to co-morbidity and symptom burden, for example pain and concentration. One NAFLD participant did however report increasing his walking and outdoor leisure pursuits in order to lose weight.

Those with ALD AB described a wide range of leisure activities and sought value in them, although one ALD AB participant, again the most recently sober, still felt unable to pursue those leisure activities of interest to him due to poor mobility.

*“I had this idea that when I stopped work I would take up hiking, spending my time on walks... I still have my brand new boots boxed upstairs.”*

ALD AB 3

The participants with ALD all described the impact alcohol had in their ability to engage in leisure activities. Prior to their dependence on alcohol they described a wide range of interests; computers, socialising, sport and travel. As with productivity and self-care, the participants with ALD's ability to engage in leisure activities were affected by their alcohol dependency; not only in lack of motivation, but through the physical degeneration caused by the disease. Alcohol was also an issue for participants in its social context. Both those with ALD and ALD AB highlighted the avoidance of those leisure pursuits associated with drinking alcohol:

*"I like a game of cards, nothing heavy, just a game of crash or something. Just something to occupy your mind really. The only trouble is, they drink there. Of course, all these times when you are on your own doesn't help either, that's why I was glad to see you today, it's somebody to talk to."*

ALD 3

### 7.3 Summary

The participants in each group reported the presence of co morbidity and symptom burden as a reason for their inability to carry out, or engage in, activity in each of the performance areas; productivity, self-care and leisure. There were however differences between the groups in their reasoning behind these limitations.

Where participants with ALD AB reported co morbidity and symptom burden problems impacting on their function, they found ways in which to compensate in order to participate in activities of worth or interest to them. The participants with NAFLD all reported being prevented from participating in activities of importance to them due to physical limitations caused by co morbidity. One NAFLD participant reported increasing their daily exercise in order to loose weight however all the participants were experiencing spiralling difficulty with their activities due to their physical deconditioning, weight, pain and breathlessness.

Physical deconditioning was impacting greatly on the participants with ALD but whereas the participants with NAFLD associated this with their co morbidities, the ALD participants attributed their difficulties in performing activities directly to their alcohol addiction; be that in a physical, environmental or social context.

In brief, the ALD AB group, with the exception of the most recently abstinent participant, were engaging in activities regardless of co morbid pain and symptom burden; the NAFLD participants were having great difficulty in engaging with activity due to obesity, breathlessness and pain and the ALD participants were prevented from engaging in activity due to alcohol dependence, muscle weakness, orthostatic symptoms and anxiety.

### 7.4 Exploring the issues affecting functional performance

Figure 40 shows the collective responses from the participants when asked to describe their usual day, explaining any difficulties they are experiencing with their activities. The responses were categorised by the themes that emerged during the interviews of the problems that affected their participation in activity



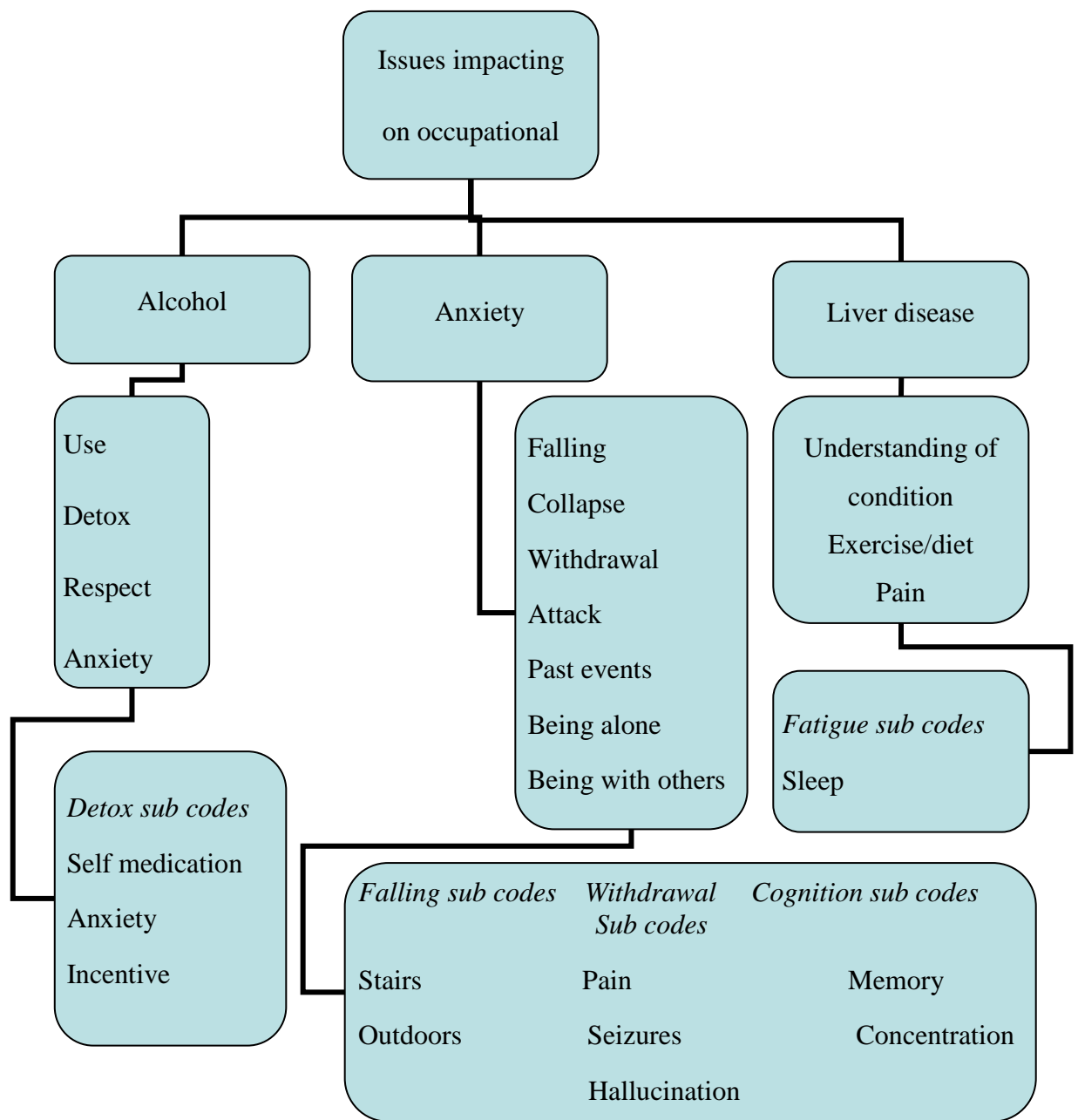


Figure 40. The issues affecting ability to be productive as described by the NAFLD and ALD and ALD AB participants.

#### 7.4.1 Alcohol

Alcohol was an unsurprising theme that emerged from the study, with ALD affecting 8 of the 12 participants. No NAFLD participant described alcohol as a problem in context of themselves or their activities.

The participants with ALD AB described their experiences of alcohol dependency and its previous impacts on productivity, self-care and leisure, but with the exception of its impact on the ‘clubhouse’ culture of which one participant now felt they had to avoid, alcohol was no longer something the participants raised as a problem directly associated with their ability to function.

For those participants living with ALD, the alcohol remained the central focus of the interviews as it directly affected every choice they made each day.

#### 7.4.2 The use of alcohol

*“The drink was getting in the way. It’s made me stop all the things that I loved to do”*

ALD 1

The use of alcohol for the participants was a complex mix of issues. Inevitably the drinking started as a social or family norm perpetuated by work, family or relationship stressors and held fast through habit, addiction and fear of detoxing.

*“I was drinking heavily because I used to work the late shift every Saturday and I used to get in at half 11, quarter to 12 at night and that was my chill-out time. I haven’t seen my kids because I am divorced through the drink. I haven’t seen my kids for about 6 years.”*

ALD 5

*“I would get up in the morning, drop her off at work and I would come back home and I was drinking. Get my paper, have something to eat, and I was drinking. Then I would go out, and I would come home, I would drink, see some people of a lunchtime and then just about every afternoon and every evening, drinking.*

ALD AB 4

### 7.4.3 Detox

The differing views of detoxing were interesting between those participants with ADL and those participants who were abstinent from alcohol, the ALD AB. For those participants in the ALD AB group, the fear of dying had been a turning point in their cycle of alcohol addiction, however, for those participants with ALD interviewed in the acute setting, being told the same life-threatening facts were secondary to the fear of withdrawal.

*“They said ‘Carry on drinking the way you are and you’ll be dead in six months’. Well I’ll tell you what it is, if that doesn’t scare the hell out of you, nothing will, and I just didn’t believe it, I said ‘You’re joking’ and he said ‘No I’m not joking, you’ll be dead within six months, you won’t see Christmas’. It was what I needed. I met the nurse and went through this programme and I stopped drinking alcohol within a week.”*

ALD AB 4

*“A few of them (friends) have tried it and then said ‘Never again, you should have seen the state of me last night’. I’ve been the same. I say ‘You don’t have to tell me, I know what it’s like’ and they say ‘We know that’. I’ve been in and out of hospital umpteen times, all with alcohol withdrawal.”*

ALD 3

The ALD participants all reported having terrifying experiences when withdrawing; seizures, shaking and panicking, and used doctors' advice as a way of self-medicating and perpetuating the use of alcohol.

*“So I started hassling my doctor, saying ‘I need some help, I need some help, I’m sick of drinking’ and he is saying ‘You cannot just stop, you cannot stop or you are going to have a seizure, you’ve got to keep drinking’”*

ALD 5

*“I always try to leave one drink in the cupboard for the next day, so if I have four cans, there’s always one there for the morning. It’s like a security blanket, and if I haven’t got it there, that’s the only time I borrow a few quid off my sister.”*

ALD 5

*“I vow to this day, and I mean it, I say I will never wake up without a drink again.”*

ALD 3

or the medical advice was simply dismissed,

*“They say ‘You keep on drinking and you are going to kick the bucket’. Well the amount of times I’ve been stabbed and shot at I just think ‘Well if I’m going to die, I’m going to die’. I couldn’t give a shit.”*

ALD 2

Other issues impacting on detox were the resources offered or the support given by family and friends. Other incentives to detox were children, grandchildren, or the want to get back to exercise, old hobbies and being fun again.

#### 7.4.4 Respect

Predominantly issues of respect, both self respect and respect from others was pertinent for all the participants from the ALD group and one participant from the ALD AB

group. One NAFLD participant noted that they felt frustrated at their inability to be productive, but this was associated with the giving up of employment rather than issues surrounding alcohol. The ALD AB who mentioned respect associated it with the issues of family or social prejudice.

*“I want to see them grow up, I’ve still got 3 little ones, the other one is grown-up. I know a lot of lads who never see their children, I couldn’t cope with that. I want to see my grandchildren grow up and I don’t want my daughters saying their father is a ‘plonky’, I don’t want that.”*

ALD AB 2

*“I want it for myself and I want my kids, and then voluntary work, a job and then when I walk around, people can’t say ‘There goes that pisshead’. I want to get rid of that reputation and get my own reputation.”*

ALD 5

A similar story came from an ALD participant being medically managed acutely for his ALD, who described overhearing medical professionals discussing one of his admissions to hospital,

*“I remember one saying ‘Just let him go, he’s a plonky’, something like that. He thought I hadn’t heard him but I did.”*

***And how did that make you feel?***

*“A bit down. He’s never been there so how does he know? Don’t criticise when you don’t understand. I felt like saying that anyway.”*

ALD 3

3 of the 4 ALD and 3 of the 4 ALD AB all praised the medical staff involved with their care and in the case of the ALD AB, their recovery. For one ALD, there was both the matter of feeling a sense of being made to feel ‘dismissed’ and not feeling of worth at a local alcohol rehabilitation centre, mixed with gratitude at being given an opportunity to become ‘clean’.

#### 7.4.5 Anxiety

Anxiety was probably the greatest symptom that impacted on function with the participants, with only one ALD AB reporting having no worries at all, although even this participant acknowledged being told he would die “changed things”. Other ALD AB described anxiety connected with co-morbidities e.g. previous heart attacks and one ALD AB described the vicious circle of the anxiety and panic experienced when they were drinking.

*“I used to have terrible panic attacks, as I say, before, when I was in the house, I used to be wanting to be out, I used to be out on the bus to Gateshead and then I would start panicking, feeling as though I was having a heart attack really, not knowing what it was, getting to Gateshead and turning around and coming straight back, then I felt secure once I got in the house, and then I would be in the house a while and wanted to go out again, you know, it was like a vicious circle. But as I say, once I got everything sorted out drink-wise, I have just completely changed, for the better.”*

ALD AB 1

The scenario was played out in the descriptions given by all the participants with ALD. The list of fears (see figure) was extensive and contradictory, for example, a fear of going out but then of staying in, of being alone or being with others, a fear of drinking or withdrawing.

*“Until I’ve had two or three cans and then I’m alright. I can go to the shop, say hello to people. At the minute, if I go to the shop, all I want to do is get there and get back, you can’t be bothered with nobody and I feel awful walking straight past. But I can’t help it.”*

ALD 3

Similarly of alcohol dependency, the participants described being fearful of a lack of comparator, but understanding that the dependency was theirs:

*“I thought ‘I’m just going to go to sleep one night and I’m not going to wake up and it will be all my own fault, because everything I’ve done, I’ve done to myself’.”*

ALD 1

All the participants with ALD reported having fallen due to dizziness associated with alcohol or withdrawal and this played an important part in their anxiety:

*“You know why I get dizzy? Because I haven’t had a drink. The doctor said ‘It’s alcohol withdrawal for you’. I’ve fallen loads of times, and I’ve been lucky because it was a flat surface, but it’s still hard on the paths. If there is grass around I try to aim for the grass, but it’s not always that simple, sometimes I just go down just like that.”*

ALD 3

This anxiety then fuelled further anxiety and resulted in a downward spiral of activity and function or of activity avoidance:

#### 7.4.6 Liver disease

All the participants in this study have a confirmed diagnosis of liver disease and yet the issue of their liver function and its impact on their activity was not at the forefront of the interview responses. Although happy to be interviewed, every NAFLD participant on first contact with the researcher expressed their ‘concern’ that their stories would not be of value as their liver disease did not affect their lives.

