UNDERSTANDING LIFESTYLE IN PATIENTS ON HAEMODIALYSIS: A MULTICULTURAL PERSPECTIVE

Thesis submitted for the degree of

Doctor of Philosophy at the

University of Leicester

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August 2018
Abstract
Understanding Lifestyle in Patients on Haemodialysis:
A Multicultural Perspective
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Background: Healthy lifestyle plays a crucial role in improving comorbidities and decreasing mortality in haemodialysis (HD) patients. However, there is no comprehensive study to address the status of lifestyle especially cross culture comparison. This thesis aimed to understand the difference of HD patients’ lifestyle between the UK and China in aspects of nutritional and physical status.

Methods: Dietary intake was assessed by 24-hour diet recall interviews in 40 UK and 43 Chinese HD patients. Physical function and activity were examined by a combination of questionnaires (1156 UK and 542 Chinese HD patients) and objective measures (30 UK and 40 Chinese HD patients, with additional evaluation of Quality of Life [QoL], symptoms and body composition). In addition, 10 UK and 44 Chinese healthy controls were evaluated for objective measures.

Results: A high prevalence of dietary insufficiency in general was revealed, but UK HD patients had a better management of micronutrients (such as iron) than Chinese HD patients. Both UK and Chinese HD patients had impaired physical function and activity that were worse in UK patients than Chinese patients. Factors influencing physical function and activity include demographic (age, gender, muscle and fat mass), clinical (nutrition, inflammation and bone derangement) and psychological factors (perceived benefits and barriers to exercise), QoL and symptoms. UK HD patients’ lower protein status and bone metabolism, higher fat mass and symptom burden, and fewer perceived exercise benefits may contribute to the lower physical function and activity than in Chinese HD patients.

Conclusion: Malnutrition and low physical function and activity existed in both UK and Chinese HD patients, with a better management of micronutrients in UK and higher physical function and activity in China. Healthy lifestyle behaviors should be improved in both cultures. Promoting communication of lifestyle between UK and China is required.
Acknowledgments

Throughout my PhD there have been so many people to whom I would like to express my gratitude to. It has been a wonderful, unique but challenging journey for me and I believe I will never forget it for the rest of my whole life.

Firstly, I would like to thank my supervisors Prof. Alice Smith, Dr. James Burton, Prof. Xiaolan Chen and Dr. Yujie Guo. Alice and James thank you for supervising and supporting me with great patience. What I have learned from you reminds me to have a rigorous attitude towards research now and in the future. Xiaolan and Yujie thank you for the selfless help you gave me when I conducted my study in China.

To my Progress Review Panel (PRP) members, I would like to thank Sally, who always encouraged me to have confidence with my PhD. Bin thank you so much for your unconditional trust and encouragement to relieve my worry and anxiety.

To my Dad, thank you for keeping your liver cancer stable in these four years, so that I wouldn’t have any concerns about your health, and for allowing me to chase my dream. Mum, my husband, my daughter and my whole family, thanks for your love to support me walking along this lonely road. To my friends in the UK, US and China, I know you are always there for me when I need. To Barry, thank you for constantly proofreading my thesis.

To my participants, I could not do anything without your cooperation. Thank you for believing me that I can do something for you.

Finally, I would like to express a special thanks to my colleagues in the Kidney Lifestyle team. Darren, Dan, Heather, Hannah, Amy, Patrick, Barbara, Soteris, Doug, Tom, Daniel and Annabel. I feel so lucky and full of gratitude to meet all of you in the UK. Darren and Dan your help and support made me stronger. I could not have completed my thesis without your support. Heather, Hannah and Amy, I will always remember the moments when I felt frustrated, you gave me numerous hugs and told me that everything would be fine. Thank you, I believe it.
Publications

Conference poster presentations

Song Y, Highton P, Clarke AL, Burton JO, Smith AC. Functional capacity and physical activity behaviour and perceptions in patients on unit-based haemodialysis. Poster presentation, UK Kidney Week, Birmingham, June 2016.


Song Y; Highton PJ; Vogt BP; Biruete A; Wilund KR; Smith AC; Burton JO. Narrowing the phosphate divide: a comparison between UK and Chinese haemodialysis patients. Poster Presentation, American Society of Nephrology Conference, New Orleans November 2017

Song Y; Highton PJ; Clarke AL; Burton JO, Smith AC. Exploring Walking Pace, Physical Activity and Readiness to Change in End Stage Renal Disease. Poster Presentation, American Society of Nephrology Conference, New Orleans November 2017
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<tbody>
<tr>
<td>6MWT</td>
<td>6 Minute Walk Test</td>
</tr>
<tr>
<td>ABI</td>
<td>Ankle Brachial pressure Index</td>
</tr>
<tr>
<td>ACEI</td>
<td>Angiotensin-Converting Enzyme Inhibitors</td>
</tr>
<tr>
<td>ADLs (ADL)</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>ALP</td>
<td>Alkaline Phosphatase</td>
</tr>
<tr>
<td>ARBs</td>
<td>Angiotensin Receptor Blockers</td>
</tr>
<tr>
<td>AV</td>
<td>arteriovenous</td>
</tr>
<tr>
<td>baPWV</td>
<td>brachial-ankle Pulse Wave Velocity</td>
</tr>
<tr>
<td>BCM</td>
<td>Body Composition Monitor</td>
</tr>
<tr>
<td>BFR</td>
<td>Body Fat Rate</td>
</tr>
<tr>
<td>BIA</td>
<td>Bioelectrical Impedance Analysis</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BNP</td>
<td>B-type Natriuretic Peptide</td>
</tr>
<tr>
<td>CA-IMT</td>
<td>Carotid Artery Intima-Media Thickness</td>
</tr>
<tr>
<td>CAVI</td>
<td>Cardio-Ankle Vascular Index</td>
</tr>
<tr>
<td>CDC</td>
<td>Centres for Disease Control and Prevention</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>CMO</td>
<td>Chief Medical Office</td>
</tr>
<tr>
<td>CNRDS</td>
<td>Chinese National Renal Data System</td>
</tr>
<tr>
<td>CoFID</td>
<td>Composition of Foods Integrated Dataset</td>
</tr>
<tr>
<td>COI</td>
<td>Cardiac Output Index</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CRF</td>
<td>Chronic Renal Failure</td>
</tr>
<tr>
<td>CRP</td>
<td>C-Reactive Protein</td>
</tr>
<tr>
<td>CSBP</td>
<td>Chinese Society of Blood Purification</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>DASI</td>
<td>Duke Activity Status Index</td>
</tr>
<tr>
<td>DMMS</td>
<td>Dialysis Morbidity and Mortality Wave II Study</td>
</tr>
<tr>
<td>DOPPS</td>
<td>Dialysis Outcomes and Practice Pattern Study</td>
</tr>
<tr>
<td>DPI</td>
<td>Dietary Protein Intake</td>
</tr>
<tr>
<td>DPPEBBS</td>
<td>Dialysis Patient-Perceived Exercise Benefits and Barriers Scale</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
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</tr>
<tr>
<td>DXA</td>
<td>Dual Energy X-Ray Absorptiometry</td>
</tr>
<tr>
<td>eGFR</td>
<td>estimated Glomerular Filtration Rate (eGFR)</td>
</tr>
<tr>
<td>EBPG</td>
<td>European Best Practice Guidelines</td>
</tr>
<tr>
<td>EE</td>
<td>Energy Expenditure</td>
</tr>
<tr>
<td>EF</td>
<td>Ejection Fraction</td>
</tr>
<tr>
<td>EQ-5D-5L</td>
<td>The Euro QOL-5 Dimensions-5 Level</td>
</tr>
<tr>
<td>EQ-VAS</td>
<td>EQ-Visual Analogue Scale</td>
</tr>
<tr>
<td>ESA</td>
<td>Erythropoiesis Stimulating Agents</td>
</tr>
<tr>
<td>ESRD</td>
<td>End Stage Renal Disease</td>
</tr>
<tr>
<td>ESWT</td>
<td>Endurance Shuttle Walking Test</td>
</tr>
<tr>
<td>FFM</td>
<td>Fat-Free Mass (FFM)</td>
</tr>
<tr>
<td>FM</td>
<td>Fat Mass</td>
</tr>
<tr>
<td>FNIH</td>
<td>Foundation for the National Institutes of Health</td>
</tr>
<tr>
<td>FTI</td>
<td>Fat Tissue Index</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
</tr>
<tr>
<td>GPAPQ</td>
<td>GP physical activity questionnaire</td>
</tr>
<tr>
<td>HCS</td>
<td>Health Contribution Score</td>
</tr>
<tr>
<td>HD</td>
<td>Haemodialysis</td>
</tr>
<tr>
<td>HDL-C</td>
<td>high-density-lipoprotein Cholesterol</td>
</tr>
<tr>
<td>Hgb</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>HGS</td>
<td>Handgrip Strength</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
</tr>
<tr>
<td>HRMs</td>
<td>Heart Rate Monitors</td>
</tr>
<tr>
<td>HRQoL</td>
<td>Health-Related Quality of Life</td>
</tr>
<tr>
<td>IDWG</td>
<td>Interdialytic Weight Gain</td>
</tr>
<tr>
<td>IL-6</td>
<td>Interleukin 6</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile Range</td>
</tr>
<tr>
<td>ISWT</td>
<td>Incremental Shuttle Walking Test</td>
</tr>
<tr>
<td>KDIGO</td>
<td>Kidney Disease Improving Global Outcomes</td>
</tr>
<tr>
<td>KDQOL-SF</td>
<td>Kidney Disease Quality of Life Short Form</td>
</tr>
<tr>
<td>KDQOL</td>
<td>kidney disease quality of life questionnaire</td>
</tr>
<tr>
<td>LM</td>
<td>Lean Mass</td>
</tr>
<tr>
<td>LTEQ</td>
<td>Leisure Time Exercise Questionnaire</td>
</tr>
<tr>
<td>LTI</td>
<td>Lean Tissue Index</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>LVM</td>
<td>Left Ventricular Mass</td>
</tr>
<tr>
<td>MAC</td>
<td>Mid-Arm Circumference</td>
</tr>
<tr>
<td>MAMC</td>
<td>Mid-Arm-Muscle-Circumference</td>
</tr>
<tr>
<td>MEMS</td>
<td>Microelectromechanical systems</td>
</tr>
<tr>
<td>METs</td>
<td>Metabolic Equivalent of Task</td>
</tr>
<tr>
<td>MICS</td>
<td>Malnutrition–Inflammation Complex Syndrome</td>
</tr>
<tr>
<td>MIS</td>
<td>Malnutrition-Inflammation Score</td>
</tr>
<tr>
<td>MQSGA</td>
<td>Modified Quantitative Subjective Global Assessment</td>
</tr>
<tr>
<td>MSSs</td>
<td>Multi-Sensor Systems</td>
</tr>
<tr>
<td>MVPA</td>
<td>Moderate to Vigorous Physical Activity</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute of Clinical Excellence</td>
</tr>
<tr>
<td>NKF</td>
<td>National Kidney Foundation</td>
</tr>
<tr>
<td>nPCR</td>
<td>normalised Protein Catabolic Rate</td>
</tr>
<tr>
<td>nPNA</td>
<td>normalised Protein Nitrogen Appearance</td>
</tr>
<tr>
<td>NS</td>
<td>Nutritional Status</td>
</tr>
<tr>
<td>NSI</td>
<td>Nutrition Screening Initiative</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratios</td>
</tr>
<tr>
<td>PA</td>
<td>Physical Activity</td>
</tr>
<tr>
<td>PAI</td>
<td>Physical Activity Index</td>
</tr>
<tr>
<td>PCS</td>
<td>Physical Component Scale</td>
</tr>
<tr>
<td>PD</td>
<td>Peritoneal Dialysis</td>
</tr>
<tr>
<td>PEW</td>
<td>Protein-Energy Wasting</td>
</tr>
<tr>
<td>POS-S</td>
<td>Palliative Care Outcome Scale–Symptoms Renal</td>
</tr>
<tr>
<td>PRT</td>
<td>Progressive Resistance Training</td>
</tr>
<tr>
<td>PTH</td>
<td>Parathyroid Hormone</td>
</tr>
<tr>
<td>QOF</td>
<td>Quality and Outcomes Framework</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>RRT</td>
<td>Renal Replacement Therapy</td>
</tr>
<tr>
<td>RS-ONS</td>
<td>Renal-Specific Oral Nutrition Supplement</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SE</td>
<td>Standard Error</td>
</tr>
<tr>
<td>SFT</td>
<td>Skin Fold Thickness</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>SGA</td>
<td>Subjective Global Assessment</td>
</tr>
<tr>
<td>SMM</td>
<td>Skeletal Muscle Mass</td>
</tr>
<tr>
<td>SPPB</td>
<td>Short Physical Performance Battery</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package of Social Sciences</td>
</tr>
<tr>
<td>STS</td>
<td>Sit-to-Stand</td>
</tr>
<tr>
<td>STS5</td>
<td>Sit-to-Stand 5</td>
</tr>
<tr>
<td>STS60</td>
<td>Sit-to-Stand 60</td>
</tr>
<tr>
<td>SVI</td>
<td>Stroke Volume Index</td>
</tr>
<tr>
<td>SWA</td>
<td>Sensewear Armband</td>
</tr>
<tr>
<td>SWT</td>
<td>Shuttle Walking Test</td>
</tr>
<tr>
<td>TAS</td>
<td>Total Activity Score</td>
</tr>
<tr>
<td>TBF</td>
<td>Total Body Fat</td>
</tr>
<tr>
<td>TCM</td>
<td>Traditional Chinese Medicine</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient Ischemic Attack</td>
</tr>
<tr>
<td>TMA</td>
<td>Thigh Muscle Mass</td>
</tr>
<tr>
<td>TSF</td>
<td>Triceps Skinfold</td>
</tr>
<tr>
<td>TTM</td>
<td>Transtheoretical Model</td>
</tr>
<tr>
<td>URR</td>
<td>Urea Reduction Ratio</td>
</tr>
<tr>
<td>USRDS</td>
<td>US Renal Data System</td>
</tr>
<tr>
<td>VPA</td>
<td>Vigorous Physical Activity</td>
</tr>
<tr>
<td>VO_{peak}</td>
<td>Peak Oxygen Consumption</td>
</tr>
<tr>
<td>VO_{max}</td>
<td>Maximal Oxygen Uptake</td>
</tr>
<tr>
<td>WBLM</td>
<td>Whole Body Lean Mass</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Chapter 1

Introduction
1.1 Overview of Chronic kidney disease

The kidney is a critical organ with multiple functions which are imperative to life. It mainly regulates water and electrolyte balance, eliminates metabolic waste products and potentially harmful foreign substances, controls acid-base balance, maintains key homeostasis components and releases hormones. Playing such a crucial role in maintenance of our health and lives, any impairments of renal function can result in a wide variety of complex and serious physical and psychological consequences.

Chronic Kidney Disease (CKD) is the term for a group of heterogeneous disorders resulting in the progressive and irreversible decline in renal function, which is defined by “kidney damage for ≥3 months based on findings of abnormal structure or function or Glomerular Filtration Rate (GFR) <60ml/min/1.73m² for >3 months with or without evidence of kidney damage (Drawz, Rahman 2015)”. Kidney damage includes either structural or functional abnormalities of the kidneys, such as albuminuria or proteinuria, or urinary sediment abnormalities. Irrespective of various possible causes, the severity of CKD can be classified into 5 stages depending on GFR and/or the presence of albuminuria (National Kidney Foundation 2002, Levin, Stevens et al. 2013).

Stage 1 and 2 are regarded as mild CKD and require confirmation with evidence of kidney damage. Stage 3 is further divided into 3a and 3b. The rationale of classification is that 3b is associated with multiple adverse outcomes including cardiovascular outcomes. Patients with stage 1 to 3a (mild-to-moderate CKD) have no physical findings specific to the decrease of kidney function and therefore they are commonly asymptomatic. A diagnosis of CKD 3-5 can be diagnosed on GFR alone. Various symptoms, such as edema, itchy skin, insomnia, muscle cramps, fatigue and so on frequently manifest in these stages of CKD, which become apparent and prominent with progressively decreased kidney function. Besides common symptoms, CKD was proved to be an independent risk factor for Cardiovascular Disease (CVD), cognitive dysfunction and hospitalization. Metabolic abnormalities, including anaemia, secondary hyperparathyroidism, and electrolyte disturbances are complications of CKD as well (Drawz, Rahman 2015).
### Table 1: Stage of chronic kidney disease by GFR and albuminuria categories

<table>
<thead>
<tr>
<th>Persistent Albuminuria Categories, Description and Range</th>
<th>Normal to mildly increased</th>
<th>Moderately increased</th>
<th>Severely increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mg/g (&lt;3mg/mmol)</td>
<td>1 if CKD</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>30-300 mg/g (3-30mg/mmol)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;300mg/g (&gt;30mg/mmol)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GFR Categories (mL/min/1.73 m²)</th>
<th>Stage, Description, and Range</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal or high ≥90</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Mildly decreased 60-89</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>Mildly to moderately decreased 45-59</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3b</td>
<td>Moderately to severely decreased 30-44</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased 15-29</td>
<td>3</td>
<td>3</td>
<td>4+</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure &lt;15</td>
<td>4+</td>
<td>4+</td>
<td>4+</td>
</tr>
</tbody>
</table>

GFR and albuminuria categories inform the risk for progression. Green indicates low risk, yellow indicates moderately increased risk, orange indicates high risk, and red indicated very high risk. The numbers in each box are recommendations for the frequency of monitoring/year. (Levin, Stevens et al. 2013).

#### 1.1.1 Incidence and prevalence

CKD is now recognized as a major and common public health problem worldwide. The rise in the number of patients is threatening the healthcare system all over the world and may reach epidemic proportions over the next decade (Bolignano, Lacquaniti et al. 2009). According to the published investigation of Public Health England in 2014, the prevalence of CKD in England was 6.1% with more than 2.62 million aged over 16 (Public Health England 2015). Up to September 2010, a cross-sectional survey of a nationally representative sample of Chinese adults showed that the prevalence of CKD in China was 10.8% with 119.5 million adults aged 18 years or older (Zhang, Wang et al. 2012). Although the prevalence of CKD in China estimated from the survey was similar to that in developed countries such as the USA (13.0%) and Norway (10.2%) (Hallan, Coresh et al. 2006, Coresh, Selvin et al. 2007), the prevalence of stage 3 and 4 of CKD was lower compared to those of developed countries. Similarly, in contrast with the 1.6% in prevalence of stage 3 CKD in China (Zhang, Wang et al. 2012), the 5.4% prevalence in the UK stage 3 patients was relatively higher. Despite the fact that diabetes and
hypertension have increased remarkably in the past 15-20 years in China (Zhang, Wang 2009), the impact of these diseases on CKD might not be felt for another 10 years (Zhang, Wang 2009). The consequence resulting from this phenomenon may lead to a dramatically high rate of prevalence of CKD in China in the foreseeable future.

1.1.2 Causes and risk factors

Although the cause of CKD depends on patient’s demographics, such as race, age and geographical area, in summary, the most common causes of CKD are diabetes and hypertension all over the world. It was revealed that CKD patients entering End Stage Renal Disease (ESRD) due to diabetes demonstrated a progressive increase over the past decade. However, glomerulonephritis, cystic kidney disease and hypertension as causes of ESRD remained relatively steady (Atkins 2005). The US Renal Data System (USRDS) demonstrated that 44% of all incidence ESRD patients suffered from diabetes mellitus (United States Renal Data System, (USRDS) 2008), which was similar to the situation that existed in the UK (Gilg, Rao et al. 2013). Following diabetes, essential hypertension and atherosclerotic renal vascular disease contribute to the most frequent causes of CKD in the UK (Kumar, Bitla et al. 2012). In China, analysis of renal biopsy data showed that the primary cause of CKD was glomerulonephritis, which was followed by diabetic nephropathy and hypertension nephrosclerosis (Xie, Chen 2008). Besides the causes associated with the incidence of CKD, it is crucial to identify risk factors which contribute to the initiation and progression of CKD. These risk factors can be classified into modifiable and non-modifiable categories, which cover susceptibility, initiation and progression factors (El Kossi, Bello et al. 2007). Improving lifestyle behaviours involving living an active life, healthy diet, ceasing smoking, and avoiding drug abuse, benefit a significant body of initiation and progression factors, so that it can prevent CKD and alleviate the deterioration of kidney function impairment.
### Table 1-2 Risk factors for Chronic Kidney disease

<table>
<thead>
<tr>
<th>Non-modifiable</th>
<th>Modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old age (S)</td>
<td>Systemic hypertension (I, P)</td>
</tr>
<tr>
<td>Male sex (S)</td>
<td>Diabetes mellitus (I, P)</td>
</tr>
<tr>
<td>Race/ethnicity (S)</td>
<td>Proteinuria (P)</td>
</tr>
<tr>
<td>Genetic disposition (S)</td>
<td>Dyslipidaemia (I, P)</td>
</tr>
<tr>
<td>Family history (S)</td>
<td>Smoking (I, P)</td>
</tr>
<tr>
<td>Low birth weight (S)</td>
<td>Obesity (I, P)</td>
</tr>
<tr>
<td></td>
<td>Infections/infestations (I)</td>
</tr>
<tr>
<td></td>
<td>Drugs and herbs/analgesic abuse (I)</td>
</tr>
<tr>
<td></td>
<td>Autoimmune disease/obstructive uropathy/stones (I)</td>
</tr>
<tr>
<td></td>
<td>Low socio-economic status (S)</td>
</tr>
</tbody>
</table>

S, Susceptibility factor; I, Initiation factor; P, Progression factors

#### 1.1.3 Overview of End Stage Renal Disease

When a patient’s GFR is less than 15ml/min/1.73m², the patient develops ESRD, which is serious, long-term chronic irreversible renal failure and requires Renal Replacement Therapy (RRT) in the form of dialysis (haemodialysis [HD] and peritoneal dialysis [PD]) or a transplant to maintain life. Kidney transplantation is an important choice for ESRD patients. It is associated with a lower risk of mortality, cardiovascular events and improved Quality of Life (QoL) compared with dialysis (Tonelli, Wiebe et al. 2011). However, the declining rate of organ donation combined with the increasing number of ESRD cases have led to a significant challenge for patients and healthcare professionals (Wolfe, Roys et al. 2010, USRDS 2008). Therefore, dialysis treatment is regarded as an essential alternative to artificially fulfill the job of the kidneys. Research found that HD is the most widely available form of dialysis with 65% of ESRD patients compared with 10% receiving PD, and the rest receive a transplant (Hall, Chertow 2007, Painter 2005).

**Haemodialysis and Peritoneal dialysis**

HD, the most common form in dialysis, usually involves thrice weekly treatments of approximately four hours. Blood is circulated through a disposable dialyser, which contains hollow fibres surrounded by a semi-permeable membrane. As blood moves through these fibres it comes into contact with purified water with added electrolytes (dialysate), which is circulated around the outside of the hollow tubes. Basically, materials are exchanged between the blood and the dialysate and this occurs across the semi-permeable membrane of the dialyzer. As a result, waste products and electrolytes in the blood move from the blood side of the membrane into the dialysate solution, resulting in adequate control of biochemistry, fluid overload, acidosis and uremic
symptoms in most patients. In PD, fluid is instilled into the peritoneal space, where it remains for a period of time, to allow waste products to diffuse from the blood into the fluid through the peritoneum as the dialysis membrane.

Nowadays, dialysis is estimated to be undertaken by more than 2 million people worldwide (Magnard, Deschamps et al. 2013b), and it is predicated that the need for dialysis will increase dramatically over the next 10 years due to a growing epidemic of obesity and diabetes (Rao A, Casula A, Castledine C 2014). In 2014, the reported incidence of ESRD in the UK and China were 115 (UK Renal Registry 2015) and 47 Per Million of Population (PMP) (Chinese National Renal Data System 2015), respectively. To date, current data indicates that there are 36,000 dialysis patients in the UK, of which 27,000 receive HD (UK Renal Registry 2015). According to the survey conducted by the Chinese Society of Blood Purification (CSBP) and the Chinese National Renal Data System (CNRDS), there were 385,000 HD cases by December 31, 2015 with prevalence at 280 PMP, compared with 65,074 HD or PD patients at the end of 2007 (Zuo, Wang et al. 2010). These findings confirm the high prevalence of HD and predict that taking care of HD patients will become an increasing burden on both families and society in the UK and China.

Symptoms and Complications

Despite significant improvement in dialysis techniques and the progress in treatment of co-morbidities, patients with ESRD still suffer from a wide variety of symptoms and complications. Dialysis patients described that the symptoms they were struggling with were up to an average of nine symptoms in one study (Yong, Kwok et al. 2009a). Also, ESRD patients with severely damaged kidney function are associated with various complications. Among them, atherosclerotic complications were certified to be the leading cause of mortality in ESRD patients (Wanner, Krane et al. 2005, Amann, Buzello et al. 2000, Burton, Jefferies et al. 2009, Levey, Beto et al. 1998). It has been reported that over 50% all deaths on HD are due to problems related to CVD (Parfrey 2000, Zoccali, Tripepi et al. 2005). The USRDS annual data reported the prevalence of cancer and Chronic Obstructive Pulmonary Disease (COPD) in HD patients showed a notable increment from 2004 to 2007 (Collins AJ 2012). A review in regard with the aging dialysis populations revealed cognitive impairment is an occult burden for ESRD, as evidenced by the fact that up to 70% of the cohort have moderate or severe cognitive impairment.
Additionally, muscle wasting (Cigarrán, Pousa et al. 2013), anaemia (Locatelli, Pisoni et al. 2004), systemic inflammation (Avesani, Carrero et al. 2006), poor mental health (Palmer, Vecchio et al. 2013, Bautovich, Katz et al. 2014), and reduced QoL (Dobsak, Homolka et al. 2012) all contribute to the numerous complications among HD patients. In order to alleviate these symptoms or complications, some require daily medication but many have to be managed rather than treated. Some symptoms can be ameliorated by encouraging patients to increase regular physical activity (PA), such as fatigue, dyspnea and sleep disturbance (Douglas, Murtagh et al. 2009, Cohen, Moss et al. 2006, Murtagh, Murphy et al. 2006, Murtagh, Addington-Hall et al. 2006, Critchley, Plach et al. 2001). Similarly, some complications can be improved through careful dietary control, fluid restriction and nutrition support (Almeras, Argiles 2009). Actually, increasing studies showed that a sedentary lifestyle and an altered nutritional status (NS) have been identified as major risk factors for adverse outcomes, which lead to a high risk of morbidity and mortality in HD population (O'Hare, Tawney et al. 2003a, Lopes, Bragg-Gresham et al. 2010). Therefore, improving a healthier lifestyle in HD patients, including promoting NS, increasing PA/exercise level and physical functioning are important integral parts of ESRD management.

1.2 Physical activity and exercise

PA and exercise have long been known to be a significant way of improving people’s physiological and psychosocial health. C J Caspersen et al. defined PA as “any bodily movement produced by the skeletal muscles that result in energy expenditure”, e.g. walking upstairs and gardening. Exercise is a subtype of PA. It is characterized with more specific and explicit plans and structures so as to obtain the improvement or maintenance of health and fitness (Caspersen, Powell et al. 1985), such as jogging or cycling. Aerobic and resistance exercise are two integral parts in an exercise program due to their different physiological effect. Aerobic exercise refers to activities stimulating and strengthening the heart and lungs, resulting in moving oxygen-rich blood throughout the body, and keeping internal vital organs working efficiently (Sigal, Kenny 2010), such as walking or jogging with continuous, repetitive movement of large muscle groups for at least 10 minutes at a time. Whereas resistance exercise refers to activities strengthening bones and muscles, resulting in improving posture and providing the strength and endurance of
daily living activities (Sigal, Kenny 2010), such as weight lifting or work against a resistance load.

1.2.1 Effects of physical activity and exercise in haemodialysis

A systematic analysis revealed that aerobic combined with resistance exercise were the best way of advocating wellness for patients with CKD (Heiwe, Jacobson 2011). Numerous studies have shown that exercise improves Peak Oxygen Consumption (VO2peak) as well as Ejection Fraction(EF), left ventricular mass(LVM), Stroke Volume Index(SVI) and Cardiac Output Index(COI) in HD patients (Johansen 2007, Deligiannis, Kouidi et al. 1999, Toussaint, Polkinghorne et al. 2008a).

Muscle wasting has been confirmed as one of the most powerful independent indicators of mortality in ESRD (Rhee, Kalantar-Zadeh 2014). The occurrence rate of skeletal muscle wasting will increase with CKD progresses (Kovesdy, Kopple et al. 2013). An exercise training rehabilitation programme(Kouidi, Iacovides et al. 1997) or both moderate and vigorous PA (Morishita, Kubo et al. 2014), have both shown to markedly improve skeletal muscle mass. One study of 16 weeks of resistance training significantly increased neuromuscular function and muscle force development (Molsted, Andersen et al. 2013).

It was estimated that around 25% of ESRD population suffer from depression (Ver, Cukor et al. 2012). The symptoms of longstanding depression has a negative impact on sleep quality, concentrating ability and activity level (Finkelstein, Wuerth et al. 2008), leading to increased hospitalizations and mortality in HD (Hedayati, Bosworth et al. 2008). Several studies of exercise in HD patients have suggested that participating in aerobic exercise training may be beneficial in relieving levels of depressed mood and have a positive impact upon other psychological problems such as anxiety (Mi Rye Suh, R N, Hyuk Jung et al. 2002, Painter, Carlson et al. 2000b, Tentori, Elder et al. 2010).

Although the aetiology of systemic inflammation is too complex to be fully elucidated (Cheema 2008), a growing number of studies revealed that it was inversely associated with muscle mass and physical fitness (Church, Barlow et al. 2002, Rahimi, Secknus et al. 2005, Albert, Glynn et al. 2004, Kaizu, Ohkawa et al. 2003a). Higher PA levels were correlated with reduced amount of Interleukin 6 (IL-6), C-Reactive Protein (CRP) and other pro-inflammatory markers(Baumgartner, Koehler et al. 1996, Bruunsgaard 2005),
all of which in circulating concentrations indicate the severity of systemic inflammation (Kalantar-Zadeh 2007, Bruunsgaard 2005).

Obviously, the combined physiological and psychological effects of exercise have a positive impact on QoL in HD population. Furthermore, studies assessed with a variety of QoL questionnaires have been directly demonstrated that increased PA improved HD patients’ QoL (Tentori, Elder et al. 2010, Mi Rye Suh, R N, Hyuk Jung et al. 2002). Mi Rye Suh et al. reported that HD patients improved QoL secondary to 12 week of an exercise program composed of bicycle ergometer, the treadmill or upper limb ergometer (Mi Rye Suh, R N, Hyuk Jung et al. 2002).

A series of Goldberg’s studies have found the metabolic effects of exercise training (Goldberg, Hagberg et al. 1980a, Goldberg, Geltman et al. 1983, Goldberg, Hagberg et al. 1980b). Exercise can decrease triglycerides and increase high-density-lipoprotein Cholesterol (HDL-C), which improve atherosclerotic heart disease. Additionally, improvement of sleep quality, reduction in antihypertensive medications, and even attenuated socio-economic indicators have also been demonstrated in several studies elucidating the effect of exercise in HD patients (Tentori, Elder et al. 2010, Miller, Cress et al. 2002, Yang, Xu et al. 2015).

1.2.2 Current situation of exercise or physical activity in haemodialysis patients between the UK and China

Whilst the importance of motivating HD patients to exercise has attracted increased attention from healthcare providers in developed countries worldwide, it is still unclear how to incorporate exercises into their daily lives. Numerous studies have shown that exercise levels among HD patients were lower than healthy (Sterky, Stegmayr 2005) or even healthy sedentary controls (Johansen, Chertow et al. 2000a, Johansen, Sakkas et al. 2003). Activity levels continued to decline by up to 3.4% each month after initiation of dialysis (Johansen, Kaysen et al. 2003). A study conducted in America showed that 59% of HD patients reported no additional PA except for Activities of Daily Living (ADLs) in a baseline investigation (Painter, Carlson et al. 2000c). Another survey regarding the relationship between exercise and limitations in PA levels among HD patients demonstrated that 56% of patients exercised less than once a week, 75% reported severe
limitations in vigorous activities, and 42% had severe limitations in moderate PA (Stack, Murthy 2008b).

In the UK, although exercise was first introduced to HD patients decades ago, physical inactivity is still a serious and highly prevalent issue. A study conducted with a total activity score (TAS) highlighted the lack of PA in patients with kidney disease (Hayhurst, Ahmed 2015). In particular, the study identified the HD patients as the most physically inactive group compared with the other groups of CKD patients and healthy control. There are few studies with regard to investigation about PA level in HD patients in China. A cross-sectional survey using convenience sampling in North China found that 26.7% HD participants were inactive and only 2.7% among them were active (Li, Li et al. 2010a). Furthermore, their dominant types of PA were only transport-related walking and household work. Despite that, studies regarding exercise intervention conducted with HD patients remain inadequate. Apart from outpatient-based renal rehabilitation programs, which were implemented only in a couple of kidney disease units, intra-dialytic exercise is the most widely used exercise form on HD patients in the UK. Whilst recent efforts have been offered on the quality and quantity of exercise interventions in HD patients, clinical trials involving these interventions have limitations, such as small sample size, no blinded controls, and lack of the understanding of participants’ exercise or PA level (Macdonald, Marcora et al. 2005, Torkington, MacRae et al. 2006, Greenwood, Naish et al. 2014b, Kirkman, Mullins et al. 2014). In China, only two studies in Hong Kong (Lo, Lo et al. 1998) and Taiwan (Liu, Chung et al. 2015) evaluated the effectiveness of two types of exercise for HD patients. There is only one study in Mainland China which implemented individualized exercise during HD session, and results revealed that exercise had improve the exercise capacity and QoL (Wu, He et al. 2014a).

1.2.3 Assessment of physical function in haemodialysis patients

Physical function refers to an individual’s ability to perform activities required in their daily lives. It includes multiple determinants, such as exercise capacity (cardiorespiratory fitness), strength, sensory function, clinical status, and environmental and behavioural factors (Painter, Stewart et al. 1999, Stewart, Painter 1997). Obviously, it is considerably difficult to cover all areas when assessing physical function. Therefore, the measurement can be tailored according to specific population and the topics of specific interest. It can be seen that the assessment of physical function mainly involves laboratory test, physical
performance tests and self-reported physical functioning questionnaires (Hlatky, Boineau et al. 1989a).

Laboratory test

Physical function can be measured using laboratory tests of oxygen uptake during a maximal exercise performed on incremental treadmill or cycle ergometer protocols (Maximal Oxygen Uptake [VO₂max]). However, with severe chronic disease, some patients are unable to meet the criteria of VO₂max. In such cases, the most commonly used marker of physical function is VO₂peak or symptom-limited VO₂peak. The specific test involves a gradually increasing velocity until the patient reaches physical exhaustion. VO₂peak is recorded when the highest VO₂ is obtained during the last stage. Koufaki P et al. confirmed that physical function measured by the VO₂ was feasible and can be safely performed with HD patients when considering specific cautions (Koufaki, Mercer 2006). However, this cardiopulmonary fitness test is not extensively implemented in HD patients due to the costs of instruments and personnel.

Physical performance tests

Physical function is more frequently evaluated by effective but simple measures based on physical performance. These objective measures cover different areas depending on various specific characteristics of interest. Walking tests are for determining mobility, including Shuttle Walking Test (SWT), 6 Minute Walk Test (6MWT) and gait speed tests. Handgrip Strength (HGS) and Sit-to-Stand test (STS) are used to evaluate muscle power or endurance of leg muscle, such as STS5, 10-STS and so on. A significant body of studies assessed physical function by using various physical performance tests to evaluate the effect of exercise interventions among HD patients (Painter, Carlson et al. 2000d, Nonoyama, Brooks et al. 2010, Parsons, Toffelmire et al. 2006). Additionally, physical performance tests play a crucial role in exploring the associated factors of physical function as well, such as anaemia (Penninx, Pahor et al. 2004), L-carnitine (Wächter, Vogt et al. 2002) and anabolic steroid (Johansen, Painter et al. 2006b).

Self-reported physical function questionnaires

Apart from objective measures, self-report questionnaires are the other optimum option for assessing physical function with HD patients. The Kidney Disease Quality of Life
Questionnaire (KDQOL) was extensively used to obtain as much information as possible on physical function in dialysis patients (Hays, Kallich et al. 1994). This questionnaire comprises an eight-point scale, which includes 10 items of questions assessing abilities to deal with the physical requirements of life, ranging from bathing or dressing to vigorous activities (Ron D. Hays et al. 1997). There were evidence to support that the low physical function level based on the poor Kidney Disease Quality of Life Short Form (KDQOL-SF™) scores was an independent and powerful predictor of adverse clinical outcomes and high risk of mortality in HD patients (Mapes, Lopes et al. 2003). Additionally, The Duke Activity Status Index (DASI) was widely utilized in renal disease and regarded as a reliable measure of physical function in CKD patients, especially the reliability is higher in estimated Glomerular Filtration Rate (eGFR) less than 35 ml/min per 1.73m² than eGFR≥35 ml/min per 1.73 m² (Ravani, Kilb et al. 2012).

1.2.4 Physical activity measurement for haemodialysis patients

Increasing PA level have been documented as a behaviour strongly associated with optimizing health and reducing morbidity and mortality in HD patients, which is consistent with recommendations made by the NICE (The national institute of clinical excellence, (NICE) 2015) and the Kidney Disease Improving Global Outcomes (KDIGO) (Levin, Stevens et al. 2013)for HD patient. A comprehensive and explicit assessment of PA is of fundamental importance in promoting HD patients to have an active lifestyle. The assessment of PA’s dimensions (frequency, duration and intensity) over the past week or month and domains (occupational, leisure time, domestic and transport) are the main topics of interests of researchers when assessing PA. Generally, the measure tools for assessing PA includes self-reported and direct measures, of those, questionnaires are most frequently used in cross-sectional studies (Ainsworth, Cahalin et al. 2015), and Multi-Sensor Systems (MSSs)were widely conducted in HD patients (Carvalho, Reboredo et al. 2014b, Avesani, Trolonge et al. 2011b).

Self-report questionnaires

A number of questionnaires were used for assessing PA level in various health status range (Armstrong, Bull 2006, Scarmeas, Luchsinger et al. 2009, Johansen, Painter et al. 2001). However, low test-retest reliability and validity and confining to the performance of heavy intensity PA in questionnaires were usually documented in the previous
literatures (Jacobs, Ainsworth et al. 1993, Shephard 2003). The GP physical activity questionnaire (GPPAQ) was usually chosen over other recognised PA questionnaires (G. Godin, R J Shephard 1985) due to its applicability over a wide age and brevity. It was developed for the routine check of cardiovascular health (NHS Health Check Program Standards 2014) and 2013/14 Hypertension Quality and Outcomes Framework (QOF) performance in the UK (Let’s Get Moving: Commissioning Guidance 2012).

The Leisure Time Exercise Questionnaire (LTEQ) was used for assessing the amount of exercise undertaken with respondents who participate in exercise and identifying preferred activities. Validity for the LTEQ was confirmed by the correlation with VO$_{2\text{max}}$(Godin, Shephard 1985). Meanwhile, the significant association of the LTEQ with lengthier and more detailed exercise questionnaires also evidenced the validity of the LTEQ (Goodman, Ballou 2004a).

**Objective measures**

Although there is no single gold-standard objective measure to assess PA, researchers have a wide range of options according to their specific interests.

**Pedometer**

Pedometer is a hip-worn mechanical sensor identifying steps based on the force generated from a typical heel-strike during ambulation. With the introduction of computer techniques, accuracy of pedometer has enhanced by the Microelectromechanical systems (MEMS). Apart from that, pedometer can also provide a valid estimation of PA intensity. However, it is understood that the ankle is the most accurate placement for tracing steps (Karabulut, Crouter et al. 2005). Hence, most pedometers with hip-worn fail to provide accurate assessment for steps. In particular, the accuracy of pedometer would be lower when participants’ steps were at slow gait speed (<2mhp) (Melanson, Knoll et al. 2004, Crouter, Schneider et al. 2003). Apparently, the compromised accuracy may restrict pedometer’s utilization in HD patients with relatively slower walking speed than general population.
Accelerometer

Accelerometer is a small wearable monitor recording acceleration on planes at sampling rates >1 time/second. Captured accelerations are then processed and calibrated to a known standard PA measure, such as doubly-labelled water (DLW), relying on a unitless intensity metric or “counts”. The doubly labelled water method is viewed as gold standard for the assessment of total energy expenditure (TEE) (Butler, Green et al. 2004). It uses stable isotopes of hydrogen and oxygen to trace the flow of water and carbon dioxide production through the body during the interval between first and last body water samples (Ainslie, Reilly et al. 2003). A single estimate of the rate of oxygen consumption can be derived from these data. When combined with a measure of resting metabolic rate, the DLW can calculate activity-related energy expenditure. Accelerometer provides Metabolic Equivalent of Task (METs) thresholds to summarize data to output the duration and frequency of PA into sedentary, light, moderate and strenuous intensities (Ainsworth, Cahalin et al. 2015). Apparently, accelerometer is capable of monitoring the dimension of PA, involving the frequency, duration, intensity of activities. Furthermore, the appeal of accelerometer is that it can measure PA with a detailed and relatively precise manner. Nowadays, triaxial accelerometer measuring acceleration on three planes provides more sensitive and precise PA due to a more comprehensive assessment of body movement than uniaxial devices. Additionally, triaxial accelerometer is capable of quantifying movement patterns during walking because it includes vertical and anterior-posterior accelerations for measuring step frequency and mediolateral accelerations for detecting specific gait-related movement (Kavanagh, Menz 2008). However, accelerometer is unable to detect non-ambulatory activities, such as weight-lifting and cycling. The reason is the limited accuracy of EE measurements with accelerometers (Matthew 2005). It only measures a single modality of PA and attempt to correct it with EE. Whereas, non-ambulatory activities do not involve a single modality. Additionally, lack of sensitivity for detecting sedentary and light intensity activities is a drawback of accelerometer as well (Butte, Ekelund et al. 2012).

Multi-sensor systems

Multi-sensor systems (MSSs) are a combination of physiological measure and mechanical sensor. It can provide precise and accurate assessment of PA level. Different
MSSs include different parameters, involving accelerometer, galvanic skin response, HR, respiration and skin or core temperature. MSSs have potential precision in measuring non-ambulatory activities because the results may come from triangulating EE estimates derived from multiple sensors (Ainsworth, Cahalin et al. 2015). While they are valid in healthy population (Rowlands, Thomas et al. 2004) and chronic diseases (Van Remoortel, Raste et al. 2012, Van Remoortel, Giavedoni et al. 2012), MSSs also have been widely adopted in the studies with kidney transplant recipients (Carvalho, Reboredo et al. 2014a) and HD patients (Carvalho, Reboredo et al. 2014a, Avesani, Trolonge et al. 2011a, Gomes, Reboredo et al. 2015). MSSs presented the results by measuring numbers of steps, time spent on different activities (lying, sitting, standing and walking), and activities intensity. Compared to questionnaires, pedometers and other monitors that measure PA through arbitrary units or estimated EE, MSSs showed higher accuracy and less variability (Van Remoortel, Raste et al. 2012).

1.3 Nutritional status in haemodialysis

1.3.1 Prevalence causes and potential comorbidities of malnutrition in haemodialysis patients

Malnutrition is a common problem involving 40-50% of ESRD patients (Basaleem, Alwan et al. 2004), with the estimated prevalence of 18-75% in HD patients (Leinig, Moraes et al. 2011). 37% of 122 HD patients in Spain had evidence of malnutrition at baseline assessment, 40.5% at 12 months and 41.4% at 24 months (Gracia-Iguacel, González-Parra et al. 2013). An NS investigation in Yemen with 50 HD patients showed that 70% of patients were moderately malnourished and severe malnutrition accounted for 20% (Basaleem, Alwan et al. 2004).

The causes of malnutrition are various, including inadequate dietary intake due to loss of appetite, gastrointestinal disturbances and anorexia, dialysis treatment, defective food assimilation and utilization occurring as a result of hypercatabolism, concomitant diseases namely systemic inflammation(Locatelli, Fouque et al. 2002a), sepsis, and CVD (Laville, Fouque 2000).

Malnutrition leads to systemic inflammation (Stenvinkel, Heimbürger et al. 2000), muscle wasting (Basaleem, Alwan et al. 2004), highly prevalence for hospitalization (Steiber, Handu et al. 2003), poor QoL and fatigue (Laws, Tapsell et al. 2000b), and
eventually causes increased mortality risk in HD patients. Nutritional parameters, including body mass index (BMI), Subjective Global Assessment (SGA) and serum albumin levels were assessed with 167 HD patients at the dialysis initiation. It was shown that reduced serum albumin (P=0.01) and malnutrition scores (P=0.02) independently predicted mortality after a ten-year of follow-up (Chan, Kelly et al. 2012). Radojica V. Stolic et al. examined BMI, treatment outcomes and biochemical parameters over a 4-year period to evaluate HD patients’ metabolic syndrome and NS. The results revealed that more than two thirds of the malnourished patients who accounted for 26.7% of the examined participants died, which indicated that there was an inverse association between malnutrition and survival rate (Stolic, Trajkovic et al. 2010).

1.3.2 Nutritional blood parameters in haemodialysis patients

Haemoglobin and serum ferritin

Anaemia is a common symptom in CKD patients with a high risk of adverse outcomes associated with increased morbidity and mortality. The primary aetiology of anaemia is the inadequate erythropoietin to support erythropoiesis due to kidney function impairment. Apart from diminished erythropoietin, the other multifactorial contributors are iron, folate and vitamin B12 deficiency, decreased red blood cell lifespan, hyperparathyroidism, inflammation, hypothyroidism and ‘uremic environment’ (US Recombinant Human Erythropoietin Predialysis Study Group 1991, Hsu, McCulloch et al. 2002, Eschbach, Adamson 1985, Kaze, Kengne et al. 2015). These factors contributed in part to the consequence that the prevalence of anaemia increased as CKD patients’ GFR declined. A number of prior studies revealed that the prevalence of anaemia in ESRD or HD patients could up to almost 100% (Afshar, Sanavi et al. 2010, Suega, Bakta et al. 2005, Astor, Muntner et al. 2002, McClellan, Aronoff et al. 2004).

Based on the latest renal data report, 20% of the UK HD patients had Hgb ≥ 12g/dl, while 59% had Hgb from 10 to 12 g/dl (UK Renal Registry 2016). The mean Hgb was 11.0g/dl in the UK HD patients. Improvement in prevention and management of anaemia has been observed in developed countries (Kaze, Kengne et al. 2015). However, the prohibitive cost of Erythropoiesis Stimulating Agents (ESA), which are administered by 19~40% patients with CKD (Covic, Nistor et al. 2014) to treat anaemia, may interfere patients from developing countries with limited healthcare resource to afford them (Afshar,
Sanavi et al. 2010, Suega, Bakta et al. 2005). Although 19.7% of Chinese HD patients had Hgb ≥ 12g/dl, only 35.8% had Hgb from 10 to 12g/dl, which was much lower than the proportionate in UK patients. Furthermore, the mean Hgb of Chinese HD patients was only 10.1 g/dl (Chinese National Renal Data System 2015).

Serum ferritin concentration is a critical and most commonly used marker playing a role in predicting iron status in HD patients (Kalantar-Zadeh, Rodriguez et al. 2004). In accordance with anaemia guidelines, intravenous iron is necessary to administer regularly to HD patients in order to maintain ferritin between 100 to 800ng/ml (National Kidney Foundation anemia working group 2001). Following the USRDS report in May 2016 (United States Renal Data System, USRDS 2017), 31.6% and 21.9% of American HD patients had serum ferritin of 801~1200 ng/ml and >1200ng/ml, respectively. The percentages with serum ferritin of ≥100μg/l (equals to ng/ml) and ≥800μg/l in UK HD patients were demonstrated by centres based on the UK Renal Registry 19th Annual Report in 2015 (UK Renal Registry 2016). It showed that 94% of the overall UK HD patients had serum ferritin ≥100μg/l, with the median of 415μg/l. It is understood that the CNRDS did not cover the investigation or collection of serum ferritin with Chinese HD patients. According to the finding of a study exploring the associated factors of cardiovascular morbidity in Chinese HD patients, the median of the serum ferritin in 1775 patients only approached 284.1 ng/ml, which was much lower than 415μg/l in the UK HD patients (Hou, Jiang et al. 2012).

**Serum calcium and phosphate**

As predictors of the mineral metabolism disorders, serum calcium and phosphate management are playing an important role in decreasing vascular calcification risk, comorbidities and mortality in HD patients (Massry, Coburn et al. 2003, Block, Klassen et al. 2004, Young, Albert et al. 2005, An, Kim et al. 2009). 560 HD patients were followed up for 9 years to evaluate survival rates and predictors of mortality. The adjusted time-dependent model revealed that hypocalcaemia, hypercalcemia and hyperphosphatemia were all significantly associated with death (Ossareh, Farrokhi et al. 2016). A study involving 119,010 American HD patients confirmed that uncorrected serum calcium <8.5 and ≥10.2mg/dl were associated with excess mortality in HD patients (Rivara, Ravel et al. 2015). The recommended target range of serum calcium is 2.2-2.5mmol/l (8.8-10.2mg/dl) for HD patients by the NICE (Steddon, Sharples 2011). 79.3%
of the UK HD patients were within the normal range and only 10.6% of patients had calcium levels less than 2.2mmol/l according to the UK Renal Registry 19th Annual report (UK Renal Registry 2016). However, 49.8% of Chinese HD patients in 2014 had calcium with 2.2-2.5mmol/l. The proportion of hypocalcaemia patients in the Chinese HD patients was up to 36.0% (Chinese National Renal Data System 2015).

Except for being an influencing factor of mineral bone disease, serum phosphate predicts the NS of HD patients as well due to the strong correlation with protein intake (Block, Klassen et al. 2004). Hyperphosphatemia is a common biochemical abnormality in HD population and leads to higher cardiovascular morbidity and mortality (Alfrey 2004, Kendrick, Chonchol 2011). It is due to the decline of kidney function, the reduced clearance of phosphate during dialysis (Al-Hejaili, Kortas et al. 2003, Kooienga 2007, Gutzwiller, Schneditz et al. 2003), poor compliance with dietary instructions (Kalantar-Zadeh 2007, Urribarri 2007, Pollock, Jaffery 2007, Poduval, Wolgemuth et al. 2003), and lack of knowledge about foods rich in phosphate(Sherman 2009, Tentori 2008, Wald 2008).The study with 119,010 U.S. HD patients revealed that patients with serum phosphate ≥6.4mg/dl had the increased mortality risk (Rivara, Ravel et al. 2015). On the basis of 2017 USRDS annual report (United States Renal Data System, USRDS 2017), 65.9% HD patients had serum phosphate levels greater than 4.5mg/dl (1.5mmol/l). It is not comparable in serum phosphate between the U.S. and UK HD patients, since these two renal data system adopt different audit standard for phosphate with 0.8~1.5mmol/l (United States Renal Data System, USRDS 2017) and1.1~1.7mmol/l(UK Renal Registry 2016), respectively. However, UK HD patients seemed to appear lower proportionate of HD patients who were beyond the Renal Association (RA) audit standard (≥1.7mmol/l) with 35.9% than U.S. HD cohorts. Additionally, Chinese HD patients had worse control of serum phosphate than their UK counterparts. 54.5% of Chinese HD patients had a serum phosphate above the standard (≥1.7mmol/l) based on the CNRDS report (Chinese National Renal Data System 2015).

**Serum potassium**

Controlling hyperkalaemia is an ever-present challenge in ESRD patients (Lin, Tu et al. 2013). The causes of hyperkalaemia are associated with poor compliance with low potassium diet, the use of Angiotensin-Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARBs), spironolactone and the unavailability
fludrocortisone and potassium binders (Sanghavi, Whiting et al. 2013). Hyperkalaemia can result in weak and paralyzed skeletal muscles, reduced conduction velocity and accelerated repolarization (Ahmed, Weisberg 2001), which may lead to the reduced physical function, disability and fatigue in dialysis patients. Importantly, all-cause mortality is also associated with hyperkalaemia. The normal range of serum potassium is 3.5-5.5mEq/L. A 3-year study with 81,013 HD patients showed that serum potassium between 4.6 and 5.3mEq/L indicated the greatest survival, whereas <4.0 or ≥5.6mEq/L was associated with the higher mortality risk (Kovesdy, Regidor et al. 2007). The distribution of serum potassium concentration in overall HD patients of each country was not showed in the USRDS, UKRR or CNRDS reports. The UKRR in 2015 hoped to obtain complete potassium data for analysis in the next report. In the Dialysis Outcomes and Practice Pattern Study (DOPPS), HD nutritional indicators were evaluated across France, Germany, Italy, Spain and the UK. Overall, the percentage of HD patients with hyperkalaemia of ≥ 6.0mmol/l was almost 20%. 10% of UK HD patients suffered from hyperkalaemia, which had the lowest proportionate among these five countries (Hecking, Bragg-Gresham et al. 2004). It is understood that there was few studies pertaining to the investigation of serum potassium concentration in Chinese HD population except for 82 urgent-start HD patients showing their mean serum potassium with 4.3±0.8 mmol/L (Jin, Fang et al. 2016).

**Serum sodium**

Net sodium balance for HD patients depends on the concentration gradient between the serum and dialysate sodium (Lambie, Taal et al. 2005). Although a higher dialysate sodium concentration was widely used in the U.S. for reducing intra-dialytic hypotension and dialysis-related complications, the consensus regarding the optimal dialysate sodium concentration has not been reached (Flanigan 2000). Therefore, ample studies have being focused on exploring the relationship between dialysate sodium and pre-dialysis serum sodium concentration, and giving insight into the importance of understanding pre-dialysis serum sodium concentration (Hecking, Karaboyas et al. 2012, Mc Causland, Brunelli et al. 2011, Jung, Lee et al. 2013). In the DOPPS involving 11,555 HD patients from 12 countries, mean serum sodium level of the overall patients was 138.5 ± 2.8 mEq/L. Mean serum sodium concentration was 138.5 ± 2.8mEq/L in the UK, which happened to be in line with the average level in the 12 countries(Hecking, Karaboyas et
A study was conducted to compare the left ventricular hypertrophy between HD and PD in Chinese patients. The result showed that the mean serum sodium concentration was 137.1±1.6mEq/L.

The DOPPS (Hecking, Karaboyas et al. 2012) and Hemodialysis (HEMO) (Waikar, Brunelli 2011) showed an unexpected finding that the lower mortality risk was observed in HD patients with higher serum sodium concentrations. The DOPPS even extended the finding to a larger and international data set. More interestingly, the lowest mortality was associated with HD patients, when their serum sodium concentration was more than 142mEq/L. The risk with higher serum sodium did not start until the concentration was more than 145mEq/L. Hyponatremia itself in the HD patients with the unique physiology may be a predictor of mortality. Additionally, sodium and caloric intake are highly correlated (Alderman, Cohen et al. 1998). The finding above was not beyond the normal serum sodium range of 135-145mEq/L. Given all the USRDS, UKRR or CNRDS did not report the distribution of serum sodium concentration in overall HD patients of the corresponding countries, the relationship of serum sodium level and survival in HD patients needs to be further explored in future study. Virtually, a significant body of studies showed that dietary sodium intake was associated with Interdialytic Weight Gain (IDWG), the pathogenesis of hypertension and hypervolemia, and left ventricular hypertrophy (Kayikcioglu, Tumuklu et al. 2008, Ozkahya, Ok et al. 2006, Maduell, Navarro 2001). A large scale and prospective trial with detailed dietary assessments unrevealed that higher dietary sodium intake was independently correlated with greater risk of mortality (Mc, Waikar et al. 2012).

Serum vitamin C

The low levels of vitamin C in HD patients were associated with anaemia due to the negative influence on iron and red cell, bone and mineral metabolism causing from the inverse correlation with both PTH and Alkaline Phosphatase (ALP) levels, inflammation and oxidative stress (Fumeron, Nguyen-Khoa et al. 2005a, Locatelli, Canaud et al. 2003). These comorbidities corroborated the evidence that patients with lower plasma vitamin C levels in HD patients suffered from shorter survival time. Vitamin C deficiency in HD patients was highly prevalent. A study found that 66% of U.S. HD participants suffered from vitamin C deficiency and 15% with severe vitamin C deficiency (Richter, Kuhlmann
et al. 2008a). As to Chinese HD patients, the proportionate of severe vitamin C deficiency was up to 35.9% (Zhang, Dong et al. 2012).

Vitamin C deficiency arise from a range of potential causes (Raimann, Levin et al. 2013). Inadequate dietary Intake and increased need of vitamin C for optimal health due to dialytic vitamin C removal are some of HD specific issues. Apart from nausea, poor appetite impacting on inadequate vitamin C intake, restriction of potassium-fortified food, such as vegetable and fruits, are the main reason of hindering vitamin C intake in HD patients. Virtually, it is still controversial with the vitamin C intake recommendation for HD patients. The concern raises due to the potential oxalate toxicity causing from high doses of vitamin C. The KDOQI guidelines declared that there was no substantial evidence to support the use of vitamin C in prevention of anaemia in CKD patients (KDOQI, National Kidney Foundation. 2006). No more than 100 mg/day is the recommendation for HD patients (Brenner 2008). However, in light of the aetiology of diet restriction and loss of vitamin C through dialysis, a consensus has been reached that supplementary vitamin C is requires. The EBPG guideline (Fouque, Vennegoor et al. 2007b) on nutrition developed a more precise recommendation that a daily allowance of 75-90mg is required for HD patients.

**Serum vitamin D**

Vitamin D is an important fat-soluble vitamin playing critical role in regulating serum calcium and phosphate concentration, bone mineralization and suppressing PTH (DeLuca 2004). Generally, the stage of serum vitamin D status can be classified into deficiency, insufficiency, hypovitaminosis, adequacy, and toxicity (Zittermann 2006). Among these categories, deficiency and insufficiency were defined as 25(OH) D concentrations with 0-25nmol/l and 25-50nmol/l, respectively. Limited sun exposure, increased age, premature birth, obesity and insufficient dietary intake are some of causes that lead to deficiency and insufficiency of vitamin D (Sadlier, Magee 2007, Zittermann 2003).

Vitamin D deficiency is highly prevalent in HD patients (Fiedler, Dorligjiv et al. 2011). In a cross-sectional study with large HD cohort conducted in the U.S., up to 96.6% patients was found to have vitamin D insufficiency and deficiency (Krassilnikova, Ostrow et al. 2014). High prevalence with deficiency and insufficiency of vitamin D also occurred in the UK HD patients. Even though a clinical guideline for cholecalciferol supplementation was implemented with patients in the UK, only 5% of patients had
optimal levels of vitamin D. 65% and 30% of patients were found to suffer from deficient and insufficient serum vitamin D (Huish, Fletcher et al. 2016). In a study exploring the serum 25 (OH) D level and its influencing factors with Chinese HD patients, the prevalence of vitamin D deficiency and insufficiency was 88.9% (Zhang, Shen et al. 2012). A significant body of studies identified the association between low vitamin D level and CVD, coronary artery calcification and bone fractures in HD patients (Souberbielle, Body et al. 2010, Goodman, Goldin et al. 2000, Drechsler, Pilz et al. 2010, Wolf, Shah et al. 2007), which negatively influenced patients’ health and survival rate (Nigwekar, Bhan et al. 2012). Reduced sunlight exposure (Clayton, Singer 2009, Korkor, Bretzmann et al. 2009), nutritional intake (Korkor, Bretzmann et al. 2009) and synthesis of cholecalciferol in the skin (Michaud, Naud et al. 2010) might be popular explanations of vitamin D deficiency and insufficiency specific to HD patients. It is lack of evidence discriminating the vitamin D source from between diet and sun exposure. However, a study conducted in Brisbane found that even in a sunny climate, vitamin D deficiency was still a common outcome in the majority of HD patients. A study showed that there was a strong association between dietary intake and serum vitamin D [25(OH) D] in HD patients (Sadlier, Magee 2007).

1.3.3 Nutritional status in haemodialysis between the UK and China

A high prevalence of malnutrition was found in the HD patients who were assessed by clinical, anthropometric and biochemical parameters relevant to NS in the UK (Huidobro, Velasco et al. 2001). No nutritional improvements occurred as dialysis was ongoing or there was no difference in nutritional markers between patients with less and more than 12 months in dialysis (Huidobro, Velasco et al. 2001). Albumin was reported with the lowest level in the UK among five European countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Some other parameters suggested as crucial measures of NS by the Clinical Practice Guidelines for Nutrition in Chronic Renal Failure (CRF), such as serum creatinine and normalised Protein Catabolic Rate (nPCR), also did not show significant higher levels than those in the other countries. Even the highest frequency of severe malnutrition was observed in the UK among these five countries (Combe, McCullough et al. 2004a).

In China, 7.4% of the global HD population (Chen, Peng et al. 2013a) has around 10% mortality rate (Cheng, Nayyar et al. 2013), which was partly attributed to high
malnutrition. A cross-sectional study with 75 HD patients from South China was conducted to evaluate the NS of patients. The findings showed that 68% of patients were reported as malnourished and 8% had severe malnutrition, based on the Malnutrition-Inflammation Score (MIS) (Chen, Peng et al. 2013b). It may imply that malnutrition was prevalent in HD patients in South China. South China is one of the wealthiest districts in China. It can be presumed that the NS in the other areas of China is similar to South China, or even worse.

1.3.4 Assessment of nutritional status in haemodialysis patients

Effective assessment of NS for HD patients is required to thoroughly understand NS. Combining the EBPG (Fouque, Vennegoor et al. 2007b) with the KDIGO recommendations (Levin, Stevens et al. 2013), the assessment of NS in HD patients mainly includes a panel of anthropometrics and biochemical measures.

**Serum albumin**

Serum albumin is recommended to be performed monthly in all HD patients as a crucial measurement of NS (Fouque, Vennegoor et al. 2007a). Although serum albumin levels are inversely influenced by acute-phase proteins, such as acute or chronic inflammation and infection, it is still viewed as an inexpensive, easy to perform and widely available measurement showing the robust correlation with NS, and high prediction in mortality risk. The outcome goal of serum albumin equals to or greater than 4.0g/dl (measured with the bromcresol green method). Serum albumin concentrations below 4.0g/dl predicated an increased risk of death (Lowrie, Lew 1990). A study showed that in keeping with serum albumin levels of 3.5 to 3.9 g/dl, the odd rates rise to 1.48, with levels of 3.0 to 3.4g/dl, the odd rate was 3.13 (Biancari, Kantonen et al. 2002).

**Serum cholesterol**

Serum cholesterol concentration of <1.5g/l predicted increased mortality risk, which appears in conflict with the conventional notion that hypercholesterolemia is a risk factor for cardiovascular mortality. However, studies showed that hypocholesterolaemia is highly associated with Malnutrition–Inflammation Complex Syndrome (MICS), which is viewed as the main cause of cardiovascular atherosclerotic disease, hypo-responsiveness and increased mortality risk in HD patients (Kalantar-Zadeh, Kilpatrick
et al. 2005). Increased cholesterol concentration appeared to be protective and paradoxically associated with a better outcome (Axelsson, Rashid Qureshi et al. 2004). The paradox is likely due to the cholesterol lowering effect of systemic inflammation and malnutrition. Therefore, evaluating serum cholesterol level is considered as a valid measurement of protein-energy NS in HD patients by guidelines (Fouque, Vennegoor et al. 2007a, Levin, Stevens et al. 2013). Actually, extended literature documented that the relationship between serum cholesterol and cardiovascular mortality demonstrated as ‘U-shaped curve phenomenon’ in HD patients (Iseki, Yamazato et al. 2002, Liu, Coresh et al. 2004c, Moradi, Streja et al. 2014), which was described that the risk for mortality increases as serum cholesterol falls below approximately 1.5g/l or rises about 2-3g/l (Fouque, Vennegoor et al. 2007b). In a Japanese study, the lower serum cholesterol concentration indicated the higher mortality in patients with low serum albumin, another marker of inflammation and malnutrition as described above. However, the higher cholesterol level was associated with higher mortality when serum albumin levels beyond 4.5 g/dl(Iseki, Yamazato et al. 2002). Similar results were found out in another study, a positive association was demonstrated between serum cholesterol concentration with overall and CVD mortality in the absence of inflammation/malnutrition (Liu, Coresh et al. 2004c).