*“I was chewing it over in my mind and I thought ‘As far as I’m concerned my problem is my breathing and my diabetes and a few other things’. What I don’t really feel I have a problem with – and I wouldn’t even know about it if I hadn’t been told by Professor (name) and other doctors – is the liver which they seem more concerned about. So you know, arguably, you are talking to the wrong person because I don’t feel that I have a liver problem, I am not aware it, I am prepared to believe what the doctors say but it’s not something that I sort of feel affects me. So I don’t know where that sort of puts me in the category of people that you should be talking to.”*

NAFLD 1

#### 7.4.7 Understanding

A reoccurring theme emerged as to the lack of understanding by the participants' of their liver disease, indeed of their knowledge of having liver disease even though a liver biopsy had been performed on each participant; and on the understanding of what liver disease is:

*“I know, according to the television there are a lot more younger ones now (with liver disease) but that is with the drink.”*

NAFLD 4

*“I mean if you said ‘liver’ to people what would they say?... ‘and onions!’ That’s what they’d say. None of my mates had ever even heard of liver disease. I hadn’t. I didn’t even know anything about it.”*

ALD AB 4

Those participants with NAFLD associated their functional difficulty with other comorbidities and had mixed feelings about the advice given therefore by medical professionals in treating their liver disease e.g. losing weight by diet and exercise. 3 of the 4 NAFLD participants described “doctors” as being prescriptive without understanding the participants’ perspective.

*“I think what is relevant is that the patients have an input, that it is not taken over and controlled by doctors who don’t have the illness because they really don’t understand all of it. Some sort of comparator factor, that is what would be helpful for us.”*

NAFLD 1

All those with ALD AB discussed their liver disease as a thing in the past and interestingly, none of the participants in the acute setting with ALD even mentioned the impact their alcohol dependency was having on their liver, or the functional difficulties that were arising due to their liver damage.



#### 7.4.8 *Exercise and weight*

Body weight was a problem for both for the ALD and NAFLD participants but was discussed by only two of the NAFLD participants; one who was trying to increase their exercise under doctor's orders and one felt unable to increase their exercise regardless of doctor's orders. In all cases, the ALD participants were notably underweight and the NAFLD participants overweight.

One of the four NAFLD participants reported adhering to advice given to address their obesity by cutting out cakes, biscuits, pies and sausage rolls and walking more. In discussion this was to prevent diabetes. The reasons given by the remaining 3 of the 4 NAFLD participants was frustration at the insistence of the doctors to lose weight and exercise more and their inability to do so.

*“Yes sometimes it’s tempting to think that doctors are a bit obsessed with health lifestyle and we’re all obese and we are all on unhealthy diets and this is what you get shoved at you constantly by the medical profession. I’m not saying they are wrong but you kind of feel ‘I’m being attacked here’, you know. You feel ‘Oh I’ve heard all this before from doctors and aren’t they just being mean and awkward about it.”*

NAFLD 1

The NAFLD participants also felt that there were barriers to exercising due to their physical difficulties i.e. general morbidity, or health status, in other words, pain or breathlessness and the exercise choices available to them.

*“You want an encouraging, comfortable environment. I happen to have a particular thing about pop music – I feel as if I am being assaulted by it. Anything that can be done to smooth the path is going to be good practice for older, not very fit people, otherwise they are probably not going to do it at all, and that would be a loss, because I am entirely sold on the idea that we should all be doing a bit of exercise and that is good practice.”*

NAFLD 1

A lack of understanding also remained for one of the participants who although having understood they needed to lose weight, was unsure about which clinic for which of their conditions had recommended it.

#### 7.4.9 Pain and Fatigue

Mention was made by the NAFLD participants about the pain and fatigue they were experiencing and again the participants felt these were either unexplained symptoms or that they were attributed to co-morbid conditions. Muscle pain was highlighted by both NAFLD and ALD and was in all the cases described as severe. Muscular pain was associated with all movement, in particular bending in NAFLD and sit-to-stand or bathing transfers in ALD.

*“At the minute, with my back, I’ve got to find that proper spot, but if I can’t, my muscles go into spasms, and I mean spasms, I could howl the place down.”*

NAFLD 4

*“It didn’t last long but it is there and it is absolutely horrendous. I think ‘Will someone just take this pain away.’”*

ALD 1

Participants with ALD AB each reported pain affecting their performance of an activity in some way, with each example being due to OA (knee, hip and wrist). Fatigue was mentioned by all NAFLD participants which one participant explained as natural tiredness e.g. staying up late and ageing, however they all noted that they were more tired or tired more quickly. For 2 of the 4 participants the fatigue was becoming a problem.

*“Well basically you just can’t be bothered with anything. All you want to do is go to sleep, but the problem is, most of time you can’t.”*

NAFLD 2

*“I’m alright as long as I am pottering around the house. It’s when I come to sit down here to watch something I can... my eyes, and I’m gone. I never used to be like that.”*

NAFLD 4

#### 7.4.10 Sleep

Sleep was a far greater problem in ALD than in the other conditions. All the ALD and one of the ALD AB reported poor sleep, and the other 3 of the 4 ALD AD reported poor sleep whilst drinking.

*“I normally used to go to bed at 10 or 11, but this drinking malarkey, you just think ‘oh I will have another drink’ and before you know it, you are looking at your watch and I was thinking ‘God, its quarter to 3 and I’m wide awake’*

ALD 1

One of the ALD reported the experience of insomnia led to such depression that they experienced suicidal thoughts.

All those participants reporting poor sleep relied heavily on the radio for comfort and company.

#### 7.4.11 Memory and Concentration

Issues of memory and concentration were highlighted in both the NAFLD and ALD AB participants as cause for concern. Participants described difficulties with word finding, ‘blinking out’ leading to poor sense of direction and conversational difficulties, and clumsiness were all attributed to a sense of embarrassment or anxiety in a social context;

*“It’s my biggest worry because I start to get embarrassed when I talk to people and I forget things, especially if I am interrupted and I can’t remember what I was talking about.”*

ALD AB 1

a functional context;

*“Yes, like when you go upstairs to go the bathroom and then forgotten what you were doing and not realising until you are downstairs again and have wet yourself.”*

ALD AB 3

and in a medical context:

*“It worries me whether I took my insulin or not.”*

ALD AB 1

Although no ALD highlighted memory or concentration as a problem, one ALD AB rated the issue:

*“Concentration and memory I would say is a bigger hindrance than the pain in my hip.”*

ALD AB 1

## 7.5 Summary

The factors impacting on the participant's ability to perform activities e.g. anxiety, alcohol and contributing co morbidities, were defined in the main, by the liver disease the participant belonged to.

The participants from the ALD AB group, whilst experiencing pain due to OA and anxiety of over exertion following a previous heart attack, were in the mostly engaging with activity in all the performance areas. The exception was the ALD AB participant most recently abstinent who was still experiencing mobility and endurance difficulty.

The participants with ALD were the group whose activity was most affected by anxiety. The depth of fear associated with the experience of alcohol withdrawal; collapse, seizure, pain along with the detrimental affect of sleep deprivation far out weighed their loss of productivity, self-care and leisure activities. The issue of respect; both self respect and respect from others, was the one factor which these participants reported as having (potential) to influence them to address their alcohol dependency and in turn, increase their engagement in activity.

The NAFLD participants were very much affected by the symptoms associated with their health status. Although pain, fatigue and cognitive difficulties are all associated with CLD, a lack of understanding about the implications of their damaged liver meant that this group attributed their inability to carry out activities to other long term conditions. The detrimental affect of this was in their non compliance of advice given to them by in the liver clinics and in the consequent possibility of a downward spiral of increased symptom burden, physical deconditioning, weight gain and further liver damage.

## Chapter 8 Discussion

This is the first study to determine that people with chronic liver disease (CLD), and people following liver transplant, are experiencing significant functional difficulty with their daily activities. The study used a self-reported functional measurement tool, specifically identified by a liver patient group, as capturing those activities pertinent to their daily lives and the functional difficulties there in. The results demonstrate clearly that more people with CLD have significantly more functional difficulty than comparator groups; this knowledge, together with the available global and national statistics confirming the rising incidence of CLD, makes a compelling case for radical and urgent improvement in the provision of services for people with CLD.

In detail, a greater proportion of people experience functional difficulty within the CLD population than in the comparator population and those with CLD who have difficulty are experiencing it to a greater degree than comparator participants' also experiencing difficulty.

These findings are incredibly important as for the first time in the CLD literature the extent to which functional difficulty is a problem along with an overview of the empirical experience of those with liver disease is given. The relevance of these findings is that it provides a better understanding of the generic disease experience, but more importantly, in the acknowledgement that under the umbrella term of CLD lie many complexities, both disease and importantly, person specific.

Also important to appreciate is the enormous impact a growing number of people with significant functional difficulty will have on resources as CLD remains the only disease in the UK top 5 'killers' increasing annually.

This is further highlighted in the finding of this study, of a small but present 2.6% increase over time in the proportion of participants now experiencing difficulty, and the implication this may have on service demands in years to come. For example, an increase in people with functional difficulty will require an increase of occupational therapy services as more people require intervention with their daily activities. The typical occupational therapy intervention for people with CLD in the UK currently is equipment provision and hospital discharge (Elliott and Newton 2010). During these

times of challenging NHS reform, where unprecedented efficiency savings, increasing importance on rehabilitation following discharge from hospital, and the impetus on avoiding unplanned hospital care (Vize, 2011) is paramount. The risk of an incredible strain being placed upon already overstretched and under staffed, front line NHS Occupational Therapy service teams, social services home loan equipment stores, community care teams and domiciliary care services is very real.

In addition, of those participants who returned their questionnaire in 2011, an increase was noted in their PHAQ scores over the three years, demonstrating an increase in functional difficulty, and although not statistically significant, it may be clinically relevant and so should not at this stage be dismissed. The accumulation of these factors, underlined this study, is the wake up call to the NHS that a new approach is needed in the service provision for people with chronic liver disease and that in light of the increasing numbers of people with CLD, this needs to be actioned urgently.

#### 8.1 Predicting mortality in CLD

Those participants who returned the PHAQ questionnaire in 2008, but who had died prior to the follow up study in 2011 were found to have significantly worse function than those who were still alive. This suggests that either people with CLD who have greater difficulty with function were more medically unwell than their disease counterparts and therefore have an increased likelihood of dying, or that decreased functional ability is a predictor of mortality. As this study has demonstrated disease severity is not independently indicative of functional difficulty, the latter explanation seems reasonable.

A review of function and mortality by Sokka and Hakkinen (2008) supports this hypothesis as the Health Assessment Questionnaire (HAQ), a predecessor to PHAQ, has been shown to be effective in predicting mortality in those with poor function in several studies of people with rheumatoid arthritis. Other self-reported functional assessment measures for example the SF-36, have been shown to predict mortality in cardiac surgery, diabetes, renal disease, cancer and HIV (Ruben, 1992a 1992 b; Konstam, 1996; Parkerson, 2000; Yerlin, 2002; Lowrie, 2003; Sokka et al 2004; Cunninham 2005; Efficace 2006; Sokka 2006a, 2008; Gupta 2007; 2006b; Kleefstra 2008; Kroenke 2008) and as such the finding of a tangible link between functional difficulty and mortality in this study may be relevant and require further investigation.

The complication of co morbidity in NAFLD and consequent prediction of mortality is answered in part by a recent study in America which noted that the significant indicators of mortality from NAFLD are being an older male of white race origin, of low education, low income, and having high BMI, hypertension, diabetes and metabolic syndrome;. It also showed that people with NAFLD had higher overall mortality and liver-related mortality than the normal population; with liver disease being the third leading cause of death among persons with NAFLD after cardiovascular disease and malignancy (Ong et al , 2008). Further investigation of these factors in our CLD cohort may be valuable in determining mortality or in better predicting individuals most at risk of developing liver disease.

## 8.2 The significant difficulty people with CLD are experiencing with hygiene and arising

The advantage of using PHAQ to measure functional difficulty in those with CLD was the tool's ability to categorise functional difficulty into domains; dressing, arising, eating, walking, hygiene, reach, grip, activity. This study has shown that the daily activities captured in the domains of arising and hygiene are significantly more difficult for people with CLD to perform. Participants with ALD and NAFLD had significantly more difficulty with arising than PSC participants as whole groups, but significantly more than PBC when comparing those with difficulty.

It may be that the significant difficulty experienced by those with ALD and NAFLD is due to physical deconditioning of the muscle groups needed to perform the gross motor transfers needed to sit to stand and transfer in and out of bed. Muscle weakness has been shown in people with CLD (Jones, 2010) and chronic alcoholic myopathy is undoubtedly a factor in the difficulty those participants with ALD have in these particular domains, with muscular atrophy most predominant in the shoulder and hip (Martin and Peters 1985; Urbano- Márquez and Fernández-Solà 2004; Vargas and Lang, 2007).

The nested qualitative study showed that participants' with NAFLD all reported being prevented from participating in activities of importance to them because of physical limitations caused by co morbidity rather than as a direct result of their liver disease. One NAFLD participant reported increasing their daily exercise in order to lose weight. However all the participants were experiencing spiralling difficulty with their activities



due to their physical deconditioning, weight, pain and breathlessness. Physical deconditioning was also shown to be impacting greatly on the participants with ALD. Whereas the participants with NAFLD associated this with their co morbidities, the ALD participants attributed their difficulties in performing activities directly to their alcohol addiction; be that in a physical, environmental or social context.

The qualitative data collected in this study indicates that exercise uptake is unlikely to be effective in participants with NAFLD due to the lack of conviction of the prescription of exercise and diet modification and for those with ALD, their alcohol dependency and physical deconditioning. Interestingly, the proximal myalgia and atrophy described by the participants with ALD is reversible with the abstinence of ethanol (alcohol) (Peters, 1985; Vary et al2004). This was demonstrated in this study by those participants from the ALD AB group, who although experiencing co morbid pain from OA, were physically active and participating fully in all aspects of day to day life.

But what of the PBC patient? Recent studies have identified people with PBC as also having muscle weakness (Newton 2006a; Blackburn 2007; Jones 2010) and yet their difficulty with the activities in the arising domain was significantly better than those with NAFLD and ALD. Evidence is available that demonstrates people with PBC have muscle weakness and significant difficulty with sit to stand (Frith 2010). This is likely to impact on their ability to get up from a chair, or in, and out, of bed. So does the significantly better performance, in this domain, of those with PBC mean that the difficulty experienced by those with ALD and NAFLD is simply dreadful? Here, insight may be given in the objective study of the participants by the researcher. Although further scientific and socio-economic study would be required, it may be that the PBC participants are more average in weight with better diets and lifestyles than those with NAFLD and ALD thus have generally better 'health', muscle strength and muscle recovery, or it may simply be that the participants in this study with PBC have more appropriate seating and higher beds, thus making the sit to stand transfer easier.

The domain of hygiene was significantly more difficult for ALD and NAFLD participants than PSC participants as whole groups, but there was no significance in the functional ability between any of the CLD groups when comparing only those with difficulty. This may clarify the hypothesis that those same weakened muscle groups necessary for both the sit to stand transfer and the bathing transfer are affecting all CLD

participants to the same degree, and whereas baths tend to come as a standard size thus creating a universal difficulty, chairs and beds can be bought to suit the user.

### 8.3 The significance of liver disease severity and poor function

Correlations with biochemical data and PHAQ showed significant relationships with difficulty in function of the CLD group as a whole with low bilirubin, low ALT and high ALB. None of these biochemical markers independently associated with function when the CLD participants were analysed as a whole group.

The independent associations of low bilirubin and low ALB with worsening function in the NAFLD participant group requires further investigation; in light of Ong et al 's (2008) study into mortality predictors in NAFLD, BMI, race, income, education and co morbidities should also be considered in conjunction with symptom burden if we are to understand more clearly the influencing factors in functional difficulty.

There was no significant difference in the functional difficulty of participants who had early stages of liver disease (pre cirrhotic) compared to those with more advanced disease (cirrhotic). Similarly, when comparing disease groups, although some associations were present between participants' biochemical results and their PHAQ total scores in ALD and NAFLD, the absence of significant differences between the cirrhotic and pre cirrhotic participants in each disease group suggests that disease severity does not determine functional difficulty in people with CLD. This reflects the findings in previous research in PBC which showed that disease severity does not influence symptom burden (Newton, 2006a; Blackburn et al , 2007).

In other words it is the accumulation of the systemic effect of liver disease that is the problem for people with CLD, not the degree of their liver damage.

### 8.4 The significance of symptom burden and poor function

The relationship between functional difficulty and increased symptom burden was demonstrated in this study as CLD participants had significant associations with poor function and increased age, increased orthostatic symptoms, increased cognitive difficulty, increased fatigue and increased day time somnolence. In each disease group functional difficulty independently associated with poorer memory and concentration, increased fatigue and increased orthostatic symptoms.

This is hugely important as growing numbers of people are being diagnosed with liver disease, and lots more people have liver disease but are not yet diagnosed (Vernon, 2011). These undiagnosed people are likely to be affected by the systemic impact of the disease even at a low level, and may already be on the downward spiral of activity avoidance, physical deconditioning and eventual difficulty with function before a diagnosis of liver disease is made. Public information campaigns, similar to that used in diabetes, stroke and heart disease (<http://guidance.nice.org.uk>) may be useful in raising awareness of liver disease, its symptoms and its management to stall the rising epidemic.

#### 8.5 The significance of age and poor function.

Increasing age correlated with functional difficulty for both NAFLD and PSC participants but not with ALD or PBC participants. This reflects elements of Frith's study in 2009 that showed increased age associating with prevalence of fibrosis in NAFLD participants and in those participants who were cirrhotic. Studies have also shown the increase in co morbidity of the NAFLD patient with increasing age (Kagansky et al, 2004; Verne, British Liver Trust 2012) and these factors would all influence an increase in functional difficulty.

More interesting are the PBC and ALD participants, as in neither condition did worsening function associate with age. We know that PBC participants are significantly older than the other disease groups and again the question is raised as to whether socio-economic factors, socio cultural, lifestyle, education or social class resulted in their being 'healthier' for their age, certainly in the context of the comparison of participants with CLD. Conversely, have the damaging effects of alcohol dependency in ALD participants rendered their age irrelevant when measuring functional difficulty even in those cirrhotic participants.

#### 8.6 The significance of day time somnolence and poor function

Day time somnolence associates with poorer functioning in PBC participants and improved function in ALD participants. This better functioning of ALD participants with higher ESS scores can be illuminated by the qualitative data which tells us that people with ALD have very poor sleep at night, therefore any sleepiness through the day would be expected as a consequence, and a probability that day time sleep would improve function by counteracting the negative influence on function of sleep

deprivation. Of course, this may not be so straight forward; studies have shown links between alcoholism and depression, low energy, social isolation and increased pain as well as day time somnolence (Allen 1980; Foster and Peters 1999; Krystal 2008). Here, the link with day time somnolence is attributed to day time drinking which in turn leads to difficulty sleeping at night. People who persistently use alcohol have been shown to find going to sleep without having an alcoholic drink more difficult, but studies show that using alcohol as a sleep aid depreciates the quality of sleep achieved. Importantly for those participants in this study who wanted to detox from their alcohol dependency and who were having suicidal thought due to insomnia, are the studies showing that insomnia perpetuates alcohol dependency and may be a predictor of alcoholism (Gillin et al 1994; Weissman et al , 1997; Peters and Foster 1998; Drummond et al, 1999; Brower et al, 2001; Brower 2003).

The findings with the PBC participants support those of Newton et al (2008) who found a significant correlation between day time somnolence and fatigue in people with PBC.

#### 8.7 The significance of fatigue and poor function

Fatigue, measured by the symptom tool FIS was found to correlate with poor function in every liver disease group. Interestingly, although people with PBC are known to be greatly affected by fatigue, only in the NAFLD and PSC participant groups did poor function associate independently with fatigue. Whilst understanding the pathogenesis and impact of fatigue in people with liver disease remains controversial, due in part to the subjective nature of fatigue, the causation of fatigue can be explained generally in two ways; peripheral fatigue and central fatigue. Typically to date, the fatigue experienced by people with CLD has been explained using the latter, central fatigue whereby the cytokines impact on neurotransmitters affecting autonomic centres, thus leading to fatigue, cognitive difficulty and autonomic symptoms (Jones, 2004; Swain, 2006). As there is much evidence to support the role of fatigue in people with PBC, it is plausible that in this study, the PSC participants are experiencing fatigue to the same degree as those with PBC. However the combined influence of symptoms such as day time somnolence and orthostatic symptoms appear to contribute to fatigue more greatly in PBC.

The incidence of fatigue in NAFLD participants may however be due to peripheral fatigue, categorised by neuromuscular dysfunction occurring with metabolic change.

Here, cardiac and +/- volume problems result in lowered blood pressure and consequent poor perfusion of brain and muscle, resulting in cognitive dysfunction, orthostatic symptom and fatigue (Swain, 2000; 2006; Chaudhuri and Behan, 2004)

Regardless of causation, the fact remains that fatigue plays an important role in the function of people with liver disease and undoubtedly contributes to the downward spiral of decreased activity and difficulty with function. Occupational therapists have long recognised the importance and impact fatigue plays in the daily ability of people to perform their activities (Cox , 1994, 1998a, 1998b, Rubal and Iwanenko, 2004) and are the ideal professional group to incorporate strategies such as time management, energy conservation and graded aerobic exercise in order to promote engagement with activity (Cook et al, 1997; Gardener 1997; Wearden et al, 1998), within a service development for people with CLD. Working with liver patient groups to negotiate best practice in this seems astute in light of the qualitative findings from this study where NAFLD participants in particular criticised the prescriptive exercise and lifestyle advice of ‘doctors’.

#### 8.8 The significance of cognition and poor function.

As with fatigue, the independent associations of poor function and increased cognitive difficulty found in this study can be arguably answered by the resulting impact of cholestasis or by cardiac and volume dysfunction. Poor cognition correlated with poor function in all the liver disease groups and was independently associated in ALD, NAFLD and PBC. Several studies have linked poor cognition with CLD (Cortez-Pinto, et al, 1999; Yaffe et al, 2004; Newton 2008, Fattakhova 2009; Hollingsworth, 2010), and this study adds to that body of work as it begins to identify the real importance of cognitive difficulty for those participants with CLD who have worsening memory and concentration. Qualitative data collected from a participant in the ALD AB group highlighted the memory problems experienced by people with ALD, possibly as residual damage from alcohol dependency were of greater distress than the pain endured from OA; in particular the participant highlighted the embarrassment of losing ‘track’ during conversations and the worry of not remembering the taking of medication. Too easily are occupational therapists channelled into seeing cognitive difficulties as a problem when discharging people from hospital as a practical safety issue without addressing the emotional aspect of living and coping with the situations that arise from

the social aspects of cognitive dysfunction. No reference was made by occupational therapists or doctors working on liver wards of advice or intervention put in place to address this significant problem (Elliott, 2010) and during the qualitative interviews, no mention was made of this area of symptom burden being appreciated, much less addressed, by any of the disease groups or participants. As occupational therapists are well equipped to work with people who have cognitive difficulties, and have techniques and equipment available to them to assist people in managing activities affected by their cognition (Ponsford, 1995; Wheatley 1996; O'Neill, 2002), the necessity of developing a quality service for people with CLD that prioritises occupational therapists and their expert skill in comprehensive cognitive assessment and intervention becomes paramount.

#### 8.9 The significance of orthostatic symptoms and poor function

An increase in orthostatic symptoms as measured by OGS correlated with worsening function in all the liver disease groups and independently associated with worsening function in participants with ALD and PBC. The prevalence of orthostatic dysfunction in CLD has been recognised by Newton (2009) and Frith (2009) and orthostatic symptoms and falling has been established in people with PBC by Frith (2010) who also highlighted fear of falling as being relevant in this area

The qualitative data in this study highlights well the problem participants with ALD have with orthostatic symptoms in the terms of dizziness on transfer (sit to stand and bathing) and bending. The likely explanation for this is blood volume, vagal nerve dysfunction, autonomic neuropathy and dehydration (Lindgren, 1997), abnormalities frequently found in patients with ALD (McAvoy, 2012). Further investigation into the self management of orthostatic symptoms e.g. education on symptom prevention, fluid intake, and a compensatory approach e.g. prescription of equipment to assist sit to stand or bed transfer, may prove beneficial to people with liver disease and could be easily incorporated into a comprehensive service for people with CLD.

#### 8.10 Functional difficulty and symptom burden in people post liver transplant.

This study has demonstrated the surprising discovery that people post transplant have significantly worse function than comparator groups, both as whole groups and as groups where only those experiencing difficulty were compared, and have greater prevalence of difficulty than comparator groups. In addition, the activities captured in

the domains of arising, eating, hygiene and reach are significantly more difficult for people who have undergone a liver transplant to perform.

The impact of fatigue, concentration and memory difficulties, day time somnolence and orthostatic symptoms have a combined effect on those post transplants' ability to function; with fatigue as measured by the symptom assessment tool FIS, being independently associated with poor function. Importantly, no association was made between the participants function and their use of immunosuppressant therapy.

Importantly the discovery that no significant difference was present in the functional ability and symptom burden of participants post transplant when compared to pre transplant disease counterparts is concerning. Ground breaking hepatocyte generation technology recently hit the headlines as the 'cure' for liver disease and as a replacement treatment for liver transplantation (The Independent 2012; Boulter, 2012); this is undoubtedly an incredibly important scientific discovery, however as the results from *this* study are suggesting that fixing the liver does not fix the person, focus needs to remain on the empirical living aspect of CLD, in particular the associated symptom burden, and services that utilise Occupational Therapists to deliver pre and post transplant interventions that engage participants in activity.

Although public domain websites offering patient information post liver transplant claim most people regain 'normal activities' after their transplant (Britishlivertrust.org 2012; NIDDK, 2012) studies show that fatigue remains a problem for this patient group (O'Carrol 2003). A study by Scott (2012) confirmed that although an improvement in daily activities was noted in post transplant people 3 months after transplant, their activity declined by the end of the first year. The accumulation of symptom burden demonstrated in his study may lend valuable insight as to the cause of this decline and be worthy of further investigation.

#### 8.11 The impact of anxiety on function

Participants with ALD were the group whose activity was most affected by anxiety. The association of depression and anxiety on function is increasingly recognised (Mehta 2007; Van Ginneken 2010; Bauke 2011; Kim 2011), however, the qualitative data elicited from those participants in the ALD group regarding the fear they have of withdrawal seems under reported in the medical literature (Allen, 2005) and as such the

emphasis on daily function is ignored in the main. This study has captured the depth of fear associated with the experience of alcohol withdrawal; collapse, seizure, pain along with the detrimental affect of sleep deprivation that far out weighed their loss of productivity, self-care and leisure activities. Recent literature from the UK Alcohol Treatment Trial accepts that treatment for people wanting to withdraw from alcohol should be seen as a complex system, incorporating cognitive, social and behavioural change (Orford, 2006) but perhaps the inclusion of activity specific goals would be beneficial. It would be naive to assume that engaging this particular client group is not difficult and complex, but perhaps a better empathy and a tailored, flexible intervention focusing on roles and activity goals, would encourage adherence to the alcohol withdrawal programmes that is currently lacking (Allen 2005; Laudet, 2009).

The issue of respect; both self respect and respect from others, was the one factor which the ALD participants reported as having (potential) to influence them to address their alcohol dependency and in turn, increase their engagement in activity. This may take a mind-set shift, drawn from better understanding, education and empathy from all parties involved in those with alcohol dependency; patient, medical and rehab staff, families and the general public, in not only appreciating the ease at which alcoholism can take hold, but in appreciating that there is life after alcohol dependency. Those participants in this study affected by ALD and alcohol dependency have allowed us the opportunity to really understand the problems and fears they experience daily, which is a candid act certainly worthy of our gratitude and respect; a first step towards change perhaps.

Further studies which appreciate the journey from alcoholism to recovery, and from recovery to participation, may be useful, if not the key, to informing future alcohol and rehabilitation programmes.



## Chapter 9 Conclusion

This study has shown the extent to which people living with CLD are experiencing functional difficulty and how significantly worse that experience is when compared to community comparators. It has shown that it is the systemic affects of liver disease and the symptom burden therein that adversely affects function and not the severity of the liver disease itself.

This study has given valuable insight to those areas of daily function most affected for people with liver disease along with the diversity and complexity therein, and has shown the correlations and associations liable for this difficulty.

This study has demonstrated that whilst for medical management the causation of the symptom burden is important, for occupational therapists well geared to play an important role in the treatment of this disease cohort, individually tailored interventions which incorporate a broad spectrum of occupational therapy skills is required.

### 9.1 Limitations

#### 9.1.1 *The database*

It is important to acknowledge that the studies presented in this thesis have a number of potential limitations.

The patient populations included in the quantitative parts of the study were drawn from clinics at the tertiary referral centre at Freeman Hospital, Newcastle. Patients attending clinics are more complex, or more symptomatic, than population based cohorts (Crook, 1986; Roy, 1990; Allison, 1996; Mailis-Gagnon, 2007). As the PBC group are, in the main, a community rather than clinic based group, their symptom and functional difficulty scores may not be as comparable as those in the NAFLD, ALD and PSC groups who are clinic cohorts. It may be that the PBC scores have lowered the functional difficulty overall of the CLD group, or increased the significant differences present between the liver disease groups. However, as this thesis has demonstrated that liver disease severity is not related to functional difficulty, the importance of the breadth of participants available, outweighs the clinic/community comparability issue.