**Body composition measurements: anthropometric parameters, Bioelectrical Impedance Analysis (BIA) and Dual Energy X-Ray Absorptiometry (DXA)**

Four-site skin fold thickness (SFT), mid-arm circumference (MAC), Mid-Arm-Muscle-Circumference (MAMC) and BMI, are anthropometric screening methods, which are cost effective and reliable to NS assessment for HD patients. SFT, including triceps, biceps, sub-scapular and ileac crest, is used to estimate body fat. MAC and MAMC provided an assessment of muscle mass. These parameters are recommended to be measured when patients start undergoing HD (Fouque, Vennegoor et al. 2007b). Accumulating evidence (Oe, Oe et al. 1998, Torun, Micozkadioglu et al. 2007) suggested that skinfold thickness measurement was still very useful for assessing body fat on HD therapy, although some other technical tools were reported to be more sensitive than it (Oe, Oe et al. 1998). A study with 90 HD patients indicated that the mean body fat obtained by skinfold thickness (13.5±6.2kg) and BIA (13.7±6.7kg) were similar, and the strongest interclass correlation was found between these two measurement tools (r=0.87) (Kamimura, Dos
Santos, Nelma Scheyla José et al. 2003). Additionally, Su CT found the significant association between declines in MAC with all-cause mortality and cardiac outcomes through the HEMO study with 1846 HD patients (Su, Yabes et al. 2013).

BMI is a simple, quick and convenient measure of evaluating body composition and malnutrition for HD patients, which is powerful to predict poor clinical outcomes. Low BMI in HD patients is associated with the high risk of co-morbidity and poor prognosis. Inversely, high BMI is regarded as protective as documented in some studies (Johansen, Young et al. 2004a, Kalantar-Zadeh, Abbott et al. 2005). However, the drawback of BMI is that it is impossible to differentiate between FM and Lean Mass (LM). Thus, researchers are confronted with challenge of distinguishing which components of body composition plays the role in the improvement of survival rate. little consensus has been reached on the relationship between specific BMI thresholds and obesity in a variety of studies (Abbott, Glanton et al. 2004, Xue, Dahl et al. 2003, Rodrigues, Santin et al. 2015). Juliana R. tested the specificity and sensitivity of BMI thresholds using skinfold thickness and waist circumference as reference (Rodrigues, Santin et al. 2015). The findings showed that BMI thresholds used for diagnosing adiposity by World Health Organization (WHO) and Nutrition Screening Initiative (NSI) were not suitable for elderly on HD, which may lead to the misclassification of BMI in this population (Rodrigues, Santin et al. 2015). The USRDS Dialysis Morbidity and Mortality Wave II Study (DMMS) (Abbott, Glanton et al. 2004) reported the relationship between 4 quartiles of BMI and 5-year survival with 1675 HD patients. The results showed that HD patients in the <21.9 quartile of BMI appeared to the worst survival. Conversely, patients with BMI≥30 decreased all-cause mortality. In another American study representing the association of initial HD access type with mortality, there was a decreased all-cause mortality when BMI was more than 25(Xue, Dahl et al. 2003). In light of the prevailing uncertainty about the target BMI for HD patients, EBPG proposed that HD patients should maintain a BMI>23.0 to keep a good nutrition (Fouque, Vennegoor et al. 2007a). BMI was specifically recommended to sustain in a range of 20 to 25 in KDIGO(Levin, Stevens et al. 2013).

Body composition reflecting NS can be measured by BIA and DXA as well. BIA is a convenient, safe and non-invasive method measuring body composition of muscle and FM (Schoeller, Alon et al. 2012, Bartok, Schoeller 2004, Albert, Hail et al. 2004). The principle of BIA is to use a change in reactance and resistance of the current passing through the various body tissues to measure body components (Chertow, Lowrie et al. 2003).
1995). Essentially, the current can more easily pass through muscle tissue (which contains a large amount of fluid) than fat tissue. It has been documented that BIA as a method for measuring fat and fat free mass (Lukaski, Bolonchuk et al. 1986) predicted body compartment changes in various clinical situations (Yanovski, Hubbard et al. 1996) and provided accurate estimates of muscle mass in pre-dialysis CKD patients (Macdonald, Marcra et al. 2006). However, the BIA is a two-compartment model. It assumes that water and mineral content are in the same proportion. Therefore, the body composition measured by the BIA in HD patients with the abnormalities of hydration status and potential renal osteodystrophy may be shown with inaccurate and unreliable results (Woodrow, Oldroyd et al. 1996c, Kamimura, Avesani et al. 2003).

In order to conduct a precise assessment for body composition with HD patients, DXA is recommended as the most accurate and reliable method commonly used in clinics for routine assessment of FM and Fat-Free Mass (FFM) (Jeong, Wu et al. 2015, Nielsen, Ladefoged et al. 1994). It is a straightforward and painless measure involving a small amount of x-ray radiation but the level of dose is quite safe for patients. In HD patients, DXA is the gold standard for estimating three principal components including FM, fat free mass and bone mineral content (Locatelli, Fouque et al. 2002b, van den Ham, E C, Kooman et al. 1999). As early as 1995, Stenver DI et al. proposed that DXA was a powerful tool for estimating the magnitude of body compartments in ESRD patients, supported by the positive correlation between fluid loss during dialysis and reduction in fat-free mass observed from DXA (Stenver, Gotfredsern et al. 1995). DXA has been extensively validated because its reproducibility for both the total body composition and regional measurements are more accurate comparing to other techniques (Heimbürg, Qureshi et al. 2000, Svendsen, Haarbo et al. 1991). However, the cost of DXA is expensive and it is not widely available, especially at some poverty areas in the developing countries. Therefore, the routine use of DXA is not recommended (Fouque, Vennegoor et al. 2007a).

**Dietary interviews**

There is no any alternatives but dietary interviews or diary can detect in time the change of food intake before other objective malnutrition parameters start changing (Fouque, Vennegoor et al. 2007a). HD patients are subject to food restrictions requiring them to limit dietary sodium, phosphate, potassium and fluid intake. Although controversy
regarding food restriction and healthy dietary pattern is present among various studies 
(Khoueiry, Waked et al. 2011, Kalantar-Zadeh, Kamyar, MD, MPH, PhD, Ikizler 2013, 
Kalantar - Zadeh, Tortorici et al. 2015), keeping minerals or water under control still 
benefits from diet restriction. However, undoubtedly, improved NS is attributed to 
adequate dietary protein and energy intake (Slomowitz, Monteon et al. 1989, Bergström, 
Fürst et al. 1993). Therefore, whilst maintaining optimal compliance of food restriction, 
balancing food restriction and maintaining adequate nutritional constituent intake 
requires a thorough understanding of dietary intake for HD patients. Routine evaluation 
of food intake is recommended to perform every 6 months after the evaluation at the first 
month of dialysis to predict NS.

A 3-day dietary recording and 24-hour diet recall interview were recommended in both 
KDIGO (Levin, Stevens et al. 2013) and EBP guidelines (Fouque, Vennegoor et al. 
2007a), as well as numerous studies investigating dietary intake (Bazanelli, Kamimura et 
dietary recall is an easy administered tool that has been validated in HD patients to assess 
the macro and micronutrient intake. In dietary interviews, relatively comprehensive and 
precise details of subject’s food and drink intake during the previous 24 hours were 
recalled and collected. The advantage of 24 hour recall are less time consuming, the fact 
that the subjects do not need to provide or prepare records of diaries (Wiggins 2002, 
Griffiths, Russell et al. 1999), and more likely to result in successful collection of data 
compare with the other diet assessments (Griffiths, Russell et al. 1999).

There are no significantly difference between 24 hour diet recall and 3-day diet diary in 
determining dietary protein and energy intake (Griffiths, Russell et al. 1999). A 3-day 
diary involving a dialysis, non-dialysis and weekend day was recommended for HD 
patients to assess dietary intake (Eknoyan, Levin 2000). Although record length of ≥ 3 
day were viewed as appropriate for usual diet representation (American Dietetic 
Association 2011), with the difference of dietary patterns due to the influence of dialysis 
process, diet intake confined to a single dialysis or non-dialysis day in 3-day diet diary 
may not represent a typical food intake reflecting diet variations. Additionally, subjects 
need to be taught to record the time of meals, methods of food preparations, and describe 
the food and drinks consumed, including the amount and composition consumed at home, 
in restaurants, and even processed foods. Whilst efficacy of the 3-day food diary is worthy
to be taken into account, patients are also confronted to the challenge of describing and recording their dietary diary.

**Subjective Global Assessment (SGA)**

The SGA (Steiber, Kalantar-Zadeh et al. 2004) is a valid and clinically useful measure tool that includes a 7-point Likert-type scale of four items (weight loss, anorexia, subcutaneous fat, and muscle mass). Subjective weightings were assigned to each of the four items to produce a global assessment. Score of 1 to 2 represented severe malnutrition; 3 to 5, moderate to mild malnutrition; and 6 to 7, normal nutrition. It has been widely used to assess NS in surgical, elderly patients (Christensson, Unossons et al. 2003), and patients with cancer (Bauer, Capra et al. 2002) or liver transplants (Stephenson, Moretti et al. 2001). In 2000, the National Kidney Foundation (NKF) KDOQI recommended that SGA can be used in nutritional assessment with the adult dialysis population (Kopple 2001a). Lower SGA score showed the higher mortality risk in dialysis patients (Chung, Lindholm et al. 2003). In a prospective, longitudinal and multi-centre study in incident HD patients, moderate and severe Protein-Energy Wasting (PEW) identified by SGA were associated with an increased mortality in 7 years of follow-up comparing to a normal NS at baseline(Krediet, Boeschoten et al. 2009).

**1.3.5 Influence of provision of food during haemodialysis treatment on haemodialysis patient**

Provision of meals during HD sessions is still a controversial issue practiced by different countries, regions and clinics. Generally, food was provided to patients during their HD treatments in most European and Asian countries. Conversely, intradialytic food consumption is banned in most American cities (Wizemann 2000, Kalantar-Zadeh, Ikizler 2013). In a survey conducted in 73 clinics from 6 continents, 85% and 65% of clinics allowed and encouraged patients to have food during treatment, respectively. However, 9 units from North American implemented ‘eating-prohibitory’ regulations (Kistler, Benner et al. 2014).

The common concerns about eating during HD sessions involved postprandial hypotension, risk of chocking or aspiration, reduced kt/v (dialysis adequacy) and infection control (Shibagaki, Takaichi 1998). Whereas, on the basis of an investigation about the most frequently reported reasons to restrict food during treatment, the vast
majority of clinicians expressed that these adverse clinical outcomes rarely occurred (Kistler, Benner et al. 2014). Lara B Pupim et al. found that intradialytic oral supplementation played an important role in reversing HD associated net negative whole body and skeletal muscle protein catabolism, consequently, improved the deranged NS that commonly exists in HD patients (Pupim, Majchrzak et al. 2006a). Daily protein intake (DPI) in most HD patients was less than 1.0g/kg based on the observation of mounting studies (Burrowes, Larive et al. 2003b, Kopple 1998), which was markedly lower than dietary protein requirement with 1.2g/kg/day(Kopple 2001b). The additional 0.2 to 0.4 g/kg/d of protein can be provided by foods during HD treatment session. Additionally to the effect of reversing protein catabolism caused by HD treatment and improving NS, eating during HD sessions motivates patients to enhance compliance and satisfaction of attending HD treatment.

1.4 Body composition of haemodialysis patients

Muscle wasting may contribute to the abnormalities in cardiac function in HD patients (Stenvinkel, Heimburger et al. 2004, Stenvinkel, Pecoits-Filho et al. 2003). A study pertaining to the relationship between body composition and arteriosclerosis revealed that decreased Thigh Muscle Mass (TMA) and accumulated abdominal visceral fat were correlated with Carotid Artery Intima-Media Thickness (CA-IMT) (Kato, Ishida et al. 2011). Meanwhile, TMA was inversely correlated with brachial-ankle Pulse Wave Velocity (baPWV), Cardio-Ankle Vascular Index (CAVI) and Ankle Brachial pressure Index (ABI).

Sarcopenia is a progressive and generalised loss of Skeletal Muscle Mass (SMM) quality and strength, which consequently leads to physical disability, poor QoL and even death (Delmonico, Harris et al. 2007, Goodpaster, Park et al. 2006). It is a predominant sign significantly marked and highly prevalent in HD patients (Domański, Ciechanowski 2012, Foley, Wang et al. 2007). A cross-sectional study with 95 ESRD patients aged over 50 years showed one third of HD patients were affected by sarcopenia (Kim, Choi et al. 2013). In another study, 549 HD patients were evaluated the prevalence of muscle wasting using different guideline definitions of sarcopenia (Tangvoraphonkchai, Hung et al. 2018). Despite the results due to the variation in guideline cut-off, high prevalence with 84.5% using the European Working Group on Sarcopenia in Older People (EWGSOP), 73.2% with North American Foundation for the National Institutes of Health
Sarcopenia Project, 75.2% and 56.6% using North American and the UK normative data, respectively, were shown in the study. Muscle gain with weight loss predicted a higher survival than muscle loss while weight gain (Kalantar-Zadeh, Streja et al. 2010). Compromised muscle strength was significantly correlated with physical inactivity, inflammation and mortality, even stronger than low muscle mass (Isoyama, Qureshi et al. 2014). Indeed, as evidenced by a number of studies, reduced muscle mass and impaired muscle strength were important predictors of adverse outcome and mortality in HD patients, which make joint effort to show the relationship between sarcopenia and prognosis of ESRD (Thomas 2007, Isoyama, Qureshi et al. 2014, Kim, Choi et al. 2013).

Protein energy wasting (PEW) is a significant symptom characterized with decreased body stores of protein and energy fuels (Fouque, Kalantar-Zadeh et al. 2008a). It is reported that 18%-75% of CKD patients suffered from PEW (Carrero, Chmielewski et al. 2008, Kalantar-Zadeh, Ikizler et al. 2003). The prevalence is higher in HD patients than other CKD patients (Carrero, Stenvinkel et al. 2013). Mounting studies have shown the robust association between PEW, comorbidity and mortality (Fouque, Kalantar-Zadeh et al. 2008b, Owen Jr, Lew et al. 1993, de Mutsert, Grootendorst et al. 2008, Fleischmann, Teal et al. 1999).

PEW is strongly associated with malnutrition (de Mutsert, Grootendorst et al. 2008) as well as loss of lean tissue mass (Carrero, Chmielewski et al. 2008). Muscle wasting is viewed as one of the most valid markers of PEW in HD patients. As mentioned before, while muscle wasting appears progressively deterioration with worsen kidney function in CKD patients (Foley, Wang et al. 2007), it is accelerated by factors commonly present in HD patients, such as acidosis, comorbidities, HD treatment and sedentary lifestyle (Fouque, Kalantar-Zadeh et al. 2008b, Du, Hu et al. 2005, Ikizler, Pupim et al. 2002). HD patients body composition is of fundamental importance for the understanding of PEW in HD patients.

Evidence documented that despite its modality exercise is beneficial to improve body composition in HD patient. Resistance exercise influenced LM and FM, while aerobic exercise impacted FM (Drenowatz, Hand et al. 2015). One study involving Progressive Resistance Training (PRT) with HD patients significantly increased SMM and decreased Body Fat Rate (BFR) (Song, Sohn 2012). Another aerobic exercise training programme
for 12 weeks with HD patients showed the potentials of preventing a decline in body composition and knee joint muscle function resulting from inactivity in CKD patients (Young, Hudson et al. 2015). Therefore, assessment of body composition can evaluate the effect of different modalities of exercise with various intensities on HD patients.

1.5 The underlying impact of culture on lifestyle between UK and Chinese haemodialysis patients

Hwu Y. et al. found that people with chronic diseases had their own evaluation system to tell which activities were good for their health because of the long medical course (Hwu, Coates et al. 2001). Furthermore, choosing some activities or not is closely associated with their culture (Kim, Bramlett et al. 1998, Kleinman 1978). A study involving 17 population samples’ nutrient intake including in the UK and China indicated that different lifestyle between western and East Asian population had protective and adverse impact on CVD (Zhou, Stamler et al. 2003). It has been reported that the intake of total fat, saturated fat and cholesterol in traditional Western diets were higher than East Asian diets. However, calcium and potassium intake of Asian diets were lower than those in Western diets (Zhou, Stamler et al. 2003). The findings corroborated the fact that culture plays a critical role in determining food selection (Blundell, Gibbons et al. 2015). The ‘Transtheoretical Model’ (TTM) is a theory of therapy used for assessing individuals’ readiness to change to a new healthier behaviour and providing strategies to guide the individuals, which is beneficial to predict future stage of change for exercise and guide practical exercise intervention (Callaghan, Khalil et al. 2010). It was revealed that culture might influence the relationships between stages of readiness to exercise and self-efficacy (Marcus, Owen 1992).

Different cultures between the UK and China may result in the disparity of the diet habits and perception of exercise. Additionally, unique traditional Chinese cultural health belief derived from the Traditional Chinese Medicine (TCM) also potentially affect Chinese HD patients’ lifestyle. The traditional Chinese culture believes that renal disease is the consequence of tiredness caused by overwork (Qu, Liang, & Chen, 2001), which impairs kidney function. There is also a strong cultural belief in China that people with chronic diseases need more rest to restore the balance of Yin and Yang (Wu, He et al. 2014b), and increase vitality and energy (Zhang, Liu et al. 2015). To some extent, overwork may equal vigorous exercise. Therefore, exercise and rest may be contradictory in Chinese
cultural health beliefs. Meanwhile, Chinese people believe that there is a strong correlation between diet and disease, so the illness may follow the principles of Yin and Yang in the choice of special food or Chinese herbs and to refuse some toxic food defined by Chinese medicine.

1.6 Aims

Malnutrition and physical inactivity are highly prevalent in HD patients, which result in high risks of morbidity and mortality. It has been known that perceptions, attitudes and habits relating to lifestyle may be influenced by culture or ethnicity. Therefore, the objective of the thesis was to gain a thorough understanding of nutritional and physical status in HD patients between the UK and China. Furthermore, the thesis was aiming to explore the disparity of the influencing factors of lifestyle between UK and Chinese HD patients. The specific aims of each chapter are shown as follows:

1. To understand and compare diet intake on dialysis and non-dialysis day between UK and Chinese HD patients;
   To explore the underlying associated factors that lead to the discrepancy of nutritional blood parameters between UK and Chinese HD patients.

In order to achieve the aims above, protein and energy intake, dietary intake of trace elements, minerals and vitamins and nutritional blood parameters were analysed and contrasted in HD patients between the UK and China. The results and discussion are shown in Chapter 4.

2. To explore the validity of the DASI and GPPAQ walking pace question with UK and Chinese HD patients

The DASI and GPPAQ walking pace question were concurrently administered with the Shuttle Walking Test (SWT) and gait speed test with the same HD cohorts in the UK and China, respectively. Validity of the DASI and GPPAQ walking pace were analysed in Chapter 5.

3. To characterise and compare physical function between UK and Chinese HD patients;
   To explore the correlation between physical function, demographics and clinical information with HD patients in the UK and China.
Both the DASI and GPPAQ walking pace question were conducted with a large sample of UK and Chinese HD patients. Physical performance tests were carried out with HD patients and healthy controls in the UK and China. Physical function obtained by self-report questionnaires and objective measures were analysed and shown in chapter 6.

(4) To characterise and compare PA level between UK and Chinese HD patients;
To explore the correlation between PA level, demographics and clinical information with HD patients in the UK and China.

The GPPAQ and LTEQ were administered with large UK and Chinese HD cohorts. The Multi-sensor systems (MSSs) were used to assess habitual PA level with HD patients and healthy controls in the UK and China. The PA level achieved by questionnaires and MSSs were shown in chapter 7.

(5) To characterise and compare self-perceived benefits and barriers to exercise between UK and Chinese HD patients;
To explore the correlation between self-perceived benefits and barriers to exercise, physical function and PA level.

The Dialysis Patient-Perceived Exercise Benefits and Barriers Scale (DPPEBBS) was conducted with the UK and Chinese HD patients. The results of questionnaires and its correlation with physical function and PA level were shown in chapter 8.

(6) To understand relationship between physical function, activity and QoL, symptoms and body composition in UK and Chinese HD patients.

The Euro QOL-5 Dimensions-5 Level (EQ-5D-5L) and Palliative Care Outcome Scale–Symptoms Renal (POS-S) were administered with UK and Chinese HD patients to assess QoL and symptoms relating to renal disease. The Body Composition Monitor (BCM) was conducted to obtain patients’ body composition. The relationship between physical function, activity and QoL, symptoms and body composition in UK and Chinese HD patients were shown in Chapter 9.
Chapter 2

Methods
2.1 Introduction

This chapter described all methods employed in Chapters 4 to 8. Essentially, the data in these chapters were extracted from 3 separate studies.

(1) The DISH study (Dietary Intake and Nutritional Status of Haemodialysis patients from the UK and China) was carried out to gain initial information on dietary intake on dialysis and non-dialysis days with HD patients in the UK and China, giving insight into HD patients’ nutritional status (NS) and the correlation between dietary intake and nutritional parameters. The data of the UK HD patients were collected by a researcher from the Leicester Kidney lifestyle Team, two PhD students from São Paulo State University and University of Illinois and the researcher. The Chinese data were collected by the researcher.

(2) The QCKD study (Increasing Physical Activity in Chronic Kidney Disease: The Patient Perspective) was carried out to gain a thorough understanding of physical function, physical activity (PA) levels and self-perceived benefits and barriers to exercise, which were all measured by questionnaires given to HD patients in the UK and China. The researcher collected the data of the patients in Leicestershire, and the rest UK data were obtained by researchers from the other regions in the UK. The study conducted in China were carried out by two Master students at Nantong University and the researcher.

(3) The COCO study (Physical Condition and Associated Factors in Haemodialysis Patients) explored the relationship of HD patients’ physical function, activity level and Quality of Life (QoL), symptoms relating to renal disease and body composition in the UK and China. The data of the UK healthy controls were collected by two researchers from the Leicester Kidney Lifestyle team. The data of the UK HD patients and all Chinese participants were collected by the researcher.

All the studies focussed on the English National Health Service (NHS) and Chinese patients who were recruited from HD units in the UK and China. Each study followed a specific protocol and participant’s characteristics were used to explore UK and Chinese HD patients’ diet intake with a 24-hour diet recall interview, levels of physical function, and PA level using questionnaires and objective measures. Considering both the QCKD and COCO studies involving HD patients’ physical status, the results of these two studies were synthesized and provided a complete presentation of physical function (Chapter 6) and PA level (Chapter 7) in UK and Chinese HD patients.
2.2 Research design

2.2.1 The DISH study

DISH was an observational study which involved HD patients from single centres in the UK and China, respectively. The study was designed to explore HD patients’ diet intake on dialysis and non-dialysis days in the UK and China and comprehensively understand their NS and the correlation between dietary intake and nutritional parameters. All the aspects of the study documentation including the UK and Chinese patients were approved by the NHS Research Ethics Committee (Ref. UHL 11329) and the Ethics Committee of the Affiliated Hospital of Nantong University (Ref.2015-12), respectively.

The study collected the UK and Chinese HD patients’ dietary intake by using the 24-hour diet recall interviews. The diet recall record included food and fluid items, amount or portion, food location of purchase, cooking method and brand. Nutritional blood parameters were obtained from the blood results of patients’ medical records. Blood nutritional parameters were taken from a single sample of blood obtained on the date closest to the dietary interview. Only results obtained within 3 months of the dietary assessment were utilised.

In order to account for the impact of the HD process on dietary intake, HD patients’ diet intake on dialysis and non-dialysis day were assessed by the researcher, respectively. The 24-hour diet recall interviews were undertaken on two normal dialysis sessions in two consecutive weeks where the patients were asked to recall their food and fluid intake on non-dialysis days for the previous 24 hours. Additionally, two more diet recall interviews on two dialysis sessions following the ones where the last interviews took place were arranged for HD patients to recall the diet intake on the dialysis days when the non-dialysis day’s dietary recall were obtained. Flow diagram of the DISH study is shown Figure2-1.
Figure 2 - Flow diagram of the DISH study

First, the patients were asked to list all food and fluid consumed in the previous 24-hours without any interruption during the 24-hour dietary recall interviews. The researcher then went through the list to ensure that nothing had been forgotten, especially snacks, condiments or supplements. Then the patients were asked to recall the details of the portion size, location of food purchased, brand of food and cooking method. The researcher then checked the list and gathered the time and location of the food and fluid consumed. Finally, the patients and researcher reviewed the list one more time to ensure accuracy.

Patients’ dietary intake on dialysis and non-dialysis days were obtained by averaging the results collected from two dialysis days and non-dialysis days, respectively. Additionally,
A weekly diet intake was computed by summing up the diet intake on dialysis days and non-dialysis days, as shown in the following formula: the weekly diet intake = the average dialysis day’s diet intake ×3 + the average non-dialysis day’s diet intake ×4. For some HD patients who have dialysis twice a week, the formula was the weekly diet intake = the average dialysis day’s diet intake ×2 + the average non-dialysis day’s diet intake ×5. A usual daily dietary intake was obtained through the weekly diet intake divided by 7 days.

Food and fluid consumed by patients was inputted into the Nutritics and Nutrition calculator, which are based on the 2015 Composition of Foods Integrated Dataset (CoFID) including McCance and Widdowson (7th edition) and China Food Composition (2nd version) nutritional databases for the UK and Chinese patients, respectively. Take a boiled egg with 60 grams for example, the “boiled egg” and the portion size of 60g was typed in the Nutritics. The software then provided a nutrient analysis for the boiled egg, such as energy at 86 kcal, protein with 8.5g and so on. Similarly, the “boiled egg” was typed or chosen in the dish list and the amount of 60g was inputted in the Nutrition calculator. The detailed nutrients of the boiled egg, such as energy at 86 kcal and protein as 8g, were presented. The nutrient analysis of a 60g boiled egg in the Nutritics and Nutrition calculator are shown in Figure2-2 and Figure2-3, respectively.
### Figure 2 - Nutrient analysis of a 60g boiled egg in the Nutritics

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (Kcal) 4% RI</td>
<td>86kcal</td>
</tr>
<tr>
<td>Energy (Kcal) 4% RI</td>
<td>357kJ</td>
</tr>
<tr>
<td>Protein 17% RI</td>
<td>5.4g</td>
</tr>
<tr>
<td>Fat 8% RI</td>
<td>1.6g</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>8.5g</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0g</td>
</tr>
<tr>
<td>Minerals &amp; trace elements</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>85mg</td>
</tr>
<tr>
<td>Potassium</td>
<td>170mg</td>
</tr>
<tr>
<td>Calcium</td>
<td>122mg</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.7mg</td>
</tr>
<tr>
<td>Iron</td>
<td>0.78mg</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.04mg</td>
</tr>
<tr>
<td>Copper</td>
<td>0.02mg</td>
</tr>
<tr>
<td>Manganese</td>
<td>16.2ug</td>
</tr>
<tr>
<td>Selenium</td>
<td>31.2ug</td>
</tr>
<tr>
<td>Iodine</td>
<td>0.01mg</td>
</tr>
</tbody>
</table>

**Vitamins**

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Amount (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (ret est) 9% RI</td>
<td>72ug</td>
</tr>
<tr>
<td>Vitamin D 38% RI</td>
<td>0.99ug</td>
</tr>
<tr>
<td>Vitamin B1 4% RI</td>
<td>0ug</td>
</tr>
<tr>
<td>Vitamin K, 0% RI</td>
<td>0.00mg</td>
</tr>
<tr>
<td>Thiamin (B1) 4% RI</td>
<td>0.03mg</td>
</tr>
<tr>
<td>Riboflavin (B2) 20% RI</td>
<td>2.3mg</td>
</tr>
<tr>
<td>Niacin total (B3) 14% RI</td>
<td>0.00mg</td>
</tr>
<tr>
<td>Niacin</td>
<td>135mg</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>0.73mg</td>
</tr>
<tr>
<td>Pantothenic Acid (B5) 12% RI</td>
<td>0.00mg</td>
</tr>
<tr>
<td>Vitamin B6 4% RI</td>
<td>0ug</td>
</tr>
<tr>
<td>Folic Acid (B9) 9% RI</td>
<td>1.2ug</td>
</tr>
<tr>
<td>Vitamin B12 48% RI</td>
<td>0ug</td>
</tr>
<tr>
<td>Biotin (B7) 20% RI</td>
<td>0ug</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0ug</td>
</tr>
</tbody>
</table>

**Other**

<table>
<thead>
<tr>
<th>Substance</th>
<th>Amount (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI (estimated)</td>
<td>0</td>
</tr>
<tr>
<td>CL</td>
<td>0</td>
</tr>
</tbody>
</table>

**CoQ10**

<table>
<thead>
<tr>
<th>CoQ10</th>
<th>Amount (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0mg</td>
</tr>
</tbody>
</table>
Participants

Inclusion criteria

HD patients aged ≥ 18 years who were willing and able to take part in the study. Participants from the UK were recruited from two HD centres in the Leicester Renal Network, and participants from China were recruited from the Affiliated Hospital of Nantong University.

Exclusion criteria

Table 2- Exclusion criteria for UK and Chinese HD patients in the DISH study

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;18 years</td>
</tr>
<tr>
<td>Patients with special medical condition which may influence dietary intake or assimilation E.g. Total Parenteral Nutrition (TPN), unusual dietary restrictions and short bowel syndrome</td>
</tr>
<tr>
<td>Clinically overt infection in the last 6 weeks</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Insufficient command of English, Mandarin or Nantong Dialects to understand the patient information sheet and give consent, or unable to understand the patient information sheet and give consent for any other reason</td>
</tr>
</tbody>
</table>
Recruitment

Before the research was started, the managers and matrons of each HD units identified potentially eligible patients in their units. The eligible patients were approached by the researcher. The study was explained and the patient information sheets were given to potential participants. The patients were allowed at least 48 hours to decide whether to participate. Written consent was obtained from all participants prior to entering the study. The GP of the UK HD patients and the consultant nephrologist of the Chinese HD patients were then informed of their participation in the research. Two copies of written consent were given to the patients and recorded in each of the patient’s medical notes, along with a copy of the Patient Information Sheet.

54 UK HD patients were approached and given a detailed explanation of the study by the researcher, out of these 54 patients, 14 refused to participate in the study. Finally, 40 patients agreed to allow their medical records to be accessed and completed all the interviews. 61 Chinese HD patients were approached and given patient information sheets. After being allowed 48 hours as consideration time, 17 patients refused to take part. Ultimately, 44 patients agreed to have their medical records accessed and completed the study. The consort diagram depicting the UK and Chinese HD patients flow through the study are showed in Figure2- 4 and Figure2- 5.
2.2.2 The QCKD study

The QCKD study was a cross-sectional multicentre study which involved HD patients in the UK and China. The study was designed to gain a thorough understanding of exercise
behaviour in HD patients in the UK and China in terms of physical function, PA level and self-perceived benefits and barriers to exercise. This study with UK and Chinese patients has received ethical approval from the NHS Research Ethics Committee: NRES Committee East Midlands-Northampton (REC reference 12/EM/0184) and the Ethical committee of the Affiliated Hospital of Nantong University (Ref. 2015-12), respectively.

The UK and Chinese HD Patients recruited in the study completed a short demographic section, followed by 4 validated questionnaires regarding exercise behaviour during their HD sessions or at home.

- The Duke Activity Status Index (DASI) is used for assessing participants’ exercise capacity.
- GP Physical Activity Questionnaire (GPPAQ) is used for assessing PA level.
- Leisure Time Exercise Questionnaire (LTEQ) is used for measuring exercise levels during individual leisure time.
- Dialysis Patient-Perceived Exercise Benefits and Barriers Scale (DPPEBBS) is used for assessing dialysis patients’ beliefs and feeling about exercise.

If the HD patients agreed to allow their medical records to be accessed, researchers extracted the patients’ clinical parameters from the medical records.

**Subjects**

**Inclusion criteria**

All patients receiving HD who were willing and able to participate in the study from the UK and the hospitals in Nantong City.

**Recruitment**

The UK HD patients were recruited from the UK. The 16 hospitals involved include Leicester General Hospital, Loughborough Hospital, Leicester Hamilton Renal Dialysis Unit, Basdon and Thurrock University hospital, The Royal London Hospital, Nottingham Hospital, Sheffield Teaching Hospitals, Dorset County Hospital, St Georges Hospital, York Teaching Hospital, Mid Essex Hospital Services NHS Trust, Royal Derby Hospital, Royal Free Hospital, Imperial College Healthcare NHS Trust, Lincoln County Hospital and Lancashire Teaching Hospital. Chinese HD patients were recruited from all
7 hospitals in Nantong city which set up HD units, including the affiliated Hospital of Nantong University, the First People’s Hospital of Nantong, the Third People’s Hospital of Nantong, the Fourth People’s Hospital of Nantong, the Sixth People’s Hospital of Nantong, Nantong geriatric rehabilitation hospital and Nantong Hospital of Traditional Chinese Medicine.

During the study process, a notice was prominently placed in the receptions of each HD units involved, informing patients that a survey about exercise behaviour was being carried out. Patients who were unwilling to take part were asked to inform the unit staff. All HD patients were approached and recruited during their dialysis sessions. The survey was briefly explained to patients. The patients who were interested in the study were then provided with the Patients Information Sheet. If the patient was then willing to complete the survey, the questionnaires which were each marked with a unique non-identifiable participant study code, were then supplied for the patients to complete during their dialysis session or at home. After the researcher collected the completed questionnaires, the patients were asked for the permission to access medical records for further information. If the patient agreed, written consent forms marked with the same code as the questionnaires were explained to the patients and obtained. Study documents were dealt with in the same way as in the DISH study. A flow diagram illustrating the study design is shown in Figure2-6.
1156 UK HD patients from 16 hospitals in the UK were recruited and completed the study. 783 Chinese HD patients who resided in Nantong, including municipal and rural regions were approached. 221 declined mainly due to lack of interest, family issue and adverse medical condition. 542 Chinese HD patients participated in the study. The recruitment rate was 69.2%.

2.2.3 The COCO study

The COCO study was an exploratory observational single centre study that involved HD patients and healthy controls from the UK and China, respectively. The study was
designed to objectively measure HD patients’ physical functions and PA levels in the UK and China. Additionally, information regarding QoL, symptoms relating to renal disease, and body composition in HD patients, and the relationship with physical function and PA levels was explored. All aspects of the study including the UK and Chinese participants were approved by the NHS Research Ethics Committee: South East Scotland REC 01 (Ethics Ref. 14/EM/1049) and the Ethical committee of the Affiliated Hospital of Nantong University (Ref. 2015-12), respectively. Participants were asked to complete a series of outcome measure assessments once only. They had the option to separate the assessment into several visits based on their own convenience or preference. The total assessment time was about 2.5 hours altogether. Based on the underlying fatigue or discomfort after the HD session, four physical performance tests were conducted with the UK and Chinese HD patients before a HD session or on a non-HD day. A multi-sensor system (Sensewear Armband [SWA]) was worn for 7 days by patients in order to assess habitual PA levels, and this was then collected by the researcher. During this time, patients completed 4 questionnaires, including the DASI, GPPAQ, Euro QOL-5 Dimensions-5 Level (EQ-5D-5L) and Palliative care Outcome Scale–Symptoms Renal (POS-S). Patients’ body composition was assessed by Body Composition Monitor (BCM) before the dialysis session. The outcome measures in the COCO study are shown in Table2- 2.

Table2- Outcome measures in the COCO study

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Measure tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Function:</td>
<td>Physical performance tests: Shuttle Walking Test (SWT), Sit to Stand (STS) 60, Handgrip Strength (HGS) and Short Physical Performance Battery (SPPB)</td>
</tr>
<tr>
<td>Habitual physical activity:</td>
<td>Multi-sensor system (SWA) over 7 days at home</td>
</tr>
<tr>
<td>Body composition:</td>
<td>Fresenius Body Composition Monitor (BCM)</td>
</tr>
<tr>
<td>Questionnaires:</td>
<td>The DASI, GPPAQ, Euro QOL-5 Dimensions-5 Level (EQ-5D-5L) and Palliative care Outcome Scale–Symptoms Renal (POS-S)</td>
</tr>
</tbody>
</table>

The healthy participants arrived at the laboratory or the University at a convenient time for a completion all outcome measures above, except for the POS-S. The flow diagram illustrating the study design is shown in Figure2- 7.
Subjects

Inclusion criteria

HD patients and healthy controls aged $\geq 18$ years who were willing and able to take part in the study from the UK and China.
**Exclusion criteria**

Table 2-3

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;18 years</td>
</tr>
<tr>
<td>Patients unable to walk e.g. amputation, unable to mobilise/wheelchair dependent</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Any element of study assessment protocol considered by own clinician to be contraindicated due to severe co-morbidity or any other reason:</td>
</tr>
<tr>
<td>Cardiovascular events (severe heart failure, myocardial infarction, unstable angina, stroke et al.) in the last 3 months;</td>
</tr>
<tr>
<td>Severe Chronic Obstructive Pulmonary Disease (COPD);</td>
</tr>
<tr>
<td>Active liver disease et al.</td>
</tr>
<tr>
<td>Clinically overt infection in the last 6 weeks</td>
</tr>
<tr>
<td>Insufficient command of English, Mandarin or Nantong Dialects to understand the patient information sheet and give consent, or unable to understand the patient information sheet and give consent for any other reason.</td>
</tr>
</tbody>
</table>

Table 2-4

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;18 years</td>
</tr>
<tr>
<td>Participants with ambulatory problem, E.g. amputation, unable to mobilise/wheelchair dependent</td>
</tr>
<tr>
<td>Any personal medical history of having kidney disease, diabetes, chronic lung disease, heart disease, cancer or any other significant long-term condition</td>
</tr>
<tr>
<td>Clinically overt infection in the last 6 weeks</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Insufficient command of English, Mandarin or Nantong Dialects to understand the information sheet and give consent, or unable to understand the information sheet and give consent for any other reason</td>
</tr>
</tbody>
</table>

**Recruitment**

Eligible patients at HD units from Leicester renal network and the affiliated hospital of Nantong University in the UK and China were identified by unit staff, respectively. The unit staff briefly explained the study to the potential patients during routine dialysis sessions. The patients who expressed an interest in participating in the study were provided with the patient information sheets and discussed the study in more details with the researcher. At least 48 hours was given to the patients to decide whether to participate. If they were interested in the study after consideration, written consent was obtained from all participants prior to entering the study. Study documents were dealt with in the same
way as in the DISH study.

The healthy participants were recruited from hospital, university and the community via leaflets. Potential healthy controls who were interested in the study were screened by assessing whether they reported a number of chronic health issues or any other problems precluding them from participation. The healthy controls with no known chronic diseases were explained to them along with further information prior to written consent being given. The healthy Chinese controls were screened after the completion of the study with HD patients. HD patients who had already completed the study were classified into age ranges (<30, 30-40, 40-50, 50-60, >60 years) and gender groups (male and female). Healthy controls were subsequently approached according to the proportion of patients from each age and gender groups. Additionally, some elderly participants with minor illnesses or well-controlled chronic health issues were deemed eligible to participate.

42 UK HD patients were approached and 12 declined to participate in the study due to lack of interest or because of concerns that it would be time-consuming. 11 healthy controls were recruited to the study and 1 dropped out. The consort diagram depicting UK HD patients and healthy controls flow through the study are showed in Figure 2-8 and Figure 2-9.
Figure 2-8: Flowchart of recruitment process and included HD patients in the UK

Figure 2-9: Flowchart of recruitment process and included healthy controls in the UK
43 Chinese HD patients were approached in the study, of these, 2 refused to take part and 1 withdrew due to a serious medical condition which developed during the study. 50 Chinese healthy controls who were age and gender-matched were screened, and 6 withdrew due to family issues or lack of interest during the study. The consort diagram depicting Chinese HD patients and healthy controls flow through the study are shown in Figure2- 10 and Figure2- 11.

**Figure2- 10** Flowchart of recruitment process and included HD patients in China
All participants involved in all aspects of the research were free to withdraw at any time without giving any reason. Patients’ medical care or legal rights were not affected. All aspects of the research conformed to the ethical principles outlined in the Declaration of Helsinki (World Medical Association 2013).

2.3 Outcome measures

2.3.1 Outcome measures in the DISH study

**Demographic characteristics** include age, gender and dialysis vintage and anthropometric parameters (Body Mass Index [BMI], MAC), which were collected from participants’ medical records.

**Protein and energy intake and intake of trace elements, minerals and vitamins**, including iron, calcium, phosphate, potassium, sodium and vitamin C and D intake. These parameters were collected from the 24-hour dietary recall interviews.

**Nutritional blood parameters** include serum albumin, cholesterol, phosphate, calcium, parathyroid hormone (PTH), Haemoglobin (Hgb), hematocrit, sodium, potassium, transferrin saturation, iron and ferritin. These parameters were collected from participants’ medical records during the month of the patients’ entry into the study.
2.3.2 Outcome measures in the QCKD study

Demographics were obtained from the demographic section which was combined with the questionnaires, including age, gender, ethnicity, dialysis vintage, smoking history (current smoker, ex-smoker or never smoked), BMI, general information about comorbidity and medication. More detailed comorbidities covered diabetes, hypertension, ischaemic heart disease, stroke/Transient Ischemic Attack (TIA), peripheral vascular disease, asthma or COPD, musculoskeletal disease, neurological disease and mental disease. Additionally, condition and symptoms reported by the patients were recorded in the study as well. Oral medications including anti-hypertensives, antidepressant, oral bicarbonate and statins were also noted.

Questionnaires were completed during the patients’ HD sessions except for patients who preferred to take questionnaires home to complete. Following a detailed explanation, patients who could write then filled in the questionnaires by themselves. For patients who were restricted in their ability to write due to arteriovenous (AV) fistula access or other issues, researchers wrote the patients answers verbatim. For patients who took the questionnaires home, the researchers collected them from the units once they had been finished.

The Duke Activity Status Index (DASI) is a self-administered questionnaire which is strongly correlated to VO2peak in development (r=0.81, P<0.0001) and validation phase (r=0.58, P<0.0001) (Hlatky, Boineau et al. 1989b) in the general population. Meanwhile, as a surrogate of VO2peak for HD patients, the DASI has also been documented as being a powerful marker of physical function (Nonoyama, Brooks et al. 2010). The DASI consists of two responses ‘yes’ and ‘no’ which refer to 12 activities of personal care, ambulation, household tasks, sexual function and recreational activities. A response of ‘no’ indicates a score of zero, and a response of ‘yes’ to each item is marked as a value based on metabolic cost by calculating Metabolic Equivalent of Task (METs), which means the Energy Expenditure (EE) of a specific physical activity. The question is weighted depending on the level of activity and the values of each specific activity are summed up to produce a numerical total score (0.00-58.2 METs).

The GP physical activity questionnaire (GPPAQ) is widely accepted for assessing PA in general practice (Weiler, Stamatakis 2010) and people’s risk of heart disease, stroke, diabetes and kidney disease as part of the NHS Health Check programme (Physical
Activity Policy, Health Improvement Directorate 2009). As a recommendation provided by NICE to identify those with “Inactive” PA and incentivise PA interventions, it was also used for patients with Chronic Kidney Disease (CKD) and renal transplant recipients (Takahashi, Hu et al. 2018, Clarke, Young et al. 2015b). The GPPAQ was designed to take less than one minute to complete and the results can categorize patients into one of four ‘Physical Activity Index’ (PAI) categories, ‘Inactive’, ‘Moderately Inactive’, ‘Moderately Active’ and ‘Active’. All those who do not achieve ‘Active’ periods have the potential to benefit from increasing their PA level. The Calculation of the four-level PAI is shown in Table2- 5. The GPPAQ walking pace question including 4 options (slow, steady, brisk and fast walking pace) is the second section of this questionnaire.

Table2- 5 Calculation of the four-level Physical Activity Index (PAI)

<table>
<thead>
<tr>
<th>PAI</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>Sedentary job and no physical exercise or cycling</td>
</tr>
<tr>
<td>Moderately inactive</td>
<td>Sedentary job and some but &lt; 1 hour physical exercise and / or cycling per week OR Standing job and no physical exercise or cycling</td>
</tr>
<tr>
<td>Moderately active</td>
<td>Sedentary job and 1-2.9 hours physical exercise and / or cycling per week OR Standing job and some but &lt; 1 hour physical exercise and / or cycling per week OR Physical job and no physical exercise or cycling</td>
</tr>
<tr>
<td>Active</td>
<td>Sedentary job and ≥ 3 hours physical exercise and / or cycling per week OR Physical job and some but &lt; 1 hour physical exercise and / or cycling per week OR Heavy manual job</td>
</tr>
</tbody>
</table>

The Leisure Time Exercise Questionnaire (LTEQ) is a self-administered assessment tool to measure exercise levels during individual leisure time (Godin, Shephard 1985). It was utilized to understand exercise level with CKD patients (Eng, Martin Ginis 2007, Beddhu, Baird et al. 2009) or dialysis patients (Stack, Molony et al. 2005b), and even in a study regarding the development of barriers and motivators of exercise questionnaire for HD patients (Goodman, Ballou 2004a). Eric D. Goodman et al. documented that the LTEQ was reviewed by the same jury of experts who evaluated the barriers and motivators questionnaire (Goodman, Ballou 2004a). The jury had the unanimous opinion that the LTEQ has appropriate applicability for HD patients. Its questions mainly record the times of strenuous, moderate, and mild exercise in the last 7 days, and weekly frequencies of these patterns of exercise are multiplied by 9, 5, and 3 METs, respectively. Therefore, summing up the values of the separate components in arbitrary units reflects
the intensity of a subject’s activity. Apart from the total exercise activity, a Health Contribution Score (HCS) (Godin 2011) to categorise respondents as “Active” ≥24 units, “Moderately Active” (14–23 units) or “Insufficiently Active” (<14 units) was calculated in order to suggest correlations between the volume of exercise and health benefits. The HCS is the sum of the frequency of the strenuous and moderate PA multiplied by 9 and 5 METs, respectively.

**The Dialysis Patient-Perceived Exercise Benefits and Barriers Scale (DPPEBBS)** was designed to assess dialysis patients’ beliefs and feeling about exercise (Zheng, You et al. 2010). It has been shown to be a valid and reliable instrument for evaluating the perceived benefits and barriers to exercise in HD patients (Zheng, You et al. 2010). There are 24 items in the DPPEBBS which are categorized into 12 benefits and 12 barrier items. The answers to the DPPEBBS are presented on a 4-point Likert-type scale, where 1 means ‘‘strongly disagree’’, 2 means ‘‘disagree’’, 3 means ‘‘agree’’, and 4 means ‘‘strongly agree’’, and the code of the barrier items is reversed. This scale consisted of six aspects, namely, daily life, symptoms, physical function, care needs, exercise-associated untoward outcomes and information on dialysis patients.

All the 4 questionnaires in the Chinese version have been validated in China except for the GPPAQ. In order to explore further possibilities and include it in the outcomes in the Chinese study, the GPPAQ was translated into Chinese by two professional translators with excellent knowledge of English and back into English iteratively by two bilinguals who had no knowledge of the original version of the questionnaire. Modifications were made in the conceptual and logistical aspects until consensus was reached by the translation group.

**Clinical information** relevant to the analysis of the questionnaire responses were obtained from patient’s medical records after asking for the patient’s consent, involving bicarbonate (mmol/L), urea (mmol/L) and creatinine (umol/L), Urea Reduction Ratio (URR) (%), albumin (g/L), C-Reactive Protein (CRP) (mg/L), triglycerides (mmol/L), cholesterol (mmol/L), phosphate (mmol/L), Alkaline Phosphatase (ALP) (iu/L), calcium (mmol/L), PTH (pmol/L), Hgb (g/dL) and haematocrit (L/L). All parameters were recorded with the pre-dialysis results. Pre-dialysis urea and creatinine were recorded with the average of three available dialysis days that are closest to the survey day. When there was no data available for the required date, the closest date
available was accepted. The results available with >3 months old were omitted from the data collection records.

2.3.3 Outcome measures in the COCO study

Questionnaires

The DASI and GP-PAQ were described in 2.3.2 (Outcome measures in the QCKD study).

The Euro QOL-5 Dimensions-5 Level (EQ-5D-5L) was originally developed by the Euro QoL group and now appears to have increased reliability and an improved ability to discriminate different levels of health over 20 years (Janssen, Birnie et al. 2008b, Pickard, De Leon et al. 2007, Janssen, Birnie et al. 2008a). It has been validated and applied to the study of patients with a variety of health status issues and a range of different populations (Janssen, Lubetkin et al. 2011, Pickard, Wilke et al. 2007, Wailoo, Davis et al. 2010), including HD patients (Faridah, Jamaiyah et al. 2010a). Additionally, the EQ-5D-5L was recommended by NICE and confirmed as being useful in the NHS patient-reported outcome measures programme (Devlin, Appleby et al. 2010). It comprised a 5-item descriptive system (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) containing 5 levels. Scores from each of the 5 dimensions are combined to give a single index value that is presented in country specific value sets. Additionally, an EQ-Visual Analogue Scale (EQ-VAS) allows the participants to judge their current health status from the worst (0) to the best health (100) they can imagine. In the study, the index value representing the participant’s QoL with 5 dimensions rather than their health status with only one overall dimension was utilized for the QoL evaluation due to its underlying accuracy (Saffari, Pakpour et al. 2013).

The Palliative Care Outcome Scale–Symptoms Renal (POS-S) was specifically developed for assessing symptom burden in patients with renal disease (Murphy, Murtagh et al. 2009). It was a reliable and valid self-reported questionnaire (Palliative care outcome scale , Gutiérrez Sánchez Daniel, Leiva-Santos et al. 2017) and has been widely used for understanding symptom burden in patients with renal disease (Sexton, Lowney et al. 2016, Brown, Collett et al. 2015). Donal J. Sexton et al. revealed that symptom burden assessed by the POS-S were the predictors of all-cause mortality in HD (Sexton, Lowney et al. 2016). The POS-S mainly measures the presence and severity of 17 symptom related diseases in the previous 7 days. The questionnaire also includes the
addition of three open fields, enabling patients to add any symptoms not listed that they had been experiencing over the past 7 days. The patient rated each symptom as absent, slight, moderate, severe, and overwhelming. The end of the questionnaire asked which symptom affected the patient the most and which symptom, if any, improved the most.

**Physical performance tests**

Physical performance tests including the Shuttle Walking Test (SWT), Sit to Stand (STS) 60, Handgrip Strength (HGS) and Short Physical Performance Battery (SPPB), were conducted for evaluating physical function with HD patients and healthy controls in the UK and China. Participants were given a chance to become familiar with the tests before they were conducted.

**SWT**

The SWT is a validated test of maximal exercise capacity in patients receiving HD and has been used in studies with dialysis patients as a vital assessment tool for physical function (Greenwood, Naish et al. 2014c, Lane, Wu et al. 2013, Wilund, Tomayko et al. 2010). It is simple to perform, well-tolerated and reproducible after a familiarization test, and is often preferred to other measures (Witham, Sugden et al. 2012, Revill, Morgan et al. 1999). The SWT includes the Incremental Shuttle Walking Test (ISWT) and Endurance Shuttle Walking Test (ESWT). Participants were asked to walk a 10-meter shuttle course at a speed controlled by an external audible bleep signal. For the ISWT, participants walked back and forth continuously at a progressively increasing pace. The test was terminated when participants failed to complete the shuttle course in the allowed time. Subsequently, the walking speed can be calculated from the ISWT performance, which equates to 85% of predicted VO$_2$peak, and this was used in the ESWT. For the ESWT, participants were asked to walk as long as they could at a constant speed and pace obtained from the participant’s ISWT performance by an external audible signal, and the total time walked was then recorded. In the study, the ESWT (meters) was calculated by multiplying the ESWT speed (meter/min) that participants achieved from the ISWT by the endurance (min) that participants walked.
HGS

The HGS is a reliable and simple assessment of muscle power (Lauretani, Russo et al. 2003) as well as an independent predictor of NS (Flood, Chung et al. 2013). Besides being a better predictor of clinical outcomes and low muscle mass (Lauretani, Russo et al. 2003), the HGS has also been reported as being a good simple measure of muscle strength in arms or legs (Cruz-Jentoft, Baeyens et al. 2010a). Additionally, it has been reported that the HGS is capable of predicting poor mobility status and disability for Activities of Daily Living (ADL) (Al Snih, Markides et al. 2004). A hand-held dynamometer was used to measure HGS three times before patients’ dialysis sessions and an average reading was obtained by averaging the three readings. Participants were asked to remain seated with the shoulder adducted elbow flexed at 90° and forearm in a neutral position (Limaye, Frankham et al. 2001, Tander, Akpolat et al. 2007, Duruoz, Cerrahoglu et al. 2003, Jamal, Leiter et al. 2006). The dynamometer was held with the side opposite to the vascular access arm by the patients and the dominant hand by the healthy controls. Participants were asked to squeeze the handle as hard as they could. 30 seconds was allowed for the interval between measurements.

STS

As well as being a surrogate for a walking test (Ozalevli, Ozden et al. 2007), an ideal tool for evaluating pulmonary rehabilitation (Vaidya, de Bisschop et al. 2016), and eliciting a comparable end-exercise physiological response to the 6 Minute Walk Test (6MWT) (Crook, Gilbert Büsching et al. 2017), the STS60 has been confirmed as a reliable and valid measure of functional outcome, especially in elderly people (Gross, Stevenson et al. 1998), COPD patients (Crook, Gilbert Büsching et al. 2017, Zanini, Aiello et al. 2015) and renal transplants (Bohannon, Smith et al. 1995). For the HD patients, Eva Segura-Ortí et al. reported the excellent test-retest reliability of the STS60 (Eva Segura-Ortí, Francisco José Martínez-Olmos 2011). Overall, STS60 is a good measure of functional ability and has been reported as being a good proxy for muscular endurance conditioning appropriate for dialysis patients (Bennett, Breugelmans et al. 2007, Kopple, Kim et al. 2015). The participant started from a seated position on a hard, upright chair, with arms folded across the chest, the feet flat on the floor and the knees bent at 90°. For the test, the subject simply stood up fully and then sat down again to the
starting position, without using their arms. For the STS60, this is the number of STS cycles achieved in 60 seconds and is a surrogate measure of muscular endurance.

**SPPB**

The SPPB was originally designed for elderly patients for testing lower extremity function (Fish 2011). It has been validated (Freire, Guerra et al. 2012) and has been widely used across diverse populations of elderly people by providing objective function measurements (Guralnik, Ferrucci et al. 2000, Volpato, Cavalieri et al. 2010). A number of studies with CKD patients reviewed the SPPB as a reliable function tool, evaluating physical function (TAŞOĞLU, Bayrakci et al. 2017, Painter, Agarwal et al. 2017) and the effect of exercise intervention (Bohm, Storsley et al. 2018). The SPPB includes a walking test (gait speed test), muscle strength test (STS5) and a balance test. Participants were asked to walk a 5m course twice at their usual walking speed with a walking aid if it was normally used. The duration times were recorded when the participant completed the 4m course and an average score was obtained from the participant’s two performances. The time taken for the participant to complete the STS cycles over 5 times as quickly as possible was then recorded for the measurement of the STS5, which is a surrogate measure of muscular power. In terms of the balance test, participant attempted to stand with 3 different movements for 10 seconds in each one. The first movement was to stand still with the feet together side by side (side-by-side). If successful, they would continue to stand with the side of the heel of one foot touching the big toe of the other foot (semi-tandem position). If successful, the final 10s position was assessed, with the heel of one foot in front of and touching the big toe of the other foot (full tandem position). These three separate tests had their own scoring system, ranging from 0 to 4. The scores from the separate tests were used to calculate the overall SPPB score.

**Physical activity level**

The SWA (BodyMedia, Inc., Pittsburgh, PA, USA) was used for assessing habitual PA levels of the UK HD patients, Chinese HD patients and healthy controls in the study. It is a typical Multi-sensor system (MSSs), which combines triaxial accelerometer with heat production, galvanic skin response, and skin temperature (David Andre, Ray Pelletier et al. 2006). In a few studies with chronic disease, it has been shown to be a valid measuring tool against the indirect calorimeter (VO$_2$) (Van Remoortel, Raste et al. 2012, Rabinovich,
Louvaris et al. 2013, Tierney, Fraser et al. 2013). Additionally, it has been widely used in HD patients (Avesani 2012, Mafra 2011). Besides duration, intensity, mode of PA that are similar with the outcomes achieved from questionnaires, SWA also provides an additional number of steps, EE and METs (David Andre, Ray Pelletier et al. 2006). The SWA was worn on the back of the upper non-vascular access arm (the triceps) for HD patients or the left arm for healthy controls, with an elastic strap. Participants were instructed to wear the SWA for 8 days (a full week) and all day long except for bathing, engaging in swimming or other water-based activities. Sensewear 7.0 software (BodyMedia, Inc., Pittsburgh, PA, USA) was used for PA data analysis.

The GENEActiv (Activinsights Ltd, Cambridgeshire, UK) was used for assessment of habitual PA level in the UK healthy controls. It is has been validated against doubly labelled water (van Hees, Renström et al. 2011). Additionally, it has been shown that the GENEActiv is valid and reliable for assessing activity intensity (Esliger, Rowlands et al. 2011, Phillips, Parfitt et al. 2013). UK healthy controls were asked to wear GENEActiv monitors on the right wrist 24 hours per day for a full week. Output derived from the GENEActiv can be classified by levels of activity intensity according to METs intensity of PAs thresholds (Zhang, Rowlands et al. 2012, Pate, Pratt et al. 1995). In the study, the minutes per day spent in moderate or vigorous activity were calculated as the outcome, which has been validated against indirect calorimetry (Esliger, Rowlands et al. 2011). It can be categorized participants’ PA level into “Active” and “Inactive” based on the PA guideline (the Chief Medical Office, (CMO) 2011). Similarly, time spent in MVPA in ≥ 10min bouts were recorded.

Patients who did not meet the criteria for the minimum accelerometer wear time of 8 hours per day on at least one HD day and two non-HD days, were excluded from the study (Prescott, Traynor et al. 2016, da Costa Rosa, Clara Suemi, Nishimoto et al. 2017, Demeyer, Heleen, PT, MSc, Burtin, Chris, PhD, PT et al. 2014). To avoid the Hawthorne effect (DÖssegger, Ruch et al. 2014) in which participants may modify their PA behaviour in response to their awareness of being monitored (Siebeling, Wiebers et al. 2012, Yap, Davis et al. 2009), the results on the first measurement day were excluded. The PA levels of participants who still met the criteria after excluding the Hawthorne effect were finally analysed. The same minimal wear times criteria were included for the healthy controls. The criteria included the minimum accelerometer wear time of 8 hours per day on at least three days and excluded the impact of the Hawthorne effect on the accelerometer data.
The Chief Medical Office (CMO) in the UK’s own PA guidelines for PA levels in adults recommends a minimum of either ≥150 min of Moderate to Vigorous Physical Activity (MVPA) in ≥ 10 min bouts or ≥75 mins of Vigorous Physical Activity (VPA) per week for adults (the Chief Medical Office, (CMO) 2011). According to the model proposed by Pate et al. for classifying the METs intensity of PAs (light, < 3METs; moderate, 3-6METs; vigorous, > 6METs) (Pate, Pratt et al. 1995), time spent on MVPA in ≥ 10 min bouts derived from the SWA were recorded. Although the utilization of <5000 steps /d as a step-defined sedentary lifestyle index still requires additional studies for further confirmation, it has been demonstrated as a multiform utility for researchers and practitioners (McKercher, Schmidt et al. 2009, Kozey-Keadle, Libertine et al. 2011, Cavanaugh, Kochi et al. 2009). Based on the numbers of steps taken, the participants were categorized as sedentary (<5000 steps/d), somewhat active (5000 to 7499 steps/d), and active (≥7500 steps/d) (Tudor-Locke, Craig et al. 2012).

The Lean tissue Index (LTI) and Fat Tissue Index (FTI)

Participants’ body composition (Lean tissue index [LTI] and fat tissue index [FTI]) were assessed using the Fresenius Body Composition Monitor (BCM) in the study. The BCM is currently a commonly used bio-impedance methodology with a 3-Compartment (3-C) model. Thus, as a tool for distinguishing OH, lean and fat tissue mass, the BCM has been extensively used for understanding the body composition of dialysis patients (Van Biesen, Williams et al. 2011, Van Biesen, Claes et al. 2013), and has played an important role in evaluating NS (Rosenberger, Kissova et al. 2014) and predicting PEW (Magnard, Deschamps et al. 2013a, Broers, Martens et al. 2015a). Patients were requested to lie flat on a bed or a couch and electrodes of the BCM were placed on one hand and foot to assess body composition before the dialysis session. The procedure usually took around two minutes.

The LTI (LTM/height²) and FTI (FTM/height²) obtained from BCM are the respective tissue masses normalized to height square. The classification of LTI and FTI were based on the reference ranges, which were derived from the BCM measurements of 1000 healthy adult subjects aged 18–75 (Fresenius Medical Care ). The reference population is age and gender specific due to the variation of the body composition throughout life and between genders. Participants in the study were classified into 3 groups by LTI and FTI, respectively. There were low LTI (LTI <10th percentile of a reference population),
normal LTI (LTI between 10th percentile and 90th percentile), and high LTI (LTI ≥90th percentile), low FTI (FTI <10th percentile of a reference population), normal FTI (FTI between 10th percentile and 90th percentile), and high FTI (FTI ≥90th percentile).

Demographics

The HD patients’ demographic information was obtained from their medical records with the patient’s consent. Healthy controls’ demographics were obtained by interviewing individuals. The demographics included age, gender, ethnicity, dialysis vintage, BMI, and general information about comorbidity and medication.

2.4 Statistical analysis

Categorical data were summarised into number and percentage of the participants. Continuous data were checked for normality of distribution using Shapiro-Wilk tests. Whilst variables with normally distributed were presented as mean ± standard deviation (SD), non-normally distributed variables were shown as median [interquartile range (IQR)]. When the comparison of two variables were presented in the same table or figure, they were shown with median (IQR) if at least one of them was non-normally distributed. Independent-sample t tests or non-parametric test were performed to compare the differences of two groups. The differences between the two groups were compared using independent t test and Mann Whitney test on parametric and non-parametric data respectively. Pearson correlation coefficient was performed to evaluate the relationship between continuous variables but only when both variables were normally distributed; otherwise Spearman’s correlation coefficient was used. The Spearman correlation coefficient was performed to evaluate the monotonic relationship between two continuous or ordinal variables, or two ordinal variables (Hauke, Kossowski 2011).

When testing for differences in the means of the dependent variable broken down by the levels of the independent variable, a one-way analysis of variance (ANOVA) or independent t-test were used if there was a categorical independent variable (with two or more categories) and a normally distributed interval dependent variable. When dependent variable was non-normally distributed, non-parametric test was used. Chi-square test was used if both dependent and independent variables are categorical or nominal.

Validation of the DASI and GPPAQ walking pace against physical performance tests
were achieved using the linear regression. Regression analysis was performed when significant difference was presented in age or gender between any two groups. Multivariable linear and multi-nominal logistic regression was used for showing the difference in a series of dependent variables representing continuous and nominal variables between any two groups after controlling for age and gender. After controlling for age and gender, dependent variables in two groups were displayed as mean (95% CI [confidence interval]: lower limitation – upper limitation), showing in the next time, there is 95% possibility for dependent variables to present with the value within the range between lower and upper limitation. ΔR² Adjusted means how much age, gender and groups explain the variance in the dependent variable.

All statistical analyses were performed using the statistical package of Social Sciences (IBM SPSS Statistics v.24, New York, USA.) Graphs were drawn with Excel 2013 (Microsoft, Washington, USA.), EDraw Max (v9.0 EDraw Mind Map, Shenzhen, China), and GraphPad Prism (v.7 Graphpad Software Inc, CA, USA). Statistical significance was taken as P<0.05.
Chapter 3

Demographics and Clinical Information of Participants in the DISH, QCKD and COCO Studies
3.1 Abstract

According to reports from the UK Renal Registry (UKRR) and the Chinese National Renal Data System (CNRDS), there are a number of differences in terms of demographics and clinical parameters between UK and Chinese HD patients. These demographic and clinical characteristics affect HD patients’ lifestyle. The aim of this chapter was to characterise and compare the demographic and clinical information of HD patients and healthy controls between the UK and China. Age and gender distributions in the UK and Chinese HD patients were consistent with those in the overall respective populations. While the mean age in the UK HD patients was older than in Chinese patients, UK HD patients had higher BMI than Chinese patients. The difference of demographics and clinical parameters between UK and Chinese HD patients may be potential associated factors that lead to the disparity of lifestyle behaviors between two cultural groups.