The inclusion of ALD, NAFLD, PBC and PSC cohorts were a reflection of previous local research interests and available databases. The subsequent building of a database

for use in the NIHR BRC liver theme included these liver diseases and as such was used in this study. The inclusion of other chronic liver diseases in this study, such as viral hepatitis, would have given a broader insight into the functional difficulty of people under the umbrella term 'CLD' and as such the omission of this disease group is regrettable.

The study concentrates on a regional cohort of participants from the North East of England, both those with CLD and the community dwelling comparator group. The exception were those participants from the post liver transplant group who may have resided elsewhere in the UK; it was necessary to include these participants however, due to the low numbers of people receiving liver transplants in the north east in the last 5 years.

### *9.1.2 The participants*

We determined the prevalence of functional difficulties in a group of chronic liver disease patients; the composition of this group may well not reflect the aetiological groups within a CLD patient group in the community which is one of the reasons we felt that it was important to represent the individual CLD groups in addition to the overall group. The proportion of PBC (19%) and ALD (23%) participants in this study is not truly representative of CLD as a whole (End of Life Care-Intelligence 2012). The patient group LIVERNORTH is a proactive patient group whose members are largely women with PBC. This dedicated patient group is a valuable resource; they are a highly motivated, research-active cohort, who tend to have a relative in-depth knowledge of their condition given the regular feedback they receive from academics at their patient support group. In addition, the PBC participants are the only cohort in the study who are geographical rather than clinical, and this therefore limits comparability between the groups.

Low numbers, (24%), of people from the ALD group returned the functional assessment tools used in this study and only subjective opinion can be given as to whether those who did respond were the less or the more symptomatic participants representative of this cohort.

| The number of participants interviewed in Chapter 7 from each disease group is low and may have affected the power of the study; therefore the results from the qualitative data

cannot be conclusive in describing their disease groups (Collier, 1995). Bias may also have been caused due to the possibility of those interested in participation as having a vested interest in the study and therefore influencing the results by having strong opinions outside of a general view.

This selection bias does not allow informational redundancy or theoretical saturation (Sandelowski, 2007), in other words there is not enough evidence when using small numbers to either state a consensus or to highlight outlying opinions. However those recruited were appropriate for participation in the context of a nested study asking specifically the impact of functional difficulty in those with ALD and NAFLD. The lack of focus on their age and gender also means that disease specific generalisations cannot be made, as social, cultural and economical aspects were not considered when analysing the data. The benefit of this are however, in the removal of the stereotyping of the participants involved.

It is possible that there is bias involved in the returning of questionnaires. One possibility is that those people who perceive themselves not to have any functional difficulty may be less likely to respond to such questions, this could lead to over stating the extent of functional difficulty. However, this reasoning is speculative and it may also be equally possible that those who do not have functional difficulty are in a position to respond more freely to questionnaires which would result in underestimating the problem. Techniques to improve response rates, and therefore reduce bias, were used in this study; participants had been previously asked if they wanted to partake in future studies, stamped addressed envelopes were provided, second round questionnaires were sent to those who did not initially respond, the questionnaires were of 'interest' to the participants and they were sent from a university (Edwards, 2002). In addition is the importance that in this study, the questionnaire used was chosen by people with liver disease; its use reduced researcher bias, it was relevant to the cohort, and it generated a large population of participants willing to share their experience of living with CLD.

### *9.1.3 Data collection*

It must be acknowledged that while this study was able to assess functional difficulty it was not involved in the collection of more invasive medical data, such as blood testing and liver biopsy. Where results of laboratory data are used they have been collected

from the Newcastle Upon Tyne NHS Foundation Trust liver database. This has the disadvantage of the clinical investigation results not being truly contemporaneous with the questionnaires. However, in an attempt to reduce this limitation the researcher used the participants most recent results available on the 3<sup>rd</sup> March 2008; in only a minority of cases were these results over 2 years old.

The choice of environment in which to conduct the semi structured interview was restricted for the ALD participants due to their being in the acute hospital setting. At times the interviews were interrupted by ward staff or other patients and the interviews were held at a time convenient to the ward rather than the participant. In addition, this ALD in-patient cohort can not represent the general ALD population as they represent a much more severe/complex patient group.

#### *9.1.4 Biochemical parameters*

The liver function test results (LFT) used in this study does not directly reflect hepatic synthetic function or hepatic compensation/decompensating. This is an important limitation to this study when discriminating between liver diseases independent of severity of hepatic damage. Although this study did not specify participants with end-stage liver disease, consideration of use the Model for End Stage Liver Disease (MELD) (Karmath et al, 2001; Weisner et al 2001; Kim et al 2008) and Child-Pugh scores (Desmet et al, 1994) would have been valuable.

#### *9.1.5 Analysis*

Limitations in data analysis are mostly found in the results for the PSC cohorts where within-cohort group, sizes were too small for meaningful statistical analysis.(Lipsey, 1990). Analysis was performed to maintain a consistent approach but it is acknowledged that these results must be interpreted with caution. Similar caution is required when interpreting the statistical results relating to those participants who had died following the 2008 survey (low sample size).

An a priori sample size calculation was not performed prior to study recruitment. As this is the first study of its kind it would not be possible to estimate effect sizes (Lipsey, 1990; Fowler, 2008). Furthermore, this study has a more pragmatic, clinical approach, using both clinical and statistical significance. This is an important and unique, hypothesis generating study, which aimed to inform future research.

### 9.1.6 Questionnaires

The PHAQ has never previously been validated for use in a purely CLD cohort; however it has been validated in several other chronic disease cohorts. The PHAQ also has the advantage over other functional assessment tools because it is validated in all age groups.

## 9.2 Future Work

There remains a dearth of evidence available to inform clinical practice of the functional difficulties experienced by people with CLD, although the need for such evidence is certainly not lacking. Importantly, as the global epidemic of CLD continues to rise, more research will be required in order to ensure that the best management, and value-for-money service provision, is available for this complex disease cohort. The work presented in this study provides evidence to contextualise the complex functional difficulty experienced by people with liver disease and the impact this increasing number of people with CLD will have on resources.

### 9.2.1 Developing results from this study

The differing results from the study between the liver disease groups warrants further study. In particular the notable greater functional difficulty of those with NAFLD and ALD in comparison with those who people who have PSC. In order to validate the findings in this thesis, future studies that compare participants' comorbidities, fitness, body mass index, diet and alcohol consumption may be insightful.

### 9.2.2 In other liver diseases

As people with other liver conditions, such as viral hepatitis, were omitted from this thesis, a repeat survey of participants from other liver disease cohorts, using the same functional and symptom assessment measurement tools, would be beneficial in capturing a broader representation of functional difficulty in CLD

### 9.2.3 An In service development

The clinical relevance of this study calls for its consideration in the development of services for people with chronic liver disease. Ideally these services should be occupational therapy strong and focus on increasing functional independence for people with CLD and include symptom management. This study has identified that functional difficulty is significant in people with CLD and therefore future studies are needed to

explore ways in which to address this problem. Such research should involve those people affected by CLD, to ensure treatment is complied with, rather than prescribed to. Examples of a possible occupational therapy programme would include initial assessment that encompasses identification of problems and goal setting. Possible interventions to achieve individual's goals may be graded exercise, cognitive training, fatigue management and lifestyle advice. The occupational therapy programme could initially mirror those used in respiratory and cardiac rehabilitation services. This would enable a 'wide-net' approach to delivering an expedient intervention for those presenting at a liver out-patient clinic. A stand alone CLD occupational therapy service delivering client-centred intervention which manages function, symptom and lifestyle would however be the ideal.

#### *9.2.4 In Occupational Therapy*

The current approach to people with CLD in occupational therapy requires urgent research as this study demonstrates the clear need for interventions that address not only the significant functional difficulty experienced by this disease cohort, but the great symptom burden that impacts on both function, and quality of life. Studies that challenge the way in which occupational therapy is delivered in the acute setting, and the development of out-patient, and community services for people with CLD, are necessary if the real issues of living with CLD are to be addressed. Such studies should reflect the take home message from this thesis, of the constellation of functional difficulty and symptom burden endured by people with CLD.

#### *9.2.5 In public awareness*

Increased effort is needed to better inform the general public of the rising problem of liver disease. This study has demonstrated that people with liver disease have a lack of understanding about their condition; often associating their symptoms with comorbidities rather than CLD. A study which a) challenges the preconceptions and stigma of liver disease, and b) increases public awareness of causal factors and symptom burden in CLD is required. Such studies and awareness campaigns should incorporate a range of media from billboard advertising to mobile phone apps to ensure the message of the campaign reaches a wide audience, encompassing people of all ages, incomes and educational levels.

### 9.2.6 *In liver transplantation*

This study has identified that people following liver transplant have significantly worse function than that of comparator populations; indeed, it is to the same degree of difficulty as that of people with CLD. Urgent research is needed into the pre, and post operative, intervention available to people undergoing liver transplantation, to ensure occupational therapy interventions that address function, are central to service provision.

## References

- Allen J, Copello A, Orford J, (2005). Fear during alcohol detoxification: views from the clients' perspective. *J Health Psychol*, 10(4):503-10
- Allen RP, Wagman AM, Funderburk FR, Wells DT, (1980). Slow wave sleep: a predictor of individual differences in response to drinking? *Biol Psychiatry*, 15: 345–348.
- Allison JJ, Kiefe CI, Centor RM, Box JB, Farmer RM, (1996). Racial differences in the medical treatment of elderly Medicare patients with acute myocardial infarction. *J Gen Intern med*, 11:736–43.
- Anstee, QM, McPhearson S, Day CP (2011) , How big a problem is non-alcoholic fatty liver disease? *BMJ*;343:d3897
- Bailey A, Starr L, Alderson M, & Moreland J, (1999). A comparative evaluation of a Fibromyalgia rehabilitation program. *Arthritis Care and Research*, 12(5):336-340.
- Barclay L, (2002). Exploring the factors that influence the goal setting process for occupational therapy intervention with an individual with spinal cord injury. *Australian Occupational Therapy Journal*, 49(1):3-13.
- Barras S, (2005). A systematic and critical review of the literature: The effectiveness of Occupational Therapy Home Assessment on a range of outcome measures. *Australian Occupational Therapy Journal*, 52: 326–336
- Barsevick AM, Dudley W, Beck S, Sweeney C, Whitner K, Nail L, (2004). A randomized clinical trial of energy conservation for patients with cancer-related fatigue. *Cancer*, 100 (6): 1302-1310.
- Bauke T, Nazaereth I, Torrez-Gonzalez et al (2011). Depression, anxiety and physical function: exploring the strength of causality. *J Epidemiol Community Health*, doi:10.1136/jech.2010.128371
- Bergman, M.M. (2011) The politics, fashions and conventions of research methods. *Journal of Mixed Methods Research*, 5 (2), 99-102
- Bjelland I, Dahl AA, Haug TT, Neckelmann D, (2002). The validity of the Hospital Anxiety and Depression Scale: an updated review. *J Psychiat Res*, 52: 69–77
- Blackburn P, Freeston M, Baker CR, Jones EJ, and Newton J, (2007). The role of psychological factors in the fatigue of Primary Biliary cirrhosis. *Liver International*, 27 (5): 654-661
- Booth ML, (2000). Assessment of physical activity: An International Perspective. *Research Quarterly for Exercise and Sport*, 71 (2):114-20.
- Boulter L, Govaere O, Bird TG, et al, (2012). Macrophage-derived Wnt opposes Notch signalling to specify hepatic progenitor cell fate in chronic liver disease. *Nature Medicine*. Available at <http://www.nature.com>. Accessed March 8th 2012
- British Liver Trust (2008) Available at: [www.britishlivertrust.org](http://www.britishlivertrust.org) Accessed on 3.04.08.



British Liver Trust (2012) Available at: [www.britishlivertrust.org](http://www.britishlivertrust.org) Accessed on 1<sup>st</sup> March 2012

Broadbent DE, Cooper PF, FitzGerald P, Parkes KR, (1982). The Cognitive Failures Questionnaire (CFQ) and its correlates. *British Journal of Clinical Psychology* 1982; 21:1-16.

Brower KJ, (2003). Insomnia, alcoholism and relapse. *Sleep Med Re.*,7(6): 523–539.

Brower KJ, Aldrich MS, Robinson EAR, Zucker RA, Greden JF, (2001). Insomnia, self-medication, and relapse to alcoholism. *American Journal Psychiatry*, 158: 399–404.

Bruce B, and Fries F, (2003).The Stanford Health Assessment Questionnaire: Dimensions and Practical Applications. *Health and Quality of Life Outcomes* 1:20

Bryman, A. (2006) Integrating quantitative and qualitative research: how is it done? *Qualitative Research*, 6 (1), 97-11

Canadian Association of Occupational therapists, (2012). Available at <http://www.caot.ca/copm/description.html>. Accessed June 10<sup>th</sup> 2012

Card TR, Solaymani-Dodaran M, West J, (2008). Incidence and mortality of primary sclerosing cholangitis in the UK: a population-based cohort study. *J Hepatology*. 2008 Jun;48(6):939-44. Epub 2008 Mar 31

Cauch-Dudek K, Abbey S, Stewart DE, Heathcote EJ, (1998). Fatigue in primary biliary cirrhosis. *GUT*, 43: 705-710.

Chalasanani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, Charlton M, MD, Sanyal AJ (2012). The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology*; Available at: [http://www.aasld.org/practiceguidelines/Documents/NonalcoholicFattyLiverDisease2012\\_25762\\_ftp.pdf](http://www.aasld.org/practiceguidelines/Documents/NonalcoholicFattyLiverDisease2012_25762_ftp.pdf). Accessed 20<sup>th</sup> September 2012.

Chamberlain A, Thornley G, Stowe J, and Wright V, (1981). Evaluation of Aids and Equipment for the Bath: II. A Possible Solution to the Problem. *Rheumatology*, 20: 38-43.

Chapparo C, and Ranka J, (1997) Occupational Performance model (Australia) Monograph 1.[www.occupationalperformance.com](http://www.occupationalperformance.com). Accessed April 23rd 2008

Charatcharoenwitthaya P, Lindor KD (Feb 2006). "Primary sclerosing cholangitis: diagnosis and management". *Current Gastroenterology Reports* 8 (1): 75

Chaudhuri A, Behan PO, (2004). Fatigue in neurological disorders. *Lancet*, 363: 978–88.

Chen YH, Rodger S, & Polatajko H, (2002). Experiences with the COPM and client-centred practice in adult neurorehabilitation in Taiwan. *Occupational Therapy International*, 9(3)167-184.

Christiansen CH, Townsend EA Ed (2004) *Introduction to occupation: the art and science of living*. Upper Saddle River, NJ: Prentice Hall

Claridge L, (2011) Rising liver death rate: food for thought. *The Lancet*, 377 (9784): 2179 – 2180,

Clavien, P.A, Killenberg, P. (2006). *Medical Care of the Liver Transplant Patient: Total Pre-, Intra- and Post-Operative Management*. Wiley-Blackwell. pp. 155. ISBN 1-4051-3032-6

Cleland J., Lee A., Hall S, (2007). Associations of depression and anxiety with gender, age, health-related quality of life and symptoms in primary care COPD patients *Fam Pract*,.24(3):217-23

Cobbold JF, Anstee QM, Thomas HC.(2010). Investigating mildly abnormal serum aminotransferase values. *BMJ*;341:c4039

Collie A, (2005). Cognition in Liver Disease. *Liver International*, 25:1-8.

Collier, D. (1995). Translating Quantitative Methods for Qualitative Researchers: The Case of Selection Bias Author(s): *The American Political Science Review*, 89, 2. 461-466

Cook NF, Boore JR, (1997). Managing patients suffering from acute and chronic fatigue. *British Journal of Nursing*, 6: 811–5.

Cortez-Pinto H, Camilom ME, Baptista A, De Oliveira A, De Moura MC, (1999) Non-alcoholic fatty liver: another feature of the metabolic syndrome? *Clinical Nutrition*, 18: 353–358.

COT (2004) Guidance on the use of the instructional classification of functioning, Disability & Health (ICF) and the OTTAWA Charter for Health Promotion in OT Services. *College of Occupational Therapists*. London:

COT (2009). College of Occupational Therapy's Curriculum Guidance for Pre registered Education. London.

COT (2011). Professional Standards for Occupational Therapy Practice College of Occupational Therapy. London.

COT Code of Ethics (2011). Available at: [http://www.cot.co.uk/sites/default/files/publications/public/Code\\_of\\_Ethics\\_2010.pdf](http://www.cot.co.uk/sites/default/files/publications/public/Code_of_Ethics_2010.pdf). Accessed 28<sup>th</sup> February 2012.

Cox DL, (1998b) The Management of Chronic Fatigue Syndrome - development and evaluation of a dedicated service. *British Journal of Therapy and Rehabilitation*, 5 (4): 205-209

Cox DL, Findley LJ, (1994). Is Chronic Fatigue Syndrome treatable in an NHS environment? *Clinical Rehabilitation*, 8 (1):76-80

- Cox DL, Findley LJ,(1998a) The Management of Chronic Fatigue Syndrome in an Inpatient Setting: Presentation of an Approach and Perceived Outcome. *British Journal of Occupational Therapy*. 61(9) :405-409
- Craig C, (2003). The International Physical Activity Questionnaire: 12-country Reliability and Validity. *Medicine and Science in Sport and Exercise*. 3(8): 1381-1395.
- Crook J, Tunks E, Rideout E, Browne G, (1986). Epidemiologic comparison of persistent pain sufferers in a specialty pain clinic and in the community. *Arch Phys Med Rehabil*;67:451–5.
- Cunningham W, Crystal S, Bozzette S, Hays R, (2005).The association of health-related quality of life with survival among persons with HIV infection in the United States. *International Medical Journal Gen*, 20: 21-7.
- Cup EH, Scholte op Reimer WJ, Thijssen MC, Kuyk-Minis MA(2003). Reliability and validity of the Canadian Occupational Performance Measure in stroke patients. *Clin Rehabil*, (4):402-9.
- Cusick A, McIntyre S, Novak I, Lannin N, Lowe K. (2006). A comparison of goal attainment scaling and the Canadian Occupational Performance Measure for paediatric rehabilitation research. *Pediatr Rehabil* ,9(2):149-57.
- Day CP, (2012). Commentary in British Liver Trust.org.uk. Accessed March 6th 2012.
- Department of Health (2012). Available at:[http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_131724.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_131724.pdf) Accessed March 28h 2012.
- Desmet, V. J., Gerber, M., Hoofnagle, J. H., Manns, M. and Scheuer, P. J. (1994), Classification of chronic hepatitis: Diagnosis, grading and staging. *Hepatology*, 19: 1513–1520.
- Drummond SP, Gillin JC, Smith TL, DeModena A, (1998). The sleep of abstinent pure primary alcoholic patients: natural course and relationship to relapse. *Alcohol Clinical and Experimental Research*. 22 (8): 1796–1802.
- Edwards P, Clarke M, DiGiuseppe C, *et al* (2002). Increasing response rates to postal questionnaires: systematic review. *BMJ*, doi: 10.1136/bmj.324.7347.1183
- Efficace F, Bottomley A, Coens C, *et al*. (2006). Does a patient’s self-reported health-related quality of life predict survival beyond key biomedical data in advanced colorectal cancer? *Eur J Cancer*, 42: 42-9.
- Elliott C, Frith J, Newton J, (2010). Occupational Therapy in chronic liver disease: a preliminary study to explore the views of Occupational Therapists and Physicians working in acute medical settings. *The British Journal of Occupational Therapy*, 73, (3):116-120
- Elliott C, Frith J, Newton JL, (2011). Functional Impairment is significant in Chronic Liver Disease. *College of Occupational Therapists’ Annual Conference*. Brighton.
- Elliott C, Newton J, (2009). Occupational Therapy in chronic liver disease: a gap in service delivery. *The British Journal of Occupational Therapy*, 72, (3):133-136

End of Life Care (2012). Available at [http://www.endoflifecare-intelligence.org.uk/resources/publications/deaths\\_from\\_liver\\_disease.aspx](http://www.endoflifecare-intelligence.org.uk/resources/publications/deaths_from_liver_disease.aspx). Accessed June 10<sup>th</sup> 2012.

Fattakhova GE, Jones DE, Frith J, Day CP, Newton JL (2009). Cognitive Symptoms and Prevalent in Non-Alcoholic Fatty Liver Disease (NAFLD) and Unrelated to the Severity of Liver Disease. *In: Hepatology: 60th Annual Meeting of the American Association for the Study of Liver Diseases.*, Boston, Massachusetts, USA: John Wiley & Sons, Inc.

Feld JJ, Heathcote EJ (October 2003). "Epidemiology of autoimmune liver disease". *J. Gastroenterol. Hepatol.* **18** (10): 1118–28

Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF, (1994). Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clinical Infectious Diseases*, 18:79-83.

Foster JH, Peters TJ, (1999). Impaired sleep in alcohol misusers and dependent alcoholics and the impact upon outcome. *Alcohol Clinical and Experimental Research*, 23 (6): 1044–1051.

Fowler FJ Jr (2008). *Survey Research Methods (4<sup>th</sup> Ed.)*. Thousand Oaks CA:SAGE

Fries JF, (1983). Toward an understanding of patient outcome measurement. *ArthritisRheum*, 26: 697–704.

Fries JF, Bruce B, Cella D, (2005). The promise of PROMIS: using item response theory to improve assessment of patient-reported outcomes. *Clin Exp Rheumatol*, 23(5 supplement 39):53–7.

Fries JF, Spitz PW, Young DY, (1982). The dimensions of health outcomes: the health assessment questionnaire, disability and pain scales. *J Rheumatol*, 9:789–93.

Fries, JF, Bruce B, Bjomer J, Rose M, (2006). Moving beyond the classic instruments assessment of physical function and disability. *Ann Rheum Dis*, 65:16-21

Frith J, Day CP, Henderson E, Burtm AD, Newton JL, (2009). Non-alcoholic fatty liver disease in older people. *Gerontology*, 55: 607–13.

Frith J, Newton JL (2009). Autonomic dysfunction in chronic liver disease. *Liver International*, 29(4), 483-489.

Frith J, Newton JL. (2010). Response: Primary biliary cirrhosis is associated with falls and significant fall related injury. *QJM*, 103(6), 438-439.

Frith JJ, Jones DE, Newton JL, (2008). Chronic Liver Disease in ageing population. *Age and Ageing*, 38: 11-18

Gardener M, (1997). Cognitive approaches. In: J Creek, ed. *Occupational therapy and mental health*. London: Churchill Livingstone.

Gillin JC, Smith TL, Irwin M, Butters N, Demodena A, Schuckit M, (1994). Increased pressure for rapid eye movement sleep at time of hospital admission predicts relapse in non-depressed patients with primary alcoholism at 3-month follow-up. *Archives of General Psychiatry*, 51: 189–197

- Goldblatt J, Taylor PJ, Lipman T, (2002). True impact of fatigue. *Gastroenterology*, 122(5):1235-41.
- Gray ML, and Fossey EM, (2002). Illness experience and occupations of people with Chronic Fatigue Syndrome. *Australian Occupational Therapy Journal* 50: 127-136.
- Graydon JE, Bubela N, Irvine D, Vincent L.(1995) Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nursing*, 18:23–8.
- Griffiths C, Rooney C, and Brock A, (2005). Leading Causes of Death in England and Wales. *Health Statistics Quarterly (Winter)*.
- Griffin, S. D. and McConnell, D. (2001), Australian occupational therapy practice in acute care settings. *Occupational Therapy International*, 8: 184–197.
- Gupta D, Granick J, Grutsch JF, Lis CG, (2007). The prognostic association of health-related quality of life scores with survival in breast cancer. *Support Care Cancer*, 15: 387-93.
- Gutteling JJ, et al, (2007). Overview of research on health-related quality of life in patients with chronic liver disease. *The Netherlands Journal of Medicine*, (65): 227-234
- Guyatt GH, Eagle DJ, Sackett B, Willan A, Griffith L, McIlroy W, *et al.* (1993). Measuring quality of life in the frail elderly. *J Clinical Epidemiology*,46:1433-44.
- Guyatt GH, Walter S, Norman G, (1987). Measuring change over time: assessing the usefulness of evaluative instruments. *Journal of Chronic Diseases*,40:171-8.
- Hagedorn R, (1997). Occupational Therapy is a complex, broadly based profession. In, *Foundations for practice in Occupational Therapy*: Churchill Livingstone.
- Hardinge, F.M, Pitson DJ, Stradling JR, (1995). "Use of the Epworth Sleepiness Scale to demonstrate response to treatment with nasal continuous positive airways pressure in patients with obstructive sleep apnoea". *Respiratory Medicine*, 89 (9):617–20.
- Harrison SA, Day CP, (2007). Benefits of lifestyle modification in NAFLD. *GUT*, 56: 1760- 1769.
- Heathcote EJ (October 2003). "[Epidemiology of autoimmune liver disease](#)". *J. Gastroenterol. Hepatol.* **18** (10): 1118–28
- Henryk Dancygier (2010). *Clinical Hepatology Principles and Practice of*. Springer.pp.895
- Herrmann C. (1997). International Experience with the Hospital Anxiety and Depression Scale: A review of validation data and clinical results. *Journal of Psychosomatic Research*, 42:17–41
- HilsabeckR, (2003). Neurocognitive changes in chronic liver disease. *J Psychosomatic Research.*, 55:121
- Ho PM, Masoudi FA, Peterson PN, (2005). Health-related quality of life predicts mortality in older but not younger patients following cardiac surgery. *American Journal Geriatric Cardiology*, 14: 176-82.

Hollingsworth G, Jones DEJ, Taylor R, Frith J, Blamire AM, Newton JL, (2010). Impaired cerebral autoregulation in primary biliary cirrhosis: implications for the pathogenesis of cognitive decline. *Liver International*, 30:878-85.

Hospital Discharge Workbook (1994). Department of health. Available at [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4003252](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4003252) - 15k. (Accessed on April 2nd 2009)

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4075214](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4075214)

Hubert HB, Bloch DA, and Fries JF,(1993). Risk factors for physical disability in an aging cohort: the NHANES I Epidemiologic Follow up Study. *Journal of Rheumatology*, 20(3):480-8.

Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A, (1997). Quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Rheumatology* 36 (5): 551-559.

Hyphantis T, Palieraki K, Voulgari PV, Tsifetaki N, Drosos AA,(2011). Coping with health-stressors and defence styles associated with health-related quality of life in patients with systemic lupus erythematosus. *Lupus*,.20:893-903

Ip WM, Woo J, Yue SY, Kwan M, Kwok T, (2006). Evaluation of the effect of energy conservation techniques in the performance of activity of daily living. *Clinical Rehabilitation*, 20: 256-261

Jacoby A, Rannard A, Buck D, Bhala N, Newton J L, James OFW, Jones DEJ, (2005). Development, validation and evaluation of the PBC-40 , a disease specific health related quality of life measure for primary biliary cirrhosis. *GUT*, 54: 1622-1629.

James OFW, Bhopal R, Howel D, Gray J, Burt AD, Metcalf JV, (1999). Primary Biliary Cirrhosis Once Rare, Now common in the United Kingdom? *Hepatology*.30(2):390-4

Johns MW, (1991). A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep*, 14: 540-545.

Johnstone, P.L. (2004) Mixed methods, mixed methodology health services research in practice. *Qualitative Health Research*, 14 (2) 259-271

Jones D, Hollingsworth K, Taylor R, Blamire A, Newton J, (2010). Abnormalities in pH Handling by Peripheral Muscle and Potential Regulation by the Autonomic Nervous System in Chronic Fatigue Syndrome. *Journal of Internal Medicine*,267(4):394-401.

Jones EA, (2004) Fatigue complicating chronic liver disease. *Metabolic Brain Disorder*, 19(3-4): 421-9.