3.2 Introduction

Kidney disease is more common as patients’ age increases. The age group with the majority of ESRD patients in the UK was 65 to 74 years (UK Renal Registry 2016). Different from diabetes as primary cause of ESRD in UK HD patients (UK Renal Registry 2016), the primary cause of ESRD is glomerulonephritis in China (Xie, Chen 2008, Chinese National Renal Data System 2015). It is understood that glomerulonephritis can occur at any age. Patients aged 2 to 15 years were the most affected age group. However, diabetes is strongly associated with patients who are around 45 years and older (Centers for Disease Control and Prevention 2014). Furthermore, ESRD due to diabetes might take longer in the progress of CKD. Therefore, Chinese HD patients ought to be relatively younger than their UK counterparts. Consistently, the average age in Chinese HD patient was 54.9 years based on the CNRDS report in 2014, which was younger than UK HD patients (Chinese National Renal Data System 2015).

ESRD incidence rate in male patients was higher than female, which was prevalent in almost every country with the exception of Estonia and Colombia (United States Renal Data System, USRDS 2017). Prevalence of ESRD patients by gender and age groups in the UK showed that males in any age groups had a higher prevalence rate than female (UK Renal Registry 2016). The percentage of males was higher than that of female in Chinese HD patients from 2011 to 2014. Male HD patients in 2014 accounted for 58.9%
of the overall Chinese HD patients (Chinese National Renal Data System 2015).

Similarly, differences in various clinical parameters are present between UK and Chinese HD patients. The mean hemoglobin (Hgb) levels of 11.0g/dl in UK HD patients was higher than 10.1g/dl in Chinese patients based on nation-wide scale reports with HD patients. Other clinical parameters, such as serum ferritin, calcium, potassium and sodium were all reported to be different between UK and Chinese HD patients (UK Renal Registry 2016, Chinese National Renal Data System 2015).

It has long been known that HD patients’ demographics, such as age and gender, influence their lifestyle (Liu 2012, Johansen, Kaysen et al. 2013, Brown, Yore et al. 2005). Furthermore, there is strong correlation between lifestyle and clinical conditions in HD patients (Kaizu, Ohkawa et al. 2003b, Johansen, Chertow et al. 2000b). Consequently, understanding of HD patients’ demographics and clinical information is a fundamental element in exploring the disparity of lifestyles between UK and Chinese HD patients. Furthermore, it can promote the understanding of the relationship between lifestyle, demographics and clinical information in HD patients.

The aims of this chapter were to characterize and compare the demographics and clinical information of all the participants involved in the studies in the UK and China, including HD patients and healthy controls.

3.3 Methods

The data included in this chapter were derived from the DISH (Chapter 2, section 2.2.1), QCKD (Chapter 2, section 2.2.2) and COCO studies (Chapter 2, section 2.2.3). The detailed methods are described in Chapter 2. Demographics of HD patients in the QCKD study were obtained from a demographic section combined with the questionnaires (Chapter 2, section 2.3.2). Demographics of healthy controls in the COCO study were collected through interviews (Chapter 2, section 2.3.3). The other demographic and clinical information of the HD patients in these three studies were all collected from the patients’ medical records (Chapter 2, section 2.3.1, 2.3.2, 2.3.3).
3.4 Results

3.4.1 Demographics and nutritional blood parameters of haemodialysis patients in the DISH study

Demographic characteristics of the UK haemodialysis patients

The demographic details of the UK HD patients in the DISH study are shown in Table 3-1. The mean age of the UK HD patients was 56.83 years, ranging from 25 to 80 years old. The percentages of male and female were 57.5% and 42.5%. The median dialysis vintage was 31.5 months. The mean Mid-Arm Circumference (MAC) and Body Mass Index (BMI) were 29.6 cm and 26.6 kg/m², respectively. Hypertension and anti-hypertensives were the most commonly reported comorbidity and medication for the UK HD patients in the study, respectively.
<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>UK HD patients (n=40)</th>
<th>n</th>
<th>Mean± SD; Median (IQR); ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>40</td>
<td>56.8±16.1</td>
</tr>
<tr>
<td>Males: Females</td>
<td></td>
<td>40</td>
<td>23:17</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td></td>
<td>40</td>
<td>31.5(15.8-60.3)</td>
</tr>
<tr>
<td>MAC (cm)</td>
<td></td>
<td>32</td>
<td>29.6±5.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>33</td>
<td>26.6±5.9</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>26</td>
<td>65%</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td></td>
<td>7</td>
<td>17.5%</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td></td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td></td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td></td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td></td>
<td>7</td>
<td>17.5%</td>
</tr>
<tr>
<td>Neurological disease</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td></td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td></td>
<td>40</td>
<td>100%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td></td>
<td>8</td>
<td>20%</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td>24</td>
<td>60%</td>
</tr>
</tbody>
</table>
**Nutritional blood parameters of the UK haemodialysis patients**

Table 3-2 shows nutritional blood parameters of the UK HD patients. All nutritional blood parameters were within the normal range except for cholesterol (3.8±1.1 mmol/L) and haematocrit levels (35.5±4.3 L/L), which were lower than the normal range (>3.9 or <5.2-7.8 mmol/L, 40.0-54.0 L/L).

<table>
<thead>
<tr>
<th>Nutritional blood parameters</th>
<th>UK HD patients (n=40)</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean± SD; Median (IQR); ratio (%)</td>
</tr>
<tr>
<td><strong>Albumin (g/L)</strong></td>
<td>39</td>
<td>38.3±3.8</td>
</tr>
<tr>
<td><strong>Cholesterol (mmol/L)</strong></td>
<td>36</td>
<td>3.8±1.1</td>
</tr>
<tr>
<td><strong>Phosphate (mmol/L)</strong></td>
<td>39</td>
<td>1.6±0.4</td>
</tr>
<tr>
<td><strong>Calcium (mmol/L)</strong></td>
<td>39</td>
<td>2.4±0.1</td>
</tr>
<tr>
<td><strong>Hgb (g/dL)</strong></td>
<td>39</td>
<td>12.1 (11.0-14.6)</td>
</tr>
<tr>
<td><strong>Haematocrit (L/L)</strong></td>
<td>39</td>
<td>35.5±4.3</td>
</tr>
<tr>
<td><strong>Sodium (mEq/L)</strong></td>
<td>39</td>
<td>135.0 (134.0-137.0)</td>
</tr>
<tr>
<td><strong>Potassium (mEq/L)</strong></td>
<td>39</td>
<td>4.4±0.8</td>
</tr>
<tr>
<td><strong>Transferrin Saturation</strong></td>
<td>34</td>
<td>Male: 25.0±6.5%; Female: 20.9±4.5%</td>
</tr>
<tr>
<td><strong>Iron (umol/L)</strong></td>
<td>33</td>
<td>Male: 12.3±3.2; Female: 10.8±2.3</td>
</tr>
<tr>
<td><strong>Ferritin (ng/ml)</strong></td>
<td>39</td>
<td>Male: 2.9±1.7; Female: 5.5±2.6</td>
</tr>
</tbody>
</table>
Demographic characteristics of Chinese haemodialysis patients

For demographic data of Chinese HD patients see Table3- 3. The mean age of Chinese HD patients was 42.5 years, ranging from 25 to 62 years old. The percentages of male and female were 48.8% and 51.2%. The median dialysis vintage was 60.0 months. The mean BMI was 21.4kg/m². Hypertension and anti-hypertensives were the most commonly reported comorbidity and medication for Chinese HD patients in the study, respectively.
<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Chinese HD patients (n=43)</th>
<th>n</th>
<th>Mean± SD; Median (IQR); ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>43</td>
<td>42.5±9.1</td>
</tr>
<tr>
<td>Males: Females</td>
<td></td>
<td>43</td>
<td>21:22</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td></td>
<td>43</td>
<td>60.0(36.0-84.0)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>43</td>
<td>21.4±2.6</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>1</td>
<td>2.3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>10</td>
<td>23%</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td></td>
<td>3</td>
<td>6.9%</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td></td>
<td>2</td>
<td>4.6%</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td></td>
<td>4</td>
<td>9.2%</td>
</tr>
<tr>
<td>Neurological disease</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td></td>
<td>43</td>
<td>100%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td></td>
<td>9</td>
<td>23%</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td>1</td>
<td>2.3%</td>
</tr>
</tbody>
</table>
Nutritional blood parameters of Chinese haemodialysis patients

Table 3-4 shows nutritional blood parameters of Chinese HD patients. Phosphate level (2.1±0.5mmol/L) was higher than the normal range (1.1-1.7mmol/L). However, haemoglobin (Hgb) (11.0 [10.1-12.0] g/dL) and haematocrit (33.7±5.7L/L) levels were lower than the normal range (11.5-17.5g/dL, 40.0-54.0L/L).

Table 3-4 Nutritional blood parameters of Chinese HD patients in the DISH study

<table>
<thead>
<tr>
<th>Nutritional blood parameters</th>
<th>UK HD patients (n=40)</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean± SD; Median (IQR); ratio (%)</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>39</td>
<td>2.1±0.5</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>39</td>
<td>2.3±0.3</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>39</td>
<td>11.0 (10.1-12.0)</td>
</tr>
<tr>
<td>Haematocrit (L/L)</td>
<td>39</td>
<td>33.7±5.7</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>39</td>
<td>136.0 (135.0-139.0)</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>39</td>
<td>5.0±0.6</td>
</tr>
</tbody>
</table>
Comparison of demographic characteristics between UK and Chinese haemodialysis patients

Comparison of demographic characteristic between UK and Chinese HD patients is shown in Table 3-5. UK patients were significantly older than the Chinese patients. Chinese patients had longer dialysis vintage than UK patients. BMI, percentage of patients who had diabetes, hypertension, asthma or COPD and mental health illness and percentage of patients who were administered with anti-hypertensives and statins administration were all significantly higher in UK patients than those in Chinese patients.

**Table 3-5 Comparison of demographic characteristics of HD patients between the UK and China in the DISH study**

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>UK HD patients (n=40)</th>
<th>Chinese HD patients (n=43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.8±16.1</td>
<td>42.5±9.1</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Males: Females</td>
<td>23:17</td>
<td>21:22</td>
<td>0.429</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td>31.5(15.8-60.3)</td>
<td>60.0(36.0-84.0)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.6±5.9</td>
<td>21.4±2.6</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>12(30%)</td>
<td>1(2.3%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26 (65%)</td>
<td>10 (23%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>7 (17.5%)</td>
<td>3 (6.9%)</td>
<td>0.141</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>1(2.5%)</td>
<td>2 (4.6%)</td>
<td>0.596</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>1(2.5%)</td>
<td>0(0.0%)</td>
<td>0.225</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>3(7.5%)</td>
<td>0(0.0%)</td>
<td>0.034*</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>7(17.5%)</td>
<td>4(9.2%)</td>
<td>0.271</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>3(7.5%)</td>
<td>0(0.0%)</td>
<td>0.034*</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>40</td>
<td>43</td>
<td>N/A</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>4(10%)</td>
<td>0(0.0%)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>8 (20%)</td>
<td>9 (23%)</td>
<td>0.567</td>
</tr>
<tr>
<td>Statins</td>
<td>24(60%)</td>
<td>1(2.3%)</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

*P< 0.05; **P< 0.01; ***P< 0.001 (2-tailed).
Comparison of Nutritional blood parameters between UK and Chinese haemodialysis patients

Comparison of nutritional blood parameters in the UK and Chinese HD patients is shown in Table 3. The UK HD patients had significantly higher Hgb and haematocrit levels than Chinese HD patients. Chinese HD patients had significantly higher phosphate, sodium and potassium concentrations than their UK counterparts.

Table 3- 6 Comparison of nutritional blood parameters of HD patients between the UK and China in the DISH study

<table>
<thead>
<tr>
<th>Nutritional blood parameters</th>
<th>UK HD patients (n=40)</th>
<th>Chinese HD patients (n=43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphate (mmol/L)</td>
<td>1.6±0.4</td>
<td>2.1±0.5</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.4±0.1</td>
<td>2.3±0.3</td>
<td>0.160</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>12.1 (110-14.6)</td>
<td>11.0 (10.1-12.0)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Haematocrit (L/L)</td>
<td>35.5±4.3</td>
<td>33.7±5.7</td>
<td>0.036*</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>135.0 (134.0-137.0)</td>
<td>136.0 (135.0-139.0)</td>
<td>0.022*</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.4±0.8</td>
<td>5.0±0.6</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

*P< 0.05; **P< 0.01; ***P< 0.001 (2-tailed).

3.4.2 Demographics and clinical information of haemodialysis patients in the QCKD study

Demographic characteristics

Table 3- 7 shows the UK HD patients’ demographic characteristics. The median age of the UK HD patients was 65.0 years, ranging from 16 to 82 years old. Ethnicity included British, South Asian, African and some other mixed or non-mixed ethnicity groups. Among these ethnicity groups, white British predominated in the subjects (59.0%), and the second most common was Southern Asian (12.7%). The current smokers accounted for 9.5% of patients but the majority of participants in the study had never been smokers in the study (49.7%). Both the median complications and medications were 2 which ranged from 0 to 6.
### Table 3: Demographics characteristics in the UK HD patients in the QCKD study

<table>
<thead>
<tr>
<th>Demographics Characteristics</th>
<th>UK HD patients (n=1156)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Age (y)</td>
<td>1126</td>
</tr>
<tr>
<td>Male/ Female</td>
<td>1132</td>
</tr>
<tr>
<td>Dialysis vintage (y)</td>
<td>1087</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>633</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>1121</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>1134</td>
</tr>
<tr>
<td>British</td>
<td>667</td>
</tr>
<tr>
<td>South Asian</td>
<td>144</td>
</tr>
<tr>
<td>African</td>
<td>101</td>
</tr>
<tr>
<td>Caribbean</td>
<td>85</td>
</tr>
<tr>
<td>Any other Asian background</td>
<td>16</td>
</tr>
<tr>
<td>Any other black background</td>
<td>15</td>
</tr>
<tr>
<td>White and black African</td>
<td>15</td>
</tr>
<tr>
<td>Irish</td>
<td>14</td>
</tr>
<tr>
<td>Bangladeshi</td>
<td>13</td>
</tr>
<tr>
<td>Any other ethnic group</td>
<td>43</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>882</td>
</tr>
<tr>
<td>Medications (count per person)</td>
<td>867</td>
</tr>
</tbody>
</table>
Clinical information

Table 3 shows the characteristics of Clinical information in the UK HD patients. The median pre-dialysis urea (17.5[14.3-21.0] vs. 2.5-6.7 mmol/L) and creatinine (688.4[553.1-860.5] vs. 79.0-118.0 umol/L), Parathyroid hormone (PTH) (45.7[21.2-93.5] vs. 1.6-9.3 pmol/L) and C-reactive Protein (CRP) (11.0[6.0-24.0] vs. <3.0 mg/L) in the UK HD patients were higher than the normal range. Urea Reduction Ratio (URR) with 74.3% in the patients was higher than 65% which is considered the minimum acceptable dose (National Kidney Foundation 2006). Conversely, the median Hgb (11.2[10.2-12.0] vs. 11.5-17.5 g/dL) and haematocrit (0.34[0.31-0.37] vs. 0.40-0.54 L/L) were slightly lower than the normal range.

Table 3. Clinical information in the UK HD patients in the QCKD study

<table>
<thead>
<tr>
<th>Clinical information</th>
<th>UK HD patients n=1156</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>840</td>
<td>22–26</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>849</td>
<td>2.5-6.7</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>760</td>
<td>79-118</td>
</tr>
<tr>
<td>URR (%)</td>
<td>672</td>
<td>&gt;65</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>872</td>
<td>35-50</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>286</td>
<td>&lt;1.7</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>544</td>
<td>&gt;3.9 or</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>861</td>
<td>&lt;5.2-7.8</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>856</td>
<td>44-147</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>852</td>
<td>2.2-2.7</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>745</td>
<td>1.6-9.3</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>879</td>
<td>11.5-17.5</td>
</tr>
<tr>
<td>Haematocrit (L/L)</td>
<td>844</td>
<td>0.40-0.54</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>581</td>
<td>&lt;3.0</td>
</tr>
</tbody>
</table>
Demographic characteristics of Chinese HD patients

Table 3 characterizes Chinese HD patients’ demographics characteristics. The median of age in Chinese HD patients was 52.0 years, ranging from 16 to 89 years. The majority of patients (69.3%) had never smoked. The median number of concomitant complications and medications was 1 and 2 with range from 0 to 6, respectively. All Chinese patients in the study had never been diagnosed with any mental disease.

Table 3- Demographics characteristics in Chinese HD patients in the QCKD study

<table>
<thead>
<tr>
<th>Demographics Characteristics</th>
<th>Chinese HD patients n=542</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Age (y)</td>
<td>542</td>
</tr>
<tr>
<td>Male/ Female</td>
<td>542</td>
</tr>
<tr>
<td>Dialysis vintage (y)</td>
<td>541</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>542</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>537</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>542</td>
</tr>
<tr>
<td>Medications (count per person)</td>
<td>542</td>
</tr>
</tbody>
</table>
Clinical information of Chinese haemodialysis patients

Table 3-10 presents the Chinese HD patients’ clinical information. The mean or median pre-dialysis urea (26.4±24.2 vs. 2.5-6.7 mmol/L) and creatinine (969.1±314.1 vs. 79.0-118.0 umol/L) levels, phosphate (1.8±0.7 vs. 1.1-1.7 mmol/L) and PTH levels (29.6 [12.8-54.1] vs. 1.6-9.3 pmol/L) in Chinese HD patients were higher than the normal range. Triglycerides, cholesterol, albumin, CRP and ALP were not described due to too much missing data in the patients’ medical records. The mean or median bicarbonate (21.6±3.5 vs. 22.0-26.0 mmol/L), Hgb (10.5 [9.4-11.5] vs. 11.5-17.5 g/dL) and haematocrit levels (32.0±13.0 vs. 40.0-54.0 L/L) were lower than the normal range.

Table 3-10 Characteristics of clinical information in Chinese HD patients in the QCKD study

<table>
<thead>
<tr>
<th>Clinical information</th>
<th>Chinese HD patients n=542</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>21.6±3.5</td>
<td>22–26</td>
</tr>
<tr>
<td>pre-dialysis Urea (mmol/L)</td>
<td>26.4±24.2</td>
<td>2.5-6.7</td>
</tr>
<tr>
<td>pre-dialysis Creatinine (umol/L)</td>
<td>969.1±314.1</td>
<td>79-118</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>39.3±5.6</td>
<td>35-50</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>1.8±0.7</td>
<td>1.1-1.7</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.3±0.3</td>
<td>2.2-2.7</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>29.6 (12.8-54.1)</td>
<td>1.6-9.3</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>10.5 (9.4-11.5)</td>
<td>11.5-17.5</td>
</tr>
<tr>
<td>Haematocrit (L/L)</td>
<td>32.0±13.0</td>
<td>40.0-54.0</td>
</tr>
</tbody>
</table>
Comparison of demographics between UK and Chinese haemodialysis patients

Table 3-11 is the comparison of the demographics between the UK and Chinese HD patients. UK HD patients were older and had higher BMI and longer dialysis vintage than Chinese HD patients (all P<0.001). Chinese patients had more female, less ex-smokers and comorbidities than their UK counterparts (all P<0.001).

Table 3-11 Comparison of demographics in the HD patients between the UK and China in the QCKD study

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>UK HD patients n=1156</th>
<th>Chinese HD patients n=542</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1126</td>
<td>542</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Median (IQR); ratio (%)</td>
<td>65.0 (53.0-74.0)</td>
<td>52.0 (45.0-63.25)</td>
<td></td>
</tr>
<tr>
<td>Male/ Female</td>
<td>1132</td>
<td>542</td>
<td>0.004**</td>
</tr>
<tr>
<td>727(64.2%)/ 405 (35.8%)</td>
<td>315(58.1%)/ 227 (41.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis vintage (y)</td>
<td>1087</td>
<td>541</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>7.0 (14.0-3.0)</td>
<td>4.0 (8.0-2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>633</td>
<td>542</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>26.0 (31.0-22.4)</td>
<td>21.7 (19.6-24.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker/ ex-smoker/ never smoke</td>
<td>1121</td>
<td>537</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>107(9.5%)/ 457(40.8%)/ 557(49.7%)</td>
<td>58(10.8%)/ 107(19.9%)/ 372 (69.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidity (count per person)</td>
<td>882</td>
<td>542</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>2(1-3)</td>
<td>1(1-2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication (count per person)</td>
<td>867</td>
<td>542</td>
<td>0.836</td>
</tr>
<tr>
<td>2(1-3)</td>
<td>2(1-3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**P< 0.01; ***P< 0.001 (2-tailed).
Comparison of clinical information between UK and Chinese haemodialysis patients

Table 3-12 shows the comparison of clinical information between UK and Chinese HD patients. The UK HD patients’ urea, creatinine and phosphate levels were significantly lower than their Chinese counterparts (all P<0.001). However, their PTH, Hgb and haematocrit levels were significantly higher than Chinese patients (all P<0.001).

Table 3-12 Comparison of clinical information between the UK and Chinese HD patients in the QCKD study

<table>
<thead>
<tr>
<th>Clinical information</th>
<th>UK HD patients n=1156</th>
<th>Chinese HD patients n=542</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean± SD; Median (IQR)</td>
<td>Mean± SD; Median (IQR)</td>
<td></td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>849</td>
<td>17.5 (14.3-21.0)</td>
<td>470</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>760</td>
<td>688.4 (860.5-553.1)</td>
<td>475</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>861</td>
<td>1.5 (1.8-1.3)</td>
<td>520</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>745</td>
<td>45.7 (21.2-93.5)</td>
<td>466</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>879</td>
<td>11.2 (12.0-10.2)</td>
<td>513</td>
</tr>
<tr>
<td>Haematocrit (L/L)</td>
<td>844</td>
<td>34.0 (31.0-37.0)</td>
<td>518</td>
</tr>
</tbody>
</table>

***P< 0.001 (2-tailed).

3.4.3 Demographics of haemodialysis patients and healthy controls in the COCO study

Demographics of haemodialysis patients and healthy controls in the UK

Demographics of the UK haemodialysis patients

Table 3-13 shows the UK HD patients’ demographic characteristics. The median age in the UK HD patients was 56.3 years, ranging from 25 to 79 years old. Ethnicity mainly included British and South Asian. Among these ethnicity groups, Southern Asian predominated in the subjects (56.7 %), and the second most common was white British (30.0%). The most frequently reported comorbidities were hypertension (76.7%) and diabetes (46.7%). The main medications administrated were anti-hypertensives (60.0%) and statins (56.7%).
Table 3: Demographic characteristics in the UK HD patients in the COCO study

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>n</th>
<th>UK HD patients n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30</td>
<td>56.3±13.8</td>
</tr>
<tr>
<td>Males: Females</td>
<td>30</td>
<td>24(80.0%)/6(20.0%)</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td>30</td>
<td>23.5(10.00-40.00)</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>25</td>
<td>1 (4.0%)/9 (36.0%)/15 (60.0%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30</td>
<td>27.1±4.6</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>17</td>
<td>56.7 %</td>
</tr>
<tr>
<td>British</td>
<td>9</td>
<td>30.0%</td>
</tr>
<tr>
<td>Caribbean</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Any other Asian background</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>Any other black background</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14</td>
<td>46.7%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23</td>
<td>76.7%</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>5</td>
<td>16.7%</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0</td>
<td>2.5%</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0</td>
<td>2.5%</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>5</td>
<td>16.7%</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>3</td>
<td>10.0%</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>18</td>
<td>60.0%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>5</td>
<td>16.7%</td>
</tr>
<tr>
<td>Statins</td>
<td>17</td>
<td>56.7%</td>
</tr>
</tbody>
</table>
Demographics of the UK healthy controls

Table 3 shows the UK healthy controls’ demographic characteristics. The median age in UK healthy controls was 45.1 years, ranging from 18 to 70 years old. Ethnicity mainly included British, South Asian and Caribbean. Among these ethnicity groups, white British predominated in the subjects (80.0%), and Southern Asian and Caribbean accounted for 10.0%, respectively. Hypertension was the only comorbidity in the group and only one participant (11.1%) had it. None of the 10 healthy controls took any medication.
<table>
<thead>
<tr>
<th>Demographics characteristics</th>
<th>UK healthy controls (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10</td>
</tr>
<tr>
<td>Males: Females</td>
<td>10</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>10</td>
</tr>
<tr>
<td>British</td>
<td>8</td>
</tr>
<tr>
<td>South Asian</td>
<td>1</td>
</tr>
<tr>
<td>Caribbean</td>
<td>1</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>0</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>0</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>0</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>0</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>0</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>0</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>0</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>0</td>
</tr>
<tr>
<td>Statins</td>
<td>0</td>
</tr>
</tbody>
</table>
Comparison of demographics between haemodialysis patients and healthy controls in the UK

Table 3-15 shows the comparison of demographic between HD patients and healthy controls in the UK. The UK HD patients were significantly older than healthy controls. More HD patients suffered from diabetes (P=0.002) and hypertension (P=0.008) than their healthy counterparts. Furthermore, they took more anti-hypertensives (P=0.001) and statins (P=0.002) than healthy controls.
Table 3: Comparison of demographics between HD patients and healthy controls in the UK in the COCO study

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>HD patients (n=30)</th>
<th>Healthy Controls (n=10)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.3±13.8</td>
<td>45.1±16.0</td>
<td>0.039*</td>
</tr>
<tr>
<td>Males: Females</td>
<td>24:6</td>
<td>6:4</td>
<td>0.220</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>1/9/15</td>
<td>0/2/6</td>
<td>0.237</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>26.6(23.9-29.8)</td>
<td>25.7(22.7-31.0)</td>
<td>0.755</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>British/South Asian/Caribbean/ Any other Asian background/Any other black background/9/17/1/2/1</td>
<td>British/South Asian/Caribbean/: 8/1/1</td>
<td></td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14(46.7%)</td>
<td>0(0.0%)</td>
<td>0.002**</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23(76.7%)</td>
<td>1 (11.1%)</td>
<td>0.008**</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>5 (16.7%)</td>
<td>0(0.0%)</td>
<td>0.092</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0(2.5%)</td>
<td>0 (0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0(2.5%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>1(3.3%)</td>
<td>0(0.0%)</td>
<td>0.466</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>5(16.7%)</td>
<td>0(0.0%)</td>
<td>0.092</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1(3.3%)</td>
<td>0(0.0%)</td>
<td>0.466</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>3(10.0%)</td>
<td>0(0.0%)</td>
<td>0.199</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>18(60.0%)</td>
<td>0(0.0%)</td>
<td>0.001***</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1(3.3%)</td>
<td>0(0.0%)</td>
<td>0.514</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>5 (16.7%)</td>
<td>0(0.0%)</td>
<td>0.132</td>
</tr>
<tr>
<td>Statins</td>
<td>17(56.7%)</td>
<td>0(0.0%)</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.01; ***P < 0.001 (2-tailed).
Demographics of participants in China

Demographics of Chinese haemodialysis patients

Table 3-16 shows Chinese HD patients’ demographic characteristics. The median age in Chinese HD patients was 48.6 years, ranging from 30 to 65 years old. The majority of patients (60%) had never smoked. The most frequently reported comorbidities were hypertension (62.5%) and ischaemic heart disease (22.5%). No one in the study was diagnosed with any mental health illness or had been administered antidepressant. The main medications were anti-hypertensives (82.5%) and oral bicarbonate (22.5%). There was no missing data for any characteristics.
Table 3: Demographic characteristics in Chinese HD patients in the COCO study

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>HD patients (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td>Mean±SD; Median (IQR); n (%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.6±9.4</td>
</tr>
<tr>
<td>Males: Females</td>
<td>22 (55%):18 (45%)</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td>74.9±42.0</td>
</tr>
<tr>
<td>Current smoker/ ex-smoker/never smoke</td>
<td>11 (27.5%)/5 (12.5%)/24 (60%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.5(20.2-25.0)</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3(7.5%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25(62.5%)</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>9 (22.5%)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>2(5.0%)</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>8(20.0%)</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>33(82.5%)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>9 (22.5%)</td>
</tr>
<tr>
<td>Statins</td>
<td>0(0.0%)</td>
</tr>
</tbody>
</table>
Demographics of Chinese healthy controls

Table 3-17 shows Chinese healthy controls’ demographic characteristics. The median age in Chinese healthy controls was 50.7 years, ranging from 30 to 73 years old. The majority of healthy controls had never smoked. Hypertension (4.5%) and anti-hypertensives (4.5%) was the only reported comorbidity and medication, respectively. There was no missing data for any characteristics.

Table 3-17 Demographics characteristics in Chinese healthy controls in the COCO study

<table>
<thead>
<tr>
<th>Demographics characteristics</th>
<th>Healthy Controls (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.7±11.2</td>
</tr>
<tr>
<td>Males: Females</td>
<td>22 (50%):22 (50%)</td>
</tr>
<tr>
<td>Current smoker/ ex-smoker/never smoke</td>
<td>10(22.7%)/2(4.5%)/32 (72.7%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.7±3.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2(4.5%)</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1(0.0%)</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>2(4.5%)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Statins</td>
<td>0(0.0%)</td>
</tr>
</tbody>
</table>
Comparison of demographics between haemodialysis patients and healthy controls in China

Table 3-18 shows the comparison of demographics between the HD patients and Healthy controls in China. The percentages of hypertension (P<0.001), ischaemic heart (P=0.001) and musculoskeletal disease (P=0.002) in the HD patients were significantly higher than those in healthy controls. Furthermore, patients administered more anti-hypertensives (P<0.001) and oral bicarbonate (P=0.001) than healthy controls.
Table 3- 18 Comparison of demographics between the HD patients and Healthy controls in China in the COCO study

<table>
<thead>
<tr>
<th>Demographics characteristics</th>
<th>HD patients (n=40)</th>
<th>Healthy Controls (n=44)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.6±9.4</td>
<td>50.7±11.2</td>
<td>0.344</td>
</tr>
<tr>
<td>Males: Females</td>
<td>22:18</td>
<td>22:22</td>
<td>0.595</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>11/5/24</td>
<td>10/2/32</td>
<td>0.082</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>22.5(20.2-25.0)</td>
<td>23.7±3.0</td>
<td>0.08</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3(7.5%)</td>
<td>0(0.0%)</td>
<td>0.104</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25(62.5%)</td>
<td>2(0.0%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>9 (22.5%)</td>
<td>0(0.0%)</td>
<td>0.001***</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0(0.0%)</td>
<td>0 (0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>2(5.0%)</td>
<td>0(0.0%)</td>
<td>0.499</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>8(20.0%)</td>
<td>0(0.0%)</td>
<td>0.002**</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1(2.5%)</td>
<td>1(2.3%)</td>
<td>0.946</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>33(82.5%)</td>
<td>2(0.0%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>9 (22.5%)</td>
<td>0(0.0%)</td>
<td>0.001***</td>
</tr>
<tr>
<td>Statins</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*P < 0.05 (2-tailed); **P < 0.01 (2-tailed); ***P < 0.001 (2-tailed)
Comparison of demographics between UK and Chinese haemodialysis patients

The comparison of demographics between UK and Chinese HD patients is shown in Table 3-19. The UK HD patients were older (P=0.011) and had higher BMI (P<0.001) than their Chinese counterparts. The percentage of female and dialysis vintage in Chinese HD patients were significantly higher than those of the UK cohorts (all P<0.001). The UK patients had more cases of diabetes (P<0.001) and mental health illness (P=0.022) and administered more statins than Chinese patients. However, more anti-hypertensives were administered in Chinese patients than those of the UK cohorts (P<0.001).
Table 3 - Comparison of demographics in HD patients between UK and China in the COCO study

<table>
<thead>
<tr>
<th>Demographics characteristics</th>
<th>UK HD patients (n=30)</th>
<th>Chinese HD patients (n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.3±13.8</td>
<td>48.6±9.4</td>
<td>0.011*</td>
</tr>
<tr>
<td>Males: Females</td>
<td>24:6</td>
<td>22:18</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>HD vintage (Months)</td>
<td>23.5 (10.0-40.0)</td>
<td>72.0 (48.0-96.0)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Current smoker/ex-smoker/never smoke</td>
<td>1/9/15</td>
<td>11/5/24</td>
<td>0.473</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>26.6 (23.9-29.8)</td>
<td>22.5 (20.2-25.0)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (46.7%)</td>
<td>3 (7.5%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (76.7%)</td>
<td>25 (62.5%)</td>
<td>0.648</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>5 (16.7%)</td>
<td>9 (22.5%)</td>
<td>0.546</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0 (2.5%)</td>
<td>0 (0.0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0 (2.5%)</td>
<td>2 (5.0%)</td>
<td>0.092</td>
</tr>
<tr>
<td>Asthma or COPD</td>
<td>1 (3.3%)</td>
<td>0 (0.0%)</td>
<td>0.190</td>
</tr>
<tr>
<td>Musculoskeletal disease</td>
<td>5 (16.7%)</td>
<td>8 (20.0%)</td>
<td>0.723</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>1 (3.3%)</td>
<td>1 (2.5%)</td>
<td>0.837</td>
</tr>
<tr>
<td>Mental Health Illness</td>
<td>3 (10.0%)</td>
<td>0 (0.0%)</td>
<td>0.022*</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>18 (60.0%)</td>
<td>33 (82.5%)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>1 (3.3%)</td>
<td>0 (0.0%)</td>
<td>0.190</td>
</tr>
<tr>
<td>Oral Bicarbonate</td>
<td>5 (16.7%)</td>
<td>9 (22.5%)</td>
<td>0.546</td>
</tr>
<tr>
<td>Statins</td>
<td>17 (56.7%)</td>
<td>0 (0.0%)</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed); **P< 0.01 (2-tailed); ***P< 0.001 (2-tailed)

3.5 Discussion

The mean age of UK HD patients was 65 years old in the QCKD study, which was conducted with a large sample of HD population. It is in agreement with the finding that 65-74 year old cohorts among the age groups account for the highest proportion of HD prevalence in UK HD patients (UK Renal Registry 2016). The mean ages of 56.3 and 56.8 years old in UK HD patients from the DISH and COCO studies were lower than the average age of the overall UK HD patients. The average age in overall Chinese HD patient was 54.9 years old, which was also similar to the mean age of 52.0 years found in
the QCKD study with large Chinese HD population (Chinese National Renal Data System 2015). Similarly, the mean age of 42.5 and 48.6 years old in Chinese HD patients from the DISH and COCO studies were lower than the average age of the overall Chinese HD patients. Obviously, the mean age of the UK HD patient groups recruited in these three studies were all older than those in Chinese patient groups, which was consistent with the findings in the nation-wide scale reports with UK and Chinese HD patients (UK Renal Registry 2016, Chinese National Renal Data System 2015). More males than females were recruited into these present studies, which was also consistent with the fact that more male HD patients suffer from ESRD found in respective reports (UK Renal Registry 2016, Chinese National Renal Data System 2015).

The mean BMI in the UK HD patient groups from these three studies were all higher than those in Chinese patient groups, which was consistent with a finding that the mean BMI in UK participants aged between 40 and 59 years old were higher than their Chinese counterparts (Zhou, Stamler et al. 2003). Mounting studies reported that high BMI confers better survival (Lowrie, Li et al. 2002, Port, Ashby et al. 2002, Beddhu, Pappas et al. 2003b). Given the relationship between body components, NS and activity (Mak, Ikizler et al. 2011), the difference in BMI between UK and Chinese HD patients may result in the disparity of lifestyle.

Although comorbidities were collected in the studies instead of primary causes of ESRD, it has been found that less Chinese HD patients suffered from diabetes than UK patients. This may corroborate the fact that diabetes is the primary cause in UK HD patients with ESRD but not in Chinese patients (Xie, Chen 2008, Chinese National Renal Data System 2015, United States Renal Data System, USRDS 2017).

Besides the disparity of demographics between UK and Chinese HD patients, the predominant findings in terms of clinical information were lower serum creatinine and higher hemoglobin and hematocrit levels in UK HD patients compared with Chinese HD patients. It indicated that UK HD patients may have worse NS, less muscle mass and anemia than Chinese patients. Better anemia status in UK HD patients compared with Chinese patients is consistent with the finding regarding anaemia in the overall HD patients between the UK and China. However, given the unclear impact of creatinine on HD patients’ lifestyle as a predictor of good NS and muscle mass, further exploration of the association between creatinine, NS and activity is required.
3.6 Conclusion

The age and gender distribution of UK and Chinese HD patients were consistent with those in the overall UK and Chinese HD populations, which may indicate patients involved in the research were good representations of their respective populations. UK HD patients were older and had higher BMI than Chinese HD patients, predicting the lifestyle between UK and Chinese HD patients may be different. Additionally, the difference of clinical parameters between UK and Chinese HD patients may also lead to the disparity of lifestyle behaviors between these two cultural groups.
Chapter 4
Comparison of dietary Intake between UK and Chinese Haemodialysis Patients
4.1 Abstract

Malnutrition is highly prevalent in HD patients with a high risk of systemic inflammation, muscle wasting, poor Quality of Life (QoL) and mortality. A thorough understanding of dietary intake provides insight into Nutritional Status (NS). Diet pattern or habits are closely associated with cultures. The aim of the study was to understand and compare diet intake between UK and Chinese HD patients. Further, the study was aiming to explore the underlying associated factors that lead to the discrepancy of nutritional blood parameters between the two cultural groups. 24-hour diet recall interviews were undertaken with patients in the UK and China during four normal dialysis sessions distributed evenly in two consecutive weeks to explore diet intake for the previous 24 hours on dialysis and non-dialysis days. Demographic and nutritional blood parameters were collected from patients’ medical records. Malnutrition was commonly present in the UK and Chinese HD patients. UK HD patients had better nutrition management in serum iron, phosphate and potassium than Chinese HD patients. Chinese patients need more attention to dietary calcium intake as part of the management of their Chronic Kidney Disease (CKD) associated mineral bone disease. Further exploration of sodium additives as well as dialysate sodium concentration is required for understanding serum sodium. Vitamin C and D deficiency are potentially highly prevalent in the UK and Chinese HD patients. Increasing vitamin intake may improve the deficiency status.

4.2 Background

The assessment of NS of HD patients is a complicated and challenging process (Pifer et al. 2002). Although diet intake is a major predictor of NS and outcome, it has been not frequently determined in previous studies. In order to update previous guidance and develop evidence-base practice guidelines regarding protein requirement for HD patients, the Renal Nutrition Group of the British Dietetic Association reviewed 2931 studies in a systematic review (Naylor et al. 2013). The research proposed that dietary assessments were poor, which was ascribed to the estimates of protein intake deriving from normalised Protein Catabolic Rate (nPCR) and normalised Protein Nitrogen Appearance (nPNA), rather than food intake records as measurements of evaluating NS (Naylor et al. 2013). No other methods of assessing NS but dietary interview or diary can detect in time the change of diet intake before nutritional blood parameters changing (Fouque, Vennegoor et al. 2007). Additionally, dietary interview has more advantages than 3-day
diet diary in obtaining complete record of intake and time consuming (Griffiths et al. 1999).

In 2002, the European Dialysis and Transplantation Nurses Association/European Renal Care Association proposed a European guideline for the nutritional care of adult renal patients, which included a number of dietary recommendations regarding nutritional intake, involving energy, protein, phosphate, potassium, sodium/fluid management, vitamins and minerals (Dietitians Special Interest Group 2002). Nutritional guidelines suggest 35 kcal/kg/d for HD patients who are less than 60 years of age as the recommended daily energy intake, and 30 to 35 kcal/kg/d for individuals aged 60 years or older. Energy expenditure in HD patients is similar to that in healthy population. The recommendations for HD patients are approximately the same comparing with the advice proposed for healthy individuals who are the same age and engaged in mild physical activity in the Recommended Dietary Allowances (RDA) (Veeneman, Kingma et al. 2005, Food and Nutrition Board 1989). The recommended Dietary Protein Intake (DPI) is 1.2 g/kg/d (Kopple 2001). However, increasing studies have shown that energy and protein intake are lower than the recommendation for HD patients (Bossola et al. 2005, De et al. 2006, Burrowes et al. 2005). Additionally, a study with Italian HD patients showed that the dietary intake of trace elements and vitamins were under the recommended values except for copper (Bossola et al. 2014).

It has been suggested that a number of supplements, such as bicarbonate, selenium supplementation and Renal-Specific Oral Nutrition Supplement (RS-ONS) were positively associated with the improvement of NS in HD patients in some studies (de Brito-Ashurst 2009, Salehi et al. 2013, Sezer et al. 2014). However, problems are still present on a wide range of different aspects of HD patients’ NS. HD patients are subject to food restrictions requiring them to limit dietary sodium, phosphate, potassium and fluid intake. Although some studies have demonstrated that restricting these micronutrients can prevent complications such as high blood pressure, fluid overload and reduced myocardial conduction velocity (Inal et al. 2014, Cupisti et al. 2013, Sanghavi et al. 2013), these restrictions contraindicated recommendations for healthy dietary habits (Hollingdale, Sutton & Hart 2008). It has been suggested that dietary restrictions during HD treatment may worsen the medical condition, induced hypoglycaemia and nutritional derangements (Kalantar-Zadeh et al. 2015). It is unclear what the best dietary approach for HD patients is highlighted by the fact that there is a lack of national and international
consensus. In fact, different countries, even different regions in a same country hold different attitudes towards food restriction (Kalantar-Zadeh, Ikizler 2013). Additionally, cultures influence dietary habits and patterns. Dietary intake assessment for HD patients not only provides data to compare with the recommended energy and protein amounts to adjust dietary pattern and habits in different cultural groups, but also is able to evaluate the regulations about food restriction or intradialytic food consumption applied by comparing dietary intake between on dialysis and non-dialysis day.

The aims of this study have previously been described in the number (1) of 1.6 section in Chapter 1. Briefly, the primary aim was to explore and compare HD patients’ nutritional intake, including protein and energy intake, dietary intake of trace elements, minerals and vitamins, and nutritional blood parameters between the UK and China.

4.3 Methods

The data included in this chapter was derived from the DISH study (Chapter 2, section 2.2.1). The detailed methods are described in Chapter 2. Briefly, in this cross-sectional study, 24-hour diet recall interviews were undertaken with HD patients in UK and China during four normal dialysis sessions distributed evenly in two consecutive weeks. Patients were asked to recall food intake for the previous 24 hours on dialysis and non-dialysis days in the interviews. Demographic and nutritional blood parameters were collected from patients’ medical records (Chapter 2, Section 2.3.1).

4.4 Results

4.4.1 Energy and protein intake

The mean age of patients in the UK and China was 56.8 and 42.5 years respectively, so 35 kcal/kg/d was utilised as the reference to assess if patients’ energy intake on dialysis, non-dialysis and an average day were adequate.
Haemodialysis patients’ energy and protein intake in the UK and China

Energy and protein intake on dialysis, non-dialysis and an average day of the UK and Chinese HD patients were all lower the recommended value of 35 kcal/kg/d and 1.2g/kg/d for HD patients. There were no differences in energy or protein intake between dialysis and non-dialysis days in the UK patients. However, Chinese HD patients showed more energy ($Z=-2.00, P=0.045$) and protein ($Z=-1.969, P=0.049$) intake on dialysis days compared to non-dialysis days. HD patients’ energy and protein intake on dialysis, non-dialysis and an average day in the UK and China is shown in Table 4-1.

Table 4-1 HD patients’ energy and protein intake in the UK and China

<table>
<thead>
<tr>
<th></th>
<th>UK HD patients (n=40)</th>
<th>Chinese HD patients (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy intake (Kcal/kg/d)</td>
<td>Protein intake (g/kg/d)</td>
</tr>
<tr>
<td>Dialysis day</td>
<td>26.24±10.95</td>
<td>0.91±0.44</td>
</tr>
<tr>
<td></td>
<td>(17.44-30.88)</td>
<td>(0.74-1.29)</td>
</tr>
<tr>
<td>Non-dialysis day</td>
<td>24.60±9.45</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>(0.66-1.11)</td>
<td></td>
</tr>
<tr>
<td>t/Z</td>
<td>$t=1.393$</td>
<td>$Z=-0.495$</td>
</tr>
<tr>
<td>P value</td>
<td>0.171</td>
<td>0.620</td>
</tr>
<tr>
<td>An average day</td>
<td>25.30±9.42</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>(0.64-1.11)</td>
<td></td>
</tr>
<tr>
<td>daily amount</td>
<td>35</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed).
Comparison of energy and protein intake in haemodialysis patients between UK and China

There was no significant difference in energy and protein intake on dialysis (Z = -0.761, P=0.447), non-dialysis (Z = -1.736, P=0.083) and an average day (Z = -1.554, P=0.120) between two cohorts from the UK and China. The comparison of energy and protein intake on dialysis, non-dialysis and average day in HD patients between the UK and China are shown in Figure 4-1 and Figure 4-2, respectively.

![Comparison of energy intake on dialysis, non-dialysis and average day in HD patients between the UK and China](image)

**Figure 4-1** Comparison of energy intake on dialysis, non-dialysis and average day in HD patients between the UK and China

The red line denotes the recommended energy of 35 Kcal/kg/d for HD patients, * denotes significant difference between dialysis and non-dialysis day within group

Data is presented as median and interquartile range (IQR)

UK HD patients n=40, Chinese HD patients n=43
Figure 4- Comparison of protein intake on dialysis, non-dialysis and average day in HD patients between the UK and China

The red line denotes the recommended protein of 1.2 g/kg/d for HD patients, * denotes significant difference between dialysis and non-dialysis day within group
Data is presented as median and IQR
UK HD patients n=40, Chinese HD patients n=43
4.4.2 Dietary intake of trace elements, minerals and vitamins

Haemodialysis patients’ iron intake in the UK and China

Both the UK and Chinese male patients’ iron intake on dialysis, non-dialysis and an average day were much higher than the recommended value 8mg for HD male patients. However, female patients’ iron intake both in the UK and China were lower than the recommended 15mg for the HD female. There were no significant differences in iron intake for either men or women between dialysis and non-dialysis days, whether in the UK or in China. HD patients’ iron intake in the UK and China is showed in the Table4-2.

Table4-2 HD patients’ iron intake in the UK and China

<table>
<thead>
<tr>
<th></th>
<th>UK HD patients (n=40)</th>
<th>Chinese HD patients (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>iron intake (mg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male (n=23)</td>
<td>Female (n=17)</td>
</tr>
<tr>
<td>Dialysis day</td>
<td>12.26 (8.12-17.46)</td>
<td>7.34 (5.01-8.16)</td>
</tr>
<tr>
<td>Non-dialysis day</td>
<td>10.23 (7.99-14.14)</td>
<td>6.91 (6.20-12.27)</td>
</tr>
<tr>
<td></td>
<td>t/Z</td>
<td></td>
</tr>
<tr>
<td></td>
<td>t=-1.196</td>
<td>t=1.736</td>
</tr>
<tr>
<td></td>
<td>Z=-0.122</td>
<td>Z=-0.796</td>
</tr>
<tr>
<td>P value</td>
<td>0.244</td>
<td>0.102</td>
</tr>
<tr>
<td>An average day</td>
<td>11.19 (8.82-16.01)</td>
<td>6.90 (5.69-10.24)</td>
</tr>
<tr>
<td></td>
<td>t/Z</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Z=0.903</td>
<td>Z=-0.426</td>
</tr>
<tr>
<td>Recommended daily amount</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Comparison of iron intake in haemodialysis patients between the UK and China

There was no significant difference in iron intake on dialysis ($Z=-1.216$, $P=0.231$), non-dialysis ($Z=-1.733$, $P=0.090$) or an average day ($Z=-1.915$, $P=0.055$) in male HD patients between two cultures. However, Chinese female patients had significantly higher iron intake than UK female patients on dialysis ($Z=-4.022$, $P<0.001$), non-dialysis ($Z=-2.549$, $P=0.011$) and average day ($Z=-3.370$, $P=0.001$).

The comparison of iron intake on dialysis, non-dialysis and average day in male and female HD patients between the UK and China are showed in Figure4-3 and Figure4-4, respectively.

![Figure4-3](image)

**Figure4-3** Comparison of iron intake on dialysis, non-dialysis and average day in male HD patients between the UK and China

The red line denotes the recommended iron of 8mg for male HD patients;
Data is presented as median and IQR;
UK male HD patients n=23, Chinese male HD patients n=21
Comparison of iron intake on dialysis, non-dialysis and average day in female HD patients between the UK and China

The red line denotes the recommended iron of 15mg for female HD patients,

†Denoted significant difference between UK and Chinese HD patients

Data is presented as median and IQR;

UK female HD patients n=17, Chinese female HD patients n=22
Calcium intake and serum calcium between UK and Chinese haemodialysis patients

Calcium intake

The median calcium intake in the UK HD patients was within the recommended amount of 500-800 mg/d. However, Chinese HD patients’ median calcium intake was below the recommended amount. There was no significant difference in calcium intake between dialysis and non-dialysis days in the UK HD patients (Z=-1.089, \( P =0.276 \)). Calcium intake on non-dialysis day was significantly higher than on dialysis day (Z=-2.801, \( P=0.005 \)) in Chinese patients (Table4- 3).

Table 4: HD patients' calcium intake in the UK and China

<table>
<thead>
<tr>
<th>Mineral intake</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>( P )</th>
<th>Average day</th>
<th>Recommended amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/d)</td>
<td>UK</td>
<td>665.0 (445.4-884.9)</td>
<td>609.2 (491.1-778.4)</td>
<td>.276</td>
<td>618.1 (520.1-777.2)</td>
<td>500-800</td>
</tr>
<tr>
<td></td>
<td>Chinese</td>
<td>300.5 (204.5-462)</td>
<td>397.5 (231.5-596.5)</td>
<td>.005**</td>
<td>360.2 (241.1-552.8)</td>
<td></td>
</tr>
</tbody>
</table>

**\( P< 0.01 \) (2-tailed).
Comparison of calcium intake between UK and Chinese haemodialysis patients

UK HD patients’ calcium consumption was significantly higher than Chinese HD cohorts (Z=-5.350, \(P<0.001\) on dialysis day; \(Z=-3.545, P<0.001\) on non-dialysis day; \(Z=-4.684, P<0.001\) on an average day). The comparison of calcium intake on dialysis, non-dialysis and an average day in HD patients between the UK and China is showed in Figure 4-5.

![Graph showing calcium intake comparison](image)

**Figure 4-5** Comparison of calcium intake on dialysis, non-dialysis and average day in HD patients between the UK and China

The red line denotes the recommended calcium intake with 500-800mg for HD patients, †Denoted significant difference between the UK and Chinese HD patients

* Denoted significant difference between dialysis and non-dialysis day within group.

Data is presented as median and IQR; UK HD patients n=40, Chinese HD patients n=43
Comparison of serum calcium between UK and Chinese haemodialysis patients

Both UK (2.37±0.10mmol/L) and Chinese HD patients’ mean serum calcium (2.31±0.25mmol/L) were within the normal range of 2.2-2.5 mmol/L. There was no significant difference in serum calcium concentration in HD patients between the UK and China (t=1.424, \( P=0.160 \)). The comparison of serum calcium concentration between UK and Chinese HD patients is demonstrated in Figure4- 6.

![Comparison of serum calcium concentration in HD patient from UK and China](image)

The red line denotes the normal range of serum calcium with 2.2-2.5 mmol/L for HD patients. Data is presented as mean± SD.
UK HD patients n=40, Chinese HD patients n=43
Phosphate intake and serum phosphorus between UK and Chinese haemodialysis patients

**Phosphate intake**

The median phosphate intake in the UK HD patients was within the recommended amount of 800-1000 mg/d. Chinese HD patients’ median phosphate intake was below the recommendation (Figure 4-7). There was no significant difference in phosphate intake between dialysis and non-dialysis days both in the UK (Z=-0.403, P=0.687) and Chinese HD patients (Z=-0.042, P=0.966) (Table 4-4).

**Table 4-4** HD patients’ phosphate intake in the UK and China

<table>
<thead>
<tr>
<th>Mineral intake</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>P value</th>
<th>Average day</th>
<th>Recommended daily amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphate (mg/d)</td>
<td>UK (n=40)</td>
<td>909.15</td>
<td>900.09</td>
<td>0.687</td>
<td>927.45</td>
<td>800-1000</td>
</tr>
<tr>
<td></td>
<td>Chinese (n=43)</td>
<td>719.5</td>
<td>734.99</td>
<td>0.966</td>
<td>697.14</td>
<td>(541.7-975.3)</td>
</tr>
</tbody>
</table>
Comparison of phosphate intake between UK and Chinese haemodialysis patients

Consumption of phosphate in the UK HD patients was significantly higher than those in Chinese HD cohorts on dialysis days ($Z=-2.06$, $P=0.039$), non-dialysis days ($Z=-2.889$, $P=0.004$) and an average day ($Z=-2.679$, $P=0.007$). The comparison of phosphate intake on dialysis, non-dialysis and an average day between UK and Chinese HD patients is showed in Figure 4-7.

![Comparison of phosphorus intake on dialysis, non-dialysis and average day in HD patients between the UK and China](image)

Figure 4-7 Comparison of phosphorus intake on dialysis, non-dialysis and average day in HD patients between the UK and China
The red line denotes the recommended phosphorus intake of 800-1000mg for HD patients;
†Denoted significant difference between the UK and Chinese HD patients;
Data is presented as median and IQR;
UK HD patients n=40, Chinese HD patients n=43
Comparison of serum phosphorus between UK and Chinese haemodialysis patients

The mean serum phosphate in the UK HD patients (1.60±0.44mmol/L) was within the normal range of 1.1-1.7mmol/L. Chinese HD patients’ mean serum phosphate (2.11±0.53mmol/L) was higher than the normal range. Serum phosphorus concentration (t=-4.739, $P<0.001$) in the UK HD patients were significantly lower than that in Chinese HD cohorts. The comparison of serum phosphorus concentration between UK and Chinese HD patients is demonstrated in Figure 4-8.

![Figure 4-8](image)

**Figure 4-8** Comparison of serum phosphorus concentration in HD patient between the UK and China

The red line denotes the normal range of serum phosphorus with 1.1-1.7 mmol/L for HD patients; † Denoted significant difference between the UK and Chinese HD patients; Data is presented as mean±SD; UK HD patients n=40, Chinese HD patients n=43.
Potassium intake and serum potassium between UK and Chinese haemodialysis patients

Potassium intake

The mean or median potassium intake in the UK and Chinese HD patients on dialysis, non-dialysis and an average day were more than the recommended daily intake of 800-1000mg (Figure4- 9). There was no significant difference in potassium intake between dialysis and non-dialysis days both in the UK (t=1.037, \( P=0.306 \)) and Chinese HD patients (\( Z=-1.618, \ P=0.106 \)) (Table4- 5).

**Table4- SHD patients' potassium intake in the UK and China**

<table>
<thead>
<tr>
<th>Mineral intake (mg/d)</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non- HD day</th>
<th>P value</th>
<th>Average day</th>
<th>Recommended daily amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>UK (n=40)</td>
<td>1996.78± 731.03</td>
<td>2120.39± 736.07</td>
<td>0.306</td>
<td>2067.41± 632.02</td>
<td>800-1000</td>
</tr>
<tr>
<td></td>
<td>Chinese (n=43)</td>
<td>1202.70± 510.41</td>
<td>1176.5 (878-1802.5)</td>
<td>0.106</td>
<td>1158.57 (859.57-1720.57)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of potassium intake between UK and Chinese haemodialysis patients

Potassium intake in the UK HD patients was significantly higher than that in Chinese patients on dialysis days ($Z=-5.698, P<0.001$), non-dialysis days ($Z=-4.347, P<0.001$) and an average day ($Z=-4.848, P<0.001$). The comparison of potassium intake on dialysis, non-dialysis and average day between UK and Chinese HD patients is showed in Figure 4-9.

![Comparison of potassium intake on dialysis, non-dialysis and average day in HD patients between the UK and China](image)

**Figure 4-9** Comparison of potassium intake on dialysis, non-dialysis and average day in HD patients between the UK and China

The red line denotes the recommended potassium intake with 800-1000mg for HD patients; 'Denoted significant difference between the UK and Chinese HD patients;

Data is presented as median and IQR;

UK HD patients $n=40$, Chinese HD patients $n=43$. 
Serum potassium between the UK and Chinese haemodialysis patients

The serum potassium (4.43±0.79mEq/L) in the UK HD patients was within the normal range of 3.5-5.5mEq/L. Chinese HD patients’ serum potassium (5.04±0.64mEq/L) was also within the normal range. The mean serum potassium concentration in the UK HD patients was significantly lower than that in Chinese HD cohorts (t=-3.844, P<0.001). The comparison of serum potassium concentration is demonstrated in Figure 4.

![Figure 4](image_url)

Figure 4. Comparison of serum potassium concentration in HD patient from the UK and China

The red line denotes the normal range of serum potassium with 3.5-5.5mEq/L for HD patients;
†Denoted significant difference between the UK and Chinese HD patients;
Data is presented as mean± SD;
UK HD patients n=40, Chinese HD patients n=43
Sodium intake and serum sodium between UK and Chinese haemodialysis patients

Sodium intake

The median sodium intake in the UK HD patients on the non-dialysis and an average day were within the recommended daily sodium intake of 2000-2300mg. The median sodium intake on the dialysis day was below the recommendation. Chinese HD patients' sodium intake on dialysis, non-dialysis and an average day were all below the recommended amount (Figure 4-11). There was no significant difference in sodium intake between dialysis and non-dialysis days with HD patients in the UK (Z=−0.551, \( P=0.582 \)) and China (Z=−0.966, \( P=0.334 \)) (Table 4-6).

Table 4-6 HD patients’ sodium intake in the UK and China

<table>
<thead>
<tr>
<th>Mineral intake (mg/d)</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non- HD day</th>
<th>( P ) value</th>
<th>Average day</th>
<th>Recommended daily amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>UK (n=40)</td>
<td>1951.03 (1347.8-2427.1)</td>
<td>2005.76 (1539.4-2790.5)</td>
<td>0.582</td>
<td>2078.52 (1482.8-2599.8)</td>
<td>2000-2300</td>
</tr>
<tr>
<td></td>
<td>Chinese (n=43)</td>
<td>553.55 (383.8-836.1)</td>
<td>471.25 (281.4-751.9)</td>
<td>0.334</td>
<td>563.34 (368.5-676.6)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of sodium intake between UK and Chinese haemodialysis patients

Consumption of sodium in the UK HD patients were significantly higher than that of Chinese patients on their dialysis days ($Z=-6.534, P<0.001$), non-dialysis days ($Z=-6.744, P<0.001$) and an average day ($Z=-6.963, P<0.001$). The comparison of sodium intake on dialysis, non-dialysis and an average day between UK and Chinese HD patients is showed in Figure4- 11.

![Figure4- 11Comparison of sodium intake on dialysis, non-dialysis and average day in HD patients between the UK and China](image_url)

*The red line denotes the recommended sodium intake with 2000-2300mg for HD patients,*

†*Denoted significant difference between the UK and Chinese HD patients*

Data is presented as median and IQR

UK HD patients n=40, Chinese HD patients n=43
Comparison of serum sodium between UK and Chinese haemodialysis patients

Both median serum sodium concentration in the UK (135.0 [134.0-137.0]mEq/L) and Chinese HD patients (136.0 [135.0-139.0]mEq/L) were with the normal range of 135-145mEq/L. The median serum sodium concentration in the UK HD patients was significantly lower than that in Chinese patients ($Z=−2.288$, $P=0.022$). The comparison of serum sodium concentration between UK and Chinese HD patients is demonstrated in Figure 4-12.

![Figure 4-12](image)

**Figure 4-12**: Comparison of serum sodium concentration in HD patient from the UK and China

The red line denotes the normal range of serum sodium with 135-145mEq/L for HD patients; †Denoted significant difference between the UK and Chinese HD patients; Data is presented as median and IQR; UK HD patients $n=40$, Chinese HD patients $n=43$
Vitamin C intake between UK and Chinese haemodialysis patients

Vitamin C intake

Both median vitamin C intake in the UK and Chinese HD patients were lower than the recommended vitamin C intake of 75-90mg on dialysis, non-dialysis and an average day (Figure4- 13). There was no significant difference in vitamin C intake between dialysis and non-dialysis day with HD patients in the UK ($Z=-4.03, P=0.687$) and China ($Z=-1.482, P=0.138$) (Table4- 7).

Table4- 7HD patients' vitamin C intake in the UK and China

<table>
<thead>
<tr>
<th>Vitamin intake</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>P value</th>
<th>Average day</th>
<th>Recommended daily amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C (mg/d)</td>
<td>UK (n=40)</td>
<td>28.04 (16.9-66.0)</td>
<td>30.21 (17.2-94.9)</td>
<td>0.687</td>
<td>39.28 (20.6-72.0)</td>
<td>75-90</td>
</tr>
<tr>
<td></td>
<td>China (n=43)</td>
<td>57.75 (31.3-77.5)</td>
<td>60.55 (37.3-86.5)</td>
<td>0.138</td>
<td>63.69 (40.6-82.6)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of vitamin C intake between UK and Chinese haemodialysis patients

UK HD patients had significantly less vitamin C intake than Chinese patients on dialysis (Z=-2.205, \( P=0.027 \)), non-dialysis (Z=-1.996, \( P=0.046 \)), and an average day (Z=-2.260, \( P=0.024 \)). The comparison of vitamin C intake on dialysis, non-dialysis and average day between UK and Chinese HD patients is showed in Figure 4-13.

![Comparison of vitamin C intake on dialysis, non-dialysis and average day in HD patients between the UK and China](image)

- The red line denotes the recommended 75-90mg of vitamin C for HD patients,
- Denoted significant difference between the UK and Chinese HD patients
- Data is presented as median and IQR.
- UK HD patients n=40, Chinese HD patients n=43
Vitamin D intake between UK and Chinese haemodialysis patients

**Vitamin D intake**

UK and Chinese HD patients consumed much less vitamin D on dialysis, non-dialysis and average day than the recommended daily vitamin D intake of 15 µg (Figure4-14). There was no significant difference in vitamin D intake between dialysis and non-dialysis day with HD patients in the UK (Z=-0.167, P=0.868) and China (Z=-1.149, P=0.250) (Table4-8).

**Table4-8 HD patients’ vitamin C intake in the UK and China**

<table>
<thead>
<tr>
<th>Vitamin intake</th>
<th>HD patients</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>P value</th>
<th>Average day</th>
<th>Recommended daily amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D (mg/d)</td>
<td>UK (n=40)</td>
<td>1.85 (0.8-4.4)</td>
<td>2.03 (0.9-3.2)</td>
<td>0.868</td>
<td>2.12 (1.0-3.9)</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Chinese (n=43)</td>
<td>1.2 (0.3-3.6)</td>
<td>1.6 (1.1-3.0)</td>
<td>0.250</td>
<td>1.94 (1.0-3.2)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of vitamin D intake between UK and Chinese haemodialysis patients

There was no significant difference in vitamin D intake between two cultural HD patients on dialysis ($Z=-1.368, P=0.171$), non-dialysis ($Z=-0.360, P=0.719$) and an average day ($Z=-0.164, P=0.870$). The comparison of vitamin D intake on dialysis, non-dialysis and an average day between UK and Chinese HD patients is showed in Figure 4.

Figure 4

Comparison of vitamin D intake on dialysis, non-dialysis and average day in HD patients between the UK and China

The recommended vitamin D daily amount for HD patients is 15µg.
Data is presented as median and IQR:
UK HD patients n=40, Chinese HD patients n=43
4.5 Discussion

4.5.1 Dietary insufficiency in UK and Chinese haemodialysis patients

Inadequate energy and protein intake and low serum cholesterol levels (3.8±1.1mmol/L) in this study indicated what is already published about the high prevalence of malnutrition in UK dialysis patients (Huidobro, Velasco & Rojas 2001, Combe et al. 2004). What is less clear is the role of Body Mass Index (BMI), which was high in this group (26.6kg/m²) and commonly viewed as a predictor of good NS when BMI≥23 kg/m²(Fouque et al. 2008, Fouque et al. 2007). As described above, it is not clear which component of body composition confers survival benefits upon HD patients or the best way to determine the correlation between BMI and NS. Assessment of body composition may be a more efficient way to evaluate NS for HD patients compared to BMI (Valtuille et al. 2015). In an Argentine study involving 9 HD units, it was reported that BMI was a reliable measure of Fat Mass (FM) for HD patients but not of muscle mass. It is also worth noting that malnutrition can still be present in HD patients, irrespective of BMI (Valtuille et al. 2015), which is compatible with both the dietary and anthropometric data (BMI ≥23kg/m²) from this study.