Jorgensen RA (2003), Non-alcoholic fatty liver disease. *Gastroenterology Nursing*, 26(4):150-4

Jørgensen, K. K., Grzyb, K., Lundin, K. E.A., Clausen, O. P. F., Aamodt, G., Schrupf, E., Vatn, M. H. and Boberg, K. M. (2012), Inflammatory bowel disease in patients with

- primary sclerosing cholangitis: Clinical characterization in liver transplanted and nontransplanted patients. *Inflamm Bowel Dis*, 18: 536–545. doi: 10.1002/ibd.21699
- Kagansky N, Levy S, Keter D, (2004). Non-alcoholic fatty liver disease – a common and benign finding in octogenarian patients. *Liver International*, 24: 588–94.
- Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, D'Amico G, Dickson ER, Kim WR (2001). A model to predict survival in patients with end-stage liver disease. *Hepatology*.33(2):464-70
- Kim SH, Oh EG, and Lee WH, (2011). Symptom experience, psychological distress, and quality of life in Korean patients with liver cirrhosis: A cross sectional survey. *Gut and Liver* (4): 150-154.
- Kirshbaum MN, (2007). A review of the benefits of whole body exercise during and after treatment for breast cancer. *Journal of Clinical Nursing*, 16(1): 104-121.
- Kitzinger, J. (2006) 'Focus Groups' , in Pope, C. & Mays, N. (eds.) *Qualitative Research in Healthcare*. 2<sup>nd</sup> edn. Oxford: Blackwell, pp. 21-30
- Kim RW, Biggins S, Kremers WK, Wiesner RH, Kamath PS, Benson JT, Edwards E, and Therneau TM (2008). Hyponatremia and Mortality among Patients on the Liver-Transplant Waiting List *Engl J Med*; 359:1018-1026.
- Kleefstra N, Landman GW, Houweling ST, *et al* (2008). Prediction of mortality in type 2 diabetes from health-related quality of life (ZODIAC-4). *Diabetes Care*, 31: 932-3.
- Konstam V, Salem D, Pouleur H, *et al*. (1996). Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. *American Journal of Cardiology*, 78: 890-5.
- Korner-Bitensky N, Desrosiers J, Rochette A (2008). A National Survey of Occupational Therapists' Practices Related to Participation Post-Stroke. *Journal of Rehabilitation Medicine*, 40 (4) 291-297
- Kraskowsky LH, Finlayson M, (2001). Factors affecting older adults' use of adaptive equipment: review of the literature. *American Journal of Occupational Therapy*, 55(3): 303-10
- Kroenke CH, Kubzansky LD, Adler N, Kawachi I, (2008). Prospective change in health related quality of life and subsequent mortality among middle-aged and older women. *American Journal Public Health*, 98(11): 2085- 2091
- Krystal AD, Mugdha T, (2008). UACP Sleep Disturbance in Psychiatric Disorders: Effects on Function and Quality of Life in Mood Disorders, Alcoholism, and Schizophrenia Effect of Sleep Disturbance on Mood Disorders. *Alcoholism and Schizophrenia Annals of Clinical Psychiatry*, (1):39–46,
- Krystal AD, Thakur M, Roth T, (2008). Sleep disturbance in psychiatric disorders: Effects on function and quality of life in mood disorders, alcoholism, and schizophrenia. *Annals of Clinical Psychiatry*, 20(1): 39-46

- Lane, L (2000). Client-Centred Practice: is it Compatible with Early Discharge Hospital-at-Home Policies? *The British Journal of Occupational Therapy*, 63, 7, 310-315(6)
- Laudet AB, Stanick V, Sands B, (2009). What could the program have done differently? A qualitative examination of reasons for leaving outpatient treatment. *Journal of substance Abuse Treatment*;37(2):182-90
- Leonardi M, Bickenbach J, Ustun TB, Kastajsek N, and Chatterji S, (2006). Comment: The definition of the ICF into Australian data dictionaries. *Disability and Rehabilitation*, 25: 676-682.
- Liddle J, and McKenna K, (2000) Quality of life: An overview of issues for use in occupational Therapy outcome measurement. *Australian Occupational Therapy Journal*, (47) 77-85.
- Lindgren S, Lilja B, Verbaan H, Sundkvist G, (1996). Alcohol Abuse Exaggerates Autonomic Dysfunction in Chronic Liver Disease. *Gastroenterology*, 31(11):1120-1124
- Lipsy LW (1990). *Design sensitivity: statistical power for experimental research*. Newbury Park, CA: SAGE.
- Lowrie E, Curtin R, Lepain N, Schatell D, (2003). Medical outcomes study short form-36: a consistent and powerful predictor of morbidity and mortality in dialysis patients. *American Journal Kidney Disease*, 41: 1286-92.
- Lundgren Pierre B (2001) Occupational therapy as documented in patients' records--part III. Valued but not documented. Underground practice in the context of professional written communication. *Scandinavian Journal of Occupational Therapy*, 8(4), 174-83.
- Mahmood S, Kida T, Izumi A et al., (2008). Assessment of Health Related Quality of Life in Chronic Liver Disease. Patients Using the Japanese Versions of CLDQ and SF-36. *The Open Gastroenterology Journal*. 2, 57-63 57
- Mailis-Gagnon A, Yegneswaran B, Lakha SF, et al, (2007). Pain characteristics and demographics of patients attending a university-affiliated pain clinic in Toronto, Ontario. *Pain Res Management*, 12(2):93-9
- Martin F, Peters T, (1985) Alcoholic muscle disease. *Alcohol*, 20:125-36.
- Matthews D, Hosker J, Rudenski, (1985) Homeostasis model. *Diabetologica*, 28:412-419
- Mattingly C, (1991). What is clinical reasoning? *American Journal of Occupational Therapy*, 45 (11): 979-986
- Mayers CA, (1995) Defining and Assessing Quality of Life. *British Journal of occupational Therapy*, 58 (4):146-150
- Mayers CA, (2003) The Development and Evaluation of the Mayers' Lifestyle Questionnaire (2). *British Journal of Occupational Therapy*, 66 (9):388-395
- Mayers CA, (1998) An Evaluation of the Use of the Mayers' Lifestyle Questionnaire. *British Journal of Occupational Therapy*, 61 (9) 393-398



- McAvoy N, and Hayes P, (2012). *Problem-based Approach to Gastroenterology and Hepatology*. Wiley Publications.
- McEvoy, P. & Richards, D. (2006) A critical realist rationale for using a combination of quantitative and qualitative methods. *Journal of Research in Nursing*, 11 (1), 66-78
- McNeely ML, Campbell KL, Rowe BH, et al. (2006). Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *Canadian Medical Association Journal*, 175: 34-41.
- McQueen J, Howe TE, Allan L, Mains D, Hardy V, (2011). Brief interventions for heavy alcohol users admitted to general hospital wards. *Cochrane Database of Systematic Reviews*,(8). DOI: 10.1002/14651858.CD005191.pub3 (Accessed March 22<sup>nd</sup> 2012)
- Mehta KM, Yaffe K, Brenes GA, Newman AB, Shorr RI, Simonsick EM, Ayonayon HN, Rubin SM, Covinsky KE (2007). Anxiety symptoms and decline in physical function over 5 years in the health, aging and body composition study, 55(2):265-70.
- Mitchell SA, Beck SL, Edwards, Hood L, Moore K, Tanner ER, (2007). *Clinical Journal of Oncology Nursing*, 11 (1).
- Modell, S. (2009) In defence of triangulation: a critical realist approach to mixed methods research in management accounting. *Management Accounting Research*, 20, 208-221
- Mountain G, Pighills A, (2003). Pre-discharge home visits with older people: time to review practice. *Health and Social Care in the Community*, (2):146–154
- National Institute for Health and Clinical Excellence (NICE) guidelines. Chronic Fatigue syndrome/myalgic encephalomyelitis. Diagnosis and management of CFS/ME in adults and children. August 2007. (<http://guidance.nice.org.uk>). Accessed 11th March 2012
- National Service Framework for long Term Conditions. [www.govpublications.com](http://www.govpublications.com): Accessed 24th April 2008
- Newton JL, Bhala N, Burt JA, Jones DEJ, (2006). Characterisation of the associations and impact of symptoms in Primary Biliary Cirrhosis using a disease specific quality of life measure. *Journal of Hepatology*, 44: 776-83.
- Newton JL, Elliott C, Frith J, Ghazala C, Pairman J, Jones DEJ (2011). Functional capacity is significantly impaired in primary biliary cirrhosis and is related to orthostatic symptoms. *European Journal of Gastroenterology and Hepatology*, 23(7), 566-572.
- Newton JL, Hollingsworth KG, Taylor R, El-Sharkawy AM, Khan Z, Pearce R, (2008). Cognitive impairment in primary biliary cirrhosis: symptom impact and potential etiology. *Hepatology*, 48: 541–549
- Newton JL, John Gibson, G Mark, Tomlinson M, Wilton K, Jones D, (2006). Fatigue in primary biliary cirrhosis is associated with excessive daytime somnolence *Hepatology*, 44(1):91-98

Newton, et al (2007). Fatigue in Non-alcoholic Liver disease is significant and associates with inactivity and excessive daytime sleepiness but not with liver disease severity or insulin resistance. In: 58th Annual Meeting of the American Association for the Study of Liver Diseases. Boston, MA: *Hepatology*, Wiley-Blackwell.

NHS Information Centre(2012). Available at: <http://www.ic.nhs.uk/>. Accessed March 28<sup>th</sup> 2012.

NHS Information Centre. Statistics on obesity, physical activity and diet: England. [http://www.ic.nhs.uk/webfiles/publications/003\\_Health\\_Lifestyles/opad11/Statistics\\_on\\_Obesity\\_Physical\\_Activity\\_and\\_Diet\\_England\\_2011.pdf](http://www.ic.nhs.uk/webfiles/publications/003_Health_Lifestyles/opad11/Statistics_on_Obesity_Physical_Activity_and_Diet_England_2011.pdf). (accessed June 8, 2011).

NIDDK, (2012) Available at [digestive.niddk.nih.gov](http://digestive.niddk.nih.gov), 2012. Accessed 7<sup>th</sup> March 2012

Nijs J, Almond F, De Becker P, Truijen S, Paul L, (2008). Can exercise limits prevent post-exertional malaise in chronic fatigue syndrome? An uncontrolled clinical trial. *Clinical Rehabilitation*, 22(5): 426-435.

O'Brien KK, Bayoumi A, Strike CL, Young NL, King K, Davis AM, (2010). How do existing HIV-specific instruments measure up? Evaluating the ability of instruments to describe disability experienced by adults living with HIV. *Health and Quality of Life Outcomes*, 8:88

O'Carroll R, Coustou M, Cossar J, Masterton G, Hayes P, (2003). Psychological outcome and Quality of life following Liver Transplant: Prospective, national, single centre study. *Liver International*, (9) 712-720.

O'Neill, (2002) Cognition-What cognition? *British Journal of Occupational Therapy*, 65(6).

O'Shea RS, Dasarathy S, McCullough AJ (2010). "Alcoholic liver disease" (PDF). *Hepatology* 51 (1): 307–28

Ong JP, Pitts A, Younossi ZM, (2008). Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease. *Epub*, 49(4): 608-12.

Orford J, Hodgson R, Copello A, John B, Smith M, Black R, Fryer K, Handforth L, Alwyn T, Kerr C, Thistlethwaite G, Slegg G, (2006). UKATT Research Team. The clients' perspective on change during treatment for an alcohol problem: qualitative analysis of follow-up interviews in the UK Alcohol Treatment Trial. *Addiction*, 101(1): 60-68.

Otis J, Guidot D (2009). Procysteine stimulates expression of key anabolic factors and reduces plantaris atrophy in alcohol-fed rats. *Alcohol Clinical and Experimental Research*, 33:1450-9.

Parkerson GR jr, Gutman RA, (2002). Health related quality of life predictors of survival and hospital utilization. *Health Care Finance Rev*, 21: 171-84.

Perlesz, A. & Lindsay, J. (2003) Methodological triangulation in researching families: making sense of dissonant data. *International Journal of Social Research Methodology*, 6 (1), 25-40

- Patanwala I, Newton JL, Jones DE, (2010). UDCA Response Criteria Identify a Sub-Group of PBC Patients with an Inherently Good Prognosis Rather Than a Specific Disease Response. 61st Annual Meeting of the American Association for the Study of Liver Diseases. Boston, MA. *Hepatology*, 52(4): 357a-8a.
- Paterson, C.(1996). Measuring outcomes in primary care: a patient generated measure, MYMOP, compared with the SF-36 health survey. *BMJ* , 312:1016-1020
- Peter TJ, Foster J, (1998). Sleep disturbance in alcohol misuse: a predictor of relapse. *Alcohol Clinical and Experimental Research*. 22 (supplement):183a
- Peters T, Martin F, Ward K (1985). Chronic alcoholic skeletal myopathy—common and reversible. *Alcohol*, 2:485
- Peterson DB,(2005).Rehabilitation Psychology, 50(2):105-112. doi: [10.1037/0090-5550.50.2.105](https://doi.org/10.1037/0090-5550.50.2.105)
- Peterson DB, *et al.* (2010). *Concepts of disability, functioning & health; Rehabilitation and Health Assessment – applying ICF guidelines*. Springer Publishing New York
- Ponsford J, (1995). *Traumatic brain injury: Rehabilitation for everyday adaptive living*. Hove: Erlbaum.
- Prince MI, James OF, Holland NP, (2000). Validation of fatigue. *J Hepatol*, 32(3):368-73
- PROMIS (2008). Available at [www.nihpromis.com](http://www.nihpromis.com), Accessed 25<sup>th</sup> February 2008
- Rast P, Zimprich D, Van Boxtel M, Jolles J, (2009). Factor structure and measurement invariance of the Cognitive Failures Questionnaire across the adult life span. *Assessment*,16:145-158.
- | Ratziu V, Bellentani S, Cortez-Pinto H, Day C, Marchesini G\_(2009). A position statement on NAFLD/NASH based on the EASL special conference. *J Hepatol*2010;53:372
- Rettig R, Sadler J, Meyer K. *et al.* (1997). Assessing health and quality of life outcomes in dialysis: a report on an Institute of Medicine workshop. *American Journal Kidney Disease*, 30:140-55.
- Reuben DB, Rubenstein LB, Hirsch SH, Hays RD, (1992). Value of functional status as a predictor of mortality: results of a prospective study. *American Journal Medicine*, 93: 663-9.
- Reuben DB, Siu AL, Kimpau S, (1992). The predictive validity of self-report and performance-based measures of function and health. *J Gerontology*, 47: 106-110.
- Robson, C. (2002) *Real World Research*. 2<sup>nd</sup> ed. Oxford: Blackwell
- Roderick P, Parkes J, Rosenberg W, Sheron N, Dillon J, Young A, Begum N, Yuen B, Goddard J, (2004). *The epidemiology and health care burden of chronic liver disease*. Final Report to British Liver Trust and Foundation for Liver Research.
- Roy R, Thomas M, Berger S, (1990). A comparative study of Canadian nonclinical and British pain clinic subjects. *Clin J Pain*, 6:276–83.

- Rubal E, Iwanenko W, (2004). Chronic Fatigue Syndrome: Is There a Role for Occupational Therapy? *Occupational Therapy in Health Care* 2004, 18, (3) 33-45.
- Rumsfeld JS, Mawhinney S, McCarthy M Jr, *et al.*, (1999). Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. *JAMA* 281: 1298-303.
- Sandelowski, M. (1995). Sample size in qualitative research. *Res. Nurs. Health*, 18: 179–183
- Schrag A, Selai C, Jahanshahi M, Quinn N, (2000). The EQ-5D—a generic quality of life measure—is a useful instrument to measure quality of life in patients with Parkinson's disease. *J Neurological Neurosurgery Psychiatry*, 69: 67-73
- Schrezenmaier C, Gehrking JA, Hines SM, Low PA, Benrud LM, Sandroni P, (2005). Evaluation of orthostatic hypotension: relationship of a new self-report instrument to laboratory-based measures. *Mayo Clinic Proceedings*, 80 330-334.
- Scott PJ and Brown VL, (2012). Resumption of Valued Activities in the First Year Post Liver Transplant. *Occupational Therapy in Health Care*, 26, (1): 48-63
- Simone M van dar Plas, Bettina E. Hansen, Josien B de Boer, Theo Stijnen, Jan Passchier, Rob A de Man and Solko W Schalm, (2007). Generic and disease specific health related quality of life of liver patients with various aetiologies: A survey. *Quality of life research*, 16: 375-388
- Snaith PR, (2003). The Hospital Anxiety and Depression Scale. *Health Quality of Life Outcomes*. 1: 29. doi: 10.1186/1477-7525-1-29
- Sokka T & Häkkinen A, (2006). Health-related, quality-of-life metrics to predict mortality and hospitalizations in community-dwelling seniors. *American Journal Geriatr Soc*, 54: 667-73.
- Sokka T, Abelson B, Pincus T, (2008). Mortality and rheumatoid arthritis: 2008 update. *Clin Exp Rheumatol* ,26 (Supplement. 51): 35-61.
- Sokka T, Häkkinen A, (2008). Poor physical fitness and performance as predictors of mortality in normal populations and patients with rheumatic and other diseases. *Clin Exp Rheumatol*, 26 (Supplement. 51):14-20.
- Sokka T, Hakkinen A, Krishnan E, Hannonen P, (2004). Similar prediction of mortality by the health assessment questionnaire in patients with rheumatoid arthritis and the general population. *Ann Rheum Dis*, 63: 494-7.
- Sokka T, Kautiainen H, Hannonen P, Pincus T, (2006). Changes in health assessment questionnaire disability scores over five years in patients with rheumatoid arthritis compared with the general population. *Rheum*, 54: 3113-8.
- Spadaro A, Lubrano E, Massimiani MP, Gaia P, Perrotta FM, Parsons WJ, *et al.* (2010). Validity, responsiveness and feasibility of an Italian version of the Canadian Occupational Performance Measure for patients with ankylosing spondylitis. *Clin Exp Rheumatol*, 28(2):215-22.

- Swain M, (2000). Fatigue in chronic disease. *Clinical Science*, 99:1–8.
- Swain M, (2006). Fatigue in liver disease: Pathophysiology and clinical management. *Can J Gastroenterol*, 20(3): 181–188.
- Texasback (2008). Available at: [http://www.texasback.com/about\\_us/patient\\_forms](http://www.texasback.com/about_us/patient_forms): Accessed February 2008
- The global burden of disease: 2004 update. Geneva, World Health Organization, 2008. [http://www.bma.org.uk/images/nhsoutcomesframework2011-2012\\_tcm41-206473.pdf](http://www.bma.org.uk/images/nhsoutcomesframework2011-2012_tcm41-206473.pdf).
- The Independent (2012). Available at: <http://www.independent.co.uk/>. Accessed 10<sup>th</sup> March 2012
- The White Paper: Our Health, our care, our say: a new direction for community services (2006)
- Turner A, (1992). *Occupational Therapy and Physical Dysfunction; Principles, skills and practice*. Churchill Livingstone.
- UK National Statistics (2008) Available at: [www.statistics.gov.uk](http://www.statistics.gov.uk) Accessed on 23.04.08.
- Urbano- Márquez A, Fernández-Solà (2004). Effects of alcohol on skeletal and cardiac muscle. *Muscle & Nerve*, 30 (6): 689–707,
- Van Ginneken B, Van Den Berg-emons H; Metselaar H; (2010). Effects of a rehabilitation programme on daily functioning, participation, health-related quality of life, anxiety and depression in liver transplant recipients. *Disability and Rehabilitation*: 32: (25): 2107-2112
- Vargas R, Lang C (2007). Alcohol Accelerates Loss of Muscle and Impairs Recovery of Muscle Mass Resulting From Disuse Atrophy. *Alcoholism: Clinical and Experimental Research*, DOI: 10.1111/j.1530-0277.2007.00548.x
- Vary T, Nairn A, Lang C, (2004). Restoration of protein synthesis in heart and skeletal muscle after withdrawal of alcohol. *Alcohol Clinical and Experimental Research*, 28:517-25.
- Verne, J (2012). Commentary in British Liver Trust.org.uk. Accessed March 6th 2012.
- Vernon G, Baranov A, Younossi ZM, (2011). Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults *Alimentary Pharmacology & Therapeutics*, 34(3): 274-285
- Vize R (2011). NHS Reforms Reality of the NHS budget squeeze. *BMJ* , 343 doi: 10.1136/bmj.d8027. Accessed March 15<sup>th</sup> 2012
- Wagle AC, Berrios GE, Ho L,(1999).The Cognitive Failures Questionnaire in psychiatry. *Comprehensive Psychiatry*, 40: 478-484
- Warren M, and Day CP, (2008). Alcoholic Liver Disease. [www.netdoctor.com](http://www.netdoctor.com). Accessed 23rd April 2008

- Wearden AJ, Morriss RK, Mullis R, (1998). Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome. *Br J Psychiatry*,172:485–90. Erratum in 1998;173:89
- Wiesner, R. H., McDiarmid, S. V., Kamath, P. S., Edwards, E. B., Malinchoc, M., Kremers, W. K., Krom, R. A.F. and Kim, W. R. (2001), MELD and PELD: Application of survival models to liver allocation. *Liver Transpl*, 7: 567–580.
- Weissman MM, Greenwald S, Nino-Murcia G, Dement WC, (1997). The morbidity of insomnia uncomplicated by psychiatric disorders. *Gen Hosp Psychiatry*, 19(4): 245–250.
- Welch A, Lowes S, (2005). Home Assessment Visits within the Acute Setting: a Discussion and Literature Review. *British Journal of Occupational Therapy*. 68: 158-164.
- Wheatley C, (1996). Evaluation and treatment of cognitive dysfunction. In: LW Pedretti, ed. *Occupational therapy skills for physical dysfunction*. St Louis: Mosby.
- Whiteford G, (2000). Occupational Deprivation: Global Challenge in the New Millennium. *British Journal of Occupational Therapy*, 63(5): 200-204
- Williams A, (2004). Patients with comorbidities: perceptions of acute care services. *Journal of Advanced Nursing*, 46: 13–22.
- Williams CD, Stengel J, Asike MI, *et al.*,(2011). Prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis among a largely middle aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology*: 140: 214-231.
- Withers N (2012). *The liver impaired patient*. Handbook of Consultation-Liaison Psychiatry. Hoyle Leigh. Springer.
- World Health Organisation (2004). The global burden of disease: 2004 update. Available at: [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4075214](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4075214). Accessed on 23.04.08.
- World Health Organisation (2011).World report on disability. Available at: [http://www.who.int/disabilities/world\\_report/2011/en/index.html](http://www.who.int/disabilities/world_report/2011/en/index.html). Accessed March 6th 2011.
- Yaffe K, Kanaya A, Lindquist K, Simonsick EM, Harris T, Shorr RI, *et al*, (2004).The metabolic syndrome, inflammation, and risk of cognitive decline. *JAMA*, 292:237–2242.
- Yelin E, Trupin L, Wong B, Rush S (2002). Functional status on mortality over 18 years among persons with rheumatoid arthritis. *J Rheumato*,29(9):1851-7

## **Exploring the impact of liver disease upon function: what's important to those people living with the symptoms?**

Ms Chris Elliott, Prof. David Jones, Prof. Julia Newton

### **PARTICIPANT INFORMATION SHEET**

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

- Part 1 tells you the purpose of the study and what will happen to you if you take part
- Part 2 gives you more information about the conduct of the study

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

#### **What is the purpose of this study?**

There are more and more people being diagnosed with chronic liver conditions. We would like to learn more about how life for people

with chronic liver disease is affected; in particular what day to day things are becoming more difficult and how important these jobs, activities, roles or responsibilities are to you.

We also want to know if you have any thoughts on what you would like from your occupational therapy service either during your hospital stay, or once you have been discharged home in relation to any difficulties you may have.

To do this, Christine Elliott, would like to talk to you in a comfortable and confidential place, for about an hour, and ask you some questions about your daily activities and what is important to you. Christine will use a tape recorder to collect the information you give and these recordings will be safely disposed of once the study is complete.

Christine will utilise the findings from this study to form the basis of a Doctor of Philosophy (PhD) degree at Newcastle University.

### **Why have I been chosen?**

We are asking a selection of people with chronic liver disease attending the Freeman Hospital Liver Clinic, people who are in hospital, or people who have recently been in hospital to take part.

The liver specialist nurses have identified from your medical records today that you would be eligible to participate in this study.

### **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. If you do withdraw from the study for any reason, data already collected with consent will be retained and used in the



study. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

### **What will happen to me if I decide to take part?**

If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form. Christine will then contact you to make an appointment convenient to you.

### **What do I have to do?**

If you would like to take part in the study, please complete the reply slip at the end of this information sheet and return it in the envelope provided to your nurse. Your care at the Freeman Hospital Liver Clinic will continue unchanged, regardless of whether you decide to take part in this study or not.

### **What are the possible benefits of taking part?**

This study is being conducted as part of the Biomedical Research Centre in Ageing (Liver Theme) Service Development Initiative. By taking part in this study, you will have the opportunity to inform the development of local services for people with chronic liver disease based at the Freeman Hospital.

### **What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in part 2.

### **Will my taking part in this study be kept confidential?**

Yes. All the information about your participation in this study will be kept confidential. The details are included in part 2.

### **Research Team contact details**

Chris Elliott – Advanced Occupational Therapist

Professor Julia Newton – Professor of Ageing and Medicine

Falls and Syncope Service

Royal Victoria Infirmary

Newcastle upon Tyne

Tel: 0191 2825237

Professor David Jones – Director of the Institute of Cellular Medicine

Newcastle University

Institute of Cellular Medicine

Newcastle upon Tyne

Tel: 0191 2225784

**This completes part 1 of the Information Sheet. If the information in part 1 has interested you and you are considering participating, please continue to read the additional information in Part 2 before making any decision.**

## **Part 2**

### **What if there is a problem?**

#### **Complaints:**

If you have any concern about any aspect of this study, you should ask to speak to a member of the Research Team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

Alternatively, you may wish to contact:

Mrs Amanda Tortice  
Research Operations Manager  
Research and Development Department  
Royal Victoria Infirmary  
Newcastle upon Tyne  
NE1 4LP  
0191 2825959

Mrs Margaret Paterson  
Patient Advice and Liaison Officer  
North of Tyne Patient Advice and Liaison Service (PALS)  
Freeman Hospital  
Newcastle upon Tyne  
0191 2837682

## **Harm:**

In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for compensation against the Newcastle upon Tyne Hospitals NHS Foundation Trust but you may have to pay your legal costs. The normal NHS complaints mechanisms will still be available to you (see above).

## **Will my taking part in this study be kept confidential?**

All information which is collected about you during the course of the research will be kept strictly confidential. Any information that leaves the hospital will have your name and address removed so that you cannot be recognised from it.

## **What will happen to the results of the research study?**

The findings from this study will form the basis of a Doctor of Philosophy (PhD) degree at Newcastle University and be published in scientific journals; however, you will not be identified in any of the reports/publications. A summary of the findings will be available at the end of the project. We can send you a copy if you are interested.

## **Who is funding the research?**

The research has been organised by Newcastle University and the Newcastle Hospitals NHS Foundation Trust and funded by the

Newcastle Hospitals NHS Foundation Trust. The Principal Investigator (Chris Elliott) will not receive any payment for including you in this study.

**Who has reviewed this study?**

This study was given a favourable ethical opinion for conduct in the NHS by Sunderland Research Ethics Committee on 08.11.2010.

**Thank you for your interest in this study**

If you have read the information above and would like to be involved in the study, please return the slip over the page in the envelope provided.

**Expression of interest form**

I would like to take part in the research study and am happy to be contacted by telephone.

Name:

Telephone number:

Best time to call:

## Appendix 2 *Ethics approval*

  
**National Research Ethics Service**

**Sunderland Research Ethics Committee**

Room 002  
TEDCO Business Centre  
Viking Industrial Park  
Jarrow  
Tyne & Wear NE32 3DT

Telephone 0191 4283563 or 4283545 Fax 0191 4283432

Helen Wilson (Co-ordinator) e-mail: [helen\\_wilson@sunderland.nhs.uk](mailto:helen_wilson@sunderland.nhs.uk)

08 November 2010

Ms Christine Elliott  
Care of the Elderly Offices  
Newcastle upon Tyne Hospitals NHS Foundation Trust  
Royal Victoria Infirmary  
Queen Victoria Road  
Newcastle upon Tyne  
NE1 4LP

Dear Ms Elliott

**Study Title:** Exploring the impact of chronic liver disease upon function; a client centred analysis of impairment, importance and satisfaction in occupational performance.  
**REC reference number:** 10/H0904/51

Thank you for your letter received 22 October 2010, responding to the Committee's request for further information on the above research [and submitting revised documentation]

The further information has been considered on behalf of the Committee by myself as Chair.

#### **Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a **favourable ethical opinion** for the above research on the basis described in the application form, protocol and supporting documentation [as revised], subject to the conditions specified below.

#### **Ethical review of research sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

#### **Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

This Research Ethics Committee is an advisory committee to the North East Strategic Health Authority  
The National Research Ethics Service (NRES) represents the NRES Directorate within  
the National Patient Safety Agency and Research Ethics Committees in England

Management permission ("R&D approval") should be sought from all NHS organisation(s) involved in the study in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System (IRAS) or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

**It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

#### Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Investigator CV	Chris Elliott	
Protocol	Version 2	01 October 2010
REC application	IRAS V3.0	30 June 2010
Covering Letter	From Chris Elliott	01 September 2010
Covering Letter		
Letter from Sponsor		12 October 2010
Participant Information Sheet	Version 2	01 October 2010
Response to Request for Further Information		
Participant Consent Form	V1	30 June 2010

#### Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

#### After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports

- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email [referencegroup@nres.npsa.nhs.uk](mailto:referencegroup@nres.npsa.nhs.uk).

**10/H0904/51**

**Please quote this number on all correspondence**

Further clarification of any issues can be obtained from the Committee Co-ordinator.