Albumin and cholesterol concentrations were not analysed for Chinese HD patients’ due to too much missing data. However, the lower energy and protein intake compared to the recommended amount still confirmed that malnutrition was commonly present in Chinese HD patients. Additionally, the BMI (21.4kg/m²) in Chinese HD patients was lower than the recommended level of ≥23kg/m² by the European Best Practice Guidelines (EBPG)(Fouque et al. 2007a) and may corroborate the evidence of malnutrition present in this study. The high prevalence of malnutrition in the UK and Chinese HD patients were consistent with the findings showed in previous studies (Bossola et al. 2005, Lacquaniti et al. 2009, Bazanelli et al. 2006). Various causes contribute to malnutrition in HD patients, such as inadequate dietary intake (Locatelli et al. 2002a), metabolic disorders (Bossola et al. 2005) and the dialysis procedure itself (Locatelli et al. 2002b). This study confirmed that insufficient energy and protein intake may result in malnutrition within the HD population both in the UK and China.

The dietary intake of Chinese HD patients consisted of low consumption of meat, seafood, dairy produce and fruit, compared with UK HD patients. Although more UK HD patients follow a vegetarian diet, the consumption of vegetables was similar between the two
populations. These different dietary habits and patterns may have contributed to the differences in nutritional intake and blood parameters observed between the two groups.

4.5.2 Provision of food during haemodialysis

Active therapeutic interventions, including intradialytic parenteral nutrition, oral nutritional supplementation, and provision of meals during HD have been shown to improve serum albumin and life expectancy (Kalantar-Zadeh et al. 2003, Ikizler 2013, Pupim et al. 2006, Pupim, Cuppari & Ikizler 2006). Based on the information collected during the study, the dialysis units in both the UK and China supplied patients with food during dialysis sessions. In the UK, the patients were provided snacks including biscuits and drinks. In China, the unit provided a lunch including rice, meat and vegetables for patients in the morning shift while snacks involving two eggs and one stuffed bun were provided for patients in the midday and evening shifts. Although energy and protein intake on dialysis day in Chinese HD patients were still lower than the recommended amount (Fouque et al. 2007), it was significantly higher than that on non-dialysis day. The finding was inconsistent with the result obtained from the HEMO study (Burrowes et al. 2003). In this cross-sectional study involving 15 clinical centres across the U.S., it was reported that dietary energy and protein intake were lower on dialysis days than on non-dialysis days. While monitoring and interventions were suggested for patients with poor appetite, counselling to increase the consumption of energy and protein, especially on HD days was of importance for HD patients. Intra-dialytic food provision with Chinese HD patients in this DISH study may provide convincing evidence to improve energy and protein intake on dialysis days for other countries, including the UK. More emphasis should be placed on NS for HD patients as well as appropriate health education reminding patients to consume adequate energy and protein (Ford et al. 2004) in both cultural groups. Meanwhile, in order to keep the balance of diet restriction and adequate nutrition intake (Burrowes et al. 2003), it is necessary for professional healthcare providers to provide counselling along with intradialytic nutrition.

4.5.3 Iron intake and serum iron in the UK and Chinese haemodialysis patients

The mean iron intake in the UK (12.4mg) and Chinese male HD patients (16.0mg) exceeded the recommended amount (8mg). Conversely, female patients in the UK (6.9mg) and China (13.3mg) had lower iron intake than the recommendation (15mg). While there
was no difference in iron intake between UK and Chinese male patients, the iron intake of female HD patients in the UK was significantly lower than that in China. The specific reasons of iron shortage within HD patients found in previous studies are possibly ascribed to the repeated loss of blood during dialysis sessions (Coyne et al. 2007), low bioavailability of iron using oral supplementation due to the parallel administration of drugs binding phosphate salts (Alleyne, Horne & Miller 2008) and lack of adequate iron intake (Szpanowska-Wohn, Kolarzyk & Chowaniec 2008). This study adds to the evidence from previously published data, that insufficient iron intake among female HD patients is a contributing factor of underlying poor iron status.

The comparison of serum ferritin between UK and Chinese HD patients was unable to be performed due to the missing data in Chinese patients. As a result, haemoglobin (Hgb) was used to estimate iron status for patients (Alvarez-Ossorio et al. 2000). UK HD patients’ Hgb level was significantly higher than Chinese patients. It was consistent with the discrepancy of Hgb in the UK and Chinese HD patients on a nation-wide scale (UK Renal Registry 2016, Chinese National Renal Data System 2015). Meanwhile, the disparity of Hgb between these two cultural groups may reveal that adverse serum iron status was present among Chinese HD patients in the study. A systematic analysis of anaemia burden concluded insufficient iron intake and diets containing poorly bioavailable iron sources were the causes of anaemia in low-income countries (Kassebaum et al. 2013), which was in agreement with the finding that Chinese female patients’ iron intake was lower compared to the recommended amount. However, it is found that UK HD patients had less iron intake than their Chinese HD counterparts, especially, in female HD patients. Interestingly, the better iron status in UK patients was shown than in Chinese patients. The finding indicated that diet is not the factor which mostly influence iron status in HD patients. It has been documented that intravenous iron that is expensive but has the advantage of much higher bioavailability than oral iron is commonly used in Western countries, but seldom used in Chinese HD patients (Li, Wang 2008). Additionally, better control of blood loss during HD and maintaining bioavailability of oral iron supplementation are potential factors as well. Chinese HD patients may need more attention to the management of iron supplementation and blood loss during HD comparing to dietary iron intake than UK HD patients. However, it is worth noting that iron deficiency is not the only cause of anaemia in patients with HD hence Hb level is a far less accurate way to assess iron status in CKD, i.e. Anaemia of
chronic diseases was the most frequent anaemia (45%) in patients with HD (Al-Rubaie, Hasan & Al-Rubay 2016).

4.5.4 Calcium intake and serum calcium in the UK and Chinese haemodialysis patients

The mean daily calcium intake in UK HD patients was within the recommended amount. Chinese patients had lower calcium intake than the recommendation. The amount of calcium contained within prescribed phosphate binders was not collected in this study, making it hard to tell whether it is wholly dietary calcium intake or intake combined with calcium-based phosphate binder that contributed to the serum calcium levels in both cultures. Prescribed medications may be one factor contributing to similar serum calcium concentrations between UK and Chinese HD patients. This finding may confirm that serum calcium is not a reliable predictor of calcium intake (Byrne et al. 2009). Despite this, UK HD patients’ dietary calcium intake was significantly higher than Chinese patients. The INTERMAP study found that calcium intake in Asian patients was lower than Western populations (Zhou et al. 2003). Calcium intake in Chinese males and females was lower than those in Western countries (US and UK) as well as other Asian populations (e.g. Japan) (Zhou et al. 2003). The result indicated that low calcium consumption in Chinese population might be associated with the development of adverse blood pressure levels and high risk of stroke (Zhou et al. 2003). Consistent with the finding from the INTERMAP study that low calcium intake is present in Chinese HD patients, Chinese HD patients may require reasonable intervention regarding the change of the dietary pattern pointing to more calcium intake. Moreover, intradialytic food provision is probably required for Chinese HD patients to be counselled and adjusted to improve the low calcium intake.

Although serum calcium levels in two groups were within the normal range and no significant difference between two cultural groups, 15(34.9%) Chinese HD patients had hypocalcaemia (<2.2 mmol/l) and none of UK HD patients suffered from it. Additionally, the percent of UK patients who were in normal range of serum calcium was up to 87.2%, whilst there were only 20 (46.5%) of Chinese patients who had normal calcium level. The result corroborated the evidence regarding the distribution of hypocalcaemia in the overall UK and Chinese HD patients with 10.6% comparing to 36.0% (UK Renal Registry 2016, Chinese National Renal Data System 2015). It may indicate the more
potential risk of mortality in Chinese HD patients than their UK counterparts. It is noteworthy that low serum calcium in HD patients is ascribed to a number of factors including reduced renal reabsorption of calcium and the inability of the kidneys to activate vitamin D (Peacock 2010). Besides the structured approach of increasing dietary calcium intake, correction of low calcium should include active vitamin D supplementation as well as possible adjustments to the dialysate calcium concentration.

4.5.5 Phosphate intake and serum phosphate in the UK and Chinese haemodialysis patients

Neither UK nor Chinese HD patients had excessive phosphate intake when compared to the recommended daily amount. However, an interesting finding regarding the comparison of phosphate intake and serum phosphate concentration was present in the study. Although protein intake was comparable between populations, UK patients reported higher phosphate intake on dialysis, non-dialysis and average day than their Chinese counterparts. Despite higher dietary intake and BMI, serum phosphate levels were lower in UK patients compared to those in China. This is consistent with serum phosphate concentration distribution in the overall UK and Chinese HD patients, which showed fewer patients with a serum phosphate above the standard in the UK HD patients than their Chinese counterparts (UK Renal Registry 2016, Chinese National Renal Data System 2015). There was no difference in the percentage of patients’ prescribed phosphate binders between two groups (UK, n%=20% [8/40]; China n%=21% [9/43]). The results above suggested that strategies to improve compliance with medications and increasing dialysis phosphate removal would have a greater impact on hyperphosphataemia than increased nutritional support in Chinese HD patients.

4.5.6 Potassium intake and serum potassium in the UK and Chinese haemodialysis patients

Potassium intake was higher than the recommended value for both UK and Chinese HD patients. The increased intake may translate to high serum levels of potassium, which may lead to a variety of comorbidities and cardiovascular mortality (Noori et al., 2010, Pun et al., 2011). Appropriate restriction of potassium-rich food and nutrition counselling are required for these two populations. Despite higher potassium intake, UK patients had lower serum potassium concentrations than Chinese patients. Besides the restriction of
potassium intake in both two cultural groups, the findings suggested that better medication management may be required to prevent hyperkalaemia than stronger dietary restriction in Chinese HD patients. Medications include Angiotensin-Converting Enzyme Inhibitors (ACEIs), potassium sparing diuretics, non-selective beta blockers, Non-steroidal anti-inflammatory drugs (NSAIDs), and unfractionate heparin, which all contribute to hyperkalaemia in HD patients (El-Sharkawy, Khedr et al. 2009). Additionally, improving compliance or vascular access problems to increase dialysis efficacy is an efficient strategy to prevent hyperkalaemia as well (El-Sharkawy, Khedr et al. 2009).

4.5.7 Sodium intake and serum sodium in the UK and Chinese haemodialysis patients

The median sodium intake in the UK HD patients was within the recommended value. The median sodium intake in Chinese patients was markedly below the recommendation. The study failed to collect the sodium additives data in both two cultural groups. However, it assumed that sodium additives intake data in Chinese HD patients would be greater than that in the UK patients (Anderson et al. 2010). Therefore, the estimated sodium intake with additives may be opposed to the measured intake. In the Dialysis Outcomes and Practice Patterns Study (DOPPS), higher mortality risk appeared in HD patients with mean serum sodium levels <140mEq/l with any groups of dialysate sodium levels compared to patients with mean serum sodium levels ≥ 140mEq/l and a dialysate sodium level of 140mEq/l (Hecking et al. 2012). Thus, both UK and Chinese HD patients with serum sodium concentration of 135.0mEq/l and 136.0mEq/l in the study had a potentially high risk of mortality. It has been reported that HD patients with mean serum sodium <137mEq/l, compared with dialysate sodium prescriptions of 140mEq/l, patients simultaneously with >140mEq/l of dialysate sodium concentration had a lower mortality risk (Hecking et al. 2012). The study failed to collect HD patients’ dialysate sodium level in the UK and China. Therefore, it is hard to compare the possible survival between UK and Chinese HD patients according to their serum sodium concentrations. The assessment of sodium intake combined with dialysate sodium concentration may be imperative to better understand the correlation between serum sodium and mortality.
4.5.8 Vitamin C in the UK and Chinese haemodialysis patients

The median vitamin C intakes in both UK and Chinese HD patients were below the recommended amount. It may in part explain the dietary restriction of vegetables and fruits recommended for HD patients (Deicher, Hörl 2003) and the high prevalence of vitamin C deficiency in HD patients all over the world (Fumeron et al. 2005, Deicher et al. 2005, Richter et al. 2008). As well as loss of the vitamin C during HD sessions, vitamin C deficiency in HD patients is primarily ascribed to food restriction of vitamin C-rich foods to avoid hyperkalaemia (Deicher, Hörl 2003). In the study, the median vitamin C intake in Chinese patients was significantly higher than that in UK patients. Interestingly, Chinese patients had lower potassium intake than their UK counterparts. A thorough understanding of dietary pattern in Chinese HD patients is noteworthy to be explored and recommended for UK HD patients in order to balance potassium restriction and adequate vitamin C intake.

4.5.9 Vitamin D in the UK and Chinese haemodialysis patients

The median vitamin D intakes in both UK and Chinese HD patients were much lower than the recommended value. The vitamin D intake in almost all the HD patients in the study was below the recommended dietary allowance (RDA) of 600IU/ day by the Institute of Medicine (IOM) (Ross et al. 2011). Insufficient vitamin D intake could lead to serum vitamin D deficiency, which was corroborated by the findings that decreased consumption of vitamin D-rich foods contribute to the high prevalence of vitamin D deficiency and insufficiency among HD patients (Krassilnikova et al. 2014). The high prevalence of vitamin D deficiency in HD patients is due to renal dysfunction which is associated with impaired conversion of 25(OH)D to 1,25(OH)2D in HD patients. Meanwhile, vitamin D deficiency is also associated with hyperparathyroidism, low serum calcium and obesity (Jean et al. 2008), which are not unusually common in HD patients. However, as we all know, the provitamin D which can convert to vitamin D or 1,25(OH)2D is initially synthesized in the skin or acquired from the diet. Therefore, insufficient sunlight exposure (Clayton, Singer 2009, Korkor, Bretzmann & Eastwood 2009) and diet rich in vitamin D intake (Korkor, Bretzmann & Eastwood 2009) may be the primary causes of vitamin D insufficiency or deficiency. The data in the study indicated dietary insufficiency as one contributing factor to vitamin D deficiency among HD patients.
It has been shown that vitamin D deficiency results in a series of adverse complications, including CVD (Wang et al. 2008), osteoporosis and fracture (Jean, Charra & Chazot 2008), consequently, leads to a high mortality risk in HD patients (Grandi, Breitling & Brenner 2010, Mitri, Muraru & Pittas 2011, Souberbielle et al. 2010, Wolf et al. 2007). Proper intervention is imperative to correct vitamin D deficiency for HD patients. It has been reported that there is strong association between vitamin D level and active vitamin D therapy (therapy with activated vitamin D) in HD patients, which significantly increase survival rate (Wolf et al. 2007). In another study, HD patients with serum 25(OH) D level <75mmol/L were administered with oral 25(OH) D3. It was found that oral vitamin D supplementation corrected most vitamin D deficiency or insufficiency in HD patients, which improved bone turnover, serum albumin, calcium and phosphate levels without any evident toxicity (Souberbielle et al. 2010). Meanwhile, a better understanding of vitamin D status with nutrition counselling to promote vitamin D intake, especially routine clinical assessment of vitamin D in China is required for HD patients.

4.5.10 Limitations

Whilst 24-hour diet recall is recommended for both well-nourished and malnourished HD patients as a routine assessment tool due to its reliable and efficient construct by European best practice guidelines (EBPG) (Fouque, Vennegoor et al. 2007), it is not without its flaws. It may underestimate actual intake with elderly patients who suffer from memory or cognition impairment (Liu, Coresh et al. 2004, Woodrow, Oldroyd et al. 1996), which are common in HD patients (Terekeci, Kucukardali et al. 2010). However, the interview including asking patients to recall their diet 5 times may partly counteract the underestimation of diet intake. Moreover, convenience sampling is easy to carry out with relatively smaller cost and time compared with probability sampling techniques. However, the convenience sample is unable to be representative of the population being studied due to the failure of being chosen at random (Etikan, Musa et al. 2016). In this study, the recruitment of 40 UK and 43 Chinese HD patients was a pragmatically selected number chosen to facilitate this exploratory feasibility trial. Additionally, missing data such as serum ferritin in Chinese patients, sodium additives serum Vitamin C and Din both two groups present in this study is another limitation as well.
4.6 Conclusion

Malnutrition was prevalent in both the UK and Chinese HD patients. Food provision during dialysis session has the potential to improve energy and protein intake for HD patients. The management of intravenous iron preparations and blood loss during HD session in Chinese HD patients may require more attention than those in their UK counterparts to improve serum iron status. Chinese patients need closer attention paying to their dietary calcium intake as part of the management of their CKD associated mineral bone disease. The management of hyperphosphatemia in Chinese dialysis patients should concentrate on more targeted prescription of phosphate binding medications management and dialysis phosphate removal, rather than dietary restriction. More attention to strengthen medication management and increase dialysis efficacy may be required to prevent hyperkalaemia than dietary restriction in Chinese HD patients. In order to gain better understanding of serum sodium in HD patients, sodium intake including additives combined with dialysate sodium concentration are required. Insufficient vitamin C and D intakes were common in both UK and Chinese HD patients, which may lead to underlying vitamin C and D deficiency. The diet pattern balancing potassium restriction and adequate vitamin C intake in Chinese HD patients could be recommended to UK patients. Proper intervention and vitamin intake counselling may enhance vitamin C and D intake and improve deficiency status.
Chapter 5

Validity of the Duke Activity Status Index (DASI) and General Practice Physical Activity Questionnaire and (GPPAQ) Walking Pace Question
5.1 Abstract

In order to determine the validity of the Duke Activity Status Index (DASI) and General Practice Physical Activity Questionnaire (GPPAQ) walking pace question in assessing physical function and gait speed in HD patients, these two questionnaires were validated against the Shuttle Walking Test (SWT) and gait speed test with the UK and Chinese HD patients, respectively. Significant positive correlation between the DASI and Incremental Shuttle Walking Test (ISWT) were shown in the two cultural groups. All categories of the measured gait speed classified by the GPPAQ walking criteria showed significant overlap of results. However, there was a significant difference between the mean gait speed of the “slow”, “steady” and “brisk” GPPAQ walking pace categories in the UK HD patients, in particular, the question was capable of identifying patients with slow pace. Although there was no significant difference between the mean gait speed of the four GPPAQ categories (P=0.107), only 1 patient reporting walking pace as “slow” exceeded the GPPAQ walking pace cut off of slow gait speed in Chinese patients. In conclusion, the DASI was valid for providing physical function measurement with HD patients. The GPPAQ walking question was potentially valuable for evaluating gait speed in the UK HD patients.

5.2 Background

Credible and applicable evidence used in research must be assessed and applied by researchers whenever possible if their work is to gain acceptance by others (Shortell, Rundall & Hsu 2007, Swan et al. 2012). Reliability and validity are important concepts in research. Reliability refers to the repeatability or reproducibility of a survey instrument’s data. It mainly composes test-retest, alternate-form and internal consistency. Of these, test-retest is the most commonly utilized indicator of survey instrument reliability. Test-retest is used for evaluating how reproducible results are by having a group of participants complete a survey at two different points in time (Litwin, Fink 1995). Validity refers to the credibility of a survey instrument, namely, it is used to evaluate if the instrument measures what it claims to measure (Litwin, Fink 1995, Pavlov et al. 2013). It consists of the content and criterion validity. The content validity covers face and construct validity, which involves whether the instrument measures at face value what it claims to and the degree to which a test captures a specific theoretical construct, respectively. However, it has been reported that the face validity only assesses the
judgement of responders rather than what the survey really measures (Pavlov et al. 2013). Additionally, a combination of different methods is required for achieving the construct of an instrument (Pavlov et al. 2013). Concurrent validity refers to the extent to which an instrument correlates with an external criterion, occurring at the same time and which is generally a well-established measurement procedure. This process has been shown to be a fast and highly appropriate way of validating the instrument; especially personal attributes, such as depression, strengths and weakness (Stephanie 2015, Andrews, Brown 1993, Blackhurst, Brandt & Kalinowski 1998). The correlation between the instrument and the well-established measurement procedure can be obtained with the Pearson correlation coefficient. The strength of this association was interpreted based on Cohen’s guidelines with r value (small: $r = 0.10$ to 0.29; medium: $r = 0.30$ to 0.49; large: $r = 0.50$ to 1.0) (Pallant 2011). Obviously, if an instrument is valid, it must be reliable according to the nature of validity and reliability. However, even if a test can be measured reliably, that does not make it a valid instrument which measures what it sets out to measure.

It has been documented that simple efficient questionnaires may be preferred to provide a wide spectrum of therapeutic results for patients compared with the time consuming and complex objective measures (Koufaki, Kouidi 2010). Furthermore, the main strength of a questionnaire’s ability to easily assess a large population making it efficient for collecting population-based information. This was the reason that the DASI and GPPAQ were chosen in the study to assess HD patients’ activity in a large sample of the population. However, poorly worded questions, ambiguous responses and non-response bias are well-known limitations of questionnaires (McLafferty 2003). Whilst the DASI has previously been used in renal disease patients (Pia Kontos et al. 2017, Pietro Ravani et al. 2012), few studies have focused on its validity in HD patients. It is understood that only one study pertaining to the reliability and validation of the DASI was conducted with stage 3-4 CKD patients. The DASI was reliable with a test-retest reliability of 71% when eGFR $\geq 35$ ml/min per 1.73$^2$ and 81% when eGFR $< 35$ ml/min per 1.73$^2$. However, another main finding in the study was that the DASI overestimated Peak Oxygen Consumption ($VO_{2peak}$) by 4.3ml/ kg per min(Pietro Ravani et al. 2012). The GPPAQ walking pace question included in the GPPAQ was usually used for categorizing participants into active or inactive groups. A study with 60-74 year old adults set a cut-off where participants who reported walking at a brisk or fast pace for $\geq 3$h/week were considered as active. The sensitivity and specificity of GPPAQ walking pace to identify
‘Active’ and ‘Inactive’ individuals against accelerometer were 39% and 70%. However, it is understood that the validity of the GPPAQ walking pace had not been explored. Therefore, establishing the validity of the DASI and GPPAQ walking pace is important for obtaining simple and efficient questionnaires to evaluate physical function or gait speed when dealing with a large group of HD patients. As described in the introduction chapter, the SWT has higher reliability and accuracy when compared to questionnaires for assessing physical function. Additionally, the Short Physical Performance Battery (SPPB) applied in the study is capable of objectively measuring HD patients’ gait speed. Therefore, examining the validity of the DASI and GPPAQ walking pace question against well-established objective measure tools is feasible and meaningful in this study. As described above, the Sit-to-Stand 60 (STS60) and handgrip strength (HGS) assess muscle endurance and strength, and the SPPB mainly assesses lower extremity mobility. Whilst the SWT, STS60, SPPB and HGS were utilized for evaluating physical function with HD patients within the thesis, only the SWT exactly measures exercise capacity, which is congruent with the construct of the DASI. Hence, the DASI was only validated against the SWT in the study.

The aims of this study have previously been described in the number (2) of Section 1.6 in Chapter 1. Briefly, this study was aiming to validate the DASI and GPPAQ walking pace question against the SWT and gait speed tests with the UK and Chinese HD patients.

5.3 Methods

The data included in this chapter was derived from the COCO study (Chapter 2, section 2.2.3). The detailed methods are described in Chapter 2. Specifically, the results of the DASI (section 2.3.2), GPPAQ walking pace question (section 2.3.2), the SWT (section 2.3.3) and the objective gait speed measure from the SPPB (section 2.3.3) were used.

As a reminder, The DASI assesses participants’ exercise capacity to perform activities ranging from self-care to household work and strenuous exercise. The SWT composes incremental and endurance SWT, which measure participants’ exercise capacity as the walking pace increases and the endurance capacity when the participants are asked to walk as long as they could at a constant walking speed. Besides the PA level assessment, the GPPAQ contains a question, which asked participants to describe their walking pace. Participants can choose one from four options regarding their own walking pace which could be categorized into slow (less than 3mph), steady (3-4mph), brisk (3-4mph) and
fast pace (over 4mph). Gait speed test from the SPPB was measured by having participants complete a 4m course at their usual walking pace.

5.4 Results

5.4.1 Demographics of haemodialysis patients

The demographics of the UK and Chinese HD patients in this chapter are shown in the Table3-13 and Table3-16 of the Chapter 3.

5.4.2 Validity of the DASI against the Shuttle Walking test in the UK and Chinese haemodialysis patients

Significant positive correlation between the DASI and ISWT with r of 0.67 ($P<0.001$) and 0.39 ($P<0.05$) were shown in the UK and Chinese HD patients, respectively (Figure5-1 and Figure5-2). However, there were no significant associations between the DASI and E SWT with r of 0.35 ($P=0.076$) and 0.28 ($P=0.098$) in two HD cohorts (Figure5-3 and Figure5-4).
Figure 5- 1. Linear regression showing DASI against the ISWT in UK HD patients

Figure 5- 2. Linear regression showing DASI against the ISWT in Chinese HD patients
Figure 5-3 Linear regression showing DASI against the Endurance Shuttle Walking Test (ESWT) in the UK HD patients

Figure 5-4 Linear regression showing DASI against the ESWT in Chinese HD patients
5.4.3 Validity of the GPPAQ walking pace question against the gait speed objectively measured by the SPPB

UK haemodialysis patients

The UK HD patients’ gait speed measured in the SPPB corresponded to their self-reported walking pace obtained from the GPPAQ (Table 5-1). Patients were categorised as “slow”, “steady” or “brisk” based on their response to the GPPAQ. No one reported his or her walking pace as “fast”. Following this the mean gait speed of each category, as measured in the SPPB, was calculated. A positive trend of measured gait speed was seen across categories, however all categories showed significant overlap of results. Only 1 (8.3%) patient correctly evaluated his/her walking pace as “steady” based on the gait speed measurement. The mean of the “steady” and “brisk” speed was lower than the range defined by the GPPAQ walking pace question criteria. However, the mean of “brisk” gait speed was higher than that of “steady” speed. There was a significant difference between the mean gait speed of the three GPPAQ categories ($P=0.008$). This was most evident with the steady walking pace which was significantly higher than slow speed ($P=0.003$).

Table 5-1 Validation of the GPPAQ walking pace against gait speed obtained from the SPPB in the UK HD patients

<table>
<thead>
<tr>
<th>N=30</th>
<th>Walking pace (GPPAQ)</th>
<th>Mean (SD) (mph) (SPPB)</th>
<th>Range (mph) (SPPB)</th>
<th>Tests of Between-Subjects Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Slow (&lt;3 mph)</td>
<td>1.75 (0.53)</td>
<td>0.71-2.50</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Steady (3-4 mph)</td>
<td>2.41 (0.42)</td>
<td>1.91-3.20</td>
<td>$P=0.008$**</td>
</tr>
<tr>
<td>1</td>
<td>Brisk (3-4 mph)</td>
<td>2.61 (0.00)</td>
<td>2.61-2.61</td>
<td></td>
</tr>
</tbody>
</table>
**Chinese haemodialysis patients**

Except for the “fast” category, the mean gait speed in the SPPB categorized by patients’ self-reported walking pace from slow to brisk also appeared to have a positive trend. However, the mean of gait speed of the “fast” group was lower than that of the brisk group. The range of gait speed obtained from the SPPB overlapped in four categories. All the walking paces reported as “brisk” and “fast” by patients were not consistent with their gait speed when objectively measured. Walking pace reported as “slow” and “steady” by 1 (6.3%) and 16 (94.1%) patients appeared inconsistent with measured gait speed from the SPPB. There was no significant difference between the mean gait speed of the four GPPAQ categories ($P=0.107$) (Table 5-2).

**Table 5-2 Validation of the GPPAQ walking pace against gait speed obtained from the SPPB in Chinese HD patients**

<table>
<thead>
<tr>
<th>N=40</th>
<th>Walking pace (GPPAQ)</th>
<th>Mean (SD) (mph) (SPPB)</th>
<th>Range (mph) (SPPB)</th>
<th>Tests of Between-Subjects Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Slow (&lt;3 mph)</td>
<td>2.20 (0.52)</td>
<td>1.36-3.58</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Steady (3-4 mph)</td>
<td>2.44 (0.30)</td>
<td>1.86-3.06</td>
<td>$P=0.107$</td>
</tr>
<tr>
<td>5</td>
<td>Brisk (3-4 mph)</td>
<td>2.68 (0.22)</td>
<td>2.42-2.98</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Fast (&gt; 4 mph)</td>
<td>2.67 (0.82)</td>
<td>2.09-3.25</td>
<td></td>
</tr>
</tbody>
</table>

**5.5 Discussion**

There were ‘large’ and ‘medium’ positive correlation between the DASI and the ISWT with $r$ of 0.67 and 0.39 in the UK and Chinese HD patients respectively, confirming that the DASI is valid for providing HD patients with a standardized assessment of physical function. The finding was consistent with a number of studies that validated the DASI against the objective measure of maximal exercise capacity. As early as 1989, a study (Hlatky et al. 1989) with 50 subjects demonstrated that the DASI provided a standardized measure of physical function and had a large correlation with the VO$_2$peak ($r=0.58$, $P<0.0001$). Coutinho-Myrrha et al. found that there was a significant positive correlation between the DASI in a Portuguese version and the VO$_2$max ($r=0.51$, $P<0.001$) in patients with CVD (Coutinho-Myrrha, Dias et al. 2014). From this study, the evidence was extended that the DASI is valid for measuring exercise capacity with HD patients.
disparity of the degree of correlation between the DASI and the ISWT between two cultural groups may be due to the difference of questionnaire versions. The DASI was designed and developed by Hlatky and colleagues in English (Hlatky et al. 1989). However, the Chinese version of the DASI was developed by cross-culturally translated and adapting (Yinian Peng 2016), which may influence the validity of the DASI in Chinese HD patients.

The VO$_{2\text{peak}}$ is viewed as the ‘gold standard’ of measuring exercise capacity. However, it is often impractical due to costs, and the fact that it is complex and physically demanding, especially in vulnerable chronic disease patients. Given its simple, progressive nature and high reliability, the SWT has been widely used in a number of studies (Billings et al. 2013, Green et al. 2001). The validation of the ISWT against VO$_{2\text{peak}}$ showed a strong relationship between measures, with $r$ values ranging from 0.54 to 0.88 in varying populations, such as obese women, patients with coronary artery bypass surgery and COPD(Jürgensen et al. 2015, Fowler, Singh & Revill 2005, Arnardóttir et al. 2006). Whilst the DASI assesses a participant’s capacity for accomplishing a particular activity, the ISWT measures participants’ physical capacity to complete a fixable shuttle course in an allowed time. Obviously, this explained the strong relationship between the DASI and the ISWT. However, the DASI does not evaluate the endurance of conducting certain activities, which may explain why there was no significant association between the DASI and ESWT in two HD cohorts.

The GPPAQ walking question appeared to have a mixed level of validity with HD patients of different cultures in the study. Gait speed classified into “steady”, “brisk” and “fast” categories in Chinese HD patients were not consistent with the standard of the GPPAQ walking pace, which was set according to the Centres for Disease Control and Prevention (CDC) (the Centres for Disease Control and Prevention, (CDC) 2015). Meanwhile, the GPPAQ walking question was unable to distinguish Chinese participants’ walking pace categories, which may indicate that the GPPAQ walking question is not reliable for Chinese HD patients. However, it showed stepwise increase in mean gait speed of the UK patients between categories. One explanation may be that the GPPAQ had never been validated with Chinese population. As mentioned in the method, the GPPAQ was only translated into Chinese for investigating more potentials in the research. Furthermore, the conversion of units of walking pace from mph to km/s for the Chinese version of the GPPAQ walking pace may be another underlying reason. Since mph is not
a commonly used unit in China. Nonetheless, it was found that slow pace reports based on the CDC criteria were in agreement with the gait speed measured with the SPPB in the UK HD patients and only one Chinese patient exceeded CDC cut off of slow gait speed, suggesting that the GPPAQ walking pace question may be valid for assessing slow pace (Kutner, Zhang et al. 2015). It have been shown in mounting studies that the vast majority of HD patients had slow gait speed(Painter, Marcus 2013, Johansen, Chertow et al. 2001, Painter, Carlson et al. 2000). Additionally, it is noteworthy that the vague classification between the “steady” and “brisk” walking pace in the GPPAQ may be an underlying limitation, which led to participants’ incapability or confusion with differentiating these two categories. Therefore, the findings may suggest that different criteria of walking pace with “slow” or “not slow” pace in the CDC is required for HD patients.

**Strengths and Limitations**

The study reported the unknown previous results regarding the relationship between the DASI and SWT, and the GPPAQ walking pace question and gait speed test. However, several limitations are still present. The DASI and GPPAQ were not administered a second time with the same HD patients in the study, therefore test-retest reliability of these two questionnaires was unable to be measured. However, according to the relationship between reliability and validity, the validation against well-established tests is arguably the most important criteria that determines the quality of the DASI and GPPAQ walking pace question. Furthermore, questionnaire validation is an overwhelming process. The process mainly includes piloting test the questionnaire on a subset of the intended population and checking reliability and validity of questionnaires. In the present study only criterion validity of the DASI and GPPAQ walking pace question were examined. Additionally, recommendations on sample size for questionnaire validation are various. Based on the statistical sophistication of Exploratory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA), sample size estimations are invariably based on ‘rules of thumb’ that number of participants to number of items ratios ranges from 3-10(Cattell 2012, Everitt 1975). Additionally, minimum sample size requirements are 50 (de Winter, Dodou et al. 2009), 100(Kline 2000), 150(Hutcheson, Sofroniou 1999), or 200(Gorsuch 1983). However, the sample size were only 30 and 40 UK and Chinese HD patients in this study, which were lower than the recommended overall sample size minima. Finally, the validity of the GPPAQ was not analyzed in the
study, although accelerometers were applied in HD patients for measuring their habitual PA level. As mentioned above, the GPPAQ is used for assessing participants’ PA level in the past 7 days. However, the accelerometers were given to patients after the GPPAQ had been taken home to complete rather than over the 7 day period preceding the completion of GPPAQ in the study. Therefore, the PA level measurements failed to correspond to the time period covered by the questionnaire. This may lead to a poor or inaccurate validation for the GPPAQ against accelerometry.

5.6 Conclusion

The DASI showed valid performance in the UK and Chinese HD patients and could be of use for providing physical function measurements with HD patients. The standard of the GPPAQ walking pace question failed to prompt HD patients to accurately report their walking pace. However, it was capable of distinguishing different categories of patients’ walking pace in UK HD patients. Specifically, the questionnaire was able to identify patients with slow walking pace, showing the possible usefulness for evaluating gait speed in the UK HD patients.
Chapter 6

Physical Function of Haemodialysis Patients in the UK and China
6.1 Abstract

Impaired physical function has been commonly reported in HD patients, which leads to a number of adverse symptoms and complications, consequently, results in a high mortality risk. In-depth exploration regarding the potential disparity of physical function with HD patients between different cultures may be beneficial to improve physical function for each cohort. In order to characterize and compare physical function between UK and Chinese HD patients and explore the contributing factors of physical function pertaining to demographics and clinical information, a combination of the Duke Activity Status Index (DASI) and GP Physical Activity Questionnaire (GPPAQ) walking pace question and physical performance tests (Shuttle Walking Test [SWT], Sit-to-Stand 60 [STS60], Short Physical Performance Battery [SPPB] and Handgrip Strength [HGS]) were conducted with HD patients in two cultural groups. Low physical function was highly prevalent in the UK and Chinese HD patients. High nutritional status (NS) or muscle mass, low inflammation, bone metabolism derangement and comorbidity were positively associated with physical function in HD patients. Anemia was negatively correlated with Chinese HD patients’ physical function. UK HD patients had significantly lower physical function than Chinese patients, which may be ascribed to the higher (Body Mass Index) BMI, lower creatinine, worse protein status and bone metabolism in UK patients compared to their Chinese counterparts.

6.2 Background

It has long been known that HD patients experience impaired physical function (Jette, Posen et al. 1977). This manifestation has been corroborated by ample studies (Diesel, Noakes et al. 1990, Johansen 1999, Van Den Ham, Eugénie C H, Kooman et al. 2005, Marcus, LaStayo et al. 2015), of these, Johansen et al. reported that levels of exercise capacity in HD patients were only 60% to 70% of age-expected levels (Johansen 1999). E.Sterky et al. conducted sit-to-stand and staircase tests to compare physical capacity between elderly HD patients and healthy controls matched for age and gender(Sterky, Stegmayr 2005). The results showed that HD patients have 50% less functional capacity than the controls. A significant body of studies have shown that reduced physical function are associated with worse symptoms and complications, increase hospitalization rates and compromise Quality of Life (QoL) (Marcus, LaStayo et al. 2015, DeOreo 1997, Li, Li et al. 2010a, Johansen, Shubert et al. 2003). Consequently, mounting studies have revealed
that declining physical function is an independent predictor of increased mortality in HD patients (DeOreo 1997, Marcus, LaStayo et al. 2015, Knight, Ofsthun et al. 2003). Given the burden caused by impaired physical function and the high prevalence profoundly affecting HD patients, assessment of physical function performed with valid and simple measurement tools, such as questionnaires or objective instruments, is urgently needed for HD patients. As described above, the DASI has been shown to be a valid questionnaire for assessing the UK and Chinese HD patients’ physical function. Whilst the DASI plays a crucial role in assessing exercise capacity for a large HD population, objective physical performance tests provide accurate and effective measure of physical function for HD patients (Cobo, Gallar et al. 2015). In the present study, subjective and objective measures were combined to gain a comprehensive understanding of physical function within the UK and Chinese HD patients. Consequently, this understanding provides insight into the potential demographics and clinical outcomes associated with physical function and may also inform the design of a patient-centred exercise prescription or intervention.

The aims of this study have previously been described in the number (3) of 1.6 section. Briefly, the primary aim of this study was to characterise and compare HD patients’ physical function between the UK and China.

6.3 Methods

The data included in this chapter was derived from the QCKD and COCO study (Chapter 2, section 2.2.2 and 2.2.3). The detailed methods are described in Chapter 2. Results from the DASI and GPPAQ walking pace question completed in the QCKD study (section 2.3.2) and physical performance tests completed in the COCO study (section 2.3.3) were analysed.

Briefly, the DASI and GPPAQ walking pace question were conducted for assessing exercise capacity and walking pace with both the UK and Chinese HD patients after recruiting them into the QCKD study. Physical performance tests include SWT, STS60, SPPB and HGS, which were utilized for measuring exercise capacity, muscle endurance, lower extremity function and muscle strength with HD patients and healthy controls in the UK and China, respectively. All these tests were assessed with patients before a HD session or on a non-HD day. For healthy controls, tests were conducted at their convenient time.
6.4 Results

6.4.1 Physical function measured by questionnaires in the UK haemodialysis patients

Demographics and clinical information

The UK HD patients in this section were from the QCKD study. Their demographics and clinical information were shown in Table 3-7 and Table 3-8.

The DASI

1109 UK HD patients completed the DASI, and the valid response rate was 96.0%. The median DASI score in the UK HD patients was 17.95 Metabolic Equivalent of Task (METs), with an IQR of 30.2-99.5 and range of 0.00-58.2. Figure 6-1 shows the histogram of the frequency of the DASI scores with 3.1% and 3.2% of patients having the minimum and maximum DASI score of 0 and 58.2 METs.

![Figure 6-1: Histogram of the frequency of the DASI scores](image-url)
Relationship between the DASI score and categorical variables of demographics and clinical information

The DASI score in male HD patients were significantly higher than that in female patients (Z=-4.529, P<0.001). There was no significant difference in DASI score between White British and South Asian patients (Z=-1.574, P=0.144), current smokers and those who have never smoked (Z=-0.906, P=0.365), ex-smokers and never smoked (Z=-0.018, P=0.986) and current smokers and ex-smoker (Z=-8.37, P=0.403).

Relationship between the DASI score and continuous variables of demographics and clinical information

The DASI score was negatively correlated to age, dialysis vintage, number of co-morbidities, high CRP and ALP levels. Conversely, higher DASI score was positively associated with urea and creatinine, phosphate, albumin and cholesterol levels. Table 6-1 shows the correlations between the DASI, demographics and clinical information.

Table 6-1: Correlations between the DASI score and continuous variables of demographics and clinical information

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>DASI Score (METs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.258</td>
</tr>
<tr>
<td>Dialysis Vintage (y)</td>
<td>Rho=-0.079</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Rho=-0.063</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>Rho=0.137</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.225</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>Rho=0.180</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Rho=-0.222</td>
</tr>
<tr>
<td>cholesterol (mmol/L)</td>
<td>Rho= 0.144</td>
</tr>
<tr>
<td>phosphate (mmol/L)</td>
<td>Rho= 0.096</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>Rho= -0.177</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho= 0.033</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho= 0.024</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho= -0.329</td>
</tr>
</tbody>
</table>

**P< 0.01; ***P< 0.001 (2-tailed).
GPPAQ walking pace

736 (63.7%) patients reported their walking pace as slow. However, only 18(1.6%) patients considered their walking pace as fast. The distribution of walking pace in the UK HD patients is demonstrated in Table 6-2.

Table 6-2 Distribution of walking pace in the UK HD patients

<table>
<thead>
<tr>
<th>GPPAQ Walking pace</th>
<th>Slow</th>
<th>Steady</th>
<th>Brisk</th>
<th>Fast</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD patients in each category n (%)</td>
<td>736 (63.7)</td>
<td>266 (23.0)</td>
<td>39(3.4)</td>
<td>18(1.6)</td>
</tr>
</tbody>
</table>

Relationship between the GPPAQ walking pace and categorical variables

Male patients’ walking pace was significantly faster than female ($X^2=4.519, P=0.034$). There was no significant difference in walking pace between ethnicities ($X^2=1.798, P=0.615$) and different types of smoking status ($X^2=2.641, P=0.852$).
Relationship between the GPPAQ walking pace and continuous variables

There were negative correlations between walking pace, age, dialysis vintage, BMI, number of co-morbidities, ALP, CRP and PTH levels. Walking pace was positively associated with creatinine, cholesterol and albumin levels. Table 6-3 shows the correlation between walking pace, demographics and clinical information.

Table 6-3 Correlation between walking speed and continuous variables of demographics and clinical information

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>Walking pace</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.208</td>
</tr>
<tr>
<td>Dialysis vintage (y)</td>
<td>Rho=-0.069</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>Rho=-0.083</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>Rho=0.059</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.153</td>
</tr>
<tr>
<td>albumin (g/L)</td>
<td>Rho=0.137</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Rho=-0.189</td>
</tr>
<tr>
<td>cholesterol (mmol/L)</td>
<td>Rho=0.111</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>Rho=-0.180</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>Rho=-0.082</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.054</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.008</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.278</td>
</tr>
</tbody>
</table>

**\( P< 0.05; **\( P< 0.01; ***\( P< 0.001 \) (2-tailed).**

6.4.2 Physical function measured by physical performance tests in the UK haemodialysis patients and healthy controls

Demographics

The HD patients and healthy controls in this section came from the COCO study. The Demographics of the UK HD patients and healthy controls are shown in the Table 3-13 and Table 3-14 of Chapter 3, respectively. The comparison of demographics between HD patients and healthy controls in the UK is shown in Table 3-15.
Physical performance tests in haemodialysis patients

The scores of physical performance tests in the UK HD patients were 329±185m in the Incremental Shuttle Walking Test (ISWT), 265 (134-1550) m in the Endurance Shuttle Walking Test (ESWT), 19± 11 in the STS60, 10 (7.8-11.3) in the SPPB and 22.93 ±10.09kg in the HGS.

Physical performance tests in healthy controls

The scores of physical performance tests in the UK healthy controls were 707±1954m in the ISWT, 2000(31962-2000) m in the ESWT and 46 ±16 in the STS60.

Comparison of physical performance tests between haemodialysis patients and healthy controls

The UK HD patients’ SWT and STS60 scores were significantly lower than healthy controls (all \( P<0.001 \)). Comparison of physical performance tests between the HD patients and healthy controls in the UK is shown in Table 6-4.

<table>
<thead>
<tr>
<th>Physical performance tests</th>
<th>HD patients (n=30)</th>
<th>Healthy controls (n=10)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD, Median (IQR)</td>
<td>n</td>
<td>Mean ± SD, Median (IQR)</td>
</tr>
<tr>
<td>ISWT (m)</td>
<td>329±185</td>
<td>27</td>
<td>707±195</td>
</tr>
<tr>
<td>ESWT (m)</td>
<td>265 (134-1550)</td>
<td>26</td>
<td>2000 (31962-2000)</td>
</tr>
<tr>
<td>STS60</td>
<td>19 ± 11</td>
<td>26</td>
<td>46 ±16</td>
</tr>
</tbody>
</table>

*** \( P<0.001 \) (2-tailed).

Comparison of physical performance tests between haemodialysis patients and healthy controls after adjusting for age

As a reminder, the HD patients were significantly older than healthy controls in the UK. After controlling for age, the mean ISWT in the HD patients and healthy controls changed to 348(95%CI: 282-414) m and 655 (95%CI: 544-765) m, respectively. The mean ESWT in HD patients and healthy controls were 764 (95%CI: 552-975) m and 1766 (95%CI: 1409-2123) m, respectively. Both of the ISWT and ESWT scores in HD patients (group=1) were significantly lower than those of healthy controls (group=2) in the UK.
(R^2_{Adjusted} = 0.569 and R^2_{Adjusted} = 0.597, both P<0.001) after adjusting for age (Table6-5 and Table6-6).

After controlling for age, the mean STS60 in HD patients and healthy controls in the UK was 20 (95%CI: 15-25) and 45 (95%CI: 36-53), respectively. The STS60 in the HD patients (group=1) was still significantly lower than that of the healthy controls (group=2) in the UK (R^2_{Adjusted} = 0.48, P<0.001) (Table6-7).

Table 6.5  Multiariable linear regression analysis for the comparison of the ISWT between HD patients and healthy controls in the UK after controlling for age

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>378.311 (69.337,687.285)</td>
<td>152.036</td>
<td>-152.036</td>
<td>.018</td>
</tr>
<tr>
<td>Age</td>
<td>-6.318 (-10.151,-2.485)</td>
<td>1.886</td>
<td>-.388</td>
<td>.002**</td>
</tr>
<tr>
<td>Groups</td>
<td>306.810 (175.186,438.434)</td>
<td>64.768</td>
<td>.549</td>
<td>.000***</td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. **P<0.01. ***P<0.001

Table 6.6  Multiariable linear regression analysis for the comparison of the ESWT between HD patients and healthy controls in the UK after controlling for age

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>987.314 (-8.656,1983.284)</td>
<td>490.084</td>
<td>-490.084</td>
<td>.052</td>
</tr>
<tr>
<td>Age</td>
<td>-22.961 (-35.317,-10.605)</td>
<td>6.080</td>
<td>-.423</td>
<td>.001***</td>
</tr>
<tr>
<td>Groups</td>
<td>1002.113 (577.827,1426.400)</td>
<td>208.777</td>
<td>.538</td>
<td>.000***</td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. ***P<0.001

Table 6.7  Multiariable linear Regression analysis for the comparison of the STS60 between HD patients and healthy controls in the UK after controlling for age

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>4.470 (-20.879,29.819)</td>
<td>12.459</td>
<td>-12.459</td>
<td>.722</td>
</tr>
<tr>
<td>Age</td>
<td>-.175 (-.486,.137)</td>
<td>.153</td>
<td>-.150</td>
<td>.262</td>
</tr>
<tr>
<td>Groups</td>
<td>24.905 (14.644,35.167)</td>
<td>5.044</td>
<td>.000***</td>
<td></td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. ***P<0.001
6.4.3 Physical function measured by questionnaires in Chinese haemodialysis patients

Demographics and clinical information

Chinese HD patients in this section were from the QCKD study. Their demographics and clinical information are shown in Table 3-9 and Table 3-10, respectively.

The DASI

All 542 Chinese HD patients completed the DASI. The median DASI score was 31.45 METs, with an IQR of 18.95-44.7 and range of 0.00-58.2. Figure 6-2 shows the histogram of the frequency of the DASI scores with 1.3% and 9.6% of patients having the minimum and maximum DASI score with 0 METs and 58.2 METs.

![Histogram of the frequency of DASI scores in Chinese HD patients](image)

**Figure 6-2 Histogram of the frequency of DASI scores in Chinese HD patients**

Relationship between the DASI score and categorical variables

There was no significant difference in the DASI score between male and female (Z=-1.742, P=0.081). There was no significant difference between current smokers and those who have never smoked (Z=-1.087, P=0.277), ex-smokers and never smoked (Z=-0.388, P=0.698) and current smokers and ex-smoker (Z=-0.676, P=0.499).
Relationship between the DASI score and continuous variables

The DASI score was negatively correlated to age and number of co-morbidities. Conversely, higher DASI score was positively associated with creatinine, phosphate, Hgb and haematocrit levels. Table 6-8 shows the correlations between the DASI, demographics and clinical information.

Table 6-8 Correlations between the DASI score and continuous variables of demographics and clinical information

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>Walking speed</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.445</td>
<td>P&lt;0.001 ***</td>
</tr>
<tr>
<td>vintage (y)</td>
<td>Rho=-0.017</td>
<td>P=0.692</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>Rho=-0.037</td>
<td>P=0.388</td>
</tr>
<tr>
<td>urea(mmol/L)</td>
<td>Rho=0.121</td>
<td>P=0.009 **</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.265</td>
<td>P&lt;0.001 ***</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.123</td>
<td>P=0.005 **</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.096</td>
<td>P=0.029 *</td>
</tr>
<tr>
<td>phosphate (mmol/L)</td>
<td>Rho=0.136</td>
<td>P=0.002 **</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.331</td>
<td>P&lt;0.001 ***</td>
</tr>
</tbody>
</table>

**P< 0.05; ***P< 0.01; ***P< 0.001 (2-tailed).

GPPAQ walking pace

224 (41.4%) patients reported their walking pace as slow. However, only 15(2.8%) patients considered their walking pace as fast. The distribution of walking pace in Chinese HD patients is demonstrated in Table 6-9.

Table 6-9 the distribution of walking pace in Chinese HD patients

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>HD patients in each category n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPPAQ Walking speed</td>
<td>Slow 224 (41.4) Steady 240 (44.3) Brisk 62 (11.5) Fast 15 (2.8)</td>
</tr>
</tbody>
</table>
Relationship between walking pace and categorical variables

There was no significant difference in walking pace between genders ($X^2=4.404$, $P=0.221$) and different smoking status ($X^2=11.902$, $P=0.064$) in Chinese HD patients.

Relationship between walking pace and continuous variables

Creatinine and Hgb levels were positively correlated with walking pace. Conversely, there was negative association between walking pace, age, BMI and number of co-morbidities. Table 6-10 shows the correlations between walking pace and continuous variables of demographics and clinical information.

Table 6-10 Correlation between walking speed and continuous variables of demographics and clinical information

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>Walking speed</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.301</td>
<td>$P&lt;0.001$ ***</td>
</tr>
<tr>
<td>Vintage (y)</td>
<td>Rho=0.006</td>
<td>$P=0.881$</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>Rho=-0.159</td>
<td>$P&lt;0.001$ ***</td>
</tr>
<tr>
<td>urea(mmol/L)</td>
<td>Rho=0.073</td>
<td>$P=0.115$</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.143</td>
<td>$P=0.002$ **</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.106</td>
<td>$P=0.016$ *</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.076</td>
<td>$P=0.086$</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.278</td>
<td>$P&lt;0.001$ ***</td>
</tr>
</tbody>
</table>

**$P<0.05$; **$P<0.01$; ***$P<0.001$ (2-tailed).

6.4.4 Physical function measured by physical performance tests in Chinese haemodialysis patients and healthy controls

Demographics

The HD patients and healthy controls in this section came from the COCO study. The demographics of Chinese HD patients and healthy controls are shown in Table 3-16 and Table 3-17 of Chapter 3, respectively.
Physical performance tests in haemodialysis patients

The scores of physical performance tests in Chinese HD patients were 440 (310-478) m in the ISWT, 625 (287-1234) m in the ESWT, 30 ± 11 in the STS60, 12 (11.00-12.00) in the SPPB and 29.54 ±9.49 kg in the HGS.

Physical performance tests in healthy controls

The scores of physical performance tests in Chinese healthy controls were 515±1071m in the ISWT, 1884 (939-2000) m in the ESWT, 46 ±16 in the STS60, 12 (12.00-12.00) in the SPPB and 36.61±10.33 kg in the HGS.

Comparison of physical performance tests between haemodialysis patients and healthy controls

All physical performance tests in the HD patients were significantly lower than those in healthy controls (all $P<0.01$). Comparison of physical performance tests between HD patients and healthy controls in China is shown in Table 6-11.

Table 6-11: Comparison of physical performance tests between HD patients and healthy controls in China

<table>
<thead>
<tr>
<th>Physical function tests</th>
<th>Chinese HD patients (n=40)</th>
<th>Chinese healthy controls (n=44)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISWT (m)</td>
<td>440 (310-478)</td>
<td>545 (448-593)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>ESWT (m)</td>
<td>625 (287-1234)</td>
<td>1884 (939-2000)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>STS60</td>
<td>30 ± 11</td>
<td>46 ±16</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>SPPB</td>
<td>12 (11.00-12.00)</td>
<td>12 (12.00-12.00)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>HGS</td>
<td>29.54 ±9.49</td>
<td>36.61±10.33</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

**$P<0.01$ (2-tailed); ***$P<0.001$ (2-tailed)**
6.4.5 Comparison of physical function measured by questionnaires between the UK and Chinese haemodialysis patients

Comparison of the DASI between UK and Chinese haemodialysis patients

The UK HD patients’ median DASI score was significantly lower than Chinese cohorts (UK vs. China: 17.95[30.2-99.5] METs vs 31.45[44.7-18.95] METs). Comparison of the DASI score between UK and Chinese HD patients is shown in Figure 6-3.

![Figure 6-3: Comparison in DASI score between UK and Chinese HD patients](image)

Figure 6-3: Comparison in DASI score between UK and Chinese HD patients
Comparison of the DASI between UK and Chinese haemodialysis patients after adjusting for age and gender

As a reminder, the UK HD patients were significantly older and had more males than their Chinese counterparts. After controlling for age and gender, the mean DASI with the HD patients in the UK and China were 22.199 (95%CI: 21.353-23.046) METs and 30.695 (95%CI: 29.465-31.925) METs, respectively. The DASI score in the UK HD patients (group=1) is significantly lower than that in Chinese HD patients (group=2) (R² Adjusted=0.240, P<0.001) (Table6- 12).

Table6- 12Multivariable linear regression analysis for the comparison of the DASI between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>â</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>41.240</td>
<td>2.266</td>
<td>&lt;.001***</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(36.796, 45.684)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.364</td>
<td>-.024</td>
<td>-.348</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td></td>
<td>(-.410, -.317)</td>
<td>(.778)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-4.246</td>
<td>.719</td>
<td>-.127</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td></td>
<td>(-5.656, -2.836)</td>
<td>(.778)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups</td>
<td>8.496</td>
<td>.778</td>
<td>.247</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td></td>
<td>(6.969,10.022)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, â: standardized Coefficients. ***P<0.001
Comparison of the GPPAQ walking pace between UK and Chinese haemodialysis patients

The percentages of “steady”, “brisk” and “fast” walking pace in the UK HD patients were less than those in Chinese cohort. However, the percentage of “slow” walking pace in the UK HD patients was more than that in their Chinese counterparts. The UK HD patients’ overall walking pace was significantly slower than Chinese HD patients ($X^2=125.349$, $P<0.001$). Comparison of walking pace categories between UK and Chinese HD patients is shown in Figure 6-4.

Figure 6-4 Comparison of walking pace categories between the UK and Chinese HD patients
Comparison of the GPPAQ walking pace between UK and Chinese haemodialysis patients after adjusting for age and gender

‘Fast’ walking pace was taken as a reference category in the multi-nominal logistic regression model. After controlling for age and gender, the UK HD patients (group=1) who had “slow” walking pace were 8.194 times than those with “Fast” pace compared to Chinese HD patients(group=2) (P<0.001). The UK HD patients with “Steady” and “Brisk” walking pace appeared 25.957 and 5.060 times than those with “fast” pace compared to Chinese HD cohorts, respectively (both P<0.001) (Table6- 13).

Table6- 13 Multi-nominal logistic regression analysis for the comparison of walking pace between the UK and Chinese HD patients adjusting for age and gender

<table>
<thead>
<tr>
<th>GPPAQ Walking pace</th>
<th>B</th>
<th>SE B</th>
<th>P</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-.2075</td>
<td>.511</td>
<td>&lt;.001 ***</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.049</td>
<td>.008</td>
<td>&lt;.001 ***</td>
<td>1.840 (1.190,2.845)</td>
</tr>
<tr>
<td>Slow</td>
<td>Gender</td>
<td>.610</td>
<td>.222</td>
<td>.006 **</td>
</tr>
<tr>
<td>[Group=1.00]</td>
<td>2.103</td>
<td>.270</td>
<td>&lt;.001 ***</td>
<td>8.194 (4.824,13.918)</td>
</tr>
<tr>
<td>Steady</td>
<td>Intercept</td>
<td>-2.403</td>
<td>.571</td>
<td>&lt;.001 ***</td>
</tr>
<tr>
<td>Age</td>
<td>.025</td>
<td>.008</td>
<td>.003 **</td>
<td>1.025 (1.008,1.042)</td>
</tr>
<tr>
<td>Gender</td>
<td>.355</td>
<td>.249</td>
<td>.154</td>
<td>1.426 (.875,2.323)</td>
</tr>
<tr>
<td>[Group=1.00]</td>
<td>3.256</td>
<td>.304</td>
<td>&lt;.001 ***</td>
<td>25.957 (14.303,47.107)</td>
</tr>
<tr>
<td>[Group=2.00]</td>
<td>0 *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brisk</td>
<td>Intercept</td>
<td>-1.749</td>
<td>.690</td>
<td>.011 *</td>
</tr>
<tr>
<td>Age</td>
<td>.007</td>
<td>.010</td>
<td>.504</td>
<td>1.509 ( .826,2.755)</td>
</tr>
<tr>
<td>Gender</td>
<td>.411</td>
<td>.307</td>
<td>.181</td>
<td>1.007 (.987,1.027)</td>
</tr>
<tr>
<td>[Group=1.00]</td>
<td>1.621</td>
<td>.345</td>
<td>&lt;.001 ***</td>
<td>5.060 (2.572,9.953)</td>
</tr>
<tr>
<td>[Group=2.00]</td>
<td>0 *</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, â: standardized Coefficients. *P<0.05, **P<0.01, ***P<0.001, Pseudo R²=0.163 *. This parameter is set to zero because it is redundant.
6.4.6 Comparison of physical function measured by physical performance tests between UK and Chinese haemodialysis patients

Except for the ESWT, all physical performance tests in the UK HD patients were significantly lower than those in their Chinese counterparts. The comparison in physical performance tests between UK and Chinese HD patients is shown in Table 6-14.

Table 6-14 Comparison in physical performance tests between the UK and Chinese HD patients

<table>
<thead>
<tr>
<th>Physical performance tests</th>
<th>UK HD patients (n=30)</th>
<th>Chinese HD patients (n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD, Median (IQR)</td>
<td>n</td>
<td>Mean ± SD, Median (IQR)</td>
</tr>
<tr>
<td>ISWT (m)</td>
<td>340 (160-510)</td>
<td>27</td>
<td>440 (310-478)</td>
</tr>
<tr>
<td>ESWT (m)</td>
<td>265 (134-1550)</td>
<td>26</td>
<td>625 (287-1234)</td>
</tr>
<tr>
<td>STS60</td>
<td>19 ± 11</td>
<td>26</td>
<td>30 ± 11</td>
</tr>
<tr>
<td>SPPB</td>
<td>10.00 (7.75-11.25)</td>
<td>26</td>
<td>12.00 (11.00-12.00)</td>
</tr>
<tr>
<td>HGS (Kg)</td>
<td>22.93 ±10.09</td>
<td>28</td>
<td>29.54 ±9.49</td>
</tr>
</tbody>
</table>

*P< 0.05; **P< 0.01; ***P< 0.001 (2-tailed)

Comparison of physical performance tests between the UK and Chinese haemodialysis patients after controlling for age and gender

After controlling for age and gender, the mean ISWT in the UK and Chinese HD patients was to 343 (95%CI: 295-392) m and 401 (95%CI: 360-443) m, respectively. There was no significant difference in the ISWT between the UK (group=1) and Chinese HD patients (group=2) after controlling for age and gender ($\Delta R^2_{Adjusted} =0.378$, $P=.085$) (Table 6-15).

After controlling for age and gender, the mean STS60 in the UK and Chinese HD patients changed to 21 (95%CI: 16-25) and 29 (95%CI: 26-33), the SPPB were 9.622 (95%CI: 8.982-10.261) and 11.098 (95%CI: 10.583-11.614) and the HGS were 22.24(95%CI: 19.252-25.227) and 30.02 (95%CI: 27.564-32.475) kg, respectively. The UK HD patients (group=1) performed lower STS60 ($\Delta R^2_{Adjusted} =0.305$, $P=.002$), SPPB ($\Delta R^2_{Adjusted} =0.366$, $P=.001$) and HGS ($\Delta R^2_{Adjusted} =0.469$, $P<.001$) than Chinese HD patients (group=2) after controlling for age and gender (Table 6-16, Table 6-17 and Table 6-18).
Table 6-15 Multivariable linear regression analysis for the ISWT between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>821.471 (591.771,1051.171)</td>
<td>114.793</td>
<td>-114.793</td>
<td>.000***</td>
</tr>
<tr>
<td>Age</td>
<td>-6.658 (-9.399, -3.916)</td>
<td>1.370</td>
<td>-.536</td>
<td>.000***</td>
</tr>
<tr>
<td>Gender</td>
<td>-143.334 (-211.173, -5.496)</td>
<td>33.902</td>
<td>-.449</td>
<td>.000***</td>
</tr>
<tr>
<td>Groups</td>
<td>58.038 (-8.315, 124.392)</td>
<td>33.160</td>
<td>.189</td>
<td>.085</td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. ***P<0.001

Table 6-16 Multivariable linear regression analysis for the STS60 between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>40.876 (20.597, 61.155)</td>
<td>10.138</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>- .396 (- .638, - .154)</td>
<td>.121</td>
<td>-.381</td>
<td>.002**</td>
</tr>
<tr>
<td>Gender</td>
<td>-6.106 (-11.720, - .493)</td>
<td>2.806</td>
<td>-.241</td>
<td>.034*</td>
</tr>
<tr>
<td>Groups</td>
<td>8.754 (3.223, 14.284)</td>
<td>2.765</td>
<td>.358</td>
<td>.002**</td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. *P<0.05, **P<0.01, ***P<0.001
### Table 6-17
**Multiariable linear regression analysis for the SPPB between UK and Chinese HD patients after adjusting for age and gender**

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE B)</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>12.448 (9.508, 15.389)</td>
<td>1.470</td>
<td>.000</td>
</tr>
<tr>
<td>Age</td>
<td>-.070 (-.105, -.035)</td>
<td>.017</td>
<td>-.436</td>
</tr>
<tr>
<td>Gender</td>
<td>-.496 (-1.356, .364)</td>
<td>.430</td>
<td>-.121</td>
</tr>
<tr>
<td>Groups</td>
<td>1.477 (.631, 2.322)</td>
<td>.423</td>
<td>.370</td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. ***P<0.001

### Table 6-18
**Multiariable linear regression analysis for the HGS between UK and Chinese HD patients after adjusting for age and gender**

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE B)</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>47.248 (33.137, 61.358)</td>
<td>7.063</td>
<td>.000</td>
</tr>
<tr>
<td>Age</td>
<td>-.277 (-.449, -.105)</td>
<td>.086</td>
<td>-.318</td>
</tr>
<tr>
<td>Gender</td>
<td>-13.669 (-17.719, -9.618)</td>
<td>2.028</td>
<td>-.638</td>
</tr>
<tr>
<td>Groups</td>
<td>7.780 (3.729, 11.831)</td>
<td>2.028</td>
<td>.378</td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. **P<0.01, ***P<0.001
6.5 Discussion

6.5.1 Physical function in the UK haemodialysis patients

The UK HD patients appeared to show a lower level of physical function as assessed by objective and subjective measures. The mean DASI score in this study’s 1109 UK HD patients was 21.02METs. It is lower than 23.8METs found in 128 UK HD patients (Greenwood et al. 2012b) and 22.2METs in 70 Scotland HD patients (Prescott 2015). This confirmed the fact that UK HD patients had impaired exercise capacity. Similarly, non-dialysis patients also had much higher DASI scores compared to the UK HD patients (38.9 METs vs. 17.95 METs) (Kurella, Ireland et al. 2004a). This provides more evidence that physical function in Chronic Kidney Disease (CKD) patients decreases as kidney function declines (Hawkins, Sevick et al. 2011). The UK HD patients in the study had significant lower physical performance scores than their age and gender-matched healthy controls as well. The performance of the SWT with 328.5m in the study were higher than the finding of a study exploring a pragmatic exercise rehabilitation programme where 128 HD patients’ baseline ISWT scores were 247.7m (Greenwood, Lindup et al. 2012c). In terms of the STS60 test, both two studies showed the same results of 19.3 (Greenwood, Lindup et al. 2012c). The SPPB and HGS scores in the study were slightly lower than those in other studies with U.S., Japanese, Brazilian HD patients (Saitoh, Ogawa et al. 2016, Leal, Stockler-Pinto et al. 2011, Kutner, Zhang et al. 2014).

There are a number of potential causes leading to impaired physical function. Increasing age and female sex were negatively associated with the UK HD patients’ physical function, which is consistent with the findings that accelerated ageing or disorders related to being old and female contributed to the declined physical functioning with HD patients in previous studies (Liu 2012, Johansen, Kaysen et al. 2013, Brown, Yore et al. 2005). However, Painter and Roshanravan in a recent study found that patients with CKD had a higher prevalence of impaired physical function and frailty, regardless of age, compared to the general population of elderly adults (Painter, Roshanravan 2013). Creatinine is a breakdown product of creatine phosphate in muscle. A number of studies have shown that serum creatinine strongly correlated with muscle mass in healthy populations (Schutte, Longhurst et al. 1981, Baxmann, Ahmed et al. 2008). When creatinine is filtered out of the blood by the kidney, there is
little to no tubular reabsorption of it. Therefore, creatinine clearance is usually used to assess glomerular filtration rate (GFR). Under unstable kidney function, serum creatinine concentration is influenced by fluctuated GFR. Serum creatinine failed to reflect skeletal muscle mass in patients with chronic kidney disease (CKD). However, referring to dialysis patients in whom renal function is minimal to non-existent, serum creatinine still can be regarded as a reliable and cost-effective surrogate marker of muscle mass (Donadio, Halim et al. 2008, Noori, Kovesdy et al. 2010, Kalantar-Zadeh, Streja et al. 2012). This notion is consistent with the finding of the positive relationship between serum creatinine and physical function in the study.

Physical function in HD patients was positively correlated with good NS (Laws, Tapsell et al. 2000), which have been defined by several nutritional blood parameters, including albumin, phosphate and cholesterol concentrations (Johansen, Chertow et al. 2000). This was consistent with the correlation between the DASI score and clinical markers in the study, suggesting that with higher levels of albumin, phosphate and cholesterol, HD patients’ physical function increases, and vice versa. The positive correlation between biochemical indexes of NS and physical function is interesting since low physical function with HD patients is associated with high mortality risks, and poor NS also predicted increased mortality. Both physical function and NS are well-documented predictors of mortality in the HD patients (Lopes, Lantz et al. 2014, O’Hare, Tawney et al. 2003). However, the interaction between physical function and NS may exist as well. Cholesterol with higher than 1.5g/l and lower than 2-3 g/l was considered as the optimal level to lower the influence of systemic inflammation and malnutrition (Liu, Coresh et al. 2004, Fouque, Vennegoor et al. 2007). The median cholesterol in this study was 1.5g/l. This may be the reason that it indicated a positive association between physical function and cholesterol. Higher phosphate levels also predict better NS in HD patients (González-Parra, Gracia-Iguacel et al. 2012). However, it is noteworthy that higher serum phosphate leads to the development of Mineral and bone disorder (MBD) with HD patients, which negatively influences physical function and PA level (Johansen, Chertow 2007). The serum phosphate level was slightly beyond the normal range in the UK HD patients, it probably explained higher phosphate level associated with the better NS but did not negatively influence on the MBD.
Additionally, physical function decreased with the higher CRP and ALP concentrations in the study. These findings indicated that there was a strong correlation between inflammation, bone metabolism derangement and physical function. It was consistent with the finding that inflamed HD patients are less active (Mafra, Deleaval et al. 2011). As an enzyme playing a critical role in removing phosphate groups from many types of molecules, ALP is a predictable biochemical marker of bone metabolism (Bergman, Qureshi et al. 2017), resulting in a high risk of mortality. Although it is not as specific as ALP as an indicator of bone turnover, PTH assessment was also recommended as an adjunctive test for bone metabolism (Rhee, Molnar et al. 2014). Meanwhile, PTH is associated with coronary artery calcification and CVD (Rhee, Molnar et al. 2014). These reasons partly explained the negative correlation between the ALP, PTH levels and physical function.

The International Task Force on Nutrition and Ageing stated that gait speed is a crucial indicator for older adults’ adverse outcomes (Van Kan, Rolland et al. 2009). HD patients have been viewed as a model of early ageing. Although it has been confirmed as a sensitive health predictor with the nature of being easily measured, limited studies focused on the association of gait speed and HD patients. Slow gait speed, defined as<3 mph (1.34 m/s) in the GPPAQ and <0.8 m/s in the SPPB, characterized with 63.7% and 31.0% of the UK HD patients in the QCKD and COCO study, respectively. The latter is similar to 34.7% of the HD patients who regarded as slow gait speed from the United States Renal Data System (USRDS) study (Kutner, Zhang et al. 2014). Besides the strong correlation between walking pace, NS, inflammation, bone metabolism and comorbidity, in the analysis BMI was shown to negatively associate with walking pace. This seems to be contradictory to the positive correlation between BMI and survival (Leavey, McCullough et al. 2001). High BMI may predict better NS and increase muscle mass (Mafra, Guebre-Egziabher et al. 2008), which are all positively associated with physical function. It is understood that BMI is a vague measure of body composition, which is hard to distinguish which part of body composition contributes high survival in HD patients. More in depth analysis of body composition would be more useful, which was shown in Chapter 9.
6.5.2 Physical function in Chinese haemodialysis patients

Although exercise capacity demonstrated with the DASI score in Chinese HD patients was higher than other HD patients (31.45 METs vs. 23.8 METs) (Greenwood, Lindup et al. 2012a), it still appeared to be lower than that in the non-dialysis patients (31.45 METs vs. 38.9 METs) (Kurella, Ireland et al. 2004b). Similarly, Chinese HD patients had higher score in all the physical performance tests than those in other studies conducted with UK, Japanese, Brazilian HD patients (440.0 vs. 247.7m in the ISWT, 30.2 vs. 19.3 in the STS60, 12.0 vs. 10.9 in the SPPB and 22.9 vs. 23.2 in the HGS) (Saitoh, Ogawa et al. 2016, Leal, Stockler-Pinto et al. 2011, Greenwood, Lindup et al. 2012, Kutner, Zhang et al. 2014). However, they had significantly lower physical function than their age and gender matched healthy population.

Surprisingly, there was no difference in exercise capacity shown with the DASI between genders. It was inconsistent with the finding that female CKD patients were negatively correlated to physical function (Hiraki, Yasuda et al. 2013). The potential explanation is that the female patients were much younger than the male patients in the study and age is a predominant factor that inversely impact on physical function in HD patients.

The correlation between physical function, albumin, cholesterol, ALP and CRP was not explored in Chinese HD patients due to too much missing data of these markers in patients’ medical records. Similar to the findings in the UK HD patients, it has been shown that more muscle mass, good NS, and decreased comorbidity were positively correlated with higher exercise capacity in Chinese HD patients. Apart from that, it has been found that there was negative correlation between anaemia and physical function. Anaemia results in fatigue or diminished muscle oxygenation (Cobo, Gallar et al. 2015), which contributes to compromised functional capacity. Essentially, anaemia has been confirmed as being a contributory factor for the decline in maximal exercise capacity (Clyne, Jogestrand et al. 1994). However, the correlation between physical function and Hgb was not shown with the UK HD patients in the study. One possible explanation may be that Chinese patients had more severe anaemia than UK patients, which was corroborated by the discrepancy in anaemia between UK and Chinese HD patients from the reports of national renal data systems (Chinese National Renal Data System 2015, UK Renal Registry 2016). A cross sectional study with the
9 largest HD units from 6 cities around China showed that anaemia was highly prevalent in Chinese HD patients. About 60% of patients were unable to achieve the Hgb target of 110g/l even though 85% of these patients were administered with erythropoietin (Zhou, Jiang et al. 2012). Similarly, the results of the DISH study confirmed the worse anaemia in Chinese HD patients than UK patients.

### 6.5.3 Comparison of physical function between UK and Chinese haemodialysis patients

Given the discrepancy of age profiles between UK and Chinese HD patients when compared to national registry data (Chinese National Renal Data System 2015, UK Renal Registry 2015), the UK and Chinese samples from this study were representative of their respective populations. It is understood that few studies focused on Chinese HD patients’ BMI level. A multi-sample cross-sectional study with a population aged 40-59 years in four countries including the UK and China found that mean BMI of Chinese participants were much lower than that of UK participants at the end of the 20th century (Zhou, Stamler et al. 2003). Despite the fact that BMI levels in the Chinese population have increased due to ‘richer diets’ and rapidly growing prosperity since the 1990s (Zhou, Stamler et al. 2003, Shankar 2010), in the study, it was still revealed that Chinese HD patients had a significantly lower BMI level than their UK counterparts.

After controlling for age and gender between the two cultures, the UK HD patients still had significantly lower physical function than their Chinese counterparts. This was shown by the UK HD patients’ worse exercise capacity obtained from the QCKD study and muscle function from the COCO study, compared to their Chinese counterparts. The higher serum creatinine, phosphate and lower PTH concentrations in Chinese HD patients than the UK cohorts may indicate that the higher muscle mass or NS, protein status and better bone metabolism in Chinese HD patients contributed to the higher physical function than the UK patients. The COCO study revealed that Chinese HD patients had higher muscle function. However, there was no significant difference in exercise capacity, assessed by the SWT, between the UK and Chinese HD patients. It has been known that decreased muscle mass or strength are causes of the reduced physical function in HD patients (Johansen, Shubert et al. 2003). In order to better understand physical function between these two cultural groups, further
exploration of the differences between body composition and their effect on physical function is needed. Another underlying reason behind it may be the disparity of BMI between these two cultural groups. It was revealed that higher BMI was significantly associated with the prevalence of physical function limitation (Ylitalo, Karvonen-Gutierrez et al. 2013). Although higher BMI levels predicted better NS or metabolically healthier (Wildman, Muntner et al. 2008), the adverse impact of higher BMI or obesity on physical function may outweigh its potential benefits being a predictor of better NS (Coakley, Kawachi et al. 1998).

6.5.4 Strengths and limitations

It is understood that this is the largest study of exploring physical function in HD patients in the UK and China. However, it does have its limitations. Convenience sampling was applied when objective measure tools were conducted in the study. The sample suffered from the inherent bias and was unlikely to be good representative of the population of being studied. However, the sample size is pragmatic for the exploratory feasibility study. Patients were recruited from dialysis units in the Leicester Renal Network and all 7 hospitals in Nantong city from China, with a total population of approximately 400 and 700 HD patients attending regularly. The number of patients required was therefore readily attainable. Additionally, the cross-sectional study conducted with questionnaires in Chinese HD patients was limited to patients who underwent their HD sessions in hospitals located in Nantong city. They may be unable to be representative of the Chinese HD population. However, these patients resided in Nantong, including municipal and rural regions. They may be a good representation of the whole Nantong HD patients. Additionally, too much missing clinical information, such as albumin and cholesterol in Chinese patients interfered the influencing factors of physical function. Although statistically significant correlations in physical function and clinical parameters in the UK and Chinese HD patients has been shown, there is a chance that a Type I error has been made due to multiple correlations being performed. Type I error can be controlled by applying a correction factor such as Bonferroni or Sidak’s, which would adjust the P value or a-level and reduce the likelihood of Type I error. There is not a statistically significant (P=0.098) difference in the ESWT between UK and Chinese HD patients. However, it may be
ascribed to the occurrence of type II error due to the small sample size in the COCO study i.e. there may be a difference, but the sample size was too small to detect it.

6.6 Conclusion

Low physical function was highly prevalent in both the UK and Chinese HD patients. In order to improve the impaired physical function in HD patients, a series of interventions enhancing NS and muscle mass and controlling inflammation, bone metabolism derangement and comorbidity may be needed. Anaemia was commonly present in Chinese HD patients, which negatively correlate with physical function. Physical function in the UK HD cohort was significantly lower than the Chinese HD cohort. This may be attributed to the higher BMI, lower creatinine, worse protein status and bone metabolism in UK patients. It is necessary to further explore which components of body composition led to the difference in BMI between two HD groups, and how muscle and fat masses affect physical function within HD patients.
Chapter 7

Physical Activity Levels in Haemodialysis Patients in the UK and China
7.1 Abstract

HD patients have substantially high risks of comorbidity and mortality, which partly attributes to sedentary lifestyle. In order to design a realistic and effective intervention for HD patients, a thorough understanding of physical activity (PA) or exercise level covering all its dimensions and domains is required. It is understood that patients’ health behaviour participation may be influenced by culture. The aim of this study was to characterise and compare PA level between UK and Chinese HD patients. While the GP physical activity (GPPAQ) and Leisure Time Exercise Questionnaire (LTEQ) subjectively assessed PA and exercise levels, the Multi-sensor system (MSSs) were utilized for objectively measuring habitual PA levels with HD patients in the UK and China. Low PA level was highly prevalent in the UK and Chinese HD patients. Impaired bone metabolism and increased age, inflammation and comorbidities were negatively correlated with HD patients’ PA level. High muscle mass and good nutritional status (NS) were positively correlated with patients’ PA participation. Anaemia in Chinese HD patients was negatively associated with PA levels. Higher muscle mass, better NS and bone metabolism, and incomplete patients transport services may contribute to the higher PA level in Chinese HD patients compared with the UK HD patients.

7.2 Background

Physical inactivity is a highly prevalent concern in HD patients all over the world. The importance of motivating HD patients to exercise has attracted increased attention from healthcare providers worldwide. However, it is still unclear how to incorporate exercise into patients’ daily lives. While the benefits of exercise for CKD patients have been highlighted by National Institute of Clinical Excellence (NICE)(The National Institute of Clinical Excellence, (NICE) 2015), they fail to provide specific exercise prescription or program information. The Clinical Practice Guidelines produced by the Kidney Disease Improving Global Outcomes (KDIGO) recommends that CKD patients should aim to conduct PA at least five times every week, with each session lasting for 30 minutes or more (Levin et al. 2013). However, the guideline does not specify the ideal modality or intensity of exercise but does suggest exercise should be individualised based on patients’ cardiovascular health.
It has been documented that people’s health status varies in different cultures (Ren, Amick 1996, Chen, Kazanjian & Wong 2009). However, limited studies examining health behaviours focused on people from different cultures (Sweeting, West 1995, Hawkins et al. 2008). Relatively few studies about exercise in HD patients in low to middle income countries such as China have been completed; with the majority of research focusing on Caucasian populations in high-income countries (Capitanini et al. 2014, de Lima et al. 2013, Johansen, Painter 2012). Little consensus has been reached on how to take care of HD patients in China, particularly when it comes to exercise. Additionally, haemodialysis units in China are heavily burdened with a large patient population. Thus, PA or exercise as a recommendation to effectively improve morbidity and mortality of HD patients is often overlooked by healthcare professionals.

Generally, previous studies have focused on limited aspects of PA or exercise levels. For example, a study measured PA levels of HD patients using the estimated number of steps/day and showed there was a positive correlation between PA level, younger patients, less morbidities, better NS and body composition, referring to higher Lean Mass (LM) and less Fat Mass (FM) (Cobo et al. 2015). Although walking steps assessment is an attractive measure to quantify PA in a simple and inexpensive way, it only involves a part of daily PA. Modalities as well as frequency and intensity of PA or exercise are missed out. Furthermore, other studies have only investigated HD patients’ activity scores, determining PA level by comparing results to established norms by age and gender(Johansen et al. 2010) or classifying patients into active or inactive categories (Lopes et al. 2014). However, in order to gain a thorough understanding of HD patients’ PA level, so as to design an effective patient-centred exercise intervention, a comprehensive assessment of PA or exercise should be utilised. This assessment should cover all dimensions of exercise prescription, such as frequency, duration and intensity of exercise, and domains, including in occupational, leisure time, domestic and transport exercise (Greenwood et al. 2014).

The aims of this study have previously been described in the number (4) of 1.6 section in Chapter 1. Briefly, the primary aim of this study was to characterise and compare HD patients’ physical activity (PA) level between the UK and China.
7.3 Methods

The data included in this chapter was derived from the QCKD and COCO study (Chapter 2, section 2.2.2 and 2.2.3). The detailed methods are described in Chapter 2. Specifically, the results of the GP Physical Activity Questionnaire (GPPAQ) (section 2.3.2), the Leisure Time Exercise Questionnaire (LTEQ) (section 2.3.2), the Sensewear armband (SWA) (section 2.3.3) and GENEActiv (section 2.3.3) were utilized.

As a reminder, the GPPAQ and LTEQ are two questionnaires, which were used for assessing PA level and exercise level during individual leisure time, respectively. The SWA and GENEActiv are two Multi-sensor system (MSSs) or generally viewed as tri-axial accelerometers, which were used for assessing habitual PA levels.

7.4 Results

7.4.1 Physical activity level measured by questionnaires in the UK haemodialysis patients

Demographics and clinical information of the UK haemodialysis patients

The UK HD patients in this section were from the QCKD study. Their demographics and clinical information are shown in Table 3-7 and Table 3-8, respectively.

GP Physical Activity Questionnaire (GPPAQ)

1093 UK HD patients provided the complete GPPAQ, and the valid response rate was 94.6%. The vast majority of patients (78.5%) remained inactive. Conversely, the lowest proportion of patients (4.2%) led an active lifestyle. The distribution of Physical Activity Index (PAI) in the UK HD patients is shown in Table 7-1.

Table 7-1 Distribution of Physical Activity Index in the UK HD patients

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Outcome</th>
<th>HD patients in each category n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPPAQ</td>
<td>PAI</td>
<td>Inactive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>907 (78.5)</td>
</tr>
</tbody>
</table>
**Relationship between GPPAQ and categorical variables**

Male patients had a significantly higher activity level than females ($X^2=17.288, P=0.001$). There was no difference in the level between White British participants and South Asian cohorts ($X^2=4.768, P=0.190$). There was also no significant difference in PA levels between different smoking statuses ($X^2=0.357, P=0.836$). The distribution of PAI in genders, ethnicities and smoking status is shown in Table 7-

**Table 7-2: The distribution of PAI in genders, ethnicities and smoking status in the UK HD patients**

<table>
<thead>
<tr>
<th>PAI</th>
<th>Gender (n=1132)</th>
<th>Ethnicity (n=761)</th>
<th>Smoking status (n=1086)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n,%)</td>
<td>Female (n,%).</td>
<td>British (n,%).</td>
</tr>
<tr>
<td>Inactive</td>
<td>568 (80.7)</td>
<td>339 (87.4)</td>
<td>538 (83.8)</td>
</tr>
<tr>
<td>Moderately</td>
<td>49 (7.0)</td>
<td>29 (7.5)</td>
<td>42 (6.5)</td>
</tr>
<tr>
<td>Active</td>
<td>44 (6.3)</td>
<td>15 (3.9)</td>
<td>33 (5.1)</td>
</tr>
<tr>
<td>Active</td>
<td>43 (6.1)</td>
<td>5 (1.3)</td>
<td>29 (4.5)</td>
</tr>
</tbody>
</table>
Relationship between the GPPAQ and continuous variables

The correlation between the GPPAQ, demographic and clinical information showed that the PA level was negatively associated with the increasing age, C-Reactive Protein (CRP), ALP levels and number of co-morbidities. Urea, creatinine and phosphate levels were positively correlated with activity level. Table 7-3 shows the Spearman’s rank correlations between PAI category, demographics and clinical information.

Table 7-3 Correlation between PAI category and continuous variables in the UK HD patients

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>PAI category</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.265</td>
<td>P&lt;0.001***</td>
</tr>
<tr>
<td>vintage (y)</td>
<td>Rho=-0.01</td>
<td>P=0.753</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Rho=-0.004</td>
<td>P=0.917</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>Rho=0.135</td>
<td>P&lt;0.001***</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.180</td>
<td>P&lt;0.001***</td>
</tr>
<tr>
<td>albumin (g/L)</td>
<td>Rho=0.109</td>
<td>P=0.002**</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Rho=-0.144</td>
<td>P=0.001***</td>
</tr>
<tr>
<td>cholesterol (mmol/L)</td>
<td>Rho=0.065</td>
<td>P=0.137</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>Rho=0.095</td>
<td>P=0.006**</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>Rho=-0.100</td>
<td>P=0.004**</td>
</tr>
<tr>
<td>URR (%)</td>
<td>Rho=0.066</td>
<td>P=0.096</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.028</td>
<td>P=0.416</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.016</td>
<td>P=0.647</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.137</td>
<td>P&lt;0.001***</td>
</tr>
</tbody>
</table>

**P< 0.01; ***P< 0.001 (2-tailed)

Leisure Time Exercise Questionnaire (LTEQ)

1063 UK HD patients completed the first question of the LTEQ, which focuses on the number of times that patients participated in different intensity exercises in a usual week. 1045 and 915 patients provided the complete responses in the frequency of activity completed long enough to work up a sweat and the types of usual exercise, respectively. The median total LTEQ score was 3.00(0.00-15.00) METs. 948 (89.2%) patients were classed as insufficiently active in their HCS, suggesting they are not active enough to benefit their health. 742 (71.0%) patients reported that they never or rarely exercise long enough to work up a sweat in a usual week. The LTEQ score, HCS
categories and percentage of patients who completed exercise ‘long enough to work up a sweat’ in a typical 7-day period are shown in Table 7-4.

**Table 7-4 LTEQ, HCS and percentage of patients that complete exercise ‘long enough to work up a sweat’ in a typical week in UK HD patients**

<table>
<thead>
<tr>
<th>LTEQ (METs)</th>
<th>UK HD patients</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>n=1063</td>
<td>3.00(0.00-15.00)</td>
</tr>
<tr>
<td>Health Contribution Score Categories</td>
<td>n=1063</td>
<td>%</td>
</tr>
<tr>
<td>Active</td>
<td>73</td>
<td>6.9</td>
</tr>
<tr>
<td>Moderately Active</td>
<td>42</td>
<td>3.9</td>
</tr>
<tr>
<td>Insufficiently Active</td>
<td>948</td>
<td>89.2</td>
</tr>
<tr>
<td>Frequency of activity completed long enough to work up a sweat</td>
<td>n=1045</td>
<td>%</td>
</tr>
<tr>
<td>Never or rarely</td>
<td>742</td>
<td>71.0</td>
</tr>
<tr>
<td>Sometimes</td>
<td>226</td>
<td>21.6</td>
</tr>
<tr>
<td>Often</td>
<td>77</td>
<td>7.4</td>
</tr>
</tbody>
</table>

The dominant type of exercise in the UK HD patients was walking, followed by cycling and swimming. Types of exercise in which patients participated during their usual life are demonstrated in Table 7-5.

**Table 7-5 Types of exercise completed by patients: number of patients reported and percentages**

- Walking (747 [81.6%])
- Cycling (65 [7.1%])
- Swimming (52 [5.7%])
- Weightlifting (24 [2.6%])
- Running (18 [2.0%])
- Aerobics (15 [1.6%])
- Tennis (14 [1.5%])
- Football (13 [1.4%])
- Table tennis (12 [1.3%])
- Dancing, yoga, badminton, fishing, Tai Chi, Golf, Cricket, Gym, Jogging (Total activities: 39 [4.3%])
Relationship between the total LTEQ score and categorical variables

Female and White British patients had significantly lower LTEQ score than their male (female /male: 0.00(0.00-12.00)/3.00(0.00-20.00), Z=-2.485, \( P=0.013 \)) and South Asian counterparts (White British/South Asian: 3.00 (0.00-12.00)/9.00 (0.00-21.00), Z=-3.849, \( P<0.001 \)). There was no significant difference in the total LTEQ score (F=0.949, \( P=0.387 \)) between different smoking status.

Relationship between the LTEQ score and continuous variables

Significant negative associations were seen between the total LTEQ score, older age, higher CRP, ALP levels and a greater number of co-morbidities. The total LTEQ score was positively correlated with creatinine levels and Urea Reduction Ratio (URR). Table7- 6 show the Spearman’s rank correlations between the LTEQ score demographics and clinical information.

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>LTEQ score</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.151</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>vintage (y)</td>
<td>Rho=-0.054</td>
<td>( P=0.083 )</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>Rho=-0.050</td>
<td>( P=0.222 )</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>Rho=0.028</td>
<td>( P=0.428 )</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.096</td>
<td>0.01*</td>
</tr>
<tr>
<td>albumin (g/L)</td>
<td>Rho=0.052</td>
<td>( P=0.138 )</td>
</tr>
<tr>
<td>cholesterol (mmol/L)</td>
<td>Rho=0.020</td>
<td>( P=0.660 )</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Rho=-0.142</td>
<td>0.001***</td>
</tr>
<tr>
<td>phosphate (mmol/L)</td>
<td>Rho=0.040</td>
<td>( P=0.259 )</td>
</tr>
<tr>
<td>ALP (iu/L)</td>
<td>Rho=-0.093</td>
<td>0.008**</td>
</tr>
<tr>
<td>URR (%)</td>
<td>Rho=0.084</td>
<td>0.036*</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.042</td>
<td>( P=0.229 )</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.002</td>
<td>( P=0.955 )</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.158</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

\(*P<0.05; \quad **P<0.01; \quad ***P<0.001 \) (2-tailed)
7.4.2 Physical activity level measured by tri-axial accelerometry of the haemodialysis patients and healthy controls in the UK

Demographics of the HD patients and healthy controls

Patients and healthy controls in this part were those who were recruited in the COCO study. For detailed information regarding their demographics the reader is asked to refer to Table3- 13and Table3- 14in chapter 3, respectively.

Physical activity level measured by Sensewear armband (SWA) in haemodialysis patients

21 (70%) UK HD patients agreed to wear the SWA, of these, 20 (95%) patients met the minimum wearing compliance (≥8 hours per day and ≥3 days with at least one HD day and two non-HD days) after excluding the impact of the Hawthorne effect. There were 17 (85.0%) male and 3 (15.0%) female in these 20 patients. The mean days of wearing SWA were 2.85 (range 2-3) and 3.85 (range 2-4) on HD and non-HD days, respectively. The mean wear hours of a usual day were 20.61±2.91, showing with 19.19±2.75 and 21.67±3.35 hours on a usual HD day and non-HD day.

The median daily steps and weekly Moderate to Vigorous Physical Activity (MVPA) were 2688 (995-6968) and 321 (82-1023) min, respectively. There was no significant difference in the percent of “sedentary” and “active” HD patients when comparing daily steps on HD days and non-HD days. However, daily steps and MVPA on HD days were significantly lower than those on non-HD days in UK HD patients. The comparison of PA levels between HD days and non-HD days in UK HD patients is shown in Table7- 7.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Steps Category</td>
<td>&lt;5000 (sedentary)</td>
<td>≥7500 (active)</td>
<td>&lt;5000 (sedentary)</td>
</tr>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>14 (70%)</td>
<td>3 (15%)</td>
<td>14 (70%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>MVPA</td>
<td>1636.5 (672.0-5701.5)</td>
<td>2917.5 (1242.25-7914.5)</td>
<td>0.030*</td>
</tr>
<tr>
<td></td>
<td>39 (2-85)</td>
<td>60 (21-188)</td>
<td>0.011*</td>
</tr>
</tbody>
</table>

*P<0.05 (2-tailed)
Physical activity level with GENEActiv in healthy controls

10(100%) UK healthy controls wore the GENEActiv. One participant’s data was missing due to a malfunction with the monitor. 9(90%) patients still met the minimum wearing compliance (≥8 hours per day and at least 3 days in the week) after excluding the impact of the Hawthorne effect. There were 5 (55.6%) males and 4 (44.4%) females in the healthy control group. The median weekly MVPA were 1426.44±318.42 min.

Comparison of PA levels between haemodialysis patients and healthy controls

The median MVPA in HD patients (1447 [1278-1712] min) was significantly lower than that in healthy control (321 [82-1023] min) (Z=-3.158, P=0.001).

Comparison of PA levels between haemodialysis patients and healthy controls adjusting for age

As a reminder, the HD patients were significantly older than healthy controls in the UK. The mean weekly MVPA in HD patients and healthy controls were 697 (95%CI: 370-1025) min and 1347 (95%CI: 839-1855) min after controlling for age, respectively. The weekly MVPA in HD patients (group=1) is significantly lower than that in healthy controls in the UK (group=2) ($R^2_{\text{Adjusted}} = .328$, $P=0.044$) (Table 7-8).

Table 7-8: Multivariable linear regression analysis for the comparison of weekly MVPA between HD patients and healthy controls after adjusting for age

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>â</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>644.544</td>
<td>799.758</td>
<td>.428</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-10.782</td>
<td>9.527</td>
<td>-.210</td>
<td>.268</td>
</tr>
<tr>
<td>Groups</td>
<td>1280.153</td>
<td>306.664</td>
<td>.394</td>
<td>.044*</td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, â: standardized Coefficients. *$P<0.05$

7.4.3 Physical activity level measured by questionnaires in Chinese haemodialysis patients

Demographics and clinical information of Chinese haemodialysis patients

Patients involved in this part came from the QCKD study, for detailed information regarding demographics and clinical information it refers to the Table 3-9 and Table 3-10 in Chapter 3, respectively.
GPPAQ

All Chinese HD patients recruited in the study provided the complete GPPAQ. 352 (64.9%) patients were physically inactive, followed by 99 (18.3%) patients with active PA level. The distribution of PAI in Chinese HD patients is demonstrated in Table 7-9.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Outcome</th>
<th>HD patients in each category n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPPAQ</td>
<td>PAI</td>
<td>Inactive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>352 (64.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderately Inactive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>49 (9.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderately Active</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42 (7.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Active</td>
</tr>
<tr>
<td></td>
<td></td>
<td>99 (18.3)</td>
</tr>
</tbody>
</table>

Relationship between GPPAQ and categorical variables

There was no significant difference in PA level between genders ($X^2=4.404, P=0.221$) and smoking status ($X^2=11.902, P=0.064$). The distribution of PAI in genders and smoking status is shown Table 7-10.

<table>
<thead>
<tr>
<th>PAI</th>
<th>Gender</th>
<th>Smoking status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n=542)</td>
<td>Female (n=542)</td>
</tr>
<tr>
<td></td>
<td>Current smoker (n=537)</td>
<td>Ex-smoker (n=539)</td>
</tr>
<tr>
<td></td>
<td>Never smoked (n=539)</td>
<td></td>
</tr>
<tr>
<td>Inactive</td>
<td>197 (62.5)</td>
<td>29 (50.0)</td>
</tr>
<tr>
<td></td>
<td>155 (68.3)</td>
<td>66 (61.7)</td>
</tr>
<tr>
<td></td>
<td>255 (68.5)</td>
<td></td>
</tr>
<tr>
<td>Moderately Inactive</td>
<td>30 (9.5)</td>
<td>5 (8.6)</td>
</tr>
<tr>
<td></td>
<td>19 (8.4)</td>
<td>12 (11.2)</td>
</tr>
<tr>
<td></td>
<td>32 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Moderately Active</td>
<td>22 (7.0)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td></td>
<td>20 (8.8)</td>
<td>6 (5.6)</td>
</tr>
<tr>
<td></td>
<td>29 (7.8)</td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>66 (21.0)</td>
<td>18 (31.0)</td>
</tr>
<tr>
<td></td>
<td>33 (14.5)</td>
<td>23 (21.4)</td>
</tr>
<tr>
<td></td>
<td>56 (15.1)</td>
<td></td>
</tr>
</tbody>
</table>
**Relationship between the GPPAQ and continuous variables**

PA levels were negatively associated with age, parathyroid hormone (PTH), and number of co-morbidities. Table 7-11 shows the Spearman’s rank correlations between PAI and the continuous variable of demographics and clinical information in Chinese HD patients.

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>PAI category</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=0.202</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>vantage (y)</td>
<td>Rho=0.003</td>
<td>P=0.945</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Rho=0.002</td>
<td>P=0.960</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>Rho=-0.011</td>
<td>P=0.819</td>
</tr>
<tr>
<td>creatinine (umol/L)</td>
<td>Rho=0.060</td>
<td>0.193</td>
</tr>
<tr>
<td>phosphate (mmol/L)</td>
<td>Rho=-0.004</td>
<td>P=0.922</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>Rho=-0.099</td>
<td>0.033*</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho=0.048</td>
<td>P=0.282</td>
</tr>
<tr>
<td>haemotocrit (L/L)</td>
<td>Rho=0.061</td>
<td>P=0.168</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.137</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>

*P< 0.05; ***P< 0.001 (2-tailed)
Leisure Time Exercise Questionnaire (LTEQ)

The median total LTEQ score was 21.00(6.00-21.00) METs. 453(83.6%) patients had an insufficiently active exercise level. 304 (56.1%) patients reported they never or rarely exercised long enough to work up a sweat in a usual week. The total LTEQ score, HCS categories and percentage of patients who complete exercise ‘long enough to work up a sweat’ in a typical 7-day period are shown in Table 7-12.

Table 7-12 The LTEQ, HCS categories and percentage of patients that complete exercise ‘long enough to work up a sweat’ in a typical week in Chinese HD patients

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Chinese HD patients (n=542)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTEQ (METs)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Total</td>
<td>21.00(6.00-21.00)</td>
</tr>
</tbody>
</table>

Health Contribution Score Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active, n (%)</td>
<td>73(13.5%)</td>
</tr>
<tr>
<td>Moderately Active, n (%)</td>
<td>16(2.9%)</td>
</tr>
<tr>
<td>Insufficiently Active, n (%)</td>
<td>453(83.6%)</td>
</tr>
</tbody>
</table>

Frequency of activity completed long enough to work up a sweat

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never or rarely, n (%)</td>
<td>304(56.1)</td>
</tr>
<tr>
<td>Sometimes, n (%)</td>
<td>167(30.8)</td>
</tr>
<tr>
<td>Often, n (%)</td>
<td>71(13.1)</td>
</tr>
</tbody>
</table>

The dominant type of exercise in everyday life was walking (85.1%), followed by running and cycling. Types of exercise participated by patients in their everyday life are demonstrated in Table 7-13.

Table 7-13 Types of exercise completed by patients: number of patients reported and percentages

- Walking (461[85.1%])
- Running (73 [13.5%])
- Cycling (25 [4.6%])
- Square Dancing (13 [2.4%])
- Aerobics (10 [1.8%])
- Fishing (8 [1.5%])
- Yoga, badminton, table tennis, basketball, swimming, push-up, Lula hoop, Tai Chi, snooker, Weightlifting (Total activities:22 [4.1%])
Relationship between the LTEQ score and categorical variables

The total LTEQ score in male patients was significantly higher than that in females (male/female: 21.00[6.00-21.00]/21.00(0.00-21.00), Z=-2.224, P=0.025).

Relationship between the LTEQ score and continuous variables

Higher LTEQ score were significantly associated with the younger age. The total LTEQ score was positively correlated with higher pre-dialysis creatinine, Hgb and haematocrit levels. Table 7-14 shows the Spearman’s rank correlations between the LTEQ score, demographics and clinical information.

Table 7-14: Spearman’s rank correlation between LTEQ score, demographics and clinical information

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>LTEQ score</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Rho=-0.120</td>
<td>0.005***</td>
</tr>
<tr>
<td>vintage (y)</td>
<td>Rho=0.043</td>
<td>P=0.315</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Rho=-0.013</td>
<td>P=0.760</td>
</tr>
<tr>
<td>urea (mmol/L)</td>
<td>Rho=-0.012</td>
<td>P=0.802</td>
</tr>
<tr>
<td>Pre-dialysis creatinine(umol/L)</td>
<td>Rho=0.096</td>
<td>0.036*</td>
</tr>
<tr>
<td>phosphate(mmol/L)</td>
<td>Rho=-0.046</td>
<td>P=0.291</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>Rho=0.019</td>
<td>P=0.686</td>
</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>Rho= 0.174</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>haematocrit (L/L)</td>
<td>Rho= 0.160</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Co-morbidities (count per person)</td>
<td>Rho=-0.070</td>
<td>P=0.101</td>
</tr>
</tbody>
</table>

*P< 0.05; **P<0.01; ***P< 0.001 (2-tailed)

7.4.4 Physical activity level measured by Sensewear Armband (SWA) of the haemodialysis patients and healthy controls in China

Demographics of haemodialysis patients and healthy controls in China

Patients and healthy controls in the section were from the COCO study. For detailed information regarding the demographics in the HD patients and healthy controls the reader is asked to refer to the Table 3-16 and Table 3-17 in chapter 3, respectively.
Physical activity level with SWA in haemodialysis patients

30 (75%) Chinese HD patients agreed to wear the SWA, of these, 23 (76.7%) patients met the minimum wearing compliance (≥8 hours per day and ≥3 days with at least one HD day and two non-HD days) after excluding the impact of the Hawthorne effect. There were 11 (47.8%) male and 12 (52.2%) female in 23 patients. The mean days of wearing SWA were 2.09 (range 1-3) and 3.78 (range 2-5) on HD and non-HD days, respectively. The mean wear hours of a usual day were 20.64±2.11, showing 19.63±3.21 and 21.43±2.18 on an average HD day and non-HD day.

The mean daily steps on an average day and weekly MVPA were 5192 ± 2741 and 664±447 min, respectively. There was no significant difference in the percent of ‘‘sedentary’’ (P=0.767) and ‘‘active’’ (P=0.459) HD patients based on the daily septs on between HD and non-HD day. Meanwhile, there were no significant difference in daily steps and weekly MVPA between on HD and non-HD day in Chinese HD patients. The comparison of PA level on between HD day and non-HD day in Chinese HD patients is shown in Table 7-15.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>HD day</th>
<th>Non-HD day</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Steps Category</td>
<td>&lt;5000 (sedentary)</td>
<td>≥7500 (active)</td>
<td>&lt;5000 (sedentary)</td>
</tr>
<tr>
<td>N (%)</td>
<td>13 (56.5%)</td>
<td>3 (13.0%)</td>
<td>12 (52.2%)</td>
</tr>
<tr>
<td>MVPA</td>
<td>4928.87±2532.39</td>
<td>5405.84±3135.59</td>
<td>0.225</td>
</tr>
<tr>
<td>92.17±70.55</td>
<td>97.43±71.94</td>
<td>0.701</td>
<td></td>
</tr>
</tbody>
</table>

PA level with SWA in healthy controls

35 (87.5%) Chinese healthy controls agreed to wear the SWA, of these, 33 (94.3%) met the minimum wearing compliance (≥8 hours per day and at least 3 days in the week) after excluding the impact of the Hawthorne effect. There were 16 (48.5%) male and 17 (51.5%) female in 33 patients. The mean days of wearing SWA were 6.73 (5-7) and 6.27 (4-7) valid wearing days, respectively. The mean wear hours of a usual day were 18.87±3.70.
The median of daily steps on an average day and weekly MVPA were 7227 (5133-10146) and 711 (378-1295) min, respectively. 7 (21.2%) and 15 (45.5%) were viewed as ‘‘sedentary’’ and ‘‘active’’ based on less 5000 and more than 7500 steps per day.

**Comparison of PA levels between haemodialysis patients and healthy controls in China**

The daily steps on an average day in HD patients were significantly lower than those in healthy controls in China. However, there was no significant difference in weekly MVPA between HD patients and healthy controls in China. The comparison of daily steps and weekly MVPA are shown in Figure7- 1 and Figure7- 2, respectively.

![Comparison of daily steps between HD patients and healthy controls in China](image.png)
Comparison of physical activity level measured by questionnaires between UK and Chinese haemodialysis patients

Comparison of demographics and clinical information between the UK and Chinese haemodialysis patients

The patients in this section were from the QCKD study. The comparison of demographics and clinical information between the UK and Chinese HD patients are shown in Table 3-11 and Table 3-12 of Chapter 3, respectively.
Comparison of the GPPAQ between UK and Chinese haemodialysis patients

The percentage of patients with “Inactive” PA in UK HD patients was more than that in Chinese HD patients. However, the percentages of patients with “Moderately Inactive”, “Moderately Active” and “Active” categories in UK HD patients was less than those in their Chinese counterparts. The UK HD patients’ overall PA level was significantly lower than Chinese HD patients ($X^2=15.209$, $P<0.001$). Comparison of PAI categories between the UK and Chinese HD patients is shown in Figure 7-3.

![Figure 7-3: Comparison of the PAI categories between UK and Chinese HD patients](image)

Figure 7-3: Comparison of the PAI categories between UK and Chinese HD patients
Comparison of the GPPAQ between UK and Chinese haemodialysis patients after adjusting for age and gender

The UK patients were significantly older and had more males than the Chinese patients in the QCKD study. ‘Active’ of PAI was taken as a reference category in the multinomial logistic regression model. After controlling for age and gender, the UK HD patients conducting ‘Inactive’ PA level appeared 4.007 times than performing ‘Active’ compared to Chinese HD cohorts (P<0.001). The UK HD patients conducting ‘Moderately Inactive’ and ‘Moderately Active’ PA level appeared 3.410 and 2.915 times than performing ‘Active’ compared to Chinese HD cohorts, respectively (both P<0.001) (Table 7-16).

Table 7-16 Multi-nominal logistic regression Analysis for the comparison of the GPPAQ

<table>
<thead>
<tr>
<th>GPPAQ</th>
<th>B</th>
<th>SE B</th>
<th>P</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-2.281</td>
<td>.456</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.045</td>
<td>.006</td>
<td>&lt;.001***</td>
<td>.000</td>
</tr>
<tr>
<td>Gender</td>
<td>.878</td>
<td>.207</td>
<td>&lt;.001***</td>
<td>.000</td>
</tr>
<tr>
<td>[Group=1.00]</td>
<td>1.388</td>
<td>.195</td>
<td>&lt;.001***</td>
<td>.000</td>
</tr>
<tr>
<td>[Group=2.00]</td>
<td>0a</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Inactive         |         |        |          |         |
| Intercept        | -1.748  | .585   | .003     |         |
| Age              | .003    | .008   | .738     | 1.003   |
| Gender           | .673    | .267   | .012*    | 1.960   |
| [Group=1.00]     | 1.227   | .259   | <.001*** | 3.410   |
| [Group=2.00]     | 0a      |        |          |         |

| Moderately Inactive |         |        |          |         |
| Intercept           | -1.858  | .623   | .003     |         |
| Age                 | .006    | .009   | .499     | 1.006   |
| Gender              | .532    | .285   | .062     | 1.702   |
| [Group=1.00]        | 1.070   | .274   | <.001*** | 2.915   |
| [Group=2.00]        | 0a      |        |          |         |

| Moderately Active  |         |        |          |         |
| Intercept          |         |        |          |         |
| Age                |         |        |          |         |
| Gender             |         |        |          |         |
| [Group=1.00]       |         |        |          |         |
| [Group=2.00]       | 0a      |        |          |         |

B: Unstandardized coefficient, SE: Standard Error, â: standardized Coefficients. ***P<0.001, Pseudo R²=0.122 * This parameter is set to zero because it is redundant.
Comparison of leisure time exercise behaviour (LTEQ) between UK and Chinese haemodialysis patients

The UK HD patients participated had significantly fewer total exercise scores than Chinese HD patients did. A lower proportion of HD patients in the UK were active than those in China based on the analysis of HCS. Conversely, more UK HD patients than Chinese patients were reported as being insufficiently active. The comparison of the total LTEQ score and HCS categories between UK and Chinese HD patients is shown in Table 7-17.

### Table 7-17 Comparison of the total LTEQ score and HCS categories between UK and Chinese HD patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>UK HD patients (n=1063)</th>
<th>China HD patients (n=542)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTEQ (METs)</td>
<td>Median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3.00(0.00-15.00)</td>
<td>21.00(6.00-21.00)</td>
<td>&lt;0.001 ***</td>
</tr>
<tr>
<td>HCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active, n (%)</td>
<td>73(6.9%)</td>
<td>73(13.5%)</td>
<td></td>
</tr>
<tr>
<td>Moderately Active, n (%)</td>
<td>42(3.9%)</td>
<td>16(2.9%)</td>
<td>&lt;0.001 ***</td>
</tr>
<tr>
<td>Insufficiently Active, n (%)</td>
<td>948(89.2%)</td>
<td>453(83.6%)</td>
<td></td>
</tr>
</tbody>
</table>

***P< 0.001 (2-tailed)
Comparison of leisure time exercise behaviour (LTEQ) between UK and Chinese haemodialysis patients after adjusting for age and gender

The mean LTEQ score in HD patients in the UK and China appeared 11.709 (95%CI: 10.367-13.051) and 19.316 (95%CI: 17.411-21.221) after controlling for age and gender, respectively. The LTEQ score in UK HD patients (group=1) was significantly lower than that in Chinese HD patients (group=2) ($R^2_{\text{Adjusted}} = .115$, $P<0.001$) (Table 7-18).

Table 7-18 Multivariable linear regression Analysis for the comparison of the total LTEQ score between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>24.036</td>
<td>3.561</td>
<td>3.561</td>
<td>.000***</td>
</tr>
<tr>
<td></td>
<td>(17.051, 31.020)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-4.616</td>
<td>1.133</td>
<td>-.099</td>
<td>.000***</td>
</tr>
<tr>
<td></td>
<td>(-6.839, -2.394)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-.228</td>
<td>.037</td>
<td>-.156</td>
<td>.000***</td>
</tr>
<tr>
<td></td>
<td>(-.302, -.155)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups</td>
<td>7.607</td>
<td>1.215</td>
<td>.159</td>
<td>.000***</td>
</tr>
<tr>
<td></td>
<td>(5.224, 9.990)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. *** $P<0.001$

7.4.6 Comparison of PA level measured by Sensewear Armband (SWA) between UK and Chinese haemodialysis patients

Comparison of demographics between UK and Chinese haemodialysis patients

The patients in this section were recruited in the COCO study. The Comparison of demographics between UK and Chinese HD patients is shown in Table 3-19 of Chapter 3.
Comparison of PA level measured by SWA between UK and Chinese haemodialysis patients

There was no significant difference in the percentage of HD patients who appeared sedentary (P=0.122) or active (P=0.314) between the UK and China. Moreover, there was no significant difference in daily steps and weekly MVPA between the UK and Chinese HD patients. The Comparison of PA level between UK and Chinese HD patients is shown in Table 7-19.

Table 7-19 Comparison of PA level between UK and Chinese HD patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>UK HD patients (n=20)</th>
<th>Chinese HD patients (n=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category N (%)</td>
<td>&lt;5000 (sedentary)</td>
<td>15 (75%)</td>
<td>12 (52.2%)</td>
</tr>
<tr>
<td>Daily Steps</td>
<td>≥7500 (active)</td>
<td>5 (25%)</td>
<td>3 (13.0%)</td>
</tr>
<tr>
<td>steps</td>
<td>2688 (995-6968)</td>
<td>4865 (3290-6576)</td>
<td>0.064</td>
</tr>
<tr>
<td>Weekly MVPA</td>
<td>321 (82-1023)</td>
<td>620 (378-1123)</td>
<td>0.330</td>
</tr>
</tbody>
</table>
7.5 Discussion

7.5.1 PA level in the UK haemodialysis patients

Along with the high prevalence of poor physical function, physical inactivity was also a common phenomenon in the UK HD patients. This may support that physical inactivity plays important role in leading to reduced physical function (Kosmadakis et al. 2010, Tawney, Tawney & Kovach 2003). Additionally to the 78.5% and 89.2% of UK HD patients from the QCKD study who were classed as inactive in physical activity index (PAI) and insufficiently active in health contribution score (HCS), 75% of the patients from the COCO did not reach the cut-off point of 5000 steps per day, which was regarded as sedentary(Tudor-Locke et al. 2012). Moreover, the UK HD patients spent significantly less time on MVPA than their age and gender-matched healthy control group. A study measuring steps using pedometers reported that 71% of HD patients were sedentary(Cobo et al. 2015), which was similar to the 75% of patients in this current study. Additionally, the UK HD patients had 2917 and 1636 steps/day on non-HD and HD days in the study, which was lower than 3767 and 2274 steps/day on non-HD and HD days in Sweden HD patients, and lower than an average 3500-4500 steps/day in the other HD patients (Nowicki, Murlikiewicz & Jagodzińska 2010, Avesani et al. 2012, Zamojska et al. 2006).

The study suggested that male HD patients had higher PA levels and performed more exercise than females, which was consistent with the finding that male HD patients’ physical function are higher than females (Liu 2012, Johansen, Kaysen et al. 2013, Brown, Yore et al. 2005).This was also in agreement with the finding in a study that male patients with ESRD participated in exercise more frequently and had fewer limitations in moderate and strenuous exercise than their female counterparts (Stack, Murthy 2008).Similar to the correlation between physical function, demographics and clinical information, PA level in the UK HD patients was negatively affected by the increased age, inflammation, worse bone metabolism and comorbidities. Conversely, higher level of muscle mass and better nutritional status (NS) were positively correlated with patients’ PA level. Additionally, underlying physical aspects related to dialysis procedure contributed to the low PA level in UK HD patients, such as 4 hours of inactivity during HD session or tiredness after the session. These contributing factors of physical inactivity were consistent with the clinical determinants and the HD
process, which were documented to be associated with reduced PA level with HD patient (Cobo et al. 2015, Violan et al. 2002).

7.5.2 PA level in Chinese haemodialysis patients

Chinese HD patients’ mean daily steps were 5192, higher than the average 3500-4500 steps/day of HD patients in the previous studies (Nowicki, Murlikiewicz & Jagodzińska 2010, Avesani et al. 2012, Zamojska et al. 2006). As well as this, they had more steps on non-HD (5405) or HD days (4928) than those in other study (Cobo et al. 2015). However, there was still 52.2% of Chinese HD patients were considered sedentary based on the cut-off point of 5000 steps/day. Additionally, besides 64.9% and 83.6% of patients showed inactive in PAI and insufficiently active in HCS, the daily steps in Chinese HD patients were significantly lower than their age and gender matched healthy controls.

It was found that male HD patients had higher exercise levels than females in this study. However, there was no difference in PA level between genders in Chinese HD patients. It is understood that household work was the Chinese HD patients’ major type of PA (Li, Li & Fan 2010). The disparity of perceptions and attitudes towards housework between genders informed by Chinese traditional beliefs may be a hidden barrier for male patients’ housework participation. Since, it is women who are subject to taking the primary responsibility in doing housework and being caregivers in Chinese traditional beliefs (Robinson 1985), especially when the patients are males.

The correlation between PA level, albumin, cholesterol, ALP and CRP were not explored as too much data was missing for these parameters. However, the results still showed the positive relationship between higher activity levels, more muscle mass and good NS in Chinese HD patients. The strong association between PA and anaemia was consistent with the independent correlation between Hgb and the number of steps with chronic HD patients in a cross-sectional study (Zamojska et al. 2006). A decline in PA level in HD patients is ascribed to impaired strength caused by anaemia. Moreover, the reduction in physical function resulted from anaemia, consequently led to the decreased physical performance (Penninx et al. 2004). Additionally, bone turnover caused by increased PTH was negatively correlated with Chinese patients’ PA level.
It is understood that PA level is lower on HD days compared with non-HD days due to lack of activity during the 4-hour HD session (Cobo et al. 2015, Majchrzak et al. 2005). However, surprisingly, there was no significant difference in PA level between dialysis and non-dialysis days in Chinese HD patients, which was inconsistent with the findings in the previous studies (Cobo et al. 2015, Violan et al. 2002). One explanation may be ascribed to the lack of patients transport services in China which was applied for dialysis patients with good quality in the UK. Chinese HD patients, especially those who resided in rural areas, usually require frequent travel between their home and HD units by public transportation, which may increase their PA levels on dialysis days.

7.5.3 Comparison of PA level between UK and Chinese haemodialysis patients

Despite more severe anaemia being present in Chinese HD patients than UK HD patients, Chinese patients showed higher activity levels than UK patients, which was in agreement with the finding reported in chapter 6 that UK HD patients had worse physical function than their Chinese counterparts. In accordance with a global investigation (Hallal et al. 2012) regarding PA levels with the same age profile, including the UK and China, the percentage of physical inactivity was 34.8% (34.5-35.1) in Europe and 17.10% (16.8-17.2) in Southeast Asia, respectively. More participants in China preferred to walk to work compared with those in Switzerland, the U.S. and Australia. Additionally, the frequency of cycling in Chinese adults (>20%) was much higher than in the UK adults (<2%). This analysis suggests that physical inactivity was more prevalent in high income countries than those in low income countries. This study extended the previous findings with HD patients in the UK and China. Underlying reasons for this difference may include: higher muscle mass, better NS and bone metabolism in Chinese HD patients versus UK HD patients. Additionally, incomplete patients transport services in China which forced patient to travel between their home and HD units by themselves may increase their PA level, consequently cause the higher activity level in Chinese HD patients than UK patients.

It is noteworthy that there was no significant difference in daily steps and weekly MVPA between the UK and Chinese HD patients in the COCO study. However, although that is not statistically significant (P=0.064) in daily steps between UK and Chinese HD patients, the difference of their value (2688 [995-6968] vs.4865[3290-
6576] in the UK and Chinese HD patients) is clinically significant. There is a chance than Type II error has been made, as a small sample size in the COCO study. The simplest method to minimize the probability of committing this type of statistical error is to increase the sample size or the power of the test to increase the chances to capture the differences in the statistical tests. The occurrence of error may confirm that UK HD patients had lower PA level than Chinese patients. However, according to the difference between the subjective and objective results of PA level, it may suggest that HD patients’ PA level is influenced by various factors, such as physical and psychological determinants(Ishii, Shibata & Oka 2010, Nantel, Mathieu & Prince 2010). Further exploration regarding the associated factors resulting in the disparity of physical function and PA levels between UK and Chinese HD patients, including HD patients’ perception of exercise is needed.

7.5.4 Strengths and limitations

It is understood that this is the study of PA level with the largest UK and Chinese HD population. However, it does have limitations. Too much missing clinical information in Chinese HD patients’ medical records led to the failure with the exploration of more influencing factors of PA levels. The GPPAQ is designed to understand participant’s PA level for discussion and motivational interviewing for anyone who is categorized into less than active (Guidance and guidelines, NICE 2013). It was widely used for collecting data from a variety of disease status issues (Takahashi, Hu et al. 2018, Clarke, Young et al. 2015b, Weiler, Stamatakis 2010). However, GPPAQ scoring is limited to employment status, physical exercise and cycling. For participants who are retired or unemployed, individuals are not classified as active unless they perform physical exercise or cycling for at least 3 hours. However, walking, housework and gardening may be particularly relevant to this population. Furthermore, whilst the reliability of the GPPAQ has been shown to be reasonable, its validity in adults between 60 and 74 years old was poor (Ahmad, Harris et al. 2015). When compared to accelerometer the GPPAQ showed low sensitivity and poor agreement for identifying active primary care patients. Actually, it has been removed from the general practice 2014/15 hypertension QOF. However, the GPPAQ is still recommended to be used in the National Health Service (NHS) health check (Public Health England 2014). Moreover, the NICE would continue to support GPPAQ’s use as a validated tool
although further studies are recommended to be explored (Guidance and guidelines, NICE 2013). Finally, the Chinese version of the GPPAQ is currently not validated for its use in adults, which is another limitation in this study. However, it has been cross-culturally translated and adapted before being applied. Additionally, similar to the potential limits of statistical analysis when using a large number of multiple correlations in Chapter 6, although it has been shown statistically significant correlation between PA level and clinical parameters, there is the possibility of the occurrence of Type I error.

7.6 Conclusion

Low PA level was highly prevalent in the UK HD patients. Increased age, more inflammation, worse bone metabolism, more comorbidities and HD process have been shown to be negatively associated with PA level of the UK HD patients. Meanwhile, high muscle mass and better NS were positively correlated with their PA levels. Similar to their UK counterparts, Chinese HD patients also presented a sedentary lifestyle. Besides high muscle mass and good NS have been shown to be positively correlated with PA level in Chinese HD patients, improved anaemia was associated with the increased PA levels. When using questionnaires to subjectively measure physical inactivity, a higher prevalence of physical inactivity was seen in the UK HD patients compared to the Chinese HD patients. Chinese HD patients’ higher muscle mass, better NS and bone metabolism, and incomplete patients transport services may contribute to the underlying causes. More potential associated factors including patients’ perception of exercise may give a more thorough understanding of PA levels with HD patients in the two cultural cohorts.
Chapter 8

Self-perceived Benefits and Barriers to Exercise in the UK and Chinese Haemodialysis patients
8.1 Abstract

While the perceived benefits of exercise motivate HD patients’ participation in exercise, perceptions of barriers to exercise inhibits their participation. Perception and attitudes towards exercise are influenced by health beliefs that are strongly correlated with cultures. The aim of this study was to understand and compare self-perceived benefits and barriers to exercise in the UK and Chinese HD patients. The Dialysis Patient-Perceived Exercise Benefits and Barriers Scale (DPPEBBS) was conducted with HD patients in the UK and China, respectively. The perception of exercise benefits in the UK and Chinese HD patients was significantly greater than that of barriers to exercise. It has been suggested that HD patients have the potential to accept exercise behaviour change intervention. The findings of perceived barriers to exercise revealed that HD patients should focus on enhancing physical and functional self-efficacy. Whilst more attention should be attracted to strengthen the management of falling for the UK HD patients, fostering patients’ understanding of how to conduct an exercise suitable for HD is required for Chinese HD patients. Older and female UK HD patients should focus more on the benefits of exercise, while attention needs to be focused both on enhancing the perception of exercise benefits and on decreasing barriers for younger and female Chinese patients, respectively. Perceived exercise benefits were significantly less in the UK HD patients compared with Chinese HD patients, which may partly explain the fact that UK HD patients had lower physical activity (PA) levels than Chinese HD patients.

8.2 Background

PA and regular exercise are recommended to optimize health, quality of life (QoL) and decrease mortality risk, but the majority of HD patients lead very sedentary lives. Great efforts have been made to encourage patients to be active. However, there are few studies that explore the contributing factors to the sedentary behaviour in HD patients (Fiaccadori et al. 2014). Identifying and understanding the influencing factors of participating in PA or exercise is required to inform the design of a personalized exercise intervention or facilitate the incorporation of exercise prescriptions into clinical practice.
Physical inactivity may be influenced not only by the poor physiological condition caused by kidney disease or dialysis itself, but also by HD patients’ perception regarding benefits and barriers to exercise. It has been shown that motivation for performing exercise may arise from a patient’s recognition of exercise benefits (Clarke et al. 2015a). It is necessary to understand HD patients’ self-perceived benefits and foster better understanding of the benefits of exercise on their kidney diseases in order to promote the motivation to exercise.

Commonly reported barriers to exercise implementation were renal symptoms and comorbidities that HD patients suffered from (Goodman, Ballou 2004a, Painter, Stewart & Carey 1999, Stack, Murthy 2008, Stack et al. 2005). One survey regarding barriers to exercise participation among HD patients revealed that 92% of participants reported at least one barrier to PA (Liu 2012). Among all the obstacles, shortness of breath (48%) and fatigue on dialysis and non-dialysis days (67 and 40%, respectively) were the most frequent barriers to PA. Lack of motivation was the second barrier closely associated with less PA, followed by the presence of a number of medical conditions and not having enough time on dialysis days. Apart from these, other studies reported that the most common barriers to PA or exercise performance were: lack of motivation, lack of confidence seeking exercise in the course of rehabilitation, insufficient understanding of the disease and negative attitudes toward exercise (Goodman, Ballou 2004a, Kontos et al. 2007, Tawney et al. 2000). Mounting evidence has demonstrated that the perceived barriers to exercise were inversely associated with exercise behaviour in HD patients (Goodman, Ballou 2004b, Delgado, Johansen 2011, Kontos et al. 2007). Thorough understanding of perceived barriers to exercise is necessary for the proper interventions development (Hefferon et al. 2013).

The aim of this chapter has previously been described in number (5) of section 1.6 in Chapter 1. Briefly, the primary aim was to explore and compare HD patients’ perceived exercise benefits and barriers in the UK and China.

8.3 Methods

The data included in this chapter was derived from the QCKD study (Chapter 2, section 2.2.2). The detailed methods are described in Chapter 2. Specifically, the DPPEBBS was used (section 2.3.2). As a reminder, the DPPEBBS assesses HD patients’ perceived benefits and barriers to exercise.
8.4 Results

8.4.1 Self-perceived benefits and barriers to exercise in the UK haemodialysis patients

Demographics

Patients in this part came from the QCKD study. UK HD patients’ demographics are shown in Table3-7 of Chapter 3.

DPPEBBS

The scores of 1-4 in exercise benefits mean from “strongly disagree” to “strongly agree”. The code of the barrier items is reversed. The median average exercise benefits and barriers score were 2.82 (2.55-3.09) and 2.42 (2.17-2.67), respectively. The mean perceived exercise benefits score was significantly higher than the barrier score (Z=-15.875, P<.001). 75.4%-78.6% patients recognized the top 5 patient perceived exercise benefits. The most frequently reported benefits were improving QoL, controlling body weight, preventing body function decline, muscle atrophy, and promoting an optimistic life. 47.2%-70.4% patients recognized the top 5 patient perceived exercise barriers. The most commonly reported barriers to exercise were predominantly physical, such as tiredness, lower extremity muscle fatigue and body pain. Additionally, patients showed concern about falling and the thirst caused from exercise. The most reported benefits and barriers to exercise are shown in Figure8-1 and Figure8-2, respectively.
Figure 8-1: The major benefits of exercise held by UK HD patients reported with DPPEBBS

Figure 8-2: The major barriers to exercise held by UK HD patients reported with DPPEBBS

**Relationship between DPPEBBS and demographics**

Average benefits score was negatively associated with increased age (rho=-0.123, \( P<0.001 \)), and female sex (\( Z=-2.203, P=0.028 \)). However, there was no association between the score of barriers to exercise, age (rho=0.038, \( P=0.253 \)) and gender (\( Z=-1.057, P=0.291 \)). Not only did White British HD patients have significantly lower
benefits scores than their South Asian counterparts ($Z=-3.362$, $P=0.001$), they also held significantly lower barrier scores than South Asian patients ($Z=-2.076$, $P=0.038$). There was no significant association between benefits (rho=-0.056, $P=0.096$), barriers scores (rho=0.004, $P=0.902$) and dialysis vintage.

**Relationship between DPPEBBS and activity questionnaires**

Exercise benefits were positively correlated with the Duke Activity Status Index (DASI) and Leisure Time Exercise Questionnaire (LTEQ) scores in the UK HD patients. Conversely, exercise barriers were negatively correlated with the DASI and LTEQ scores. Exercise benefits ($F=4.315$, $P=0.005$) and barriers scores ($F=8.001$, $P<0.001$) were significantly different between physical activity index (PAI) categories. The benefit scores in “Inactive” patients (2.84±0.48) were significantly lower than in “moderately active” (3.03±0.44, $P=0.011$) and “active” ones (3.02±0.60, $P=0.016$). The barrier score in “Inactive” patients (2.44±0.42) were significantly higher than in “moderately active” (2.19±0.49, $P<0.001$) and “active” ones (2.20±0.60, $P<0.001$). The correlation between benefits and barriers scores, the DASI and LTEQ is shown in Table 8-1.

**Table 8-1** Correlation between benefits and barriers scores, the DASI and LTEQ

<table>
<thead>
<tr>
<th>Activity questionnaires</th>
<th>Self-perceived benefits of exercise</th>
<th>Self-perceived barriers to exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASI score (METs)</td>
<td>Rho=0.201 $P&lt;0.001$***</td>
<td>Rho=-0.297 $P&lt;0.001$***</td>
</tr>
<tr>
<td>LTEQ score (METs)</td>
<td>Rho=0.225 $P&lt;0.001$***</td>
<td>Rho=-0.253 $P&lt;0.001$***</td>
</tr>
</tbody>
</table>

$P<0.001$***

**8.4.2 Self-perceived benefits and barriers to exercise in Chinese haemodialysis patients**

**Demographics**

Patients in this part came from the QCKD study. Chinese HD patients’ demographics are shown in Table 3-9 of chapter 3.
The median average exercise benefits and barriers scores were 2.92 (2.67-3.17) and 2.42 (2.08-2.67), respectively. The mean perceived exercise benefits score was significantly higher than the barrier score ($Z=-15.219, P<.001$). 82.4%-87.8% patients recognized the top 5 patient-perceived exercise benefits. The most frequently reported benefits were promoting an optimistic life, preventing muscle atrophy, improving mood, self-care abilities, and QoL. 41.9%-70.1% patients recognized the top 5 patient-perceived exercise barriers. The most commonly reported barriers were predominantly physical, such as: tiredness, lower extremity muscle fatigue and body pain. Additionally, patients lacked an understanding of how to do exercise and had concern about thirst caused from exercise. The most reported benefits and barriers to exercise are shown in Figure 8-3 and Figure 8-4, respectively.