Yours sincerely



*PP* **Mr Paddy Stevenson**  
Chair

Email: [Helen.Wilson@suntppt.nhs.uk](mailto:Helen.Wilson@suntppt.nhs.uk)

*Enclosures:* "After ethical review – guidance for researchers"

*Copy to:* Dr Lesley Hall  
R & D  
Newcastle Hospitals NHS Trust



The Newcastle upon Tyne Hospitals   
NHS Foundation Trust

Royal Victoria Infirmary  
Queen Victoria Road  
Newcastle upon Tyne  
NE1 4LP

AT/NG

Tel: 0191 233 6161  
Fax: 0191 201 0155

20 January 2011

Professor J. Newton  
Professor of Aging and Medicine  
Institute of Aging and Health  
University of Newcastle  
Care of the Elderly Offices  
Royal Victoria Infirmary  
Newcastle upon Tyne  
NE1 4LP

Dear Professor Newton,

<b>Trust R&amp;D Project:</b>	<b>5427</b>
<b>Title of Project:</b>	<b>Exploring the impact of chronic liver disease upon function</b>
<b>Principal Investigator:</b>	<b>Professor Julia Newton</b>
<b>Number of patients:</b>	<b>30</b>
<b>Funder (proposed):</b>	<b>BRC</b>
<b>Sponsor (proposed):</b>	<b>The Newcastle upon Tyne Hospitals NHS Foundation Trust</b>
<b>REC number:</b>	<b>10/H0904/51</b>

Having carried out the necessary risk and site assessment for the above research project, Newcastle upon Tyne Hospitals NHS Foundation Trust grants NHS R&D approval for this research to take place at this Trust dependent upon:

- (i) you, as Principal Investigator, agreeing to comply with the Department of Health's Research Governance Framework for Health and Social Care, and understanding their responsibilities and duties (a copy of responsibilities prepared by the Trust R&D Office is enclosed)
- (ii) you, as Principal Investigator, ensuring compliance of the project with all other legislation and guidelines including Caldicott Guardian approvals and compliance with the Data Protection Act 1998, Health and Safety at Work Act 1974, any requirements of the MHRA (eg CTA, EudraCT registration), and any other relevant UK/European guidelines or legislation (eg reporting of suspected adverse incidents).
- (iii) where applicable, you, as Principal Investigator, should also adhere to the GMC supplementary guidance *Good practice in research* and *Consent to research* which sets out the good practice principles that doctors are expected to understand and follow if they are involved in research – see [http://www.gmc-uk.org/guidance/ethical\\_guidance/5991.asp](http://www.gmc-uk.org/guidance/ethical_guidance/5991.asp)

### **Sponsorship**

***The Newcastle upon Tyne Hospitals NHS Foundation Trust will act as Sponsor for this project, under the Department of Health's guidelines for research in health and social care.***

***In addition, the Trust has a Research Governance Implementation Plan, agreed with the Department of Health, in order to fully comply with Research Governance and fulfil the responsibility of a Sponsor.***

***As the Trust is acting as Sponsor for the research and where some of the research is taking place outside of Newcastle upon Tyne, then all costs must be met for research governance audit visits to those sites. It is the responsibility of the PI to provide confirmation to the Trust of who will pay these costs. Audit is required under the Research Governance Framework for Health and Social Care. (Please note that the Trust randomly audits 10% of approved research projects annually.)***

Any changes to the study protocol, other study documents (eg, Patient Information Sheets and Consent forms), or any other amendments to the study must be submitted to the Ethics Committee and MHRA (if relevant) for review – see <http://www.nres.npsa.nhs.uk/applications/after-ethical-review/amendments/> for guidance). The R&D office must also review these notices of amendments in parallel with ethical and regulatory review so that implications of the amendment can be assessed. Therefore, you must send a copy of all amendment documents to the R&D office at the same time you are submitting these to the Ethics Committee/MHRA. If changes or amendments to the study have implications for costs or use of resources, you must also submit details of these changes to the R&D office.

It is also the Principal Investigator's responsibility to ensure that all staff involved in the research have Honorary Research Contracts or the necessary letters of access. These need to be issued prior to commencing the research.

In addition, unless otherwise agreed with the Trust, the research will be covered for negligence under the CNST (Clinical Negligence Scheme for Trusts), however cover for no-fault harm is the responsibility of the Principal Investigator to arrange if required.

Please also note that for any NHS employee who generates Intellectual Property *in the normal course of their duties*, it is recognised that the Intellectual Property Rights remain with the employer and not the employee.

Yours sincerely



Amanda Tortice  
**Research Operations Manager**

Enc: Principal Investigator Responsibilities Document

CC: Mr G Regan, Finance Department, Room 203, Cheviot Court, Freeman Hospital  
Dr S Louw, Clinical Director, Freeman Hospital  
Christine Elliott, Trial Coordinator

#### Appendix 4 **Qualitative interview topic guide**

Introductions and thanks for taking part in interview. Reiterate permission to use tape recorder and explain confidentiality.

1) I'm interested in your day to day experience of living with liver disease. I would like you to describe a typical day in your life for me, from getting up to going to sleep at night.?

(Listen to participant and repeat points back to them).

2) How well do you manage those day to day activities (link to productivity depending on what they say, e.g. going to work, housework, volunteering etc.)?

3) How well do you manage those day o day activities (link to self care e.g. bathing, dressing etc)?

4) How well do you manage those day to day activities (link to leisure e.g. socialising, exercise, clubs etc.)?

(Listen to participant and repeat points back to them).

5) Can you tell me more about some of the problems you experience in doing these activities (go back to points they have raised)?

- direct to HAD if appropriate (see attached)
- direct to CFQ if appropriate (see attached)
- direct to COPM if appropriate (see attached)

## Appendix 5 HAD

### I feel tense or 'wound up':

- Most of the time
- A lot of the time
- Time to time; occasionally
- Not at all


### I still enjoy the things I used to enjoy:

- Definitely as much
- Not quite so much
- Only a little
- Hardly at all


### I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly
- Yes, but not too badly
- A little, but it doesn't worry me
- Not at all


### I can laugh and see the funny side of things:

- As much as I always could
- Not quite so much now
- Definitely not so much now
- Not at all


### Worrying thoughts go through my mind:

- A great deal of the time
- A lot of the time
- From time to time but not too often
- Only occasionally


### I feel cheerful

- Not at all
- Not often
- Sometimes
- Most of the time


### I can sit at ease and feel relaxed:

- Definitely
- Usually
- Not often
- Not at all


### I feel as if I am slowed down:

- Nearly all the time
- Very often
- Sometimes
- Not at all


### I get a sort of frightened feeling like 'butterflies' in the stomach:

- Not at all
- Occasionally
- Quite often
- Very often


### I have lost interest in my appearance:

- Definitely
- I don't take so much care as I should
- I may not take quite as much care
- I take just as much care as ever


### I feel restless as if I have to be on the move:

- Very much indeed
- Quite a lot
- Not very much
- Not at all


### I look forward with enjoyment to things:

- As much as I ever did
- Rather less than I used to
- Definitely less than I used to
- Hardly at all


### I get sudden feelings of panic:

- Very often indeed
- Quite often
- Not very often
- Not at all


### I can enjoy a good book or radio or TV programme:

- Often
- Sometimes
- Not often
- Very seldom


## Appendix 6 Cognitive Failure Questionnaire

		Very often	Quite often	Occasionally	Very rarely	Never
1.	Do you read something and find you haven't been thinking about it and must read it again?	1	2	3	4	5
2.	Do you find you forget why you went from one part of the house to the other?	1	2	3	4	5
3.	Do you fail to notice signposts on the road?	1	2	3	4	5
4.	Do you find you confuse right and left when giving directions?	1	2	3	4	5
5.	Do you bump into people?	1	2	3	4	5
6.	Do you find you forget whether you've turned off a light or a fire or locked the door?	1	2	3	4	5
7.	Do you fail to listen to people's names when you are meeting them?	1	2	3	4	5
8.	Do you say something and realise afterwards that it might be taken as insulting?	1	2	3	4	5
9.	Do you fail to hear people speaking to you when you are doing something else?	1	2	3	4	5
10.	Do you lose your temper and regret it?	1	2	3	4	5
11.	Do you leave important letters unanswered for days?	1	2	3	4	5
12.	Do you find you forget which way to turn on a road you know well but rarely use?	1	2	3	4	5
13.	Do you fail to see what you want in a supermarket (although its there?)	1	2	3	4	5
14.	Do you find yourself suddenly wondering whether you've used a word correctly?	1	2	3	4	5
15.	Do you have trouble making up your mind?	1	2	3	4	5
16.	Do you find you forget appointments?	1	2	3	4	5
17.	Do you forget where you put something like a newspaper or a book?	1	2	3	4	5

18.	Do you find you accidentally throw away the thing you want to keep and keep what you meant to throw away—as in the example of throwing away the matchbox and putting the used match in your pocket?	1	2	3	4	5
19.	Do you daydream when you ought to be listening to something?	1	2	3	4	5
20.	Do you find you forget peoples' names?	1	2	3	4	5
21.	Do you start doing one thing at home and get distracted into doing something else (unintentionally)?	1	2	3	4	5
22.	Do you find you can't quite remember something although its "on the tip of your tongue"?	1	2	3	4	5
23.	Do you find you forget what you came to the shops to buy?	1	2	3	4	5
24.	Do you drop things?	1	2	3	4	5
25.	Do you find you can't think of anything to say?	1	2	3	4	5

## Appendix 7 Canadian Occupational Performance Measure

### Canadian Occupational Performance Measure (COPM)

Authors: Mary Law, Sue Baptiste, Anne Carswell, Mary Ann McColl, Helene Polatajko, Nancy Pollock

Client Name:		
Respondent (if not client):		
DOB:	ID#:	Gender:
Date of Assessment:	Planned Date of Reassessment:	Actual Date of Reassessment:
Therapist:		
Facility/Agency:		
Program:		

#### STEP 1: IDENTIFICATION OF OCCUPATIONAL PERFORMANCE ISSUES

To identify occupational performance problems, ask clients to identify daily activities which they want to do, need to do or are expected to do but can't do, don't do, or aren't satisfied with how they do.

#### STEP 2: RATING IMPORTANCE

Using scoring card provided, ask client to rate, on a scale of 1 to 10, the importance of each activity

##### STEP 1A: Self-Care

###### Personal Care

(e.g., dressing, bathing, feeding, hygiene)

---

---

---

---

###### Functional Mobility

(e.g., transfers, indoor, outdoor)

---

---

---

---

###### Community Management

(e.g., transportation, shopping, finances)

---

---

---

---

##### IMPORTANCE


##### STEP 1B: Productivity

###### Paid/Unpaid Work

(e.g., finding/keeping a job, volunteering)

---

---

---

---

###### Household Management

(e.g., cleaning, laundry, cooking)

---

---

---

---

###### Play/School

(e.g., play skills, homework)

---

---

---

---

##### IMPORTANCE


DOB:

ID#

**STEP 1C: Leisure**

Quiet Recreation  
(e.g., hobbies,  
crafts, reading)

Active Recreation  
(e.g., sports,  
outings, travel)

Socialization  
(e.g., visiting, phone  
calls, parties,  
correspondence)

IMPORTANCE


**STEP 3: SCORING**

Confirm with the client the 5 most important problems and record them below. Using the scoring cards, ask the client to rate each problem on performance and satisfaction, then calculate the total scores. Total scores are calculated by adding together the performance or satisfaction scores for all problems and dividing by the number of problems.

**STEP 4: RE-ASSESSMENT**

At an appropriate interval for re-assessment, the client again scores each of the problems selected for performance and satisfaction.

**Initial Assessment:**

Occupational Performance Problems:

1. \_\_\_\_\_
2. \_\_\_\_\_
3. \_\_\_\_\_
4. \_\_\_\_\_
5. \_\_\_\_\_

PERFORMANCE 1

SATISFACTION 1


**Reassessment:**

PERFORMANCE 2

SATISFACTION 2


**SCORING:**

Total score =  $\frac{\text{Total performance or satisfaction scores}}{\text{Number of problems (1-5)}}$

PERFORMANCE SCORE 1

SATISFACTION SCORE 1

--	--

PERFORMANCE SCORE 2

SATISFACTION SCORE 2

--	--

**STEP 5: COMPUTING CHANGE SCORES**

CHANGE IN PERFORMANCE = Performance Score 2

	-	Performance Score 1	=	
--	---	---------------------	---	--

CHANGE IN SATISFACTION = Satisfaction Score 2

	-	Satisfaction Score 1	=	
--	---	----------------------	---	--

**ADDITIONAL NOTES AND OBSERVATION:**

Initial Assessment:

Reassessment:



Appendix 8 PHAQ

**HEALTH ASSESSMENT QUESTIONNAIRE (PROMIS HAQ®)**

Name: \_\_\_\_\_ Date: \_\_\_\_\_

**Please tell us your ability to carry out your daily activities by placing an "X" in the box which best describes your abilities:**

<b>Are you able to:</b>	WITHOUT ANY DIFFICULTY	WITH A LITTLE DIFFICULTY	WITH SOME DIFFICULTY	WITH MUCH DIFFICULTY	UNABLE TO DO
Dress yourself, including shoelaces and buttons?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shampoo your hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stand up from an armless straight chair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Get in and out of bed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cut your food using eating utensils?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lift a full cup or glass to your mouth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Open a new milk carton?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Walk a block on flat ground?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Climb up five steps?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Wash and dry your body?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Take a tub bath?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Get on and off the toilet?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Reach and get down a 5 pound object from above your head?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bend down to pick up clothing from the floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Open car doors?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**For each of the following questions, please answer by placing “X” in the appropriate box.**

	<b>Yes</b>	<b>No</b>
To get around, do you usually need a walking stick, crutches, walker, wheelchair or help from another person?	<input type="checkbox"/>	<input type="checkbox"/>
To stand up from a sitting position, do you usually need a special chair, a raised toilet seat, or help from another person?	<input type="checkbox"/>	<input type="checkbox"/>
To get dressed, do you usually need a buttonhook, zipper pull or other gadget, or help from another person?	<input type="checkbox"/>	<input type="checkbox"/>
To reach something, do you usually use long-handled appliance or help from another person?	<input type="checkbox"/>	<input type="checkbox"/>

**Your ACTIVITIES:** To what extent are you able to carry out your everyday activities such as walking, climbing stairs, carrying groceries or moving a chair?

<b>COMPLETELY</b>	<b>MOSTLY</b>	<b>MODERATELY</b>	<b>A LITTLE</b>	<b>NOT AT ALL</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Your PAIN:** How much pain have you had IN THE PAST WEEK?

On a scale of 0 to 100 (where zero represents “no pain” and 100 represents “severe pain”), please record the number below.

--	--	--

**Your HEALTH:** Please rate how well you are doing on a scale of 0 to 100 (0 represents “very well” and 100 represents “very poor health”), please record the number below.

--	--	--

**Your TIREDNESS OR FATIGUE:** Please rate how tired or fatigued you have been IN THE LAST WEEK?

On a scale of 0—100 (0 represents no fatigue and 100 represents severe fatigue), record the number below.

--	--	--

Appendix 9 NAFLD ALT and PHAQ Correlation