![Figure 8-3: The major benefits of exercise held by Chinese HD patients reported with DPPEBBS](image-url)
Figure 8 - The major barriers to exercise held by Chinese HD patients reported with DPPEBBS

Relationship between DPPEBBS and demographics

Female patients reported significantly higher barriers scores than male (Z=-3.348, P=0.001). However, there was no significant difference in exercise benefits scores between genders (Z=-0.938, P=0.348). There was no significant correlation between benefits score and dialysis vintage (rho=-0.023, P=0.596). However, barrier scores were positively correlated with dialysis vintage (rho=0.093, P=0.032). Increasing age was positively correlated with benefits score (rho=0.131, P=0.002), but positively correlated with barriers score (rho=0.158, P<0.001).

Relationship between DPPEBBS and activity questionnaires

There was no significant correlation between benefits scores and the DASI score. However, the barriers to exercise score was negatively correlated with the DASI score. Exercise benefits (F=4.659, P=0.003) and barriers scores (F=13.841, P<0.001) were significantly different between PAI categories. “Active” patients perceived more benefits than “inactive” ones (2.91±0.43 vs. 2.87±0.45, P<0.001). The barrier score in “active” patients were significantly lower than in “moderately active” (2.34±0.43, P=0.01), “moderately inactive” (2.36±0.47, P=0.002) and “inactive” (2.45±0.42, P<0.001). Exercise benefits were positively correlated with the LTEQ
scores. Conversely, barriers were negatively correlated with the LTEQ scores. The correlation between benefits and barriers scores, the DASI and LETQ are shown in Table 8-2.

### Table 8-2 Correlation between benefits and barriers scores, the DASI and LTEQ

<table>
<thead>
<tr>
<th>Activity questionnaires</th>
<th>Self-perceived benefits of exercise</th>
<th>Self-perceived barriers to exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASI score (METs)</td>
<td>Rho=0.007 P=0.871</td>
<td>Rho=-0.404 P&lt;0.001***</td>
</tr>
<tr>
<td>LTEQ score</td>
<td>Rho=0.202 P&lt;0.001***</td>
<td>Rho=-0.297 P&lt;0.001***</td>
</tr>
</tbody>
</table>

8.4.3 **Comparison of self-perceived benefits and barriers to exercise between UK and Chinese haemodialysis patients**

**Comparison of demographics between UK and Chinese haemodialysis patients**

The comparison of demographics between UK and Chinese HD patients is shown in Table 3-11 of Chapter 3.

**Comparison of perceived benefits and barriers to exercise between UK and Chinese haemodialysis patients**

UK HD patients (2.91 [2.55-3.09]) had a significantly lower mean average perceived benefits of exercise score than Chinese patients (2.92 [2.67-3.17]) (Z=-3.363, P=0.001). However, there was no significant difference in the mean average perceived barriers to exercise score between the two cohorts (Z=-1.590, P=0.112). The comparisons in exercise benefits and barriers scores between UK and Chinese HD patients are shown in Figure 8-5 and Figure 8-6, respectively.
Figure 8-5: Comparison in benefits score between UK and Chinese HD patients

Z = -3.363, P = 0.001***

Figure 8-6: Comparison in barriers score between UK and Chinese HD patients

Z = -1.590, P = 0.112
Comparison of perceived benefits of exercise between UK and Chinese haemodialysis patients after adjusting for age and gender

The mean perceived benefits of exercise score with HD patients in the UK and China was 2.838 (95%CI: 2.806-2.870) and 2.905 (95%CI: 2.864-2.947) after controlling for age and gender, respectively. The benefits score in the UK HD patients (group=1) was significantly lower than that in Chinese HD patients (group=2) ($R^2_{\text{Adjusted}} = .015$, $P=0.014$) (Table 8-3).

Table 8-3 Multivariable linear regression analysis for the comparison of perceived benefits of exercise between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>2.940</td>
<td>.083</td>
<td>.083</td>
<td>.000</td>
</tr>
<tr>
<td></td>
<td>(2.778, 3.103)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.055</td>
<td>.026</td>
<td>-.055</td>
<td>.035*</td>
</tr>
<tr>
<td></td>
<td>(-.107, -.004)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-.002</td>
<td>.001</td>
<td>-.050</td>
<td>.068</td>
</tr>
<tr>
<td></td>
<td>(-.003, .000)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups</td>
<td>.067</td>
<td>.027</td>
<td>.067</td>
<td>.014*</td>
</tr>
<tr>
<td></td>
<td>(.013, .121)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B: Unstandardized coefficient, SE: Standard Error, β: standardized Coefficients. *$P<0.05$

8.5 Discussion

The perceived benefits and barriers to a behaviour are of importance in the health promotion model (N.J. Pender 1996). It has been documented that the greater perception of benefits to exercise facilitated individuals’ exercise participation, while the greater perception of barriers to exercise impede them engaging in exercise (Brown 2005, Cuaderes, Parker & Burgin 2004, Grubbs, Carter 2002). Unsurprisingly, whilst motivation for performing exercise is related to HD patients’ recognition of exercise benefits (Clarke et al. 2015b), perceived barriers to exercise negatively impact on exercise engagement with HD patients (Goodman, Ballou 2004b, Delgado, Johansen 2011, Kontos et al. 2007). These are consistent with the findings in this study, which showed that perception of exercise benefits was positively associated with physical function and activity level but perceived barriers to exercise negatively affect them in both the UK and Chinese HD patients. Both UK and Chinese HD patients perceived more benefits than barriers, which is similar with the Jordanian ESRD patients who had a higher mean score of benefits than that of barriers (Darawad, Khalil 2013), and with American HD patients who reported more salient motivators compared with
barriers (Goodman, Ballou 2004b). This study showed that a high percentage of patients recognized a range of potential exercise benefits in the UK and Chinese HD patients, which is in agreement with reports from prior studies (Johansen, Painter 2012, Delgado, Johansen 2012, Jhamb et al. 2016), suggesting openness to an appropriate exercise behaviour change intervention. Moreover, UK and Chinese HD patients had a better understanding of the direct benefits of exercise, such as preventing muscular atrophy and improving mood. Additionally, some benefits items in the questionnaire that are shared with the general population, involving promoting an optimistic life and better QoL, were grounded in HD patients’ perceptions. However, indirect benefits of exercise, including relieving pain, preventing other diseases, and especially decreasing medical costs in Chinese HD patients need to be understood by patients. The findings in this study regarding common barriers to exercise for patients, suggested that exercise intervention for the UK HD patients should focus on enhancing physical and functional self-efficacy, including management of the risk of falling. Additionally to reinforcing physical and functional self-efficacy, fostering patients’ understanding of how to conduct appropriate exercise suitable for HD and widening exercise information resources are essential to increase the motivation of exercise participation in Chinese HD patients.

It has been documented that Chinese HD patients were younger than HD patients in the other countries (UK Renal Registry 2016, United States Renal Data System, USRDS 2015, Chinese National Renal Data System 2015). Interestingly, younger Chinese HD patients perceived fewer exercise benefits than older ones, which is consistent with results reported by Jordanian (Darawad, Khalil 2013). During the survey, a few young Chinese patients mentioned that they quit their jobs when they had been diagnosed with ESRD. The life of unemployment and/or self-pity may weaken their ability to meet the responsibilities necessary to support their family. As a result, they might lose interest in or passion for doing anything including increasing awareness of the health benefits of exercise. However, UK HD patients perceived fewer exercise benefits with age increases. Additionally, it has been showed that Chinese female HD patients reported more barriers, and UK female HD patients held fewer benefits for exercise than their respective male counterparts. There were no findings pertaining to the correlation between demographics and perceived benefits and barriers to exercise in HD patients in a previous study (Goodman, Ballou 2004b).
This study extends the findings that exercise counselling or education for the UK HD patients needs to focus more attention on the benefits of exercise for older and female patients. Meanwhile, more attention should be put on increasing motivation and removing barriers to exercise for younger and female Chinese HD patients, respectively.

Although there was no significant difference in perceived barriers between UK and Chinese HD patients, Chinese HD patients perceived more benefits of exercise than the UK patients. This may increase Chinese patients’ motivation for engaging in exercise and consequently increase PA level more than their UK counterparts (Clarke et al. 2015b). Fostering HD patients’ recognition of exercise benefits, especially for the UK HD patients, is essential for increasing motivation of patients’ exercise participation. As described in the previous physical function chapter, UK HD patients had lower physical function than Chinese HD patients, which might explain the possibility that UK patients with worse physical function may lack motivation of an understanding of exercise benefits. It may be supported by the positive correlation between exercise capacity (the DASI score) and benefits of exercise which was reported in this study. However, although this is statistically significant in perceived exercise benefits between UK and Chinese HD patients, the median difference (0.01) is not clinically significant. So this may mean there is no meaningful difference between the populations. Additionally, it has been shown that the effect of improving QoL was regarded as the main exercise benefit and physical symptoms are considered the main barrier to exercise by HD patients. Therefore, further exploration of the contributing factors of PA levels, including QoL and symptoms, may be required to understand HD patients’ activity in the UK and China.

**Limitations**

The DPPEBBS is a validated questionnaire which further explores the specific perception of dialysis patients about exercise. However, it was originally developed in China. Therefore, the terminology on its English version may be slightly unclear to English speakers. In this study, a supplementary explanatory sheet was used to aid comprehension. Additionally, the first question which refers to the cost of dialysis treatment is not relevant to National Health Service (NHS) patients. This question was deleted with a single strikethrough and not required for UK participants to complete.
Thus, there were only 11 items about exercise benefits left in the English version. However, the results of the DPPEBBS were described with the average scores of exercise benefits and barriers. This may have partly eliminated the impact of questionnaire modification. Variance explained by age, gender and group in perceived benefits of exercise was only 1.5%. It indicates that many other factors associated with exercise benefits were not included in the model in the study. Additionally, dependent variables for linear regression should be continuous or scalar. However, score from the DPPEBBS is ordinal. The ordinal regression may be the most appropriate analysis rather than the linear regression.

8.6 Conclusion

UK and Chinese HD patients perceived more benefits than barriers. The majority of UK and Chinese HD patients recognized a range of exercise benefits, suggesting openness to exercise behaviour change intervention. In-depth understanding of indirect exercise benefits is required for HD patients in two cultural groups. Exercise intervention for HD should focus on enhancing physical and functional self-efficacy, including management of the risk of falling for the UK patients and providing more information about exercise engagement for Chinese patients. While more attention to exercise benefits needs to be focused on old and female patients in UK HD patients, young and female Chinese HD patients should have more attention put on understanding benefits and removing barriers to exercise. UK HD patients perceived fewer exercise benefits than Chinese HD patients, which in part explains the lower PA level in UK HD patients compared with Chinese patients.
Chapter 9

Relationship between Physical Function, Activity and Quality of Life, Symptoms and Body Composition in UK and Chinese haemodialysis Patients
9.1 Abstract

In previous results, the BMI in UK HD patients were higher than Chinese patients, but this was coupled with dietary insufficiency and was negatively correlated with physical function. These findings may be inconsistent with previous research indicating that higher BMI predicts better survival in HD patients. Poor Quality of Life (QoL) and symptom burden in HD patients lead to high mortality risk. It was found in previous results that improving QoL and the impact of symptoms were the commonly reported exercise benefit and barrier by both UK and Chinese HD patients. Therefore, the aim of this study was to explore the relationship between physical function, activity and QoL, symptoms and body composition in UK and Chinese HD Patients. The Euro QOL-5 Dimensions-5 Level (EQ-5D-5L), Palliative Care Outcome Scale–Symptoms Renal (POS-S) and Body Composition Monitor (BCM) were used to assess QoL, symptom burden and body composition. Physical performance tests and triaxial accelerometer were used for evaluating physical function and PA levels. There was a negative correlation between low QoL in the UK HD patients and physical function and PA levels. QoL scores were higher in the Chinese group and did not demonstrate any correlation with physical function and PA level. The most commonly reported symptoms in the UK and Chinese HD patients were physical, including pain, fatigue and weakness, which significantly affected physical function and PA levels. Higher BMI in the UK HD patients when compared to Chinese patients was ascribed to high Fat Mass (FM). Poorer QoL, greater impact of symptoms and higher FM may explain the lower physical function and activity level in the UK HD patients compared with their Chinese counterparts.

9.2 Background

Several studies indicate that higher BMI conveys survival advantage in HD patients (Lowrie, Li et al. 2002, Port, Ashby et al. 2002, Beddhu, Pappas et al. 2003). However, there were mixed consequences regarding which body component confers the survival. Some studies ascribed survival advantage in HD patients to both increased fat and muscle mass (Huang, Tighiouart et al. 2010) or independent higher muscle mass (Mafra, Guebre-Egziabher et al. 2008), whilst others attributed the positive finding to higher FM (Kalantar-Zadeh, Kuwae et al. 2006, Beddhu, Pappas et al. 2003). However, Kamyar Kalantar-Zadeh et al. also revealed that negative relationship between QoL
and FM percentage (Kalantar-Zadeh, Kuwae et al. 2006). The influence of FM for HD patients requires reconsideration and further exploration. UK HD patients had significant higher BMI than Chinese HD patients in all studies of this thesis. Meanwhile, high BMI failed to predict good NS and was negatively correlated with physical function. Therefore, to determine whether fat or muscle mass contributed to the disparity of BMI between UK and Chinese HD patients and which body component negatively associated with NS and physical function is necessary.

It was found in previous results that HD patients in both the UK and China have impaired physical function. It is widely known that muscle functionality and muscle mass are not congruent. In another words, reduced muscle strength or muscle functionality is unable to explain the muscle mass status (Hughes, Frontera et al. 2001). Both loss of skeletal muscle mass (SMM) and strength are independent predictors of mortality in HD patients (Cruz-Jentoft, Baeyens et al. 2010). Therefore, assessment of muscle mass may provide additional diagnostic and prognostic information to physical function evaluation. Low protein or energy intake and reduced muscle mass are integral diagnosis criteria of Protein-Energy Wasting (PEW) (Mak, Ikizler et al. 2011). As found in the DISH study, both the UK and Chinese HD patients had lower daily protein and energy intake than the recommended amount. Therefore, body composition measurement gives insight into the understanding of PEW and provides valuable information for the multidimensional nutritional assessment in HD patients (Broers, Martens et al. 2015).

QoL plays an important role in evaluating the strategies to improve the well-being of HD patients or prevent adverse outcomes (Fukuahara, Lopes et al. 2003), impact of illness and the quality of healthcare (Wan, Chen et al. 2015, Fukuahara, Yamazaki et al. 2007, Dashti-Khavidaki, Sharif et al. 2013). Furthermore, it has been confirmed that improved QoL is beneficial in improving dialysis outcomes (Chambers, Germain et al. 2010). Additionally, it is an efficient predictor in identifying risks of hospitalization and mortality in HD patients (Mapes, Lopes et al. 2003). However, large studies have confirmed that HD patients experience poor QoL (Yang, Griva et al. 2015a, Yang, Lau et al. 2015, Faridah, Jamaiyah et al. 2010, Kang, Lee et al. 2015a, Katayama, Miyatake et al. 2014, Okubo, Kai et al. 2014, Walters, Hays et al. 2002). Impaired QoL is affected by a number of factors in HD patients, such as increased age, female gender,
lack of formal education, multiple co-morbidities, medications (Sa'ed H Zyoud, Dala N Daraghmeh et al. 2016), and even cultures (Hicks, Cleary et al. 2004a).

HD patients also suffer from multiple physiological and psychological symptoms (Gutiérrez Sánchez Daniel, Leiva-Santos et al. 2017). Over 50% of dialysis patients reported that the most prevalent physiological symptoms were fatigue, pain, muscle cramps, difficulty sleeping and sexual dysfunction (Weisbord, Fried et al. 2005, Weisbord, Fried et al. 2007, Rosas, Joffe et al. 2001, Palmer 2003). A study of 60 HD patients found that more than half experienced weakness, difficulty sleeping and depression (Gutiérrez Sánchez Daniel, Leiva-Santos et al. 2017). Yong et al. revealed that the five most prevalent and intense symptoms amongst Hong Kong HD patients were fatigue, aversion to the cold, pruritus, lower torso weakness and difficulty sleeping. All symptoms were also inversely associated with QoL and survival (Yong, Kwok et al. 2009).

The findings regarding perception of exercise indicated that the most frequently reported patients-perceived benefits of exercise in UK HD patients was the improvement of QoL, which was also recognized in the top 5 exercise benefits for Chinese HD patients. Meanwhile, the most commonly reported patients-perceived barriers to exercise were physical symptoms in both UK and Chinese HD patients. In order to understand how well these factors influence physical function and PA, a thorough understanding of QoL and symptoms related to renal disease is required.

The aim of this chapter has previously been described in number (6) of section 1.6 in Chapter 1. Briefly, the primary aim was to understand the relationship between physical function, activity and QoL, symptoms and body Composition in UK and Chinese HD Patients.

9.3 Methods

The data included in this chapter was derived from the COCO study (Chapter 2, section 2.2.3). The detailed methods are described in Chapter 2. Specifically, the results of the EQ-5D-5L, POS-S and BCM (section 2.3.3) were used.

Briefly the EQ-5D-5L and POS-S were administered to UK and Chinese HD patients to assess QoL and symptoms relating to renal disease. The BCM was used to assess
HD patients’ body composition, including Lean Tissue Index (LTI) and fat tissue index (FTI). Physical performance tests (Shuttle Walking Test [SWT], Sit-to-Stand 60 [STS60], Short Physical Performance Battery [SPPB] and Handgrip Strength [HGS]) and triaxial accelerometer (Sensewear Armband [SWA]) were used to assess physical function and PA level. The purpose of exploring the correlation between physical function and symptoms was to understand the continuous impact of symptoms on physical function. Among these 4 physical performance tests, only SWT needs a period of time to complete. It takes around one minute to perform STS60, SPPB and HGS. Therefore, only SWT was used for showing HD patients’ physical function when evaluating the correlation between physical function and symptoms. Additionally, some symptoms in the POS-S are not closely related with exercise, such as mouth problems, changes in skin and so on. In this study, symptoms assumed to be connected to exercise, (pain, shortness of breath, weakness or lack of energy, drowsiness, poor mobility, restless legs and difficulty sleeping) were chosen to show the relationship between symptoms, physical function and PA level. Moderate to Mild Physical Activity (MVPA) as an outcome derived from SWA was obtained for assessing HD patients’ PA level. MVPA refers to the time that participants spend on moderate and vigorous intensities of PAs, which involves duration and intensity of exercise. It is a more comprehensive and efficient outcome measure compared with daily steps. Therefore, only MVPA was selected to be an outcome of PA level.

9.4 Results

9.4.1 QoL, symptom burdens and body composition in the UK haemodialysis patients

Demographics

Patients in the part were recruited in the COCO study. For detailed information regarding demographics the reader is asked to refer to Table3- 13 in chapter 3.

Quality of life

29 (96.7%) UK HD patients completed the EQ5D-5L. The mean index value was 0.68 (±0.26) with a range of 0.054-1.
Symptom burden relating to renal disease

The most commonly reported renal symptoms in the UK HD patients was ‘‘weakness’’ (97%), with the highest mean score of impact (1.79 ±1.01), while the least experienced symptom was ‘‘mouth problem’’ (17%), with the lowest mean score of impact (0.31±0.76). The most commonly experienced renal symptoms with percentage of patients reporting each symptom and mean (± SD) impact scores of renal symptoms in the UK HD patients are shown in Figure 9-1 and Table 9-1 (in descending order). The 5 most commonly reported symptoms and all other symptoms reported by participants with a percentage above 50% are highlighted in red and yellow, respectively.

![Figure 9-1 Renal symptoms reported in a usual week by UK HD patients](image-url)
Table 9- Impact scores for each of the renal symptoms in UK HD patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mean Impact Score ±SD (on a scale of 0 [not at all] to 4 [Overwhelmingly])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>1.79±1.01</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>1.76±1.21</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>1.48±1.24</td>
</tr>
<tr>
<td>Itching</td>
<td>1.48±1.24</td>
</tr>
<tr>
<td>Restless legs</td>
<td>1.38±1.18</td>
</tr>
<tr>
<td>Pain</td>
<td>1.34±1.17</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>1.24±1.15</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>1.10±1.11</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.90±1.01</td>
</tr>
<tr>
<td>Changes in skin</td>
<td>0.86±0.99</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.83±1.14</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>0.83±0.93</td>
</tr>
<tr>
<td>Feeling depressed</td>
<td>0.79±1.05</td>
</tr>
<tr>
<td>Feeling anxious</td>
<td>0.72±0.80</td>
</tr>
<tr>
<td>Vomiting (being sick)</td>
<td>0.45±1.02</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0.45±0.69</td>
</tr>
<tr>
<td>Mouth problems</td>
<td>0.31±0.76</td>
</tr>
</tbody>
</table>

**Relationship between QoL and physical function and PA level**

The index value of QoL significantly correlated with all the physical performance tests and PA level. HGS had a medium positive association with the index value. The associations between index value, whilst other physical function tests (ISWT, STS60, SPPB) and PA level (weekly MVPA) were all large. The correlation between QoL and physical function and PA level is shown in Table 9-2.

Table 9-2 Correlational relationship between QoL (EQ5D-5L index value), physical function (ISWT, STS60, SPPB, and HGS) and PA level (Weekly MVPA) in UK HD patients

<table>
<thead>
<tr>
<th>QoL Index value</th>
<th>ISWT</th>
<th>ESWT</th>
<th>STS60</th>
<th>SPPB</th>
<th>HGS</th>
<th>PA level (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index value</td>
<td>.759*</td>
<td>.562*</td>
<td>.611*</td>
<td>.612*</td>
<td>.390*</td>
<td>.732**</td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed); **P< 0.01 (2-tailed).
**Relationship between symptom burden, physical function and PA level**

The Incremental Shuttle Walking Test (ISWT) was negatively correlated with “pain”, “shortness of breath”, “weakness”, “poor mobility” and “restless legs”. PA level was significantly negatively correlated with “pain” and “poor mobility”. “Poor mobility” showed the largest correlation with physical function and PA level. Correlation between impact of symptoms, physical function and PA level is shown in Table 9.

Table 9- Correlational relationship between impact of renal symptoms, physical function (SWT) and PA level (Weekly MVPA) in the UK HD patients

<table>
<thead>
<tr>
<th>Renal Symptoms</th>
<th>N</th>
<th>Median (range)</th>
<th>Physical Function</th>
<th>PA level (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ISWT</td>
<td>ESWT</td>
</tr>
<tr>
<td>Pain</td>
<td>29</td>
<td>1(0-4)</td>
<td>-0.412*</td>
<td>-0.361</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>29</td>
<td>1(0-4)</td>
<td>-0.500**</td>
<td>-0.226</td>
</tr>
<tr>
<td>Weakness</td>
<td>29</td>
<td>2(0-4)</td>
<td>-0.412*</td>
<td>-0.089</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>29</td>
<td>1(0-3)</td>
<td>-0.325</td>
<td>-0.095</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>29</td>
<td>1(0-4)</td>
<td>-0.577**</td>
<td>-0.335</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>29</td>
<td>2(0-4)</td>
<td>-0.187</td>
<td>-0.052</td>
</tr>
<tr>
<td>Restless legs</td>
<td>29</td>
<td>1(0-4)</td>
<td>-0.483*</td>
<td>-0.356</td>
</tr>
</tbody>
</table>

*P < 0.05 (2-tailed); **P < 0.01 (2-tailed).

**Body composition**

44.8% and 72.4% of the UK HD patients showed low LTI and high FTI, respectively.
Relationship between body composition, physical function and PA level

LTI was positively associated with physical function tests and PA level. Except for the HGS, FTI was negatively associated with the other physical function tests and PA level. The association between LTI, FTI, physical function and PA is shown in Table 9-4.

Table 9-4 Correlational relationship between body composition (LTI, FTI), physical function (SWT, STS60, SPPB, HGS) and PA level (Weekly MVPA) in UK HD patients

<table>
<thead>
<tr>
<th>Body composition</th>
<th>N</th>
<th>Mean(±SD)</th>
<th>Physical Function</th>
<th>PA level (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ISWT</td>
<td>ESWT</td>
</tr>
<tr>
<td>LTI (kg/m²)</td>
<td>29</td>
<td>13.99±3.76</td>
<td>.513**</td>
<td>.394*</td>
</tr>
<tr>
<td>FTI (kg/m²)</td>
<td>29</td>
<td>12.29±5.18</td>
<td>-.600**</td>
<td>-.660**</td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed);  **P< 0.01 (2-tailed)

9.4.2 QoL, symptom burdens and body composition in Chinese haemodialysis patients

Demographics

Patients in the section were from the COCO study. For detailed information regarding demographics in Chinese HD patients the reader is asked to refer to the Table 3-16 in chapter 3.

Quality of life

All Chinese HD patients (n=40) completed the EQ5D-5L questionnaires. The mean index value was 0.95 (±0.08) with a range of 0.652-1.

Symptom burden relating to renal disease

The most common reported renal symptoms in Chinese HD patients was ‘Itching’ (75%), with the highest mean score (± SD) of impact (1.10±0.87), while the least experienced symptom was ‘Diarrhoea’ (15%), with the lowest mean (±SD) score of impact (0.15±0.36). The common experienced renal symptoms with percentage of patients reporting each symptom and mean impact scores of renal symptoms in Chinese HD patients were shown in Figure 9-2 and Table 9-5 (in descending order). The 5 most commonly reported symptoms and all other symptoms reported by
participants with a percentage above 50% are highlighted in red and yellow, respectively.

Figure 9 - Renal symptoms reported in a usual week by Chinese HD patients
Table 9- Impact scores for each of the renal symptoms in Chinese HD patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mean Impact Score ±SD (on a scale of 0 [not at all] to 4 [Overwhelming])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching</td>
<td>1.10±0.87</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>1.08±1.00</td>
</tr>
<tr>
<td>Mouth problems</td>
<td>0.80±0.88</td>
</tr>
<tr>
<td>Weakness or lack of energy</td>
<td>0.78±0.70</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0.75±0.81</td>
</tr>
<tr>
<td>Pain</td>
<td>0.70±0.82</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>0.60±0.67</td>
</tr>
<tr>
<td>Changes in skin</td>
<td>0.58±0.68</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.48±0.72</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>0.43±0.59</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>0.35±0.70</td>
</tr>
<tr>
<td>Feeling anxious</td>
<td>0.35±0.58</td>
</tr>
<tr>
<td>Restless legs</td>
<td>0.30±0.52</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.28±0.51</td>
</tr>
<tr>
<td>Vomiting (being sick)</td>
<td>0.28±0.45</td>
</tr>
<tr>
<td>Feeling depressed</td>
<td>0.23±0.48</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0.15±0.36</td>
</tr>
</tbody>
</table>

Relationship between QoL, physical function and PA level

There was no significant association between QoL, physical function and PA level in Chinese HD patients, which is shown in Table 9- 6.

Table 9- Correlational relationship between QoL (EQ5D-5L index value), physical function (ISWT, ESWT, STS60, SPPB, HGS) and PA level (Weekly MVPA) in Chinese HD patients

<table>
<thead>
<tr>
<th>QoL Index value</th>
<th>Physical Function</th>
<th>PA level (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISWT</td>
<td>0.249</td>
<td></td>
</tr>
<tr>
<td>ESWT</td>
<td>0.221</td>
<td></td>
</tr>
<tr>
<td>STS60</td>
<td>0.106</td>
<td></td>
</tr>
<tr>
<td>SPPB</td>
<td>0.154</td>
<td></td>
</tr>
<tr>
<td>HGS</td>
<td>0.233</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.020</td>
<td></td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed); **P< 0.01 (2-tailed).
Relationship between symptom burden, physical function and PA level

The ISWT was negatively correlated with “difficulty sleeping”. The Endurance Shuttle Walking Test (ESWT) was negatively correlated with “pain” and “weakness”. There was no association between the impact of symptoms and PA level. Table 9-7 shows the correlation between impact of renal symptoms and physical function (SWT) and PA level (Weekly MVPA) in Chinese HD patients.

**Table 9-7** Correlational relationship between impact of symptoms, physical function (SWT) and physical activity level (Weekly MVPA) in Chinese HD patients

<table>
<thead>
<tr>
<th>Renal Symptoms</th>
<th>N</th>
<th>Median (range)</th>
<th>Physical Function ISWT</th>
<th>ESWT</th>
<th>Physical activity (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>40</td>
<td>1(0-3)</td>
<td>-.147</td>
<td>-.481**</td>
<td>-.124</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>40</td>
<td>0(0-2)</td>
<td>-.079</td>
<td>-.165</td>
<td>.000</td>
</tr>
<tr>
<td>Weakness</td>
<td>40</td>
<td>1(0-2)</td>
<td>-.235</td>
<td>-.411*</td>
<td>-.366</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>40</td>
<td>1(0-3)</td>
<td>.066</td>
<td>.082</td>
<td>.088</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>40</td>
<td>0(0-3)</td>
<td>-.232</td>
<td>-.222</td>
<td>.129</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>40</td>
<td>1(0-3)</td>
<td>-.342*</td>
<td>-.246</td>
<td>-.269</td>
</tr>
<tr>
<td>Restless legs</td>
<td>40</td>
<td>0(0-2)</td>
<td>.122</td>
<td>.070</td>
<td>.292</td>
</tr>
</tbody>
</table>

*P < 0.05 (2-tailed); **P < 0.01 (2-tailed).

Body composition

37.8% and 45.9% of Chinese HD patients showed low LTI and high FTI, respectively.
Relationship between body composition, physical function and PA level

There was a significant and positive association between the LTI, physical performance tests and PA level. The negative association was shown between FTI, ISWT and HGS. The relationship between body composition, physical function and PA level in Chinese HD patients is shown in Table 9-8.

Table 9-8 Correlational relationship between body composition (LTI, FTI) and physical function (SWT, STS60, SPPB, HGS) and physical activity level (Weekly MVPA) in Chinese HD patients

<table>
<thead>
<tr>
<th>Body composition</th>
<th>N</th>
<th>Mean (SD)</th>
<th>ISWT</th>
<th>ESWT</th>
<th>STS60</th>
<th>SPPB</th>
<th>HGS</th>
<th>PA level (Weekly MVPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTI (kg/m²)</td>
<td>37</td>
<td>13.61 (2.11)</td>
<td>.523  **</td>
<td>.456  **</td>
<td>.569  **</td>
<td>.359  *</td>
<td>.699  **</td>
<td>.460  *</td>
</tr>
<tr>
<td>FTI (kg/m²)</td>
<td>37</td>
<td>8.78 (3.26)</td>
<td>-.403  *</td>
<td>-.302</td>
<td>-.288</td>
<td>-.152</td>
<td>-.325  *</td>
<td>-.139</td>
</tr>
</tbody>
</table>

*P < 0.05 (2-tailed); **P < 0.01 (2-tailed)

9.4.3 Comparison of QoL, symptom burdens and body composition between UK and Chinese haemodialysis patients

Comparison of demographics between UK and Chinese haemodialysis patients

Table 3-19 (Chapter 3) compares demographics between UK and Chinese HD patients.

Comparison of QoL between UK and Chinese haemodialysis patients

UK HD patients (0.68±0.26) had significantly lower index value than their Chinese counterparts (0.95 ±0.08) (t=-6.457, P<0.001). Comparison of QoL (index value) between UK and Chinese HD patients is shown in Figure 9-3.
Comparison of QoL between UK and Chinese haemodialysis patients after controlling for age and gender

UK patients were significantly older and had more males than the Chinese patients. After controlling for age and gender, the mean index value in UK and Chinese HD patients were 0.681 (95%CI: 0.612-0.750) and 0.951 (95%CI: 0.894-1.009), respectively. UK HD patients (group=1) had significant worse QoL than their Chinese counterparts (group=2) after controlling for age and gender ($R^2_{\text{Adjusted}}=0.364$, $P<0.001$) (Table 9).

Table 9. Multivariable linear regression analysis for the QoL between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>.539</td>
<td>.163</td>
<td>.002</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>(.213,.865)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.002</td>
<td>.002</td>
<td>-.093</td>
<td>.384</td>
</tr>
<tr>
<td></td>
<td>(-.006,.002)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-.029</td>
<td>.048</td>
<td>-.062</td>
<td>.552</td>
</tr>
<tr>
<td></td>
<td>(-.124,.067)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups</td>
<td>.270</td>
<td>.047</td>
<td>.604</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td></td>
<td>(.177,.363)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, $\beta$: standardized Coefficients. ***$P<0.001$
Comparison of symptoms between UK and Chinese haemodialysis patients adjusting for age and gender

UK HD patients suffered from a significantly greater impact in their symptoms than their Chinese counterparts, in relation to pain ($Z=-2.419$, $P=0.016$), shortness of breath ($Z=-2.774$, $P=0.006$), weakness ($Z=-4.175$, $P<0.001$), poor mobility ($Z=-4.245$, $P<0.001$), difficulty sleeping ($Z=-2.335$, $P=0.020$) and restless legs ($Z=-4.273$, $P<0.001$).

After controlling for age and gender, UK HD patients suffered greater impact from pain ($R^2_{Adjusted}=0.111$, $P=0.003$), shortness of breath ($R^2_{Adjusted}=0.138$, $P=0.003$), weakness ($R^2_{Adjusted}=0.306$, $P<0.001$), poor mobility ($R^2_{Adjusted}=0.278$, $P<0.001$), difficulty sleeping ($R^2_{Adjusted}=0.212$, $P=0.001$), and restless legs ($R^2_{Adjusted}=0.266$, $P<0.001$) than their Chinese counterparts (group=2). Unadjusted (mean±SD) and adjusted (mean [95%CI: lower bound-upper bound]) impact of symptoms related to renal disease between UK and Chinese HD patients is shown Table9-10.

Table9-10 Unadjusted and adjusted symptoms related to renal disease between UK and Chinese HD patients

<table>
<thead>
<tr>
<th>Renal Symptoms</th>
<th>UK HD patients</th>
<th>Chinese HD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted impact (mean±SD)</td>
<td>Adjusted impact Mean (95%CI: lower bound-upper bound)</td>
</tr>
<tr>
<td>Pain</td>
<td>1.34±1.17 (1.06-1.81)</td>
<td>1.43 (1.06-1.81)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>1.10±1.11 (0.78-1.45)</td>
<td>1.11 (0.78-1.45)</td>
</tr>
<tr>
<td>Weakness</td>
<td>1.79±1.01 (1.55-2.20)</td>
<td>1.88 (1.55-2.20)</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>1.48±1.24 (1.09-1.84)</td>
<td>1.46 (1.09-1.84)</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>1.76±1.21 (1.51-2.31)</td>
<td>1.91 (1.51-2.31)</td>
</tr>
<tr>
<td>Restless legs</td>
<td>1.38±1.18 (1.01-1.68)</td>
<td>1.34 (1.01-1.68)</td>
</tr>
</tbody>
</table>

*Denoted significant difference in unadjusted impact of symptoms between UK and Chinese HD patients, †$P<0.05$; ††$P<0.01$; †††$P<0.001$ (2-tailed);
* Denoted significant difference in adjusted impact of symptoms between UK and Chinese HD patients; *$P<0.05$ (2-tailed), **$P<0.01$, ***$P<0.001$ (2-tailed)
Comparison of LTI and FTI between UK and Chinese haemodialysis patients

There was no significant difference in the percentage of low LTI between UK and Chinese HD patients. However, the UK HD patients had a higher proportion of high FTI than their Chinese counterparts. The number and percentage of LTI and FTI in different categories, and the comparison of low LTI and high FTI between UK and Chinese HD patients is shown in Table 9-11. Similarly, there was no significant difference in LTI between UK and Chinese HD patients (t=0.490, P=0.627). UK HD patients had higher FTI than Chinese HD patients (t=3.187, P=0.003). The comparison of LTI and FTI between the UK and Chinese HD patients are shown in Figure 9-4 and Figure 9-5.

Table 9-11 Comparison of percentage of low LTI and high FTI between the UK and Chinese HD patients

<table>
<thead>
<tr>
<th>Body composition</th>
<th>Category</th>
<th>UK HD patients n (%)</th>
<th>Chinese HD patients n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTI</td>
<td>Low</td>
<td>13 (44.8)</td>
<td>14 (37.8)</td>
<td>0.566</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>15 (51.7)</td>
<td>23 (62.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>1 (3.5)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>FTI</td>
<td>Low</td>
<td>0 (0.0)</td>
<td>1 (2.7)</td>
<td>0.039*</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>8 (27.6)</td>
<td>19 (51.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>21 (72.4)</td>
<td>17 (45.9)</td>
<td></td>
</tr>
</tbody>
</table>

*P< 0.05 (2-tailed)
Comparison of LTI and FTI between UK and Chinese haemodialysis patients after adjusting for age and gender

After controlling for age and gender, the mean FTI in UK and Chinese HD patients were 12.338 (95% CI: 10.786–13.890) and 8.741 (95% CI: 7.379–10.102), respectively. UK HD patients (group=1) had significantly higher FTI than their Chinese counterparts (group=2) after controlling for age and gender ($R^2_{\text{Adjusted}} = -.221$, $P=0.001$) (Table 9-12).

Table 9-12: Multivariable linear regression analysis for the FTI between UK and Chinese HD patients after adjusting for age and gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>$\beta$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>7.321</td>
<td>3.607</td>
<td>3.607</td>
<td>.047</td>
</tr>
<tr>
<td>(.112,14.531)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.092</td>
<td>.044</td>
<td>.044</td>
<td>.043*</td>
</tr>
<tr>
<td>(.003,.181)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>2.833</td>
<td>1.099</td>
<td>.246</td>
<td>.012*</td>
</tr>
<tr>
<td>(.636,5.031)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups</td>
<td>-.397</td>
<td>1.071</td>
<td>-.397</td>
<td>.001***</td>
</tr>
<tr>
<td>(-5.737,-1.456)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Unstandardized coefficient, SE: Standard Error, $\beta$: standardized Coefficients. *$P<0.05$, **$P≤0.001$
9.5 Discussion

UK HD patients in this study had similar QoL with index value of 0.68±0.26 with that in patients from Korea (0.70 ± 0.20) (Kang, Lee et al. 2015b) and Taiwan (0.65 ±0.23) (Sakthong, Kasemsup 2012). The level of QoL is lower for UK HD patients than for Japanese HD patients with 0.75 ± 0.17 (Katayama, Miyatake et al. 2014) and higher than for Palestine 0.37 ± 0.44 (Sa’ed H Zyoud, Dala N Daraghmeh et al. 2016) and Singaporean patients 0.60 ± 0.21(Yang, Griva et al. 2015b). Surprisingly, Chinese HD patients had a remarkably higher QoL with the index value of 0.95±0.08 than HD patients from other countries. Socioeconomic factors, such as education levels and residency in different regions, healthcare systems, and clinical parameters, including age, female, dialysis vintage and comorbidities all affect HD patients’ QoL (Sa'ed H Zyoud, Dala N Daraghmeh et al. 2016, Hicks, Cleary et al. 2004b). These associated factors could explain the variations in QoL levels for HD patients in different countries. Meanwhile, the various relationship between QoL, patterns of medical practice and mortality among international ESRD patients showed that QoL is culture-specific (Rayner, Pisoni et al. 2003, Bleyer, Hylander et al. 1999, Held, Brunner et al. 1990, Hicks, Cleary et al. 2004c). Age is a powerful determinant of QoL in HD patients (Iliescu, Coo et al. 2003, Valderrábano, Jofre et al. 2001), which may explain the high QoL in Chinese HD patients who are younger than other HD patients (Chinese National Renal Data System 2015, UK Renal Registry 2015, United States Renal Data System, USRDS 2015). Sa’ed H. Zyoud attributed low QoL to physical inactivity in female HD patients in developing countries (Zyoud, Daraghmeh et al. 2016). However, as discussed in the previous chapters, Chinese female HD patients showed the similar PA level to male patients due to the possibility that Chinese women are expected to take primary responsibilities in doing housework and being caregivers in traditional Chinese culture (Wai - Ying 2001). The high PA level in Chinese female HD patients may contribute to a high QoL level. It has been shown that increasing PA or exercise levels improves the levels of QoL in HD patients(Painter, Carlson et al. 2000, Mi Rye Suh, R N, Hyuk Jung et al. 2002), which is consistent with the finding that a positive relationship between QoL, physical function ad PA level was present in the UK HD patients. It also can corroborate HD patients’ perception that exercise can improve QoL, which was the predominant self-perceived exercise benefit. However, the high
prevalence of optimal QoL level in Chinese HD patients could not determine a correlation with physical function and PA level.

It has been highlighted that the commonly reported symptoms related to renal disease focus on physiological complaints with both UK and Chinese HD patients, such as weakness, pain, itching, shortness of breath, poor mobility and so on, which were consistent with the reports from previous investigations with HD patients (Murtagh, Addington-Hall et al. 2007b, O'Connor, Corcoran 2012). In the current study, 97% of UK HD patients suffered from weakness, which showed a higher proportion than 60.2% in HD patients who experienced weakness from Iran (Omrani, Fallahi et al. 2015). 63% of Chinese HD patients reported experiencing weakness. 69% of UK HD patients and 53% of Chinese patients reported experiencing pain in the study, which is higher than 50% of Canadian HD patients with pain (Davison 2003). Similarly, 76% and 75% of UK and Chinese patients who suffered from itching was higher than 55% of HD patients from a systematic review (Murtagh, Addington-Hall et al. 2007b).

It is noted in the study that physical symptoms, including pain, short of breath, weakness, mobility and leg restless negatively affected Incremental Shuttle Walking Test (ISWT) in the UK HD patients. There was a significantly negative correlation between Shuttle Walking Test (SWT), pain, weakness and difficulty sleeping in Chinese HD patients. Meanwhile, poor mobility and pain significantly associated with UK HD patients’ PA level. This indicated that physical function may increase as symptoms improve, and that consequently, PA levels could possibly be augmented as well. These results were in agreement with the findings that physical outcomes are direct determinants of physical function and maintenance of PA in previous studies (Merkus, Jager et al. 1999, Curtin, Bultman et al. 2002, Knight, Ofsthun et al. 2003, van Stralen, De Vries et al. 2009). Likewise, the increasing PA level may potentially to lead to decreased symptom burden and increased physical function, which has been confirmed by previous studies (Windsor, Nicol et al. 2004a, Sarna, Conde 2001, Windsor, Nicol et al. 2004b). The walking speed used in the ESWT is determined by the performance in the ISWT, which equates to 85% of predicted Peak Oxygen Consumption (VO_{2peak}) achieved from the ISWT. This may explain the finding that there was no significant correlation between symptoms and ESWT in the UK HD patients. Since, the impact of symptoms on the performance in the ISWT may lead to a lower walking speed compared to participants’ actual capacity. Thus, symptoms may
not influence HD patients’ performance in a low level of the ESWT. Chinese HD patients reported that only weakness, pain and difficulty sleeping affected exercise capacity, the potential low impacts of these symptoms might not be great enough to affect patients’ PA level.

Nearly half of the UK HD patients in the study appeared to have a low LTI based on the norms obtained from 1000 healthy volunteers (Fresenius Medical Care). The mean LTI (13.99 kg/m²) in the UK cohort was higher than the average value of 12.7 kg/m² in HD patients from 3 European centres (Wizemann, Wabel et al. 2009). It was also higher than the one in 37,345 HD patients from 17 European countries (median: 14.3 vs. 12.2 kg/m²) (Marcelli, Usvyat et al. 2015). 72.4% of UK HD patients had high FTI. The mean FTI in UK HD patients was higher than that in other European HD patients (12.29 vs. 8.2 kg/m²) (Wizemann, Wabel et al. 2009).

Compared with the previous findings, the LTI of Chinese HD patients was higher than that in HD patients from other European studies (mean: 13.6 vs 12.7 kg/m²; median: 15.30 vs. 12.2 kg/m²) (Wizemann, Wabel et al. 2009, Marcelli, Usvyat et al. 2015). However, Chinese HD patients showed lower FTI than European HD patients (mean: 7.7 vs 8.2 kg/m²; median: 6.7 vs 9.8 kg/m²) (Wizemann, Wabel et al. 2009, Marcelli, Usvyat et al. 2015). This may be an underlying explanation for the finding that there was no significant correlation between FTI, muscle capacity and PA level in Chinese HD patients.

Positive associations between higher BMI and better survival in HD patients have been confirmed by a number of studies (Johansen, Young et al. 2004, Kalantar-Zadeh, Abbott et al. 2005, Port, Ashby et al. 2002). However, controversy has been raised due to the fact that higher BMI with higher Fat Mass (FM) had an increased prevalence of inflammation, atherosclerosis, CVD and all-cause mortality (Pecoits - Filho, Nordfors et al. 2002, Menon, Wang et al. 2003). The underlying explanations for the conflicting findings could be that the increased death risks caused by obesity (high BMI with high FM) were not so much as occurs in malnutrition (low muscle and FM). Essentially, only well-nourished HD patients with high BMI and high muscle mass had the lowest mortality risk (Beddhu, Pappas et al. 2003, Beddhu 2004). The findings in the study provided evidence that increased LTI contributed to the high physical function and PA
levels. Conversely, the higher FTI negatively affected activity outcomes in HD patients.

Loss of muscle mass (sarcopenia) and a decline in muscle strength (myopathy) may contribute to HD patients’ reduced functional capacity and physical inactivity (Beddhu 2004). This was corroborated by the finding of the significant positive correlation between LTI, physical function and PA level in UK and Chinese HD patients in this study. However, there was no significant difference in LTI between UK and Chinese HD patients, which may partly explain the finding that there was no significant difference in exercise capacity and PA level in this study. The higher BMI in the UK HD patients than Chinese patients was ascribed to the increased FM. Based on the negative correlation between the FTI, physical function and PA level, the higher FM may contribute to the lower physical function and PA levels in the UK HD patients than Chinese patients found in the QCKD study. It could explain the finding that UK HD patients with higher BMI than Chinese patients showed lower physical function and PA level compared with their Chinese counterparts. Additionally, it has been reported that the FTI contributes to adverse clinical outcomes (Pecoits - Filho, Nordfors et al. 2002, Menon, Wang et al. 2003, Cordeiro, Qureshi et al. 2009), which may lead to serious symptom burdens. This is consistent with the findings which indicated that UK HD patients had greater symptom burdens and poorer QoL when compared to Chinese HD patients.

The relationship between body components and BMI in UK and Chinese HD patients found in this study is also presumably applicable in the QCKD and DISH studies. Thus, it could be concluded that high BMI with high FM is unable to determine the good NS for HD patients. Additionally, the effect of serum creatinine as the predictor of muscle mass has not been confirmed, which is required to be further explored.

**Limitations**

The POS-S is a reliable and valid questionnaire which specially assesses symptom burden in patients with renal disease (Murphy, Murtagh et al. 2009). It has been translated into different languages and validated with a variety of patients with different stages of renal disease (Gutiérrez Sánchez Daniel, Leiva-Santos et al. 2017). However, there is currently no valid Chinese version of the POS-S. In the study, the English version of POS-S was translated to Chinese by two professional translators.
who had medical knowledge and back into English by two more translators who had no knowledge of the original version of the questionnaire but had medical background. Adaptations in the conceptual aspect were made until consensus was reached by the translation group and professional healthcare providers. Actually, the POS-S only refers to 17 symptoms that are commonly related to renal disease. It was not necessary to adapt the questionnaire in terms of logistical aspects, which may have guaranteed the quality of the Chinese version of POS-S.

9.6 Conclusion

The impaired QoL in the UK HD patients was correlated with low physical function and PA level. There was no significant correlation between Chinese HD patients’ good QoL, physical function and PA level. UK and Chinese HD patients’ symptom burdens relating to renal disease mainly referred to physical discomforts. These physical symptoms significantly affected UK HD patients’ exercise capacity and PA level. The few symptoms and low impact on Chinese HD patients may be the reason why symptoms did not influence PA levels. The higher BMI in UK HD patients than Chinese patients was ascribed to high FM, which may explain the finding that UK HD patients had lower muscle function and PA level. Poorer QoL, greater impact from symptom burdens as well as higher FM in UK HD patients may contribute to lower physical function and PA level compared with Chinese HD patients.
Chapter 10

General Discussion
Healthy lifestyle behaviors play a crucial role in the initiation and progression of Chronic Kidney Disease (CKD), and can prevent the deterioration of kidney function (EI Kossi, Bello et al. 2007). The European Dialysis and Transplantation Nurses Association/European Renal Care Association have proposed a series of recommended dietary intake amount for maintaining good nutritional status (NS) with HD patients. Moreover, the National Institute of Clinical Excellence (NICE) recommends regular exercise and even the Kidney Disease Improving Global Outcomes (KDIGO) suggests physical activity (PA) at least five times every week for HD patients to improve medical conditions and complications, and consequently decrease their high risk of mortality. However, it has been widely reported that malnutrition is highly prevalent in HD patients. Additionally, most HD patients have very sedentary lives. Dietary patterns and habits, and perceptions and attitudes towards exercise are strongly associated with lifestyle. It is understood that these factors are influenced by cultures. Therefore, to comprehensively understand HD patients’ lifestyle, the studies presented in this thesis have been designed to explore and compare HD patients’ nutritional status (NS) and physical activity between UK and China.

The dietary intake of UK and Chinese HD patients was evaluated, alongside demographics and nutritional blood parameters that provided insight into the underlying disparity of nutritional components between UK and Chinese HD patients. A high prevalence of malnutrition was present in both UK and Chinese HD patients. UK HD patients had better micronutrients management, such as iron, phosphate and potassium, than Chinese patients. However, there was no significant difference in energy and protein intake between UK and Chinese patients.

The understanding of physical function and PA in UK and Chinese HD patients was obtained by a combination of questionnaires and objective measures, which were conducted in two separate studies. Both UK and Chinese HD patients had impaired physical function and PA level. Although there was no significant difference in habitual PA level objectively measured by triaxial accelerometers between UK and Chinese patients, physical function and self-reported PA level with a large HD population were lower in UK patients than Chinese patients.

Demographic (age, gender, muscle and fat mass), clinical (nutrition, inflammation and bone derangement) and psychological parameters (perceived benefits and barriers to
exercise), QoL and symptoms were potential influencing factors of physical function and activity level in UK and Chinese patients. Anaemia in Chinese HD patients was negatively correlated with physical function and activity levels. Lower protein status and bone metabolism, higher fat mass and symptom burden, and fewer perceived exercise benefits in UK HD patients may contribute to the lower physical function and activity level than in Chinese HD patients.

Figure 10-1 shows schematic representation of the order of the studies presented in this thesis, which reported the primary conclusions and additional problems that need to be explored in the following chapters.
Primary Conclusions:

- Malnutrition was highly prevalent in UK and Chinese HD patients.
- UK HD patients had better nutrition management than Chinese patients.

Additional problems that need to be further explored:

- Body composition is necessary to be explored to better understand the relationship between BMI and NS.

Chapter 5: Validity of the DASI and GPPAQ walking pace question

Primary Conclusions:

- The DASI is valid for assessing physical function in UK and Chinese HD patients.
- The GPPAQ walking pace question showed possible valuable for providing walking pace assessment in UK HD patients.

Chapter 6: Physical Function of Haemodialysis Patients in UK and China

Primary Conclusions:

- Both UK and Chinese HD patients had impaired physical function and a low PA level.
- UK HD patients had lower physical function and PA levels than Chinese patients.

Additional problems that need to be further explored:

- Link between creatinine, NS and muscle mass and in-depth understanding of the relationship between body components and physical function.

Chapter 7: Physical activity level of Haemodialysis Patients in UK and China

Primary Conclusions:

- Both UK and Chinese HD patients had impaired physical function and a low PA level.
- UK HD patients had lower physical function and PA levels than Chinese patients.

Additional problems that need to be further explored:

- Link between creatinine, NS and muscle mass and in-depth understanding of the relationship between body components and physical function.

Chapter 8: Self-perceived benefits and barriers to Exercise in UK and Chinese HD patients

Primary Conclusions:

- UK and Chinese HD patients were found to perceive more benefits than barriers to exercise.
- The self-perceived benefits of exercise were fewer in UK HD patients than Chinese patients.

Additional problems that need to be further explored:

- Improving QoL and impact of symptoms were the commonly reported exercise benefits and barriers. The relationship between physical function, activity and QoL and symptoms is required to be explored.

Chapter 9: Relationship between physical function, activity and quality of life, symptoms and body composition in UK and Chinese HD patients

Primary Conclusions:

- The high fat mass contributed to high BMI in UK HD patients. High BMI with high fat mass was not able to explain good NS. High fat mass was negatively correlated with physical function and PA level in HD patients.
- The effect of serum creatinine as the predictor of muscle mass has not been confirmed.
- Poorer QoL, more impact of symptom burdens as well as higher fat mass in UK HD patients may contribute to lower physical function and activity level compared with Chinese HD patients.

Figure 10: Schematic representation of the order of the studies presented in this thesis
The whole thesis provided the evidence for improving lifestyle with HD patients in the UK and China. Comparison of nutritional status, physical function and activity level between UK and Chinese HD patients revealed the disparity of lifestyle between two cultural groups and the potential influencing factors of these lifestyle behaviours. These findings can promote UK and Chinese HD patients to learn from each other to efficiently adapt lifestyle.

Referring to the study of nutrition in UK and Chinese HD patients, insufficient energy and protein intake is the predominant problem. Health education pertaining to nutrition (Ford et al. 2004), dietary instruction or counselling are required to encourage HD patients to consume more energy and protein (Burrowes et al. 2003). Meanwhile, intradialytic food provision in Chinese HD patients has the potentials to improve energy and protein intake. It is worthwhile to be further explored and recommended to UK HD patients. Additionally, findings in this study suggested that Chinese HD patients should pay more attention to supplementation, medication management and dialysis efficacy than dietary intake compared with UK HD patients. The source of funding for dialysis therapy varies between UK and China (Prasad, Jha 2015). All treatments of HD patients on the NHS is free for UK residences (NHS trusts 2018). However, in China, although HD patients living in urban areas who are employed can get generous insurance coverage, patients who live in rural areas may need to make substantial co-payments (Prasad, Jha 2015). In recent years, medical insurance in China has broadened the coverage and decreased in the self-pay percentage (Zhou, Zeng et al. 2017). However, Chinese HD patients still need to undertake enormous financial pressure for their medication administrations, and even healthcare system bears great expenditure of clinical examination. These socioeconomic factors may lead to inadequate supplementation or medication usage and insufficient input to HD patients in China. Furthermore, poor healthcare systems and busy HD units with tension from large population in China are unable to provide efficient HD to eligible patients (Prasad, Jha 2015). However, it is long been known that the UK has well-established HD systems. Other environmental factors such as lack of the counselling from renal dietitians or non-specialist dietitians in China may contribute to the poor nutrition management in Chinese HD patients. As a matter of fact, although specific physiotherapists or kinesiologists are rarely available at dialysis units within the UK to provide education or instructions for patients’ exercise engagement, the services are
particularly underdeveloped in China, which may exacerbate patients’ lack of access and even awareness to seek their disease-appropriate exercise information (Pang, Kurosawa 2003). It is presumed that professional healthcare providers, such as doctors and nurses at HD units in China may need to take responsibilities of counselling nutrition and exercise information with HD patients. Therefore, it is worthy to gain a thorough understanding of their perceptions about HD patients’ nutritional status and exercise participation, especially for Chinese healthcare providers (Jhamb, McNulty et al. 2016, Greenwood, Naish et al. 2014).

Apart from findings above, the controversial relationship between high BMI (26.6 kg/m²) (Fouque et al. 2008, Fouque et al. 2007) and malnutrition in the UK HD patients indicated that patients’ body composition needs to be explored in order to better understand the relationship between BMI and NS. This exploration was described in Chapter 9. The comparison of body composition between UK and Chinese HD patients revealed that the high BMI in UK HD patients was ascribed to high fat mass (FM) rather muscle mass. This finding may indicate that high fat mass is not correlated with good NS. Similarly, higher fat mass in UK HD patients than Chinese patients partly explained the lower physical function and activity level compared with Chinese patients, which were found in Chapters 6 and 7. Numerous studies have reported that higher BMI predict better survival in HD patients (Johansen, Young et al. 2004, Kalantar-Zadeh, Abbott et al. 2005, Port, Ashby et al. 2002). However, the negative correlation between high BMI with high FM, NS, physical function and activity level is unable to support the notion above. It corroborated the finding that only high BMI with high muscle mass confirmed the positive relationship between BMI and survival (Beddhu, Pappas et al. 2003, Beddhu 2004).

Although UK HD patients had higher BMI than their Chinese counterparts, malnutrition was highly prevalent both in UK and Chinese HD patient as well as there was no difference in energy intake between two cultural groups. UK HD patients possibly have had higher energy intake or BMI than Chinese patients before started HD, which has been confirmed by the finding that mean BMI of Chinese general population was lower than in the UK (Ramachandran, Snehalatha 2010). Adaption of dietary pattern and habits to prevent obesity in the UK may be required. Moreover, lower PA level in UK HD patients than Chinese patients found in this study may
indicate UK patients had less calories consumption, which further deteriorates patients’ physical function and activity.

10.1 Practical Implications

A series of findings within the thesis aimed at comparing diet intake and nutritional blood parameters between UK and Chinese HD patients. Based on these findings practical implications have been shown as follows:

(1) Energy, protein and vitamin C and D intake need to increase in UK and Chinese HD patients.

(2) More attention should be given to intravenous iron supplementation and the control of blood loss during dialysis in female patients, phosphate binding medications management and dialysis removal with phosphate, and medication management and increase dialysis efficacy to prevent hyperkalaemia than nutritional support in Chinese HD patients.

(3) Excessive potassium intake in UK and Chinese HD patients needs to be controlled.

A number of findings in terms of physical function and PA level in UK and Chinese HD patients were shown within the thesis. Based on these findings the following practical applications have been derived:

(1) Given the strength that the GPPAQ walking pace question may be valid for assessing slow pace in HD patients, the question can be changed to two categories of “slow” and “not slow” walking pace with the criteria from the CDC, which is more suitable for HD patients.

(2) Although the GPPAQ is still recommended by the NICE, the reaction of the GP hypertension QOF and the finding that it is not a valid tool for assessing PA in older adults, question its continued use in National Health Service (NHS) health checks. Currently pedometers and accelerometers are being used for the measure of PA level. Pedometers only measure steps and do not determine exercise intensity. Accelerometers are able to assess steps as well as the intensity. However, they are usually expensive and uncomfortable to wear. Nevertheless, with the improvements of technology, effective, portable and cheap accelerometers will be
a good option to replace invalid questionnaires for providing more robust measures of PA level.

10.2 Future research

10.2.1 Nutrition

(1) This thesis reports that the energy and protein intake on HD days were significantly higher than that on non-HD day in Chinese HD patients. It is concluded that intra-dialytic food provision may contribute to the finding. Moreover, high phosphate and potassium intake reported as concerns in the provision of meals during HD treatment (Kalantar-Zadeh, Tortorici et al. 2015) did not be found higher on HD day than those on non-HD day. That food during HD sessions is provided or banned with HD patients is still an issue which is worth being further explored.

(2) The findings showed Chinese HD patients had higher vitamin C intake but lower potassium intake than UK patients. It is widely known that the low vitamin C intake in HD patients is primarily to fulfill the aim of avoiding hyperkalaemia. It would seem appropriate to understand diet pattern and habits in terms of the balance of sufficient vitamin C intake and restriction of potassium intake in Chinese HD patients.

(3) Given the finding that HD patients had severely insufficient vitamin D intake, increasing vitamin D intake and vitamin D supplementation in combination have the potential to correct vitamin D deficiency and insufficiency. It has been reported that vitamin D supplementations improved the complications in HD patients, including improving excessive bone turnover and reducing plasma levels of vascular adhesion molecules (Assimon, Salenger et al. 2012, Jean, Terrat et al. 2008). Future investigation can further explore the role of vitamin D supplementations.

10.2.2 Activity

In light of impaired physical function and low PA level in both UK and Chinese HD patients, a series of realistic and effective exercise interventions based on the findings in this thesis can be designed and implemented.
(1) Interventions can be conducted with UK and Chinese HD patients to confirm the role of some influencing factors in improving physical function and PA level. These factors include improved NS and bone metabolism derangement, increased muscle mass and decreased FM, comorbidities and physical symptoms.

(2) The majority of HD patients in the UK and China viewed walking as their favorite modality of exercise, which is consistent with the findings evidenced in the previous studies (Clarke, Young et al. 2015a, Chen, Wang et al. 2014). For dialysis patients, regular walking for 6 months improved their physical capacity, health-related QoL and post-dialysis fatigue symptoms (Malagoni, Catizone et al. 2008). Therefore, exercise intervention can be designed with HD patients by first focusing on walking and then build other types of exercise into their daily walking.

(3) In order to promote professional healthcare providers to support HD patients’ healthy lifestyle behaviours, especially in China, it is required to understand their perceptions and attitudes towards patients’ nutrition management and exercise participation. Additionally, it has been found that family support and encouragement were key elements in motivating patients’ involvement in exercise (Clarke et al., 2015). Therefore, one of future directions can focus on exploring and adapting these environmental factors or supportive strength.

(4) Given the findings of self-perceived benefits and barriers to exercise, exercise interventions focusing on physical and functional self-efficacy can be recommended to UK and Chinese HD patients. Meanwhile, interventions should include the strategies to alleviate concerns about falling for UK HD patients. For Chinese HD patients, more attention to obtain information of exercise implementation is required for designing intervention.

(5) HD patients’ other psychological determinants, such as stage of change relating to exercise and exercise self-efficacy to explore their confidence in implementing exercise when facing some situations, can be assessed to further explore the impact of perceptions or attitudes towards exercise. Furthermore, qualitative studies can be conducted to further identify the underlying impact of culture on patients’ perceptions about facilitators and barriers to exercise between UK and Chinese HD patients.
(6) It has been found that a high percentage of patients recognized a range of direct exercise benefits in UK and Chinese HD patients. Other benefits, especially indirect exercise benefits can be advised with HD patients. Interventions about increase awareness of exercise benefits are worthwhile conducting with HD patients to motivate their exercise participation.

(7) Currently intra-dialytic exercise is the most commonly implemented exercise interventions with UK HD patients. However, few studies have reported the intra-dialytic exercise in Chinese HD patients(Yin, Wan 2016). It has been documented that intra-dialytic exercise is safe and effective(Greenwood, Naish et al. 2014b). Moderate-intensity intra-dialytic exercise conducted for 6 months have confirmed the effect of increasing VO_{2peak} and self-reported physical function(Cheema, Singh 2005, Smart, Steele 2011). Additionally, intra-dialytic exercise also plays important roles in reducing cardiovascular risk and improving arterial stiffness(Toussaint, Polkinghorne et al. 2008). However, the clinical trials reporting these conclusions have many limitations, including small sample sizes, insufficient exercise dose and variable reported outcomes(Young, March et al. 2018). Therefore, larger and longer-term clinical trials are suggested to be conducted in order to obtain credible conclusions. Meanwhile, implementation of intra-dialytic exercise and understanding of its effect with Chinese HD patients are especially needed.

**Strengths and Limitations**

This thesis reported previous unknown data on the disparity of lifestyle between UK and Chinese HD patients, including diet intake, physical function and activity level. Understanding of influencing factors that result in these differences is able to promote these two cultural groups to effectively improve lifestyle behaviours. Additionally, the work of the thesis showed previously unknown prevalence of low physical function and self-reported physical inactivity in UK and Chinese HD patients. Meanwhile, the combination of valid questionnaires and objective measures ensured large HD cohorts are accessible and the reliability and accuracy of the assessments.

Studies in China only involved HD patients from Nantong, one city in the East of China. It is unlikely to be representative of the whole Chinese HD patients due to geographic and economic differences among cities and regions in China.
The mean BMI of UK HD patients in the DISH, QCKD and COCO studies were all higher than those in Chinese HD patients. However, HD patients’ body composition were only explored in the COCO study. The finding that high BMI was ascribed to high fat mass may be not applicable to the HD patients from the QCKD and DISH. In the thesis, this finding was used as an underlying associated factor explaining the relationship between BMI, NS and activity level. 

Having a small sample size in the DISH study particularly in the COCO study limits the power of the analysis. Another adverse consequence of a small sample is the increase of type 2 error, which is the failure to reject a false null hypothesis so as to cause false negatives. Additionally, all of the studies in the thesis are un-randomized and there is no blinding. There may be some selection bias in which patients were chosen to be part of the studies. Therefore, the sample obtained may be not entirely representative of the HD population intended to be analyzed. Taking a random sample of the HD population can reduce the likelihood of selection bias.

10.3 Conclusion

The body of work presented in this thesis highlights the high prevalence of malnutrition, low physical function and physical activity level in UK and Chinese HD patients. UK HD patients had better control of micronutrients than Chinese HD patients. Chinese HD patients had a higher physical function and activity level than UK patients. UK HD patients need to focus more attention on decreasing fat mass, bone metabolism management, improvement of protein status and QoL, remission of symptoms and more exercise benefits acquisition compared with Chinese patients. The importance of maintaining a healthy lifestyle should be emphasised in two cultural groups and this can be achieved by promoting continued communication between the UK and China.
# Appendices

A list of appendices in this thesis

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Appendix A Ethics approval letter
A.1 The DISH study

24 October 2016

Dr Alice C Smith
Honorary Senior Lecturer
UHL
Leicester Kidney Exercise Team, Academic Unit
Leicester General Hospital
Leicester
LE5 4PW

Dear Dr Smith

Study Title: DISH: Dietary patterns, food Security, and nutritional status of Haemodialysis patients
REC reference: 14/SS/1016
IRAS project ID: 156831

Thank you for sending the progress report for the above study dated 20 October 2016. The report will be reviewed by the Chair of the Research Ethics Committee, and I will let you know if any further information is requested.

It was noted in your annual report that you recruited 40 participants who have completed the trial. The initial application to Ethics was for 12 participants and a subsequent amendment increased this to 20 participants. Please note that the Committee received no notification that you had increased this to 28 and then to 40 participants.

The favourable ethical opinion for the study continues to apply for the duration of the research as agreed by the REC.

14/SS/1016: Please quote this number on all correspondence

Yours sincerely

S. Wylie
REC Manager

E-mail: sandra.wylie@nhslothian.scot.nhs.uk

Copy to: Mrs Carolyn Maloney, University Hospitals of Leicester NHS Trust
A.2 The QCKD study

Health Research Authority

NRES Committee East Midlands - Northampton
The Old Chapel
Royal Standard Place
Nottingham
NG5 6FS

Telephone: 0115 8239425
Facsimile: 0115 8239214

13 June 2012

Dr Alice Smith
Senior Renal Research Scientist
University Hospitals of Leicester
Renal Research Laboratory
Medical Sciences Building
University of Leicester
LE1 9HN

Dear Dr Smith,

Study title: Increasing Physical Activity in Chronic Kidney Disease: The Patient Perspective (QCKD)
REC reference: 12/EM/0184

Thank you for your letter of 31 May 2012, 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 the Vice-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

NHS 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).

Non-NHS sites

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.

Management permission ("R&D approval") should be sought from all NHS organisations 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 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 the 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:

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Statement of compliance
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review
Reporting requirements
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
• Notification of serious breaches of the protocol
• 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.

Feedback

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.

Further information is available at National Research Ethics Service website > After Review

12/EM/0184 Please quote this number on all correspondence

With the Committee’s best wishes for the success of this project

Yours sincerely

[Signature]

Mr Mike Newman
Vice Chair

Email: jessica.parfremen@notspct.nhs.uk

Enclosures: "After ethical review – guidance for researchers"
Copy to: R&D Contact/Sponsor – UHL
A.3 The COCO study

21 July 2014

Dr Alice C Smith
Honorary Senior Lecturer
UHL
Leicester Kidney Exercise Team, Academic Unit
Leicester General Hospital
Leicester
LE5 4PW

Dear Dr Smith

<table>
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Thank you for your email of 21 July 2014, 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 the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Ms Tracy Leavesley, NRESCommitteeEastMidlands-Derby@nha.net

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.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list
of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations 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 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

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the 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).

Ethical review of research sites

NHS 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).
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Statement of compliance

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After ethical review

Reporting requirements

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
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study
The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

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 HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

We are pleased to welcome researchers and R & D staff at our NRES committee members’ training days – see details at http://www.hra.nhs.uk/hra-training/

14/EM/1049 Please quote this number on all correspondence

With the Committee’s best wishes for the success of this project.

Yours sincerely

Mr Peter Korczak
Chair

Email: NRESCommittee.EastMidlands-Derby@nhs.net

Enclosures: “After ethical review – guidance for researchers”

Copy to: Mrs Carolyn Maloney, University Hospitals of Leicester NHS Trust
A.4. Ethics approval letter in Chinese study

根据《赫尔辛基宣言》及卫生部关于《涉及人的生物医学研究伦理审查办法（试行）》（2007年）的有关规定，
伦理委员会对该项目进行伦理审查。意见如下：

1. 该试验研究对肾病患者和常规透析患者进行问卷调查，根据调查结果进行针对性的锻炼指导，研究过程
考虑了严格执行医疗常规。

2. 项目研究中考虑了知情同意程序，符合伦理规范。

3. 请按伦理委员会批准的知情同意书开展该研究，保护
受试者的健康与权利。

4. 在研究过程中，如变更主要研究者或研究方案、知情
同意书等有任何修改，请报伦理委员会批准。

5. 项目结束后请及时向伦理委员会提交结题报告。

同意

主任签字：

日期：二〇一五年十月十九日

伦理委员会联系电邮：0513-85052390；E-mail: hunlibr@126.com
Appendix B Patients information sheet (PIS) and Consent form
B.1 The DISH study

B.1.1 PIS in the UK study

DISH: DIetary patterns, food Security, and nutritional status of Haemodialysis patients from the U.K.

Patient Information Sheet

Version 2 14th July 2014

You are being invited to take part in a research study. Before you decide, 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. 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 the study?

People on haemodialysis often need to eat more energy and protein in their diets, but many do not manage to eat enough. This can lead to malnutrition which increases patients risk and is one of the causes of muscle weakness, tiredness, and a reduced physical capacity.
It is important to understand why people on haemodialysis become malnourished so that steps can be taken to reduce the problem. In this study, we will interview patients on haemodialysis about their diet and where they buy their food. We will also ask them to fill in a short questionnaire about their ability to afford food, and will request to take some information from their medical records about their nutritional status.

This is a feasibility study and the data collected will be used in the design of a larger study in the future. We will analyse the data collected from the study to evaluate how the dietary habits of haemodialysis patients, and their ability to afford food, might affect their nutritional status.

A similar study has been carried out in America, and we will compare the food intake and habits of American dialysis patients with those from the Leicester region in the UK.

**Why have I been chosen?**

You have been chosen because you are receiving regular haemodialysis at a unit in the Leicester region.

We are doing this research so we can understand better the relationship between dietary habits, the ability to afford food and the nutritional status of people receiving haemodialysis.

Altogether we will ask 12 patients to take part in the study.
**Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive.

**What will happen to me if I take part?**

During the study, we will ask you to continue your life in the usual way. You should follow your usual recommended diet and take your medicines as prescribed.

If you decide to take part we will ask you about the food you have eaten and where you bought it from in four separate interviews. We can either hold the interviews in person during your regular haemodialysis sessions, or we can interview you over the telephone, which ever you prefer. In each of these interviews, a member of the research team will ask you about the food that you ate on one particular day. This would either be the day before the interview, or the day before that. These interviews are called “24-hour dietary recall” and each one will take about 15-30 minutes. During the 24-hour dietary recall interviews the researcher will ask you to list everything that you have eaten or drank during the 24-hour period in question, and then will go through the list with you to collect details on where you bought the food, how it was cooked, and the portion sizes you ate, and to ensure that nothing was missed. The researcher will be aiming to get as true a picture of what you ate as possible and will not judge any of your food choices but will ask some questions to make sure that they have recorded your intake as accurately as possible.
We want to get good overall picture of your diet. Some people eat differently on dialysis days, so two of the interviews will be about your diet on dialysis days, and the other two about non-dialysis days. Also, some people may find they can’t always afford to eat so well at some times of the month. Therefore we will arrange the four dietary interviews so that two of them are during the first week of the month and two are during the last week of the month.

In summary, the four dietary recall interviews will relate to the following days:

1. A dialysis day in the last week of the month
2. A non-dialysis day in the same last week of the month
3. A dialysis day in the first week of the following month (i.e. the next week)
4. A non-dialysis day in the same first week of the month

- The interviews about the non-dialysis days will be held during your dialysis session the next day
- The interviews about the dialysis days will either be held on the telephone the next day, OR during your next dialysis session (2 days later), whichever you prefer.

We will also ask you to fill in a questionnaire called the Food Security Questionnaire, which is about your ability to afford food. It takes about 5-10 minutes to complete. We will only ask you to fill this in once, and you can do this during a dialysis session.

With your permission we will also extract blood test results relating to your nutritional status from your medical records. We can get this from your last routine monthly blood test – you do not need to give an extra blood sample.
All of the information we collect will be stored anonymously using a study participant code and will not be identifiable as belonging to you.

**What are the possible disadvantages and risks of taking part?**

The main disadvantage of taking part is the time commitment involved. The study will involve 4 interviews in total, which will last around 15-30 minutes each, and the completion of the Food Security Questionnaire which will take about 10 minutes. However, these will be arranged with participants at a practical time that suits them during their normal dialysis sessions, with the option of having the two dietary recall interviews where you are asked to remember your dietary habits for dialysis days, carried out over the phone.

**What are the possible benefits of taking part?**

There are no direct benefits to you of taking part in this research. We hope that the results of the study will help us understand how the dietary habits haemodialysis patients, and their ability to afford food, relates to their nutritional status. This will help us to better understand the causes and effects of malnutrition in haemodialysis patients and to design research studies that may lead to improved treatments for other haemodialysis patients in the future.

**What happens when the research study stops?**

Your usual clinical care will continue unchanged.
**What if something goes wrong?**

In the very unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone’s negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

If you wish to make a complaint about the study you can contact the UHL Patient Information and Liaison Service by post to PILS, The Firs, Glenfield Hospital, Leicester LE39QP, telephone 0808 1 788337 (free phone number), or email pils@uhl-tr.nhs.uk

**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 about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

With your permission, we will inform your GP that you are taking part in this study.

We want to compare the data we get from this study with similar data collected from American patients from the University of Illinois. Therefore, your data may be shared with the American researchers, but it will be completely anonymous and no one will be able to identify who you are from this information.

While you are taking part in the study, your contact details will be made available to the researchers so that they can contact you to arrange the details of your research study appointments.

**What will happen to the results of the research study?**
We expect the results of the research to become available from 2015. We will publicise the results in posters and leaflets in clinical areas so you can read them while you are there, and we will write a report about them in our Kidney Research Newsletter. If you would like us to send you a written report of the results, or if you would like to receive our Kidney Research Newsletter, please ask the researcher or contact the Chief Investigator, Dr Alice Smith (contact details at the end of this document).

The results may also be published in a medical journal. All information will be anonymised so you will not be identified in any report or publication.

**Who is organising and funding the research?**

The research is being organised and funded by the Leicester Kidney Exercise Team at the John Walls Renal Unit, Leicester General Hospital and is led by Dr Alice Smith, Honorary Senior Lecturer.

Any research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be reviewed by an NHS Research Ethics Committee before it can go ahead. This study has been reviewed by the Proportionate Review Subcommittee of the South East Scotland Research Ethics Committee 01, and given a favourable opinion which means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.

**Contact for Further Information**

If you would like any further information about this study please contact the Chief Investigator Dr Alice Smith, or Dr James Burton on 0116 252 3061.
Alternatively, if you have questions about the study and you would prefer to ask someone not directly involved with the research team, you can contact the University Hospitals of Leicester Research and Development Office, Leicester General Hospital, LE5 4PW, by phone on 0116 258 8351, or email RDAdmin@uhl-tr.nhs.uk

Thank you for reading this Information Sheet, and for considering taking part in this study.

Dr Alice Smith

Leicester Kidney Exercise Team, Academic Unit, Leicester General Hospital, LE5 4PW.

Tel 0116 258 4346 Email kidney.exercise@uhl-tr.nhs.uk

You will be given a copy of this information sheet and signed consent form to keep
B.1.2 PIS in Chinese study

DISH-C: 中国血液透析患者的饮食类型，食品保障和营养状态

患者信息表

2014-7-14

尊敬的患者朋友:

您正在被邀请参与我们的研究。但是在您做出决定之前，请您先了解我们研究的目的和内容。请仔细阅读下面的信息，您也可以和其他人讨论后做出决定。如果有任何问题或是您想获得更多的信息请向我们咨询。

研究目的

血液透析患者经常需要摄入更多的能量和蛋白，但是很多人并没有做到。能量与蛋白的摄入不足会引起营养不良，进而导致肌肉无力，疲劳，造成体力活动能力下降。

理解血液透析患者营养不良的原因是我们采取措施，解决问题的第一步。在本研究中，我们将会询问到您的饮食以及购买食物的地点。我们也会请您填写一张关于您对食物购买能力的调查问卷，还将从您的病历中获得一些涉及营养状态的数据。

这是一个可行性的研究，获得的数据将会被用于将来更深入的研究。我们将会分析数据以评估血液透析患者的饮食习惯和购买食物的能力，进而进一步评价其营养状态。

一个类似的研究已经在美国和英国开展，另有在巴西的研究也即将进行，之后我们会将四个国家的数据进行比较，以获得更有用的信息。
为什么选择我？

您之所以被选择是因为您正在南通地区接受常规的血液透析治疗。此研究的目的是为了更好的理解血透患者饮食习惯、食物购买能力与营养状态的关系。

我必须参加吗？

您是否参加完全取决于您的决定。如果您决定参加，我们将会请您签署一份知情同意书。但是，即使您决定参加本研究，您也有权利勿需给出任何理由的随时退出研究。您退出研究的决定或是拒绝参加的决定都不会影响到您的治疗。

如果我参加此项研究将需要做些什么？

在整个研究过程中，请继续保持您正常的生活习惯和治疗。

如果您决定参加本研究，我们将会和您进行四次的访谈。在每次的访谈中，我们会询问并记录您所摄入的食物以及购物食物的地点。你可以选择我们访谈的方式，在您透析的过程中或者进行电话联系。在每一次的访谈中，研究者将会问您在特定某一天的饮食，可能是透析的前一天或是大前天。这些访谈我们称之为“24小时饮食回顾”，每一次将持续15-20分钟。在每一次“24小时饮食回顾”中，研究者会请您列举您所摄入的任何东西（食物，水，饮料等），之后您还会被问到某些细节问题，包括您购买食物的地点，如何烹饪以及摄入的量。研究者的目标是尽可能的对您的饮食有深入的了解，而不是对您食物的选择做出评价。

我们的目的是为了全面的了解您的饮食。我们知道，有些患者在透析日和非透析日饮食是不同的，所以我们四次的访谈将有两天涉及到透析日的饮食，两天为非透析日的饮食。另外，某些患者会发现他们在一个月的某些日子里无法负担他们所需的饮食，因此我们将两次访谈安排在月初，两次安排在月末。
具体来说，四次“24小时饮食回顾”会有如下的安排：

1. 月末最后一周的透析日
2. 月末最后一周的非透析日
3. 月初第一周的透析日（接下来的一周）
4. 月初第一周的非透析日

关于非透析日的访谈将会在第二天的透析日进行。

关于透析日的访谈可以按照您的意愿在第二天进行电话联系或在您下一次的透析日（2天后）进行。

我们也会请您填写一份“食物保障问卷”，这份问卷涉及到您对食物的购买能力。填写问卷的时间为5-10分钟。在整个研究过程中，您仅会被要求填写这一份问卷，而且可以在透析过程中完成。

如果您允许，我们将会从您的病历中提取某些涉及到营养状态的血液检查数据。我们会从您上一次的常规检查中获得数据，不需对您进行抽血检查。

所有收集到的信息都会通过一个研究编号进行匿名使用，整个过程中不会涉及到您的任何个人信息。

我参加此项研究可能的不利或危险是什么？

参加本次研究最大的影响就是您的时间。这个研究包括四次访谈，每次会花费您15-20分钟。另外，“食物保障问卷”也会耽误您10分钟左右。但是我们会将访谈安排在您透析过程中的合适时间，或者我们会在合适的时间里和您电话联系。

我参加此项研究的好处是什么？

抱歉的说，您参加本研究没有任何直接的好处。我们希望这个研究的结果能够帮助理解血液透析患者的营养状态与饮食习惯和食物购买能力的关系。这样，我们
就能更好的理解血透患者营养不良的原因以及影响因素，从而设计出有效的干预措施促进血透患者的治疗。

当研究结束时会发生什么？

常规的临床治疗依旧正常进行。

如果研究不顺利会怎么样？

参加本研究会伤害到您的可能性几乎为零，所以我们也没有什么特殊的补偿措施。如果您对我们的研究过程有任何的不满，您可以向医院的投诉部门就行投诉。

我参加此项研究的数据信息会被保密吗？

在本研究中所收集的任何数据信息将会被严格的保密。任何被带出医院的信息都将不会包含您的姓名和地址，以确保您的个人信息不会被泄露。经过您的允许，我们将会告知您的主治医生您参与了此项研究。

我们会将此次收集到的数据与美国伊利诺斯大学、英国莱斯特地区以及巴西的研究数据相比较，因此您的信息将会和其他国家的研究者共享，但是共享将会是完全匿名的，没有人可以从数据信息中确认您的身份。

如果你参与了本研究，你的联系方式将会被这个研究的研究者们所共享，以便于我们可以更好的为您做研究的安排。
研究的结果将如何处理？

我们预期研究的结果将于2015年底完成。我们将会把研究结果以海报或手册的方式在病房里展示，这样您就可以在到达医院的时候看到。另外，我们也会将结果形成报告或者文章。如果您有需要，请联系我们或护士（联系方式显示在下方），我们会将报告或文章邮寄或直接送到您手上。

谁组织或资助此项研究？

本研究是由宋艳副教授（南通大学）以及南通大学附属医院组织负责。

谁将对本研究进行评价监督？

任何涉及到患者病历信息或使用到其规定或设施的研究都应在开展之前通过伦理委员会的审查。本研究已经经南通大学附属医院伦理委员会办公室审核通过，意味着伦理委员会认定您的权利在本研究中将会被充分的保护和尊重，对您的影响以及对您利益的冲突已经被减少到最低，另外，在您做出决定之前，您已经被给予充分的信息说明。

更多的信息

如果您想获得更多关于此项研究的信息，请联系研究者宋艳，手机（86）1386190853

固定电话：0513-85051784，电子邮件：suyayanshu@hotmail.com

感谢您阅读患者信息表，请考虑参与此项研究！
B.1.3 Consent form in the UK study

University Hospitals of Leicester NHS Trust

LEICESTER GENERAL HOSPITAL
Gwendolen Road
Leicester
LE5 4PW

Leicester Kidney Exercise Team
University of Leicester Academic Unit
Tel 0116 258 4346
Email idney.exercise@uhl-tr.nhs.uk

CONSENT FORM

DISH: Dietary patterns, food Security, and nutritional status of Haemodialysis patients from the U.K.

Name of Researcher: Dr Alice Smith

1. I confirm that I have read and understand the DISH Patient Information Sheet version 2 dated 14th July 2014 for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that my contact details will be made available to the research staff involved in this project so that they can contact me to arrange details of my research study appointments, and I give permission for them to do so.

4. I understand that a researcher will access my medical records to extract relevant information to be used anonymously for the purposes of this research study only, and I give permission for this.

5. I understand that my GP will be informed of my taking part in this study.

6. I understand that the information collected as part of this study may be shared with researchers from the University of Illinois, USA, but that all such information will be anonymous with no personal or identifiable details included. I give permission for my information to be shared in this way.

7. I understand that relevant sections of my medical notes and/or data may be looked at by responsible individuals from the study team, the Sponsor, Research Ethics Committee, NHS Trust or from regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to access my records.

8. I agree to take part in the study.

Name of Patient ____________________________ Date __________ Signature __________________________

Researcher __________________________ Date __________ Signature __________________________
B.1.4 Consent form in Chinese study

知情同意书

DISH-C：中国血液透析患者的饮食类型、食品保障和营养状态。

研究负责人：宋艳。

1. 我已经认真阅读并了解DISH 2014-7-14第二版的患者信息表，并且有权利提出问题。

2. 我参加本研究是完全自愿的，我可以在任何时候选择退出，不需任何理由，该决定不会影响我的治疗和合法权益。

3. 我同意我的联系方式可以被本研究的研究者们共享，以便安排研究进程。

4. 我同意本研究的研究者可以查阅我的病历，但仅限于做研究使用，相关信息均做匿名处理。

5. 我同意我的主治医生会告知我参与了此项研究。

6. 我同意在本研究中收集的数据信息会被美国伊利诺斯大学的研究者共享，所有的数据不包括个人身份信息。

7. 我授权研究小组的负责人、研究赞助者、研究伦理委员会、美国国家医疗服务体系以及和本研究相关的监管机构可以查阅我病历的相关数据和信息。

8. 我同意参加此项研究。

参与者签名：

日期：

研究者签名：

日期：
B.2 The QCKD study

B.2.1 PIS in the UK study

University Hospitals of Leicester NHS Trust
LEICESTER GENERAL HOSPITAL
Gwendolen Road
Leicester
LE5 4PW
Tel: 0116 249 0490

Physical Activity for Kidney Patients: Your Opinions

Part 1

QCKD Part 1 Participant Information Sheet

Version 4 dated 17th September 2014

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Leading an active lifestyle is beneficial for health, and research shows that this is true for people with kidney problems as well as for everyone else. We want to develop ways to help kidney patients increase their activity levels. First of all, it is important for us to understand more about the current activity levels of kidney patients, and how kidney patients feel about exercise. The purpose of this research is to collect this information.

This research study has two separate parts. Part 1 is a survey of kidney patients’ exercise habits. Part 2 involves small group and one-to-one discussions about exercise. At the moment, we would just like to ask you to participate in Part 1.

Why have I been chosen?

You have been chosen because you are a patient attending a kidney clinic. We will ask up to 1200 patients to do the survey.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and you will be free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive in any way.
What will happen to me if I take part?

If you agree to participate, you will be asked to fill in some questionnaires about exercise, which should take no more than 10-15 minutes. You can fill them in while you are in the clinic waiting area or during your routine dialysis session, and the researcher will collect them from you when you have finished, or else you can leave them with the clinic reception or renal unit staff.

The questionnaires will be marked with a code: they will not have your name or any other identifiable information on them. We can analyse the information you provide on the form without knowing who you are.

However, the information will be even more valuable to us if we can add to it some of your clinical information obtained from your medical records. Therefore, the researcher will ask for your permission to access your records and extract the required information: your blood and urine results, blood pressure, weight, ethnicity, any other medical conditions, and the drugs you are taking.

If you agree, this information will be extracted from your records and will be added to the study database in an anonymous form, separately to any information from which you could be identified. If you agree to this, you will be asked to sign a consent form.

Finally, the researcher will ask you if you are interested in possibly participating in Part 2, when we will talk to patients in more detail about physical activity and exercise. If you may be interested in Part 2, we will ask you to fill in a Contact Form so we can give you more information at a later date. This does not mean you have to take part: the study will be explained to you nearer the time, and you will be free to decide whether or not you wish to participate. We will only be able to talk to a limited number of volunteers in Part 2, so even if you do agree to take part, we may not invite you to participate if too many patients volunteer for it.

On the Contact Form, you can also choose to be informed about other research projects in the future. If you fill in the Contact Form, we will store it securely, separately from your survey form and clinical information, and we will only use it to contact you for the purposes you have chosen.
Confidentiality

Questionnaires and clinical information will be labelled with a code instead of your name, and all your responses and data will be stored securely and separately from your personal details.

What do I have to do?

You just need to fill in the survey form and give it back to us. Other than that, we ask you to continue your life in the usual way. You should follow your usual recommended diet, and take your other medicines as prescribed.

What are the possible disadvantages and risks of taking part?

The only disadvantage of taking part is that you will need to spend a few minutes filling in the survey form while you are in the clinic waiting room or during your normal dialysis session.

What are the possible benefits of taking part?

There are no direct benefits to you of taking part in this research.

What happens when the research study stops?

Your usual clinical care will continue unchanged.

What if something goes wrong?

In the very unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone’s negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

If you wish to make a complaint about the study you can contact the UHL Patient Information and Liaison Service by writing to PILS, Gwendolen House, Gwendolen Road, Leicester LE5 4QF, or telephoning 08081 788337 (free phone number)
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 labelled with a code instead of your personal details. We will keep a separate list of the codes and patient identities. If you prefer to remain completely anonymous, you can return your questionnaire without your name or personal details.

What will happen to the results of the research study?

We expect the results of the research to become available in 2015. We will publicise the results with posters and leaflets in clinical areas so you can read about them while you are there, and we will write a report about them in our Exercise Newsletter. If you would like us to send you a written report of the results, or if you would like to receive our Exercise Newsletter, please ask the researcher or contact the Chief Investigator, Dr Alice Smith (contact details at the end of this document). The results will also be published in a medical journal. All information will be anonymised so you will not be identified in any report or publication.

Who is organising and funding the research?

The research is being organised by Senior Research Scientist Dr Alice Smith and staff at the John Walls Renal Unit, and funded by a research grant from the British Renal Society.

Who has reviewed the study?

All research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be approved by an NHS Research Ethics Committee before it goes ahead. This study has been reviewed by the NHS Research Ethics Committee East Midlands - Northampton. Approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.
Contact for Further Information

If you would like any further information about this study please contact the Chief Investigator Dr Alice Smith, or Dr James Burton on 0116 252 3061.

Dr Alice Smith,

Leicester Kidney Exercise Team,

C/O Dr Barratt’s secretary,

John Walls Renal Unit,

Leicester General Hospital, LE5 4PW.

Tel 0116 252 5033

Email kidney.exercise@uhl-tr.nhs.uk

Thank you for reading this, and for considering taking part in this study.

You will be given a copy of this information sheet and if applicable, your signed consent form to keep.
尊敬的患者：

您将被邀请参与我们的研究。在您做出决定之前，请您先了解我们研究的目的和内容。请仔细阅读下面的信息，您也可以和其他人讨论后做出决定。如果有任何问题或是您想获得更多的信息都请向我们咨询。

本研究的目的是什么？

保持积极锻炼的生活方式对健康是大有裨益的。研究者发现这条原则对于肾脏疾病的患者来说同样适用。我们想帮助肾脏病患者增加他们的活动量。因此，了解肾脏病患者目前的活动水平以及对锻炼、活动的态度显得尤为重要。本研究的目的就是为了收集这样的信息。

本研究包括两部分。第一部分涉及肾脏病患者活动、锻炼习惯的调查。第二部分涉及对于患者进行锻炼、活动方面的焦点团体访谈和一对一访谈。现阶段，我们邀请您参与的是第一部分。

为什么选择我？

您被邀请参加本研究是因为您是肾脏病患者，我们将要组织1900名肾脏患者参与本研究。

我必须参加吗？

您是否参加完全取决于您的意愿。如果您决定参加，我们将会请您签署一份知情同意书。即使您已决定参加本研究，您也有权利随时退出研究，不需任何理由。您拒绝参加或退出研究的决定都不会影响到您的治疗和合法权益。
如果我参加此项研究将需要做些什么？

如果您同意参加本研究，您将会被要求填写一份关于锻炼、活动的量表，这可能会花费您10-15分钟。您可以在候诊或透析过程中填写。当您完成后，我们的研究者会来收取，您也可以把量表放到护士站或交给我们的医务人员。

我们将会给您一个研究编号，您的姓名或任何身份认证信息都不会出现在量表上，因此请不用担心您的个人信息会被泄露。为了使本研究更为有意义，我们将通过您的授权，从您的病历中提取与肾脏疾病以及运动相关的血液、尿液检查结果，比如钙、磷、尿素、肌酐浓度，蛋白肌酐比，体重，腹腰围，服药情况以及病史等临床数据。如果您同意上述要求，我们会请您签署一份知情同意书，同意这部分信息将会被从您的病历中提取并以匿名的形式用于本研究。

最后，研究者将会询问您是否愿意参与本研究的第二部分。在这一部分研究中，我们将涉及到关于您更多的活动水平和锻炼的信息。如果您对第二部分感兴趣，我们会请您填写一份联系表，以便今后向您了解更多的信息。当然，这也并不意味着您必须参加，我们将会在开展第二部分研究时再向您进行详细的解释，到那时您再决定是否参与。这里我们要说明的是，在第二部分研究中，我们只能邀请有限的参与者，所以即使您同意参与，我们也可能会因为人数过多而无法将您纳入其中。

在联系表中，您也能选择是否愿意被通知将来我们可能要开展的研究。如果您填写了联系表，我们会将它妥善保存，并与调查量表、临床信息分开放置，避免个人信息泄露的问题。在您同意参与研究的前提下，我们才会和您联系。

保密原则

研究者在您的调查量表和临床信息中使用研究编号代替您的姓名。本研究中收集到的所有信息与数据也将会和您的个人信息分开放置，并妥善保存。
我需要做什么？

您所需要做的只是填写调查量表然后把它交给我们。您无需为了本研究改变您的生活习惯。

参加本研究会有什么可能的坏处和风险吗？

参与本研究唯一的影响就是需要您在候诊或透析过程中花费几分钟来协助研究者填写量表。

参加本研究有什么潜在的好处？

参加本研究没有直接的好处。

当研究结束时会发生什么？

你常规的临床治疗护理一切正常进行。

如果研究不顺利会怎么样？

参加本研究会伤害到您的可能性几乎为零，所以我们也没有什么特殊的补偿措施。如果您对我们的研究过程有任何的不满，您可以向医院的投诉部门进行投诉。

我参与此项研究的信息会被保密吗？

在本研究中所收集的任何数据信息将会以研究编码标记，而不是您的姓名。我们会对编号信息和您的身份信息分开放置。如果您想保持完全的匿名，您也可以收回不包含您姓名或其他个人信息的量表。

研究的结果将如何处理？
本研究预期于 2015 年底完成。我们将会把研究结果通过海报或手册的方式在病房展示，这样您就可以在就医期间看到。另外，我们也会将结果形成报告或文章。如果您有需要，请联系我们或护士（联系方式显示在下方），我们会将报告或文章直接邮寄或送达给您。

谁组织或资助此项研究？

本研究是由宋艳副教授（南通大学）以及南通大学附属医院组织负责。

谁将对本研究进行评价监督？

任何涉及到患者病历信息或使用到其规定或设施的研究都应在开展之前通过伦理委员会的审查。本研究已经经南通大学附属医院伦理委员会办公室审核通过，意味着伦理委员会认定您的权利在本研究中将会被充分的保护和尊重，对您的影响以及对您利益的冲突已经被减少到最低，另外，在您做出决定之前，您已经被给予了充分的信息说明。

更多的信息

如果您想获得更多关于此项研究的信息，请联系研究者宋艳，手机（86）1386190853 固定电话：0513-85051784。电子邮件：suyayanshu@hotmail.com

感谢您阅读患者信息表，请考虑参与此项研究！

在同意参与此项研究之后，

您将会受到此份患者信息单以及签过姓名的知情同意书的复印件！

谢谢！
B.2.3 Consent form in the UK study

**University Hospitals of Leicester NHS Trust**

**LEICESTER GENERAL HOSPITAL**

Gwendolen Road
Leicester
LE5 4PW
Tel: 0116 249 0490

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**Participant**

Code: ..........................................

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**CONSENT FORM**

Title of Project: **Physical Activity Opinions in Kidney Patients: Part 1**

Name of Researcher: Dr Alice Smith

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1. I confirm that I have read and understand the QCKD Part 1 Participant Information Sheet v4 dated 17th September 2014 for the above study and have had the opportunity to ask questions.

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2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

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3. I agree to a researcher accessing my medical records to extract relevant information to be used anonymously for research purposes.

---

4. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

---

5. I agree to take part in the above study.

---

**Name of Participant**

Date

Signature

**Name of Researcher**

Date

Signature

---

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B.2.4 Consent form in Chinese study

知情同意书

肾脏疾病患者的体力活动：第一部分

研究者姓名：宋艳

1. 我已经阅读并了解QCKD第一部分2014-9-17的患者信息表，并且有权利提出问题。

2. 我参加本研究是自愿的，我可以在任何时候选择退出，不需任何理由，该决定不会影响我的治疗和合法权益。

3. 我同意本研究的研究者使用我的病历，以便提取相关的信息做匿名使用。

4. 我同意我病历的相关部分以及本研究所收集到的数据可能会被英国国家医疗服务体系以及和本研究相关的监管机构查阅。

5. 我同意参加本研究。

______________________________
参与者签名

日期

______________________________
研究者签名

日期
B.3 The COCO study

B.3.1 PIS in the UK study

UK HD patients

You are being invited to take part in a research study. Before you decide, 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. 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 the study?**

Kidney disease can affect the health of the heart and blood vessels and can also cause muscle wasting which leads to muscle weakness, tiredness, and a reduced physical capacity. This tends to get worse for patients on dialysis, and even though a kidney transplant can really benefit patients and restore kidney function, some of the negative effects often still remain.

Our previous research has shown that exercise can help kidney patients get fitter, strengthen the muscles and improve the health of the heart and blood vessels. This suggests that regular exercise might be very helpful for kidney patients, but we don’t yet know what types of exercise will be best for people at different stages of kidney disease.
We still need to understand more about the current physical condition and physical activity habits of kidney patients, including those with less severe kidney failure, those on dialysis and people with a kidney transplant, and how these relate to other important health-related factors, and quality of life.

This study is designed to collect this information, which will help us to carry out the best future research on exercise for kidney patients.

We will invite kidney patients to undertake a series of tests and measurements of walking ability, everyday physical activity levels, body composition and heart health, to have a blood test and a urine test, and to fill in some simple questionnaires. The tests will be done at a hospital research centre and the patient can choose whether to do them in two visits of about 2 hours each, or three shorter visits.

We will analyse the data collected from the study to help us to evaluate how exercise might benefit kidney patients and to design future research studies about exercise and the health of kidney patients.

**Why have I been chosen?**

You have been chosen because you have non-dialysis kidney disease (CKD), or you are on a form of dialysis, or you have a kidney transplant.

Altogether we will ask 60 kidney patients to take part in the study, and also 20 healthy people of the same age and sex, who do not have kidney disease.

**Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive.
What will happen to me if I take part?

During the study, we ask you to continue your life in the usual way. You should follow your usual recommended diet and take your other medicines as prescribed.

If you decide to take part we will arrange for you to attend the research centre for 2 or 3 visits for assessments. These visits will be flexible and scheduled at your convenience – you can choose whether to come for two longer visits or three shorter ones.

At one of these visits we will ask you to arrive in a “fasted” state – this means not having eaten or drunk anything except water since the previous night. This is needed for the blood test. You can choose which visit this will be, and we will arrange it for the morning so you don’t have to be hungry for too long! We will take the blood as soon as you arrive and then we will offer you tea or coffee and some breakfast such as toast or cereal. If it suits you, you can choose to call by briefly one morning just for the blood test, and do all the other assessments on other occasions.

We will also ask you to carry on with your life as normal while wearing a wrist-watch style activity monitor for one week.

Assessments

During the research visits, researchers will carry out the tests listed below. More detailed information about all these tests can be in Appendix 1 at the end of this Information Sheet. We will arrange the dates and times of the assessment visits to suit you.

Physical performance tests: Your physical performance will be tested using walking tests, sit to stand tests (rising from chair), hand grip strength test and balance tests. We will show you how to do the tests and allow you to practice before you do the test for real.

Blood vessel health: We will use a very easy and non-invasive test called Pulse Wave Velocity (PWV) to measure the health of your blood vessels.

Heart Function: Another easy and non-invasive test, called Cardiac Bio-reactance, will be used to measure the function of the heart.
Body fat and muscle: We will measure these using two safe, non-invasive techniques; DEXA and BIA.

Height, weight, and waist and hip circumference: We will measure these once in the same way as your doctor, nurse or dietician uses during clinic visits.

Blood samples: We will take one 30ml (2 tablespoon) blood sample from a vein in your arm. As explained above, you need to refrain from eating or drinking anything other than water on the morning of the blood test.

Urine sample: we will ask you to provide a 20ml urine sample at your convenience during one of the study visits.

Habitual physical activity: We will ask you to wear a wrist-watch style activity monitor continuously for 7 days that will measure how much physical activity you do.

Food diary: we will ask you to record everything you eat and drink for 7 days in a food diary which we will give you to take home with you.

The Kidney Transplant Questionnaire: A member of the research team will ask you 25 questions about some of the problems that kidney transplant patients commonly experience in their day to day lives. You will only complete this questionnaire if you are a kidney transplant patient.

Other questionnaires: We will ask you to do a quick and simple questionnaire assessment of your “cognitive function” – that is, memory and problem-solving. The researcher will go through this with you, and it will take about 15 minutes. We will also ask you to fill in a series of questionnaires to assess your quality of life, the impact of any symptoms you suffer from, your level of fatigue, your physical activity habits and opinions, and your feelings about the likelihood of falling. We will explain these questionnaires to you and allow you to fill them in during the quiet time while you are resting between your walking tests, at other times during your visits or, if you prefer, you can take some, or all, of the questionnaires home with you to complete in your own time.
Clinical information: With your permission we will extract information related to your kidney transplant and general health from your medical records. This information will be stored anonymously using a study participant code and will not be identifiable as belonging to you.

**What are the possible disadvantages and risks of taking part?**

The main disadvantage of taking part is the time commitment involved in the hospital visits for assessments (2 or 3 visits in total). We will reimburse your travel expenses and car parking for these visits.

Taking blood samples from your arm may cause slight pain or some bruising afterwards, but is not dangerous.

At the visit involving the blood test, we will ask you to arrive in a “fasted” state – this means not having eaten or drunk anything except water since the previous night. You can choose which visit this will be, and we will arrange it for the morning so you don’t have to be hungry for too long! We will take the blood as soon as you arrive and then we will offer you tea or coffee and some breakfast such as toast or cereal. If it suits you, you can choose to call by the hospital briefly one morning just for the blood test, and do all the other assessments on other occasions.

You will need to fill in a series of questionnaires, which takes about half an hour. You will be given quiet time during a rest period to do this, or you can take them home to complete if you prefer.

We will fit you with an accelerometer, which is a lightweight waterproof device worn on the wrist like a watch. We will ask you to wear it continuously for 7 days. The device is not uncomfortable and should not cause you any problems.

**What are the possible benefits of taking part?**

There are no direct benefits to you of taking part in this research. We hope that the results of the study will help us understand how the physical condition of kidney patients relates to their overall health, and to design research studies that will lead to improved treatments for other kidney patients in the future.
What happens when the research study stops?

Your usual clinical care will continue unchanged.

What if something goes wrong?

In the very unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone’s negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

If you wish to make a complaint about the study you can contact the UHL Patient Information and Liaison Service by post to PILS, The Firs, Glenfield Hospital, Leicester LE3 9QP, telephone 08081 788337 (free phone number), or email pils@uhl-tr.nhs.uk

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 about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

While you are taking part in the study, your contact details will be made available to the researchers so that they can contact you to arrange the details of your research study appointments.

With your permission, your own GP will be notified of your participation in the study.

What will happen to any samples collected during the research?

Blood samples and urine samples collected as part of the research will be stored in the research laboratory, and may be used in laboratory tests at the Universities of Leicester and Loughborough. All samples will be labelled with an anonymous code and it will not be possible to identify you. Any tests carried out on the samples collected are part of a research programme and any results will not be used as a basis for diagnosis or treatment, either now or in the future.
We would like to keep any samples remaining after the end of this research for use in future studies that obtain ethical approval, such as measurement of newly-discovered factors associated with heart health or immune function, or to investigate in more detail any new findings that may emerge from the COCO study. At the end of COCO, we would like to either use your remaining samples in further research straight away, or transfer them to a research sample storage bank for use in studies that follow later on. However, if you would prefer your samples not to be used in such future research, you can indicate this on the Consent Form. In this case, we will destroy any of your samples that remain after the end of COCO.

**What will happen to the results of the research study?**

We expect the results of the research to become available from 2016. We will publicise the results in posters and leaflets in clinical areas so you can read them while you are there, and we will write a report about them in our Kidney Research Newsletter. If you would like us to send you a written report of the results, or if you would like to receive our Kidney Research Newsletter, please ask the researcher or contact the Chief Investigator, Dr Alice Smith (contact details at the end of this document).

The results will also be published in a medical journal. All information will be anonymised so you will not be identified in any report or publication.

**Who is organising and funding the research?**

The research is being organised by the Leicester Kidney Exercise Team at the John Walls Renal Unit, Leicester General Hospital and is led by Dr Alice Smith, Honorary Senior Lecturer. The study is partly funded by the Leicester Kidney Care Appeal.

Any research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be approved by an NHS Research Ethics Committee before it can go ahead.

This study has been reviewed by the NHS Research Ethics Committee East Midlands (Derby). Approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.
Contact for Further Information

If you would like any further information about this study please contact the Chief Investigator Dr Alice Smith, or Dr James Burton on 0116 258 4346.

Dr Alice Smith,

Leicester Kidney Exercise Team, Academic Unit,

Leicester General Hospital, LE5 4PW.

Tel 0116 258 4346 Email kidney.exercise@uhl-tr.nhs.uk

Thank you for reading this Information Sheet, and for considering taking part in this study.

You will be given a copy of this information sheet and signed consent form to keep
Appendix 1

Details of the Tests and Measurements

This section of the information sheet describes the assessment tests in more detail. Each assessment will be carried out once.

Physical performance tests: We will carry out two different tests of physical function and performance: a shuttle walk test and a sit-to-stand test.

The shuttle walk test has two parts. You will be asked to walk around two cones placed on the floor 10 metres apart, at a speed timed by a recorded bleep sound. For the first part, the bleep signal gets a little faster every minute so that you have to increase your walking speed to keep up. The test is stopped when you can no longer walk fast enough to keep up with the bleep. This test measures your maximum physical capacity. After this you will have a rest and the researcher will calculate a walking speed that equates to 85% of your maximum capacity. For the second part of the test, you will walk at this 85% speed (in time with a steady bleep) for as long as you can. The test is stopped when you can no longer keep walking at that speed. This test measures your stamina. Before doing these tests, you will be taught how to do it and allowed to practice.

The gait speed test measures your normal walking speed over a short distance (4 metres). We will use a laser gate device to accurately time you as you walk this short distance at your usual, comfortable walking pace.

The sit-to-stand test measures how easily you can stand up from a chair without using your hands. First of all we will measure how many times you can do this in 1 minute. Then we will time how long it takes you to perform 5. You will be given a chance to practice beforehand, and time to recover between each test.
The handgrip strength test is a quick and simple technique that provides a good overall estimate of your strength. We use a device called a dynamometer which you hold in your hand. The researcher will show you what to do and will give you a chance to practice before doing the test for real. You will sit comfortably with your elbow by your side and arm bent at a right angle. You will hold the dynamometer and squeeze it as hard as you can to generate the strength reading. You will do this three times with each hand and we will use the maximum reading as your strength measurement.

The balance tests are a very quick and simple way of measuring how good your balance is in 3 different standing positions. The researcher will show you what to do. You start with your feet together side by side and try to stand perfectly still for 10 seconds (timed by the researcher). If you are able to do this, you then move one foot forward a bit so that the heel is alongside the toe of your other foot, and again try to stand perfectly still for 10 seconds. Finally, you move one foot directly in front of the other and again try to stand still for 10 seconds.

Blood vessel health (Pulse Wave Velocity): This non-invasive test measures how long it takes a pulse to travel between two points, a point on your neck and a point at the top of your leg. We will place a sensor on each of these points and use a computer to measure how long a pulse takes to travel between them. We will also measure your blood pressure using a cuff in the same way your doctor usually measures it. It is a completely painless procedure, but you will be asked to remain still and not talk whilst the measurement is being taken. The pulse is easy to detect, but it is hard to find at the top of the leg through thick clothing, so you will be asked to wear light weight clothing or shorts for this assessment. It should take no longer than 5 minutes, including the time for you to get comfortable and for the researcher to position the sensors correctly.

Heart Function (Cardiac Bio-reactance): This is a safe, simple, non-invasive test which measures several aspects of heart function. The test involves lying on a couch and having four sticky electrodes (like those used for ECG which you may have had before) placed on your chest. A small, painless electric current is then passed through your body. The test is quick and will take around five minutes.
**Body fat and muscle**: These will be measured in two ways. An x-ray device called DEXA, often used in the NHS to assess the strength of bones, will be used and a technique called BIA will also be used.

**DEXA** scans are quick and painless and involve lying on an X-ray table so that the body can be scanned. This test uses a very small amount of x-ray radiation, which is equal to the dose you would receive from the natural background radiation by living in Leicester for about 10 days. The radiation dose is also less than the difference in yearly dose from natural sources between different locations in the United Kingdom.

**BIA** is a simple, safe and quick procedure which involves lying flat on a couch for around 2 minutes and having two sticky electrodes (similar to those used for ECG which you may have experienced) placed on one hand and foot. A small electric current which causes no pain is then passed down one side of your body.

**Height, weight and waist circumference**: Height and weight will be measured in the same way as your doctor uses during clinic visits by a member of the research team. We will also measure waist and hip circumference using a tape measure.

**Blood Sample**: We will take a blood sample from you from a vein in your arm. The sample will be 30ml (2 tablespoons) and will be used to measure for markers of inflammation.

**Urine Sample**: We will give you a container to collect some of your urine when you need to go to the toilet during one of the study visits.

**Habitual physical activity**: Habitual physical activity: We will ask you to wear a wrist-watch style activity monitor continuously for 7 days that will measure how much physical activity you do. The watch is waterproof and does not have to be removed while washing. We will request that you do not remove the watch during the 7 days.
Food diary: we will give you a food diary containing enough record sheets for 7 days. In this we will ask you to record everything you eat and drink for 7 days. The researcher will explain how to fill this in and you will take it home with you.

The Kidney Transplant Questionnaire: A researcher sit down with you in a quiet private room to ask 25 questions about problems which can affect your quality of life as a kidney transplant patient. These questions will be read out to you in a standard way and the researcher will record your answers on the questionnaire form. This questionnaire is only relevant for people with a kidney transplant. If you are on dialysis or have early CKD, you won’t need to fill it in.

Other Questionnaires: The researcher will ask you to do a simple questionnaire test of memory and problem-solving, which will take about 15 mins. We will also give you a series of questionnaires to complete yourself. Some or all of these can be filled out during assessment visits, or you may take them home to complete them there if you prefer. These are assessing your quality of life, the impact of symptoms associated with your kidney transplant, your level of fatigue, your physical activity habits and opinions, and your fear of falling.

Clinical parameters: With your permission we will extract information related to your kidney disease and general health from your medical records. This will include age, gender, ethnicity and postcode, your recent blood and urine tests results, other health problems you may suffer from, and the drugs you are taking. This will be stored anonymously using a study participant code and will not be identifiable as belonging to you.
You have been referred for a Dual Energy X-ray Absorptiometry (DXA) Scan. The information in this leaflet will explain what will happen before, during, and after this procedure and also answer any questions that you may have.

**What is a DXA Scan?**
A DXA scan is the most accurate and reliable way of measuring body composition, i.e. percentage body fat and lean mass. The scanner uses X-rays, which pass through bone and soft tissue. The X-rays are detected by the scanner which then calculates your body composition data.

**Are there any risks?**
Although DXA uses X-rays, this is at a very low dose and any risks are negligible.

**Before your DXA Scan**
A DXA scan may not be suitable:
- if you have severe mobility problems
- if you are unable to lie flat for a few minutes
- if you are pregnant, or think you may be
- if your weight exceeds 204 kg (32 stone)
- if you have had an X-ray with barium, contrast dye or a nuclear medicine test within the last 72 hours

When you come for your scan, you should try to wear light clothes that have no metal (e.g. zips, bras, buckles, belts, buttons and studs). Tight waistbands should also be avoided. You will then be able to have the scan in your own clothes rather than having to change into a hospital gown.
You will also be asked to remove any jewellery (including piercings), watches or hair accessories. You should inform the operator of any internal artefacts that may be seen in your scan (e.g. metal implants, pacemaker, surgical pins etc.).

What will happen during the scan?

You will be asked to lie on a firm couch while the scanner arm passes over you. You will not be in a tunnel, although the scanner arm may pass near your face. You will not need to have an injection. The scan will take around 10 minutes. The operator will be in the room with you during the scan.

Does it hurt?

The scan itself is painless. However, you will need to lie flat during the scan, which some people find uncomfortable.

When happens to the information collected?

The results will be provided to your study coordinator.

Who should I contact if I have any questions?

If you have any questions about your scan or the information in this leaflet you should contact your study coordinator.
Healthy controls

University Hospitals of Leicester

NHS

Trust

Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

Leicester Kidney Exercise Team

University of Leicester Academic Unit
Tel 0116 258 4346
Email Kidney.exercise@uhl-tr.nhs.uk

COCO: CardiOvascular Risk Factors and Physical COndition in Kidney Patients

Control Information Sheet

Version 2 23rd November 2015

You are being invited to take part in a research study. Before you decide, 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. 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 the study?

Kidney disease can affect the health of the heart and blood vessels and can also cause muscle wasting which leads to muscle weakness, tiredness, and a reduced physical capacity. For some people, a kidney transplant can be really beneficial and restore kidney function, but some of the negative effects often still remain.

Exercise can help healthy people get fitter, strengthen the muscles and improve the health of the heart and blood vessels. However, we do not know if kidney patients can also benefit in the same way from regular exercise. The Leicester Kidney Exercise Team are carrying out a number of research studies to investigate how exercise might help patients with kidney disease, including people on dialysis and those with a kidney transplant.
Altogether we will ask 60 kidney patients and 20 healthy controls to take part in the study. If you are aware that you do have a significant long term health problem, please tell the researchers that you don’t think you are suitable as a healthy control in this study. You don’t have to tell them any details about your condition.

**Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

**What will happen to me if I take part?**

During the study, we ask you to continue your life in the usual way. You should follow your usual diet and activities, and if you are on any prescribed medicines you should continue taking them as normal.

If you decide to take part we will arrange for you to attend for 2 or 3 visits for assessments. These visits will be flexible and scheduled at your convenience – you can choose whether to come for two longer visits or three shorter ones.

At one of these visits we will ask you to arrive in a “fasted” state – this means not having eaten or drunk anything except water since the previous night. This is needed for the blood test. You can choose which visit this will be, and we will arrange it for the morning so you don’t have to be hungry for too long! We will take the blood as soon as you arrive and then we will offer you tea or coffee and some breakfast such as toast or cereal. If it suits you, you can choose to call by briefly one morning just for the blood test, and do all the other assessments on other occasions.

We will also ask you to carry on with your life as normal while wearing a wrist-watch style activity monitor for one week, and recording everything you eat and drink over 7 days.

**Assessments**

During the visits, researchers will carry out the tests listed below. More detailed information about all these tests can be in Appendix 1 at the end of this Information Sheet. We will arrange the dates and times of the assessment visits to suit you.

1. **Physical performance tests:** Your physical performance will be tested using walking tests, sit to stand tests (rising from chair), hand grip strength test and balance tests. We will show you how to do the tests and allow you to practice before you do the test for real.
2. Blood vessel health: We will use a very easy and non-invasive test called Pulse Wave Velocity (PWV) to measure the health of your blood vessels.

3. Heart Function: Another easy and non-invasive test, called Cardiac Bio-reactance, will be used to measure the function of the heart.

4. Body fat and muscle: We will measure these using two safe, non-invasive techniques; DEXA and BIA.

5. Height, weight, and waist and hip circumference: We will measure these once in the same way as your doctor, nurse or dietician uses during clinic visits.

6. Blood samples: We will take one 30ml (2 tablespoon) blood sample from a vein in your arm. As explained above, you need to refrain from eating or drinking anything other than water on the morning of the blood test.

7. Urine sample: we will ask you to provide a 20ml urine sample at your convenience during one of the study visits.

8. Habitual physical activity: We will ask you to wear a wrist-watch style activity monitor continuously for 7 days that will measure how much physical activity you do.

10. Food diary: we will ask you to record everything you eat and drink for 7 days in a food diary which we will give you to take home with you.

11. Questionnaires: We will ask you to do a quick and simple questionnaire assessment of your “cognitive function” – that is, memory and problem-solving. The researcher will go through this with you, and it will take about 15 minutes. We will also ask you to fill in a series of questionnaires to assess your quality of life, the impact of any symptoms you suffer from, your level of fatigue, your physical activity habits and opinions, and your feelings about the likelihood of falling. We will explain these questionnaires to you and allow you to fill them in during the quiet time while you are resting between


**What are the possible disadvantages and risks of taking part?**

The main disadvantage of taking part is the time commitment involved in the hospital visits for assessments (2 or 3 visits in total). We will reimburse your travel expenses and car parking for these visits.

Taking blood samples from your arm may cause slight pain or some bruising afterwards, but is not dangerous.

At the visit involving the blood test, we will ask you to arrive in a “fasted” state – this means not having eaten or drunk anything except water since the previous night. You can choose which visit this will be, and we will arrange it for the morning so you don’t have to be hungry for too long! We will take the blood as soon as you arrive and then we will offer you tea or coffee and some breakfast such as toast or cereal. If it suits you, you can choose to call by the hospital briefly one morning just for the blood test, and do all the other assessments on other occasions.

You will need to fill in a series of questionnaires, which takes about half an hour. You will be given quiet time during a rest period to do this, or you can take them home to complete if you prefer.

We will fit you with an accelerometer, which is a lightweight waterproof device worn on the wrist like a watch. We will ask you to wear it continuously for 7 days. The device is not uncomfortable and should not cause you any problems.

We will ask you to complete a food diary, in which you write down everything you eat and drink over a period of 7 days.

**What are the possible benefits of taking part?**

There are no direct benefits to you of taking part in this research. We hope that the results of the study will help us understand how the physical condition of kidney patients relates to their overall health, and to design research studies that will lead to improved treatments for kidney patients in the future.
**What happens when the research study stops?**

You will carry on with your normal routine.

**What if something goes wrong?**

In the very unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone’s negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

If you wish to make a complaint about the study you can contact the UHL Patient Information and Liaison Service by post to PILS, The Firs, Glenfield Hospital, Leicester LE3 9QP, telephone 08081 788337 (free phone number), or email pils@uhl-tr.nhs.uk

**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 about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

While you are taking part in the study, your contact details will be made available to the researchers so that they can contact you to arrange the details of your research study appointments.

When you enter the study we will ask you to provide the researchers with the name and contact details of your own GP. In the unlikely event that one of the tests we carry out as part of the study shows any abnormal results, we will inform your GP so that he or she can decide what further action to take.

**What will happen to any samples collected during the research?**

Blood samples and urine samples collected as part of the research will be stored in the research laboratory, and may be used in laboratory tests at the Universities of Leicester and Loughborough. All samples will be labelled with an anonymous code and it will not
used as a basis for diagnosis or treatment, either now or in the future.

However, there is a small chance that one of the tests we carry out during the study may show an abnormal result. In this case, we will contact your own GP so that he or she can decide what action to take.

We would like to keep any samples remaining after the end of this research for use in future studies that obtain ethical approval, such as measurement of newly-discovered factors associated with heart health or immune function, or to investigate in more detail any new findings that may emerge from the COCO study. At the end of COCO, we would like to either use your remaining samples in further research straight away, or transfer them to a research sample storage bank for use in studies that follow later on. However, if you would prefer your samples not to be used in such future research, you can indicate this on the Consent Form. In this case, we will destroy any of your samples that remain after the end of COCO.

**What will happen to the results of the research study?**

We expect the results of the research to become available from 2016. We will write a report about them in our Kidney Research Newsletter. If you would like us to send you a written report of the results, or if you would like to receive our Kidney Research Newsletter, please ask the researcher or contact the Chief Investigator, Dr Alice Smith (contact details at the end of this document).

The results will also be published in a medical journal. All information will be anonymised so you will not be identified in any report or publication.

**Who is organising and funding the research?**

The research is being organised by the Leicester Kidney Exercise Team at the John Walls Renal Unit, Leicester General Hospital and is led by Dr Alice Smith, Honorary Senior Lecturer. The study is partly funded by the Leicester Kidney Care Appeal.

Any research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be approved by an NHS Research Ethics Committee before it can go ahead.

This study has been reviewed by the NHS Research Ethics Committee East Midlands (Derby). Approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits.
and that you have been given sufficient information on which to make an informed decision.

**Contact for Further Information**

If you would like any further information about this study please contact the Chief Investigator Dr Alice Smith, or Dr James Burton on 0116 258 4346.

Dr Alice Smith,
Leicester Kidney Exercise Team, Academic Unit,
Leicester General Hospital, LE5 4PW.
Tel 0116 258 4346 email kidney.exercise@uhl-tr.nhs.uk

Thank you for reading this Information Sheet, and for considering taking part in this study.

You will be given a copy of this information sheet and signed consent form to keep
Appendix 1

Details of the Tests and Measurements

This section of the information sheet describes the assessment tests in more detail. Each assessment will be carried out once.

Physical performance tests: We will carry out two different tests of physical function and performance: a shuttle walk test and a sit-to-stand test.

The shuttle walk test has two parts. You will be asked to walk around two cones placed on the floor 10 metres apart, at a speed timed by a recorded bleep sound. For the first part, the bleep signal gets a little faster every minute so that you have to increase your walking speed to keep up. The test is stopped when you can no longer walk fast enough to keep up with the bleep. This test measures your maximum physical capacity. After this you will have a rest and the researcher will calculate a walking speed that equates to 85% of your maximum capacity. For the second part of the test, you will walk at this 85% speed (in time with a steady bleep) for as long as you can. The test is stopped when you can no longer keep walking at that speed. This test measures your stamina. Before doing these tests, you will be taught how to do it and allowed to practice.

The gait speed test measures your normal walking speed over a short distance (4 metres). We will use a laser gate device to accurately time you as you walk this short distance at your usual, comfortable walking pace.

The sit-to-stand test measures how easily you can stand up from a chair without using your hands. First of all we will measure how many times you can do this in 1 minute. Then we will time how long it takes you to perform 5. You will be given a chance to practice beforehand, and time to recover between each test.

The handgrip strength test is a quick and simple technique that provides a good overall estimate of your strength. We use a device called a dynamometer which you hold in your hand. The researcher will show you what to do and will give you a chance to practice before doing the test for real. You will sit comfortably with your elbow by your side and
bent at a right angle. You will hold the dynamometer and squeeze it as hard as you can to generate the strength reading. You will do this three times with each hand and we will use the maximum reading as your strength measurement.

The **balance tests** are a very quick and simple way of measuring how good your balance is in 3 different standing positions. The researcher will show you what to do. You start with your feet together side by side and try to stand perfectly still for 10 seconds (timed by the researcher). If you are able to do this, you then move one foot forward a bit so that the heel is alongside the toe of your other foot, and again try to stand perfectly still for 10 seconds. Finally, you move one foot directly in front of the other and again try to stand still for 10 seconds.

These physical performance tests are easy to do and are widely used in patients with many chronic diseases, including kidney disease. If you are not used to exercise you may feel rather breathless after the shuttle walk tests, and you may experience some mild muscle stiffness later. These are normal effects of unaccustomed exercise, and nothing to worry about.

**Blood vessel health** (Pulse Wave Velocity): This non-invasive test measures how long it takes a pulse to travel between two points, a point on your neck and a point at the top of your leg. We will place a sensor on each of these points and use a computer to measure how long a pulse takes to travel between them. We will also measure your blood pressure using a cuff in the same way your doctor usually measures it. It is a completely painless procedure, but you will be asked to remain still and not talk whilst the measurement is being taken. The pulse is easy to detect, but it is hard to find at the top of the leg through thick clothing, so you will be asked to wear light weight clothing or shorts for this assessment. It should take no longer than 5 minutes, including the time for you to get comfortable and for the researcher to position the sensors correctly.

**Heart Function** (Cardiac Bio-reactance): This is a safe, simple, non-invasive test which measures several aspects of heart function. The test involves lying on a couch and having four sticky electrodes (like those used for ECG which you may have had before) placed
on your chest. A small, painless electric current is then passed through your body. The test is quick and will take around five minutes.

**Body fat and muscle:** These will be measured in two ways. An x-ray device called DEXA, often used in the NHS to assess the strength of bones, will be used and a technique called BIA will also be used.

**DEXA** scans are quick and painless and involve lying on an X-ray table so that the body can be scanned. This test uses a very small amount of x-ray radiation, which is equal to the dose you would receive from the natural background radiation by living in Leicester for about 10 days. The radiation dose is also less than the difference in yearly dose from natural sources between different locations in the United Kingdom.

**BIA** is a simple, safe and quick procedure which involves lying flat on a couch for around 2 minutes and having two sticky electrodes (similar to those used for ECG which you may have experienced) placed on one hand and foot. A small electric current which causes no pain is then passed down one side of your body.

**Height, weight and waist circumference:** Height and weight will be measured in the same way as your doctor uses during clinic visits by a member of the research team. We will also measure waist and hip circumference using a tape measure.

**Blood Sample:** We will take a blood sample from you from a vein in your arm. The sample will be 30ml (2 tablespoons) and will be used to measure for markers of inflammation.

**Urine Sample:** We will give you a container to collect some of your urine when you need to go to the toilet during one of the study visits.

**Habitual physical activity:** Habitual physical activity: We will ask you to wear a wrist-watch style activity monitor continuously for 7 days that will measure how much physical activity you do. The watch is waterproof and does not have to be removed while washing. We will request that you do not remove the watch during the 7 days.
Food diary: we will give you a food diary containing enough record sheets for 7 days. In this we will ask you to record everything you eat and drink for 7 days. The researcher will explain how to fill this in and you will take it home with you.

Questionnaires: The researcher will ask you to do a simple questionnaire test of memory and problem-solving, which will take about 15 mins. We will also give you a series of questionnaires to complete yourself. Some or all of these can be filled out during assessment visits, or you may take them home to complete them there if you prefer. These are assessing your quality of life, the impact of symptoms associated with your kidney transplant, your level of fatigue, your physical activity habits and opinions, and your fear of falling.
B.3.2 PIS in Chinese study

Chinese HD patients

COCO : 肾脏疾病患者的心血管危险因素及体力状态

患者信息单

2015-11-23

您正在被邀请参与我们的研究。但是在您做出决定之前，请您先了解我们研究的目的和内容。请仔细阅读下面的信息，您也可以和其他人讨论后做出决定。如果有任何问题或是您想获得更多的信息请向我们咨询。

研究目的

肾脏疾病影响心血管健康的同时也会引起肌肉萎缩，后者会导致肌肉无力，疲劳以及体力下降。这些反应在透析患者身上表现的更为突出。虽然肾移植能够使患者受益，恢复肾功能，但是某些消极的影响依旧存在。

我们之前的研究发现运动能够帮助肾病患者增强肌肉能力，促进心血管健康。这些发现提示我们常规的运动可能对肾病患者非常有益，但是我们并不知道何种运动对肾病不同阶段的患者有最佳的帮助。因此我们需要对肾病患者，涉及透析前，透析和肾移植的患者，他们的体力状况以及活动水平有更深的了解，包括与健康相关因素和生活质量的关系。此项研究设计收集这些信息，这将会帮助我们为肾脏病人的运动方面开展更好的研究。

我们将邀请肾病患者进行一系列的研究，包括行走能力，每日活动水平，身体结构构成，以及心脏健康，血液和尿液检查以及填写一些简单量表。这些测试将会在医院的研究中心进行。您可以选择两次，每次大约 2 小时，或者三次短时间的测试。

为什么选择我？

您被邀请参加本研究是因为您是肾脏病患者，我们将要组织60名肾脏患者以及同年龄和性别的没有肾脏疾病的健康人参与本研究。
我必须参加吗？

您是否参加完全取决于您的意愿。如果您决定参加，我们将会请您签署一份知情同意书。即使您已决定参加本研究，您也有权利随时退出研究，不需任何理由。您拒绝参加或退出研究的决定都不会影响到您的治疗和合法权益。

如果我参加此项研究需要做些什么？

整个研究不会影响到您的正常生活，我们不需要您做出任何调整，请您还是按照医嘱调整您的饮食与药物服用。

如果您愿意参加此项研究，我们将安排您进行 2-3 次的评估测试。这些测试是灵活的，可以根据您方便的时间来安排的。您可选择来两次或者三次完成它。

在其中的一次测试之前我们会请您禁食—这意味着前一天晚上您就不能进食或饮用任何除了水之外的饮品。这是为了血液检查之用。您可以选择方便的时候，我们也会把检查放在早上，这样可以减少您饥饿的时间。在您到达之时，我们会马上为您抽血，然后会为您提供早餐。在要求您佩戴测量活动量仪器的那一周里请您继续正常的生活节奏，无需做出任何调整。

评估

在研究期间，研究者将进行下面列出的测试。关于所有这些测试的更详细的信息可以在本信息表的附录 1 中找到。我们会根据您的需要，安排评估的时间和时间。

身体活动能力测试：你的身体表现将通过行走测试、坐立测试（从椅子上站起来）、握力测试和平衡测试来测试。我们将向您展示如何进行测试，并允许您在真正进行测试之前进行实践。

血管健康：我们将使用一种非常简单和非侵入性的测试，叫做脉搏波速度（PWV）来测量你的血管的健康状况。

心脏功能：另一种简单的、非侵入性的测试，叫做心脏生物电抗，将被用来测量心脏的功能。
身体脂肪和肌肉：我们将使用两种安全的、非侵入性的技术来测量它们：DEXA和BIA。

身高、体重、腰围和臀围：我们将以你的医生、护士或营养师在门诊就诊时使用的方式来测量这些指标。

血样：我们将从你手臂上的静脉中取出一个30ml（2汤匙）的血样。如上所述，在验血时，你需要避免吃或喝除水以外的任何东西。

尿样：我们会要求您在某次评估期间方便的时候提供一个20ml的尿样。

习惯性体力活动：我们会要求你连续7天佩戴腕表式的活动监测器，以测量你做了多少体力活动。

饮食日记：我们会要求你把你7天的饮食都记录在饮食日记里，我们会请你带回家记录。

肾移植问卷：研究小组的一个成员会问你25个问题，关于肾移植患者日常生活中经常遇到的一些问题。如果你是肾脏移植病人，你必须填写这份问卷。

其他的问卷调查：我们会让你做一个快速简单的问卷调查评估你的认知功能，也就是记忆力和解决问题的能力。研究者会和你一起检查，大约需要15分钟。我们还会要求你填写一系列的问卷来评估你的生活质量，你所遭受的任何症状的影响，你的疲劳程度，你的身体活动习惯和观点，以及你对摔倒可能性的感觉。我们将解释这些问卷，并请你在安静的环境里填写。您可以在你的行走测试休息期间，或者其它评估时间，或者如果你愿意，你可以带一些，或全部问卷带回家完成。

临床参数：经您同意，我们将从您的病历中提取有关您的肾脏疾病和一般健康的信息。这将以研究参与者代码匿名的方式使用，属于您个人的信息不会被识别。
参加本研究会有什么可能的缺点和风险吗？

参与本研究主要的影响就是您花在上面的时间（总共2-3次）。我们将要补偿您每次的车费和停车费。

抽取血液标本可能会引起轻微的疼痛或皮肤青紫，但是都没有危险性。在血液检查的那次评估中，我们会请您禁食—这意味着从前一天晚上您就不能进食或饮用任何除了水之外的饮品。这是为了血液检查之用。您可以选择方便的时候，我们也会把检查放在早上，这样可以减少您饥饿的时间。在您到达之时，我们会马上为您抽血，然后会为您提供早餐。

您还需要填写一些量表，这大概要占用您半个小时。您可以在休息时在安静的环境中完成量表，或者选择带回家去完成它们。

除此之外，我们还请您使用一个运动加速器来评估您的活动水平。这是一个防水佩戴在胳膊上的小型测量仪。我们需要您持续佩戴7天。这个仪器不会让您不舒服也不会引起任何问题。

参加本研究有什么潜在的好处？

参加本研究没有直接的好处。我们希望研究的结果能帮助我们理解肾病患者的体力状态和健康的关系，以便今后能设计出可以改善肾病患者治疗的研究方案。

当研究结束时会发生什么？

您常规的临床治疗护理一切正常进行。

如果研究不顺利会怎么样？

参加本研究会伤害到您的可能性几乎为零，所以我们没有什么特殊的补偿措施。如果您被某人的失职带来伤害，您有理由采取法律行动，但是您可能需要自己支付费用。如果您对我们研究过程有任何的不满，您可以向医院的相关部门进行投诉。
若您对研究有任何的不满，您可以向医院的伦理委员会联系。电话：0513-85052390 邮箱：lunlib@126.com 地址：江苏省南通市西寺路20号南通大学附属医院13号楼3楼伦理委员会办公室

我参与此项研究的信息会被保密吗？

在本研究中所收集的任何数据信息将会以研究编码标记，而不是您的姓名。您留在医院里的任何涉及您个人身份信息的文件都会被去除，您的个人隐私会得到保护。在您参与研究期间，研究者会保留您的联系方式以便和您及时沟通研究的相关信息。

再得到您的允许之后，我们会通知您的主治医生您参与了此项研究。

研究的结果将如何处理？

本研究预期于2016年完成。我们将会把研究结果通过海报或手册的方式在病房展示，这样您就可以在就医期间看到。另外，我们也会将结果形成报告或文章。如果您有需要，请联系我们或护士（联系方式显示在下方），我们会将报告或文章直接邮寄或送达给您。

谁组织或资助此项研究？

本研究是由宋艳副教授（南通大学）以及南通大学附属医院组织负责。

谁将对本研究进行评价监督？

任何涉及到患者病历信息或使用到其规定或设施的研究都应在开展之前通过伦理委员会的审查。本研究已经经南通大学附属医院伦理委员会办公室审核通过，意味着伦理委员会认定您的权利在本研究中将会被充分的保护和尊重，对您的影响以及对您利益的冲突已经被减少到最低，另外，在您做出决定之前，您已经被给予了充分的信息说明。

更多的信息

如果您想获得更多关于此项研究的信息，请联系研究者宋艳，手机（86）1386190853 固定电话：0513-85051784。电子邮件：suyayanshu@hotmail.com

感谢您阅读患者信息表，请考虑参与此项研究！
附件

测量评估细节

这个部分为本研究评估内容的细节介绍。每个评估只进行一次。

1. 身体活动能力测试：穿梭行走试验有两个部分。您将会被要求跟着外部的提示音来绕着相距10米的两个标志物来回的走动。在第一部分，提示音每分钟都会加快一点以提示您需要加快步速跟上节奏。当您没法再加快速度以跟上提示音，测试结束。这一部分测试最大的活动能力。之后请您休息一下。研究者会用您最大活动能力的85%计算出步速。在第二部分，我们请您以计算出来的步速继续绕着标记物往返走动。在这一部分中，步速不变，请您尽可能的完成往返的次数。同样，如若您无法以此步速跟上提示音，测试结束。穿梭行走试验第二部分测试的是耐力。在正式测量之前，您将被告知如何进行测量并且会给您练习的机会。

步速试验是通过一段短距离（4m）测量您正常的步速。我们将用激光门仪器来精确的在您通过这段短距离时计时。

坐-立试验测量的是您不借助手的帮助从椅子上站立的能力。首先，我们要测量您一分钟内进行此项试验的次数。然后我们将记录您快速完成5次试验所用的时间。您会先有一段练习的时间，在每次测试之间也会有休息的时间。

手持式力量测试是一种快速而简单的技术，可以对您的力量进行全面的评估。我们使用一种叫做测功仪的装置，您可以拿在手里。研究人员会告诉您该做什么，并给您一个练习的机会，然后再做真正的测试。您可以舒服地坐着，肘放在身体两侧，手臂弯曲成直角。您将握住测功器，尽可能用力挤压，以产生强度读数。您将用每只手做三次，我们将使用最大读数作为您的力量测量。

平衡测试是一种非常快速和简单的方法，用来测量您在3个不同的站立位置时的平衡能力。研究人员会告诉您该做什么。您把双脚并排放在一起，试着保持完全静止10秒钟（研究者计时）。如果您能做到这一点，您就把一只脚向前挪一点，这样脚后跟就会和另一只脚的脚趾
并排，然后再试着保持完全静止10秒钟。最后，您把一只脚直接放在另一只脚的前面，然后再试着站立10秒钟。

2. 血管健康（脉搏波速度）：这个非侵入性的测试测量了脉搏在两点之间传播的时间，一个点在您脖子上，一个点在您的脚的顶部。我们将在每一个点上放置一个传感器，并使用计算机来测量脉冲在它们之间传播的时间。我们也会用袖带测量您的血压，就像您的医生通常测量血压一样。这是一种完全无痛的过程，但您会被要求在测量过程中保持静止不说话。脉搏很容易检测到，但是通过厚的衣服很难在脚的顶部找到，所以您会被要求穿轻便的衣服或短裤进行评估。它应该不超过5分钟，包括让您感到舒适和研究者正确定位传感器的时间。

3. 心脏功能（心脏生物电抗）：这是一种安全、简单、无创的检测方法，可以检测心脏功能的几个方面。这个测试包括躺着沙发上，用四个粘贴的电极（就像您以前可能有的心电图一样）。小的，无痛的电流通过您的身体。整个测量过程很快，大约需要5分钟。

4. 身体脂肪和肌肉：这些将以两种方式测量。一种被称为DEXA的X光设备将会被使用，这种设备通常被用于英国国家医疗服务系统（NHS），用于评估骨骼的强度。一种叫做BIA的技术也将被使用。

DEXA扫描仪扫描快速、无痛，检查者躺在一张X射线桌子上面，身体可以被扫描。这项测试使用的X射线辐射量非常少。

BIA检测过程简单、安全、快速。被检查者平躺在沙发上约2分钟左右，两个带有粘性的电极（类似于那些您可能经历过的用于心电图的）分别置于一只手和脚。一股不会引起疼痛的小电流就会从您身体的一侧流过。

5. 身高、体重和腰围：身高和体重的测量方法与您的医生在门诊就诊时所使用的方法相同。我们还将用卷尺测量腰围和臀围。

6. 血液样本：我们将从您手臂上的静脉中抽取血液样本。样本容量为30ml（2汤匙），用于检测炎症标志物。
7. 尿液样本：我们会给您一个容器，当您需要去厕所的时候收集您的一些尿液。

8. 习惯性体力活动：我们会要求您佩戴活动加速器，持续7天，以测量您做了多少体力活动。我们要求您除了在洗澡、游泳在接触水的时候拿下监测仪，其余时间请持续佩戴。

9. 食物日记：我们会给您一个食物日记，里面有足够7天的记录。在这本日记中，我们将要求您记录下您在7天内吃的所有东西。研究者会解释如何填写，我们请您会把它带回家做记录。

10. 肾脏移植调查问卷：一名研究人员和您一起坐在一个安静的私人房间里，就影响肾脏移植患者生活质量的问题问您25个问题。这些问题将以一种标准的方式向您宣读，研究者将在调查表上记录您的答案。本问卷仅适用于肾移植患者。如果您正在透析或有早期的CKD，您将不需要填写它。

11. 其他调查问卷：研究人员会让您做一个简单的关于记忆和解决问题的调查问卷，大约需要15分钟。我们也会给您一系列的问卷请您自己完成。有些或所有这些可以在评估期间填写，或者您可以带回家完成，如果您喜欢的话。这些是评估您的生活质量，与肾脏移植相关的症状的影响，您的疲劳程度，您的身体活动习惯和观点，以及您对跌倒的恐惧。

12. 临床参数：经您同意，我们将从您的病历中提取有关您的肾脏疾病和一般健康的信息。这将包括年龄、性别、种族和邮编、您最近的血液和尿液检测结果、您可能遭受的其他健康问题，以及您正在服用的药物。这将以研究参与者代码匿名的方式使用，属于您个人的信息不会被识别。
DXA对扫描患者信息传单

向您推荐进行双能量X射线吸收测量(DXA)扫描。本小册子中的信息将解释在此过程之前、期间和之后将发生的事情，并回答您可能提出的任何问题。

**DXA扫描仪是什么？**

DXA扫描是测量身体成分的最准确和最可靠的一种方式。如：身体的脂肪和肌肉百分比。扫描仪使用X射线，通过骨骼和软组织。扫描仪会检测到X光，然后计算出你的身体成分数据。

**DXA扫描有风险吗？**

尽管DXA测定仪使用X射线，但是这种剂量非常低并且风险可以忽略不计。

DXA测定前，以下情况可能不适合DXA检测：

- 如果你有严重的移动障碍
- 如果你不能平躺几分钟
- 如果你已经怀孕，或认为你可能已经怀孕
- 如果你的体重超过204公斤
- 如果你接触X射线与钡，请在过去72小时内对比染色或扫描测。

请你应该尽量穿着没有金属(如拉链、胸罩、扣、腰带、按钮和钉)的衣服。也要避免紧身腰带。这样，你就可以穿自己的衣服上去进行扫描，而不用换上医院的长袍。你也将被要求移除任何珠宝(包括穿孔)、手表或发饰。操作员将会告知你任何内部物品也要去除(例如金属植入物、起搏器、外科针等)。

**在扫描期间会发生什么事？**
你将被要求躺在沙发上同时扫描器手臂经过你。你不是在隧道里，尽管扫描器的手臂可能会经过你的脸。你不需要打针。扫描大约需要10分钟。在扫描过程中操作员会和你在房间里。

扫描疼吗？

扫描本身是无痛苦的。然而，在扫描过程中，你需要平躺，有些人会觉得不舒服。

何时信息收集？

请将研究结果将提供给你的研究者。

你应该和谁联系？

如果你扫描过程或有任何关于这个小册子的问题，你应该联系你的研究者。
Healthy controls

COCO: 肾脏疾病患者的心血管危险因素及体力状态

健康对照组信息单

2015-11-23

您正在被邀请参与我们的研究。但是在您做出决定之前，请您先了解我们研究的目的和内容。请仔细阅读下面的信息，您也可以和其他人讨论后做出决定。如果有任何问题或是您想获得更多的信息请向我们咨询。

研究目的

肾脏疾病影响心血管健康的同时也会引起肌肉萎缩，后者会导致肌肉无力，疲劳以及体力下降。这些反应在透析患者身上表现的更为突出。虽然肾移植能够使患者受益，恢复肾功能，但是某些消极的影响依旧存在。

运动可以帮助健康的人变得更健康，增强肌肉，改善心脏和血管的健康。然而，我们不知道肾脏病人是否也能从定期锻炼中获得同样的好处。莱斯特肾脏锻炼小组正在进行多项研究，以研究锻炼可能如何帮助肾病患者，包括透析患者和肾移植患者。

为了帮助我们的研究，我们需要了解目前肾脏病人的身体状况和身体活动习惯，以及这些与健康相关的其他重要因素，以及生活质量的关系。我们还需要了解这些因素在肾脏病人和同年龄、同性别的健康人中的差异。

这项研究旨在收集这些信息，这将有助于我们开展关于肾病患者运动的最佳未来研究。

我们将邀请肾脏患者进行一系列的行走能力、日常身体活动水平、身体成分和心脏健康的测试和测量，进行血液测试和尿液测试，并填写一些简单的问卷。

我们也会请一些年龄和性别相同的健康人做同样的测试，这样我们就可以比较结果，以研究肾病对患者的影响。
测试将在医院研究中心进行，参与者可以选择两次，每次大约 2 小时，或者三次短时间的测试。我们将分析从研究中收集的数据，以帮助我们评估锻炼对肾脏病人的益处，并设计未来关于锻炼和肾脏病人健康的研究。

为什么选择我？

您之所以被选中，是因为您的年龄与参与这项研究的一些肾脏病人差不多，就您所知，您有不错的健康状况，没有任何已知的疾病。一组健康的人参加这样的研究被称为“健康对照组”。

我们正在做的这项研究是为了更好地了解肾病患者的身体活动与健康和生活质量之间的关系，以及肾病患者和健康人之间的差异。

我们将邀请 60 名肾脏患者和 20 名健康对照者参与这项研究。

如果您意识到您有严重的长期健康问题，请告诉研究者您认为您不适合在这项研究中作为一个健康的对照。您不必告诉他们您的具体情况。

我必须参加吗？

您是否参加完全取决于您的意愿。如果您决定参加，我们将会请您签署一份知情同意书。即使您已决定参加本研究，您也有权利随时退出研究，不需任何理由。您拒绝参加或退出研究的决定都不会影响到您的治疗和合法权益。

如果我参加此项研究将需要做些什么？

整个研究不会影响到您的正常生活，我们不需要您做出任何调整。请您还是遵循您的日常饮食和活动，如果您正在服用任何处方药，您应该继续正常使用。

如果您愿意参加此项研究，我们将安排您进行 2-3 次的评估测试。这些测试是灵活的。您可以选择两次，每次大约 2 小时，或者三次短时间的测试。
在其中的一次测试之前我们会请您禁食—这意味着从前一天晚上您就不能进食或饮用任何除了水之外的饮品。这是为了血液检查之用。您可以选择方便的时候，我们也会把检查放在早上，这样可以减少您饥饿的时间。在您到达之时，我们会马上为您抽血，然后会为您提供早餐。在要求您佩戴测量活动检测仪的那一周里请您继续正常的生活节奏，无需做出任何调整。

**评估**

在研究期间，研究者将进行下面列出的测试。关于所有这些测试的更详细的信息可以在本信息表的附录 1 中找到。我们会根据您的需要，安排评估的时间和时间。

身体活动能力测试: 你的身体表现将通过行走测试、坐立测试 (从椅子上站起来)、握力测试和平衡测试来测试。我们将向您展示如何进行测试，并允许您在真正进行测试之前进行实践。

血管健康: 我们将使用一种非常简单和非侵入性的测试，叫做脉搏波速度 (PWV) 来测量你的血管的健康状况。

心脏功能: 另一种简单的、非侵入性的测试，叫做心脏生物电抗，将被用来测量心脏的功能。

身体脂肪和肌肉: 我们将使用两种安全的、非侵入性的技术来测量它们; DEXA 和 BIA。

身高、体重、腰围和臀围: 我们将以你的医生、护士或营养师在门诊就诊时使用的方式来测量这些指标。

血样: 我们将从你手臂上的静脉中取出一个 30ml (2 汤匙) 的血样。如上所述，在验血时，你需要避免吃或喝除水以外的任何东西。

尿样: 我们会要求您在某次评估期间方便的时候提供一个 20ml 的尿样。

习惯性体力活动: 我们会要求你连续 7 天佩戴腕表式的活动监测器，以测量你做了多少体力活动。

饮食日记: 我们会要求你把你 7 天的饮食都记录在饮食日记里，我们会请你带回家记录。
肾移植问卷: 研究小组的一个成员会问你25个问题，关于肾移植患者日常生活中经常遇到的一些问题。如果你是肾脏移植病人，你必须填写这份问卷。

其他的问卷调查：我们会让你做一个快速简单的问卷调查评估你的认知功能，也就是记忆力和解决问题的能力。研究者会和你一起检查，大约需要15分钟。我们还会要求你填写一系列的问卷来评估你的生活质量，你所遭受的任何症状的影响，你的疲劳程度，你的身体活动习惯和观点，以及你对摔倒可能性的感觉。我们将解释这些问卷，并请你在安静的环境里填写。您可以在你的行走测试休息期间，或者其他评估时间，或者如果你愿意，你可以带一些，或者全部问卷带回家完成。

临床参数：经您同意，我们将从您的病历中提取有关您的肾脏疾病和一般健康的信息。这将以研究参与者代码匿名的方式使用，属于您个人的信息不会被识别。

参加本研究会有什么可能的缺点和风险吗？

参与本研究主要的影响就是您花在上面的时间（总共2-3次）。我们将要补偿您每次过来的车费和停车费。

抽取血液标本可能会引起轻微的疼痛或皮肤青紫，但是都没有危险性。在血液检查的那次评估中，我们会请您请您禁食——这意味着从前一天晚上您就不能进食或饮用任何除了水之外的饮品。这是为了血液检查之用。您可以选择方便的时候，我们也会把检查放在早上，这样可以减少您饥饿的时间。在您到达之时，我们会马上为您抽血，然后会为您提供早餐。

您还需要填写一些量表，这大概要占用您半个小时。您可以在休息时在安静的环境中完成量表，或者选择带回家去完成它们。

除此之外，我们还请您使用一个运动加速器来评估您的活动水平。这是一个防水佩戴在胳膊上的小型测量仪。我们需要您持续戴7天。这个仪器不会让您不舒服也不会引起任何问题。

我们会要求您完成一份饮食日记，您在日记中写下您在7天内吃的和喝的所有东西。
参加本研究有什么潜在的好处？

参加本研究没有直接的好处。我们希望研究的结果能帮助我们理解肾病患者的体力状态和健康的关系，以便今后能设计出可以改善肾病患者治疗的研究方案。

当研究结束时会发生什么？

您将继续您的日常生活。

如果研究不顺利会怎么样？

参加本研究会伤害到您的可能性几乎为零，所以我们也没有什么特殊的补偿措施。如果您被某人的失职带来伤害，您有理由采取法律行动，但是您可能需要自己支付费用。如果您对我们的研究过程有任何的不满，您可以向医院的相关部门进行投诉。

若您对研究有任何的不满，您可以向医院的伦理委员会联系。电 话：0513-85052390  邮  箱 lunlib@126.com  地  址：江苏省南通市西寺路20号南通大学附属医院13号楼3楼 伦理委员会办公室

在研究过程中收集的样本会如何处理？

作为研究的一部分，采集的血液样本和尿液样本将被储存在研究实验室中。所有的样本都将被贴上匿名的标签，从上面不可能识别您的信息。对采集的样本进行的任何检测都是研究计划的一部分，任何结果都不会作为诊断或治疗的基础，无论是现在还是将来。

然而，我们在研究过程中进行的任何的一项测试可能显示出异常结果的可能性很小。在这种情况下，我们将告知您，以便您可以决定采取什么措施。
我们想保持任何剩余样品待本研究结束后经伦理批准用于未来的研究，如测量新发现的与心脏健康相关的因素或免疫功能，或详细调查任何可能来自本研究的新发现。在研究结束时我们希望将您的剩余样本直接用于进一步研究，或者将它们转移到一个研究样本存储库中，以便以后的研究中使用。但是，如果您希望您的样品不用于今后的研究，您可以在同意书上注明。在这种情况下，我们将销毁您们在研究结束后留下的任何样品。

研究的结果将如何处理？

本研究预期于2016年完成。我们将会把研究结果通过海报或手册的方式在病房展示，这样您就可以在就医期间看到。另外，我们也会将结果形成报告或文章。如果您有需要，请联系我们或护士（联系方式显示在下方），我们会将报告或文章直接邮寄或送达给您。关于您的任何个人信息都不会出现在报告或文章中。

谁组织或资助此项研究？

本研究是由宋艳副教授（南通大学）以及南通大学附属医院组织负责。

谁将对本研究进行评价监督？

任何涉及到患者病历信息或使用到其规定或设施的研究都应在开展之前通过伦理委员会的审查。本研究已经经南通大学附属医院伦理委员会办公室审核通过，意味着伦理委员会认定您的权利在本研究中将会被充分的保护和尊重，对您的影响以及对您利益的冲突已经被减少到最低，另外，在您做出决定之前，您已经被给予了充分的信息说明。

更多的信息

如果您想获得更多关于此项研究的信息，请联系研究者宋艳，手机（86）13861908536，固定电话：0513-85051784，电子邮件：suyayanshu@hotmail.com

感谢您阅读患者信息表，请考虑参与此项研究！

在同意参与此项研究之后，

您将会受到此份患者信息单以及签过姓名的知情同意书的复印件！谢谢！
附件

测量评估细节

这个部分为本研究评估内容的细节介绍。每个评估只进行一次。

1. 身体活动能力测试：穿梭行走试验有两个部分。您将会被要求跟着外部的提示音来绕着相距10米的两个标志物来回的走动。在第一部分，提示音每分钟都会加快一点以提示您需要加快步速跟上节奏。当您没法再加快速度以跟上提示音，测试结束。这一部分测试最大的活动能力。之后请您休息一下。研究者会用您最大活动能力的85%计算出步速。在第二部分，我们请您以计算出来的步速继续绕着标记物往返走动。在这一部分中，步速不变，请您尽可能的完成往返的次数。同样，如若您无法以此步速跟上提示音，测试结束。穿梭行走试验第二部分测试的是耐力。在正式测量之前，您将被告知如何进行测量并且会给您练习的机会。

步速试验是通过一段短距离（4m）测量您正常的步速。我们将用激光门仪器来精确的在您通过这段短距离时计时。

坐-立试验测量的是您不借助手的帮助从椅子上站立的能力。首先，我们要测量您一分钟内进行此项试验的次数。然后我们将记录您快速完成5次试验所用的时间。您会先有一段练习的时间，在每次测试之间也会有休息的时间。

手持式力量测试是一种快速而简单的技术，可以对您的力量进行全面的评估。我们使用一种叫做测功仪的装置，您可以拿在手里。研究人员会告诉您该做什么，并给您一个练习的机会，然后再做真正的测试。您可以舒服地坐着，肘放在身体两侧，手臂弯曲成直角。您将握住测功器，尽可能用力挤压，以产生强度读数。您将用每只手做三次，我们将使用最大读数作为您的力量测量。

平衡测试是一种非常快速和简单的方法，用来测量您在3个不同的站立位置时的平衡能力。研究人员会告诉您该做什么。您把双脚并排放在一起，试着保持完全静止10秒钟（研究者计时）。如果您能做到这一点，您就把一只脚向前挪一点，这样脚后跟就会和另一只脚的脚趾
并排，然后再试着保持完全静止10秒钟。最后，您把一只脚直接放在另一只脚的前面，然后再试着站立10秒钟。

2. 血管健康（脉搏波速度）：这个非侵入性的测试测量了脉搏在两点之间传播的时间，一个点在您脖子上，一个点在您腿的顶部。我们将在每一个点上放置一个传感器，并使用计算机来测量脉冲在它们之间传播的时间。我们也会用袖带测量您的血压，就像您的医生通常测量血压一样。这是一种完全无痛的过程，但您会被要求在测量过程中保持静止不说话。脉搏很容易检测到，但是通过厚的衣服很难在腿的顶部找到，所以您会被要求穿轻便的衣服或短裤进行评估。它应该不超过5分钟，包括让您感到舒适和研究者正确定位传感器的时间。

3. 心脏功能（心脏生物电抗）：这是一种安全、简单、无创的检测方法，可以检测心脏功能的几个方面。这个测试包括躺在沙发上，在您的胸部放置四个粘贴的电极（就像您以前可能有过的心电图一样）。小的，无痛的电流通过您的身体。整个测量过程很快，大约需要5分钟。

4. 身体脂肪和肌肉：这些将以两种方式测量。一种被称为DEXA的X光设备将会被使用，这种设备通常被用于英国国家医疗服务体系（NHS），用于评估骨骼的强度。一种叫做BIA的技术也将被使用。

DEXA扫描仪扫描快速、无痛，检查者躺在一张X射线桌子上面，这样身体可以被扫描。这项测试使用的X射线辐射量非常少。

BIA检测过程简单、安全、快速。被检查者平躺在沙发上约2分钟左右，两个带有粘性的电极（类似于那些您可能经历过的用于心电图的）分别置于一只手和脚。一股不会引起疼痛的小电流就会从您身体的一侧流过。

5. 身高、体重和腰围：身高和体重的测量方法与您的医生在门诊就诊时所使用的方法相同。我们还将用卷尺测量腰围和臀围。

6. 血液样本：我们将从您手臂上的静脉中抽取血液样本。样本容量为30ml（2汤匙），用于检测炎症标志物。
7. 尿液样本: 我们会给您一个容器，当您需要去厕所的时候收集您的一些尿液。

8. 习惯性体力活动: 我们会要求您佩戴活动加速计，持续7天，以测量您做了多少体力活动。我们要求您除了在洗澡、游泳在接触水的时候拿下监测仪，其余时间请持续佩戴。

9. 食物日记: 我们会给您一个食物日记，里面有足够7天的记录。在这本日记中，我们将要求您记录下您在7天内吃的所有东西。研究者会解释如何填写，我们请您会把它带回家做记录。

10. 肾脏移植调查问卷: 一名研究人员和您一起坐在一个安静的私人房间里，就影响肾脏移植患者生活质量的问题问您25个问题。这些问题将以一种标准的方式向您宣读，研究者会在调查表上记录您的答案。本问卷仅适用于肾移植患者。如果您正在透析或有早期的CKD，您将不需要填写它。

11. 其他调查问卷: 研究人员会让您做一个简单的关于记忆和解决问题的调查问卷，大约需要15分钟。我们也会给您一系列的问卷请您自己完成。有些或所有这些可以在评估期间填写，或者您可以带回家完成，如果您喜欢的话。这些是评估您的生活质量，与肾脏移植相关的症状的影响，您的疲劳程度，您的身体活动习惯和观点，以及您对跌倒的恐惧。

12. 临床参数: 经您同意，我们将从您的病历中提取有关您的肾脏疾病和一般健康的信息。这将包括年龄、性别、种族和邮编、您最近的血液和尿液检测结果、您可能遭受的其他健康问题，以及您正在服用的药物。这将以研究参与者代码匿名的方式使用，属于您个人的信息不会被识别。
DXA对扫描患者信息传单

向您推荐进行双能量X射线吸收测量（DXA）扫描。本小册子中的信息将解释在此过程之前、期间和之后将发生的事情，并回答您可能提出的任何问题。

DXA扫描仪是什么？

DXA扫描是测量身体成分的最准确和最可靠的一种方式。如：身体的脂肪和肌肉百分比。扫描仪使用X射线，通过骨骼和软组织。扫描仪会检测到X光，然后计算出您的身体成分数据。

DXA扫描有风险吗？

尽管DXA测定仪使用X射线，但是这种剂量非常低并且风险可以忽略不计。

DXA测定前，以下情况可能不适合DXA检测：

• 如果您有严重的移动障碍

• 如果您不能平躺几分钟

• 如果您已经怀孕，或认为您可能已经怀孕

• 如果您的体重超过204公斤

• 如果您接触X射线与钡，请在过去72小时内对比染色或扫描测。

请您应该尽量穿着没有金属（如拉链、胸罩、扣、腰带、按钮和钉）的衣服。也要避免紧身腰带。这样，您就可以穿自己的衣服上去进行扫描，而不用换上医院的长袍。您也将被要求移除任何珠宝（包括穿孔）、手表或发饰。操作员将会告知您任何内部物品也要去除（例如金属植入物、起搏器、外科针等）。

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在扫描期间会发生什么事？

您将被要求躺在沙发上同时扫描器手臂经过您。您不是在隧道里，尽管扫描器的手臂可能会经过您的脸。您不需要打针。扫描大约需要10分钟。在扫描过程中操作员会和您在房间里。

扫描疼吗？

扫描本身是无痛苦的。然而，在扫描过程中，您需要平躺，有些人会觉得不舒服。

何时信息收集？

请将研究结果将提供给您的研究者。

您应该和谁联系？

如果您扫描过程或有任何关于这个小册子的问题，您应该联系您的研究者。
B.3.3 Consent form in the UK study

UK HD patients

University Hospitals of Leicester

Study Code
COCO

Leicester Kidney Exercise Team
University of Leicester Academic Unit
Leicester General Hospital
Leicester LE5 4PW
Tel 0116 258 4346

CONSENT FORM
COCO: CardiOvascular Risk Factors and PhysicalCondition in Kidney Patients
Name of Researcher: Dr Alice Smith.

1. I confirm that I have read and understand the COCO Patient Information Sheet version 5 dated 23rd November 2015 for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that my contact details will be made available to the research staff involved in this project so that they can contact me to arrange details of my research study appointments, and I give permission for them to do so.

4. I understand that my GP will be informed of my taking part in this study.

5. I understand that the samples collected as part of the research may be stored in research laboratories at the University of Leicester or Loughborough University and used in laboratory tests there.

6. I give permission for any of my samples which remain after the end of the current study to be used in further studies which obtain ethical approval, or stored in a research tissue bank. (If you prefer that this does not happen, please tick “NO” and your samples will be destroyed at the end of the COCO study).

7. I understand that any tests carried out on the samples collected are part of a research programme and any results will not be used as a basis for diagnosis or treatment, either now or in the future.

8. I understand that relevant sections of my medical notes and/or data may be looked at by responsible individuals from the study team, the Sponsor, Research Ethics Committee, NHS Trust or from regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to access my records.

9. I agree to take part in the above study.

Name of Patient ___________________________ Date ____________ Signature _______________________

Researcher ___________________________ Date ____________ Signature _______________________

Yes NO
UK Healthy controls

University Hospitals of Leicester
Leicester Kidney Exercise Team
University of Leicester Academic Unit
Leicester General Hospital
Leicester LE5 4PW
Tel 0116 258 4346

Study Code
COCO

CONTROL CONSENT FORM
COCO: Cardiovascular Risk Factors and Physical Condition in Kidney Patients
Name of Researcher: Dr Alice Smith

1. I confirm that I have read and understand the COCO Control Information Sheet version 2 dated 23rd November 2015 for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that my contact details will be made available to the research staff involved in this project so that they can contact me to arrange details of my research study appointments, and I give permission for them to do so.

4. I understand that the samples collected as part of the research may be stored in research laboratories at the University of Leicester or Loughborough University and used in laboratory tests there.

5. I give permission for any of my samples which remain after the end of the current study to be used in further studies which obtain ethical approval or stored in a research tissue bank. (If you prefer that this does not happen, please tick “NO” and your samples will be destroyed at the end of the COCO study.)

6. I understand that any tests carried out on the samples collected are part of a research programme and any results will not be used as a basis for diagnosis or treatment, either now or in the future.

7. However, I understand that in the unlikely event that any of the research tests involved in the study reveal results that are relevant to my health, a doctor who is part of the research team will inform my GP so that appropriate action can be taken. I agree to provide the name and contact details of my GP for this purpose only.

8. I understand that relevant sections of my data may be looked at by responsible individuals from the study team, the Sponsor, Research Ethics Committee, NHS Trust or from regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to access my records.

9. I agree to take part in the above study.

Name of Participant Date Signature

Researcher Date Signature

Please initial box.

YES NO

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B.3.4 Consent form in Chinese study

Chinese HD patients

患者知情同意书

患者姓名

日期

签名

研究者

日期

签名

研究代码

coco

患者知情同意书

肾病患者的心血管风险和身体状况

研究者：宋艳

请在此处打“√”

1. 我已阅读并理解 2015 年 11 月 23 日的关于该研究的肾病患者信息单
   并已询问了相关问题。

2. 我自愿参与该研究项目，并且无需提交任何理由、随时有退出该研究的自由，我的临床治疗和合法权利都不会受到影响。

3. 研究组相关工作人员已获得我的联系方式，因此他们可以联系我并安排相关研究细节。

4. 我的主治医生也将知晓我参与研究。

5. 我已获知这个研究所收集的标本将被存放于南通大学附属医院实验室。

6. 对于该项研究结束时余留的标本，我允许其存放于研究资料库或用于符合伦理学要求的后续研究。

7. 所收集的标本进行的任何实验都是该研究项目中的一部分，不管现在还是将来，任何结果都不用作诊断或治疗的基础。

8. 研究小组、资助者以及研究相关的伦理组织，所有这些相关责任人能获得我的医学相关信息和（或）数据。

8. 我同意加入该项研究。
Healthy controls

健康对照组知情同意书

肾病患者的心血管风险和身体状况

研究者：宋艳

请在此处打“√”

1. 我已阅读并理解 2015 年 11 月 23 日的关于该研究的健康对照组信息单并已询问了相关问题。

2. 我自愿参与该研究项目，并且无需提交任何理由，随时有退出该研究的自由，我的临床治疗和合法权利都不会受到影响。

3. 研究组相关工作人员已获得我的联系方式，因此他们可以联系我并安排相关研究细节。

4. 我已获知这个研究所收集的标本将被存放于南通大学附属医院实验室。

5. 对于该项研究结束时余留的标本，我允许其存放于研究资料库中或用于符合伦理学要求的后续研究。（如果你不同意，请选择“否”，该研究结束时，你的标本将被废弃）

6. 所收集的标本进行的任何实验都是该研究项目中的一部分，不管现在还是将来，任何结果都不用作诊断或治疗的基础。

7. 若在研究中发现任何涉及本人健康，且并不令人乐观的研究结果，研究者应当通知我以便采取适当措施。

8. 研究小组、资助者以及研究相关的伦理组织，所有这些相关责任人能获得我的医学相关信息和（或）数据。

9. 我同意加入该项研究。

患者姓名__________________ 日期__________ 签名__________________

研究人员__________________ 日期__________ 签名__________________
Appendix C. Interview record and questionnaires using in this thesis
C.1 The DISH study

C.1.1 UK HD patients

24-Hour Dietary Recall Instructions

Separate interviews will be conducted for a dialysis day and non-dialysis days in each of the first and last weeks of a month to account for variations in eating patterns associated with treatment. The interviews will be conducted using a modified version of the USDA 5-pass method:

1. Ask the patient to confirm that the day in question was either a dialysis or non-dialysis day
2. Ask the patient to recall everything eaten during the 24-hours in question.
   1. Start by asking the patient to list all foods and beverages consumed during the 24-hours. Do not interrupt and allow the patient to finish.
   2. Go through the list a second time prompting for anything that may have been forgotten such as beverages, snacks, and condiments.
   3. Gather details on the portion sizes, cooking methods, brands, etc. Be sure to ask them the point of purchase (supermarket, convenience store, q uick service restaurants, restaurant, etc.). Try to get the specific name of the place when possible.
   4. Review the list and prompt for details regarding the time and location of the foods and beverages consumed.
   5. Review the recall one additional time to ensure accuracy.

The interviewer should remember:

1. Be objective. Do not give any opinions of the food choices, whether good or bad. Remind the patient that he or she will not be judged, and therefore should be honest in disclosing everything consumed.
2. Do not over-prompt, which can sway a response.
3. Probe to record all supplements, especially probing for protein bars or meal replacement drinks (some examples: Ensure, Boost, Glucerna).
4. Be sure to record enough detail. The below tips can help with this.

Tips

- Be very careful about recording objective portion sizes. For example, 1 small bowl of cereal will mean different things to different people. Be sure to record the kind of cereal (eg Cheerios) and the kind of milk (eg semi-skimmed). Volume (in ml, tablespoons, teaspoon etc), weight (in grams or ounces), or dimensions (in cm or inches) are appropriate units.
- Packaging can be very helpful but participants will rarely provide this information. If you do have packaging, you can record the amount in grams or ounces.
VOLUME: 1 teaspoon = 5 ml; 1 tablespoon = 15ml; 1 fl. oz = 2 Tablespoons
1 pint = 568ml; 1 litre = 2.1 pints

WEIGHT: 1 lb = 16 oz (not the same as fluid ounces!); 1 ounce = 28 grams

COMMON PORTION APPROXIMATIONS:
1 cup ≈ size of your fist; ½ cup ≈ half of your fist or one hand cupped
1 Tablespoon ≈ size of your thumb
1 Teaspoon ≈ size of your thumbnail
3 oz/84g (meat) ≈ size of the palm of your hand
1 oz (crisps) ≈ two cupped hands

- You cannot usually convert between volume and weight yourself. It is easy to make a mistake. For example, 1 cup of crisps does not weigh 8 oz (actually it weighs about 1 oz.)! In this case, you must look on the label to see the weight, or just record volume.
- Remember to record whether a food was measured before or after cooking. This especially applies to oatmeal, pasta, rice, meats, and fish. During the cooking process, grains will gain and meats will lose water weight & volume. (Example: 1 cup dry pasta = 2 cups cooked pasta).
- Record all fluids consumed, including water and ice.
- Condiments such as sugar, butter, cream cheese, mayo, salad dressings, and sour cream can add many calories, and must be kept track of carefully. Always ask if there was anything else eaten alongside.
- For multi-ingredient foods, it is best to record all components. Otherwise, you must specify the brand. Examples of multi-ingredient foods: sandwiches, pizza, soup, salads, etc.
- Here are some examples to help you:

<table>
<thead>
<tr>
<th>Incorrect</th>
<th>Correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 bowl cereal</td>
<td>1 fist Frosted Flakes</td>
</tr>
<tr>
<td>1 bagel</td>
<td>1 medium plain bagel (3” diameter)</td>
</tr>
<tr>
<td>1 container yogurt</td>
<td>1 container Yoplait blueberry lowfat yogurt (6oz)</td>
</tr>
<tr>
<td>1 cup oatmeal (also applies to rice, pasta, etc)</td>
<td>1 cup cooked oatmeal, OR ½ cup dry oatmeal with ½ cup water</td>
</tr>
<tr>
<td>1 glass milk</td>
<td>200ml skimmed milk</td>
</tr>
<tr>
<td>1 ham &amp; cheese sandwich</td>
<td>1 sandwich: -Lean ham, 3 oz; -Swiss cheese, 1 oz -Whole wheat bread: 2 slices; -Mayo: 2 Tb</td>
</tr>
<tr>
<td>Food Item</td>
<td>Description</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lettuce</td>
<td>2 leaves</td>
</tr>
<tr>
<td>Tomato</td>
<td>2 slices, 3” diameter</td>
</tr>
<tr>
<td>Cheeseburger</td>
<td>1 cheeseburger:</td>
</tr>
<tr>
<td></td>
<td>- 1 beef patty 3 oz</td>
</tr>
<tr>
<td></td>
<td>- 1 slice American cheese, 1 oz</td>
</tr>
<tr>
<td></td>
<td>- Mayo: 1Tb</td>
</tr>
<tr>
<td></td>
<td>- Ketchup: 1 tsp</td>
</tr>
<tr>
<td></td>
<td>- Mustard: 1 tsp</td>
</tr>
<tr>
<td></td>
<td>- Onions, pickles, lettuce, tomato</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong>, record size, toppings &amp; fast food brand</td>
</tr>
<tr>
<td>Pizza</td>
<td>1/8th of veggie pizza from 16” pizza</td>
</tr>
<tr>
<td>Chips</td>
<td>1 small bag of Walkers plain crisps</td>
</tr>
<tr>
<td>Potato (applies to all fruits &amp;</td>
<td>1 medium potato or 3” diameter</td>
</tr>
<tr>
<td>vegetables)</td>
<td></td>
</tr>
<tr>
<td>Cake</td>
<td>1 slice of chocolate, three-layer round cake (1/8th cake)</td>
</tr>
<tr>
<td>Cookie</td>
<td>1 chocolate chip cookie, 2 ¼ inch diameter</td>
</tr>
<tr>
<td>Chocolate bar</td>
<td>1 snickers bar</td>
</tr>
</tbody>
</table>

Before taking recall, ask if yesterday was a typical eating day for them. If it was out of the ordinary, wait and do another day.

Examples that could affect intake: Major medical procedures, sickness, hospitalization, stress, travel, social events, our testing, etc.
DISH Study Diet Recall Record Sheet

<table>
<thead>
<tr>
<th>Time</th>
<th>Food Item</th>
<th>Amount/Portion</th>
<th>Additional Info</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(location, cooking method, brand)</td>
</tr>
</tbody>
</table>

Remember to probe for beverages, snacks, condiments, side dishes, desserts, etc.

**EXTRA BEVERAGES** – such as water, ice, or soda consumed throughout the day, but not mentioned earlier. Don’t forget alcohol!

**SUPPLEMENTS** – any additional shakes or bars, such as Ensure, Boost or Glucerna?
### C.1.2 Chinese HD patients

**DISH 饮食回顾记录表**

研究编号：_______ 访谈日期：_______ 访谈次数（1-4）：_____

饮食回顾日期：_________ 透析日？ 是 / 不是

<table>
<thead>
<tr>
<th>时间</th>
<th>食物</th>
<th>量/分量</th>
<th>附加信息（地点，烹饪方法，食品商标）</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>注意提醒摄入的饮品，零食，调味品，配菜，甜品等</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>额外的饮品 – 之前未提及的一天中摄入的水，冰或苏打等，不要忘记酒精类饮品！</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>补充剂 – 任何额外的蛋白粉，能量棒等</td>
</tr>
</tbody>
</table>

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C.2 The QCKD study

C.2.1 UK HD patients

Section 1: About You

These questions ask a few details about you which will help us make sense of the research findings. Please tick the boxes to indicate your answers or write the information where indicated.

1. Are you Male □ Female □

2. What was your age in years at your last birthday? ______ Years

3. Do you smoke? Yes, I am a current smoker □
   No, I have never smoked □
   I used to smoke but I gave up ______ years ago □

4. When was your kidney problem first diagnosed? ______ years ago

5. Which of the following statements best describes you?
   I am a kidney patient but I don’t need any form of dialysis and I don’t have a transplant □
   I am on unit-based haemodialysis □ I am on home haemodialysis □
   I am on peritoneal dialysis with exchanges during the day □
   I am on overnight peritoneal dialysis □ I have a functioning kidney transplant □
   Other (please explain):
6. Are you diabetic?  Yes ☐  No ☐

7. Have you ever had a heart problem or a stroke?  Yes ☐  No ☐

8. Do you have any other medical conditions as well as kidney disease?  
   Yes ☐  No ☐
   If yes, please write here what other conditions you have:

9. Is there anything else which makes physical activity difficult for you?  
   Yes ☐  No ☐
   If yes, please briefly explain:

10. What is your ethnic group?  
    Choose ONE section from A to E, then tick the appropriate box to indicate your ethnic group:

    **A : White**
        ☐ British
        ☐ Irish
        ☐ Any other White background (please write in) ...

    **B : Mixed**
        ☐ White and Black Caribbean
        ☐ White and Black African
        ☐ White and Asian
        ☐ Any other mixed background (please write in)

    **D : Black or Black British**
        ☐ Caribbean
        ☐ African
        ☐ Any other Black background (please write in) ...

    **E : Chinese or other ethnic group**
        ☐ Chinese
        ☐ Any other (please write in)
        ☐ Not stated
        ☐ I prefer not to say
### Section Two: About your physical activity and exercise habits

#### 2A: DUKE ACTIVITY STATUS INDEX

Can you: (please circle yes or no)

<table>
<thead>
<tr>
<th></th>
<th>Activity Description</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Take care of yourself, that is, eat, dress, bathe or use the toilet?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Walk indoors, such as around your house?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Walk a block or two on level ground?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Climb a flight of stairs or walk up a hill?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Run a short distance?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Do light work around the house like dusting or washing dishes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Do moderate work around the house like vacuuming, sweeping floors or carrying groceries?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Do garden work like raking leaves, weeding or pushing a lawn mower?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Have sexual relations?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis or throwing a ball?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Participate in strenuous sports like swimming, singles tennis, football, basketball or skiing?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**2B : GP PHYSICAL ACTIVITY QUESTIONNAIRE**

1. Please tell us the type and amount of physical activity involved in your work:

   (if you do not work, please tick box a)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Please tick one box only</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>I am not in employment (e.g. retired, retired for health reasons, unemployed, fulltime carer etc)</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>I spend most of my time at work sitting (such as in an office)</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>I spend most of my time at work standing or walking. However, my work does not require much intense physical effort (e.g. shop assistant, hairdresser, security guard, childminder, etc.)</td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>My work involves definite physical effort including handling of heavy objects and use of tools (e.g. plumber, electrician, carpenter, cleaner, hospital nurse, gardener, postal delivery worker etc)</td>
<td></td>
</tr>
<tr>
<td>e</td>
<td>My work involves vigorous physical activity including handling of very heavy objects (e.g. scaffolder, construction worker, refuse collector, etc.)</td>
<td></td>
</tr>
</tbody>
</table>

Continued overleaf ....
2B : GP PHYSICAL ACTIVITY QUESTIONNAIRE *continued*

2. During the **last week** how many hours did you spend on each of the following activities?

*Please answer whether you are in employment or not*

<table>
<thead>
<tr>
<th>Please tick one box only on each row</th>
<th>None</th>
<th>Some but less than 1 hour</th>
<th>1 hour but less than 3 hours</th>
<th>3 hours or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Physical exercise such as swimming, jogging, aerobics, football, tennis, gym workout etc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Cycling, including cycling to work and during leisure time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Walking, including walking to work, shopping, for pleasure etc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Housework or Childcare</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Gardening or DIY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. How would you describe your usual walking pace? Please tick one box only.

- Slow pace (i.e. less than 3 mph)
- Steady average pace
- Fast pace (i.e. over 4 mph)
- Brisk pace
2C : LEISURE TIME EXERCISE QUESTIONNAIRE

1. If you currently exercise, how many times in the last 7 days have you done the following type of exercise?

   a) **Strenuous exercise**  (Heart beats rapidly, i.e. running, jogging, squash, basketball, vigourous swimming, long distance bicycling)

       Number of times____________________

   b) **Moderate exercise**  (Not exhausting, i.e. fast walking, tennis, easy bicycling, volleyball, badminton, easy swimming)

       Number of times____________________

   c) **Mild exercise**  (Minimal effort, i.e. fishing, golf, easy walking)

       Number of times____________________

2. In a 7 day period how often do you engage in any regular activity long enough to **work up a sweat** (heart beats rapidly)

   *Often □ Sometimes □ Never/Rarely □*

3. **What activities do you usually do when you exercise?**

   *Walking □ Cycling □ Running □
   Swimming □ Weightlifting □ Aerobics □
   Basketball □ Football □ Badminton □
   Table Tennis □ Tennis □ Hiking □

   *Others □*

   *(please state)*
Dialysis Patient-perceived Exercise Benefits and Barriers Scale

Name .................................................. Hospital Number ..................................................

Date this form filled in .............................. Code (for staff use only) .................................

This is a questionnaire about your beliefs and feelings about exercise for dialysis patients. Please indicate the degree to which you agree or disagree with Statements 2-24 by ticking the columns for Strongly Agree, Agree, Disagree or Strongly Disagree. Then answer the two questions at the end.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Exercise helps reduce my total medical costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Exercise helps reduce my body pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Exercise can postpone a decline in body function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Exercise prevents muscular atrophy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Frequent tiredness impedes my exercise participation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Exercise improves my mood</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Exercise improves bone diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Exercise is adverse to the health of dialysis patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. I worry about a fall during exercise</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Exercise improves my appetite</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Frequent lower-extremity muscle fatigue impedes my exercise participation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. I lack an understanding of the benefits of exercise</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Exercise helps me lead an optimistic and active life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Exercise is not suitable for me since I have other comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Body pain impedes my exercise participation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Exercise improves my quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Continued on next page
Dialysis Patient-perceived Exercise Benefits and Barriers Scale

Name .................................................. Hospital Number ..................................................

Date this form filled in .............................. Code (for staff use only) ..............................

This is a questionnaire about your beliefs and feelings about exercise for dialysis patients. Please indicate the degree to which you agree or disagree with Statements 2-24 by ticking the columns for Strongly Agree, Agree, Disagree or Strongly Disagree. Then answer the two questions at the end.

Continued from previous page

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>17. I lack an understanding of the knowledge of how to carry out exercise</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. I worry that exercise may make me feel thirsty</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. Exercise is not suitable for me since I have kidney disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Exercise can keep my body weight at a steady level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. I worry that exercise may affect my arteriovenous fistula</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Exercise helps enhance my self-care abilities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Exercise will keep me from having other diseases (e.g., cold)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. Outdoor exercise adds a burden to my family since I need their company while I am out</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What other benefits do you think exercise has?

What other factors do you think can impede your exercise participation?

Page 2 of 2

Thank you for taking the time to fill in this questionnaire

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C.2.2 Chinese HD patients

第一部分：个人信息

下面的问题涉及您的一些个人信息。您的回答会使研究更有意义。请在您选择项处的方框内打“√”或在提示处写下您的答案。

1. 您是  男性 □       女性 □

2. 您的年龄？______ 岁

3. 您抽烟吗？ 是的，我抽烟 □  不，我从不抽烟 □
   我已经戒烟 ______ 年 □

4. 您的肾脏疾病是什么时候诊断出来的？______ 年前

5. 下列哪个陈述最符合您的状况？

   我是肾脏疾病患者，但是我不需要任何形式的透析，我也没有肾脏移植  □
   我是在透室行血液透析的患者 □  我是在家里行血液透析的患者 □
   我是持续性不卧床腹膜透析患者 □
   我是持续循环式腹膜透析患者 □
   我是肾脏移植者 □
   其他（请解释）：__________________

6. 您有糖尿病吗？ 是 □     否 □

7. 您曾经有过心脏问题或中风吗 是 □     否 □

8. 除了肾脏疾病之外，您有其他健康问题吗？
9. 有什么其他问题会使您的体力活动产生困难吗？

是 ☐ 否 ☐

若有，请简单的解释：____________________________

10. 您的种族是？

:请从A到E中选择一项符合您的打“✓”

A：白人

☐ 英国人

☐ 爱尔兰人

☐ 其他白人(请填写)

B：混血

....

☐ 白人与加勒比黑人

☐ 白人与非洲裔黑人

☐ 白人与亚裔

☐ 其他混血(请填写)

D：黑人或英国黑人

☐ 加勒比

☐ 非洲人

☐ 其他黑人(请填写)

E：中国人或其他人种

☐ 中国人

☐ 其他(请填写)

☐ 我不想回答

............................................
第二部分：关于您的体力活动和锻炼习惯

2A : DUKE 活动状况指标

您是否可以执行这些活动，请圈出符合您的情况

| 1 | 照顾自我的日常活动，比如：吃饭，穿衣，洗澡和上厕所 | 是 | 否 |
| 2 | 在室内行走，例如在你的屋内走动？ | 是 | 否 |
| 3 | 到户外，在平地行走到下一个街口或巷口？ | 是 | 否 |
| 4 | 爬一层楼梯或走上一小段上坡路？ | 是 | 否 |
| 5 | 做短距离的跑步？ | 是 | 否 |
| 6 | 做一些轻度的家务，例如擦拭家具或洗碗？ | 是 | 否 |
| 7 | 做一些中度的家务，例如使用吸尘器，扫地或提一些杂货食品？ | 是 | 否 |
| 8 | 做一些重度的家务，例如洗刷地板或搬移较重的家具？ | 是 | 否 |
| 9 | 做庭院工作，像扫落叶，除杂草或操作电动割草机？ | 是 | 否 |
| 10 | 性交活动？ | 是 | 否 |
| 11 | 参与中度的休闲活动，例如打高尔夫球，保龄球，双人网球，跳交谊舞或投掷球？ | 是 | 否 |
| 12 | 参与费力的运动，例如：游泳，单人网球，足球，篮球或滑雪？ | 是 | 否 |
### 2B : GP 体力活动量表

请告诉我们您工作时涉及到的体力活动的种类和活动量
（若您不工作，请在1的空格内打 “√”）

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>我不工作</td>
<td>请选择</td>
</tr>
<tr>
<td></td>
<td>（例如：退休，因健康问题退休，失业，专职照料者）</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>我工作的大部分时间都是坐着</td>
<td></td>
</tr>
<tr>
<td></td>
<td>（例如：我的工作是在办公室）</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>我工作的大部分时间是站着或行走，但是我的工作不需要强烈的体力消耗</td>
<td></td>
</tr>
<tr>
<td></td>
<td>（例如：店员，理发师，保安，保育员等）</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>我的工作涉及到一定的体力消耗，包括处理一些重的物件和使用工具</td>
<td></td>
</tr>
<tr>
<td></td>
<td>（例如：水管工，电工，木工，清洁工，护士，园丁，邮件投递员）</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>我的工作涉及强烈的体力消耗，包括处理非常重的物件</td>
<td></td>
</tr>
<tr>
<td></td>
<td>（例如：脚手架工，建筑工人，垃圾收集工人）</td>
<td></td>
</tr>
</tbody>
</table>

未完待续....
### 2B：GP 体力活动量表

2. 在过去的一周内您花在下列活动上的时间有多少？

请先回答您是否工作

<table>
<thead>
<tr>
<th></th>
<th>请在每一行选择一个答案</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>没有</td>
</tr>
<tr>
<td>a  运动，比如游泳，慢跑，有氧运动，足球，网球，去健身房等</td>
<td></td>
</tr>
<tr>
<td>b  骑脚踏车，包括上班或空闲时间</td>
<td></td>
</tr>
<tr>
<td>c  行走，包括步行上班，购物或休闲等</td>
<td></td>
</tr>
<tr>
<td>d  家务活或照顾孩子</td>
<td></td>
</tr>
<tr>
<td>e  园艺或 DIY</td>
<td></td>
</tr>
</tbody>
</table>

2. 您怎么描述您一般的步伐节奏（步速）？请选择

- 慢速
- 稳定的步速
- 轻快的步速
- 快速
2C：休闲时间身体活动测量问卷

1. 想一想一周里，你闲暇时间从事下列运动的频率有几次？

2. a）费力的活动（心跳很快，例如：快跑、慢跑、壁球，篮球，比赛性的游泳，长距离脚踏车）

   次数__________________

   b) 中等费力活动（未筋疲力尽，例如：快走，网球，慢慢地骑脚踏车，排球，羽毛球，非比赛的游泳）

   次数__________________

   c）轻度活动（轻度费力，例如：钓鱼，高尔夫，散步等）

   次数__________________

3. 想一想一周里，您常不常从事规律运动到流汗的程度（心跳很快的程度）？

   经常□         偶尔□         不曾（很少）□

4. 当您锻炼时，您经常从事的运动有哪些？

   步行□          骑脚踏车□        跑步□
   游泳□          举重□            有氧运动□
   篮球□          足球□            羽毛球□
   乒乓球□       网球□            徒步□
   其他□

   （请列出）__________________
透析患者锻炼益处/障碍量表

填写指导：请您对以下每个条目的陈述内容表明自己的看法：非常同意、同意、不同意、非常不同意，请在相应的态度栏划“√”。

<table>
<thead>
<tr>
<th>序号</th>
<th>陈述内容</th>
<th>非常同意</th>
<th>同意</th>
<th>不同意</th>
<th>非常不同意</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>锻炼有利于减少我总的医疗费用开支。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>锻炼有助于减轻身体疼痛。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>锻炼能延缓躯体功能衰退。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>锻炼可以防止肌肉萎缩。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>我常感到疲倦妨碍我进行锻炼。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>锻炼能使我感到心情比较好。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>锻炼能改善肾病。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>锻炼不利于透析患者的身体健康。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>我担心锻炼时会跌倒。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>锻炼可以使我的胃口较好。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>我常感到下肢乏力妨碍了我进行锻炼。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>我缺乏对锻炼益处的了解。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>锻炼有助于我乐观、积极的生活。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>我有其他合并症不宜锻炼。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>身体疼痛妨碍了我进行锻炼。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>锻炼能提高我的生活质量。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>我缺乏透析患者如何进行运动锻炼的信息。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>我担心锻炼引起口渴。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>我患有肾脏病不宜锻炼。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>锻炼可以使我的体重控制较平稳。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>我担心锻炼会影响动静脉内瘘。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>锻炼能提高我的生活自理能力。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>锻炼可以减少我患其他病（如感冒）的次数。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>我外出需要家人陪伴，到户外锻炼为他们增添了负担。</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

您认为锻炼还能为您带来哪些方面的益处？

________________________________________________________________________

您认为还有哪些方面妨碍了您参加锻炼

________________________________________________________________________
C.3 The COCO study

C.3.1 UK HD patients and healthy controls

The Duke Activity Status Index (DASI) and GP Physical Activity Questionnaire (GPPAQ) have previously been shown in C.2.1 UK HD patients of section C.2 the QCKD study in Appendix C.

Health Questionnaire (English version for the UK)

Under each heading, please tick the ONE box that best describes your health TODAY

**MOBILITY**
- I have no problems in walking about
- I have slight problems in walking about
- I have moderate problems in walking about
- I have severe problems in walking about
- I am unable to walk about

**SELF-CARE**
- I have no problems washing or dressing myself
- I have slight problems washing or dressing myself
- I have moderate problems washing or dressing myself
- I have severe problems washing or dressing myself
- I am unable to wash or dress myself

**USUAL ACTIVITIES** *(e.g. work, study, housework, family or leisure activities)*
- I have no problems doing my usual activities
- I have slight problems doing my usual activities
- I have moderate problems doing my usual activities
- I have severe problems doing my usual activities
- I am unable to do my usual activities

**PAIN / DISCOMFORT**
- I have no pain or discomfort
- I have slight pain or discomfort
- I have moderate pain or discomfort
- I have severe pain or discomfort
I have extreme pain or discomfort

ANXIETY / DEPRESSION
- I am not anxious or depressed
- I am slightly anxious or depressed
- I am moderately anxious or depressed
- I am severely anxious or depressed
- I am extremely anxious or depressed
We would like to know how good or bad your health is TODAY.

This scale is numbered from 0 to 100. 100 means the best health you can imagine. 0 means the worst health you can imagine.

Mark an X on the scale to indicate how your health is TODAY.

Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = [ ]
### POS-S RENAL – PATIENT COMPLETION

Below is a list of symptoms, which you may or may not have experienced. Please put a tick in the box to show how you feel each of these symptoms has affected you and how you have been feeling over the past week.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not at all</th>
<th>Slightly but not bothered</th>
<th>Moderately</th>
<th>Severely</th>
<th>Overwhelmingly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Weakness or lack of energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Nausea (feeling like you are going to be sick)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting (being sick)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Constipation</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Mouth problems</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Itching</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Restless legs or difficulty keeping legs still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Feeling anxious</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Feeling depressed</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Changes in skin</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Any other symptoms</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Which symptom has affected you the most? __________________________________________

Which symptom has improved the most? __________________________________________

---

Palliative care Outcome Scale – Symptoms

www.pos-pal.org

www.csi.kcl.ac.uk
C.3.2 Chinese HD patients and healthy controls

The Duke Activity Status Index (DASI) and GP Physical Activity Questionnaire (GPPAQ) have previously been shown in C.2.2 Chinese HD patients of section C.2 the QCKD study in Appendix C.

健康问卷（中国大陆简体中文版）
在每个标题下，请在能最恰当地描述您今天的一个方格上打“√”

行动能力
我四处走动没有困难
我四处走动有一点困难
我四处走动有中度困难
我四处走动有严重的困难
我无法四处走动

自我照顾
我自己洗澡或穿衣没有困难
我自己洗澡或穿衣有一点困难
我自己洗澡或穿衣有中度困难
我自己洗澡或穿衣有严重困难
我无法自己洗澡或穿衣

日常生活（如工作、学习、家务、家庭或休闲活动）
我进行日常生活没有困难
我进行日常生活有一点困难
我进行日常生活有中度的困难
我进行日常生活有严重的困难
我无法进行日常生活

疼痛或不舒服
我没有疼痛或不舒服
我有一点疼痛或不舒服
我有中度的疼痛或不舒服
我有严重的疼痛或不舒服
我有非常严重的疼痛或不舒服
焦虑或沮丧
我没有焦虑或沮丧
我有一点焦虑或沮丧
我有中度的焦虑或沮丧
我有严重的焦虑或沮丧
我有非常严重的焦虑或沮丧
最后，我们想知道您今天的健康状况的好坏。

- 这个刻度尺上有从 0 到 100 的数字。
- 100 代表您想象中最好的健康状况。
- 0 代表您想象中最差的健康状况。
- 请在刻度尺上打一个“X”，指出您今天的健康状况如何。
- 现在，请在下面的空格里写下您在刻度尺上标出的那个数字。

您今天的健康状况 = [ ]
息照护结局量表—症状—肾脏

下列是一组您可能存在或者不曾经历的症状。在过去的一周内，这些症状在多大程度上影响到您？请在相应的方框内打勾。（每行仅选择一个）

<table>
<thead>
<tr>
<th>症状</th>
<th>完全没有（未受到影响）</th>
<th>轻微地（但是没有影响到想要止住它）</th>
<th>中度地（限制了某些活动或注意力集中）</th>
<th>严重地（活动或注意力明显受到影响）</th>
<th>完全地（无法思考其他事情）</th>
</tr>
</thead>
<tbody>
<tr>
<td>疼痛</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>气促（呼吸短促）</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>虚弱或乏力</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>恶心（有要生病的感觉）</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>呕吐（生病）</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>食欲不佳</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>便秘</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>口腔问题（牙龈肿胀，牙龈出血，舌苔发白，嘴巴发苦，口干等）</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>困倦</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>活动不便</td>
<td>完全没有（未受到影响）</td>
<td>轻微地（但是没有影响到想要止住它）</td>
<td>中度地（限制了某些活动或注意力集中）</td>
<td>严重地（活动或注意力明显受到影响）</td>
<td>完全地（无法思考其他事情）</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------</td>
<td>-----------------</td>
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<td>-----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>瘙痒</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>睡眠障碍（入睡困难，早醒，多梦）</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>不宁腿或腿部难以保持静止</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>感觉焦虑</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>感觉抑郁</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>皮肤改变（色素沉着，角化等）</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>腹泻</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>其他症状：</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

哪个（些）症状最为严重地影响到您？
哪个（些）症状改善最多？


BASALEEM, H.O., ALWAN, S.M., AHMED, A.A. and AL-SAKKAF, K.A., 2004. Assessment of the nutritional status of end-stage renal disease patients on maintenance...


BERGMAN, A., QURESHI, A.R., HAARHAUS, M., LINDHOLM, B., BARANY, P., HEIMBURGER, O., STENVINKEL, P. and ANDERSTAM, B., 2017. Total and bone-
specific alkaline phosphatase are associated with bone mineral density over time in end-stage renal disease patients starting dialysis. *Journal of nephrology*, 30(2), pp. 255-262.


associated with reduced dietary intake in hemodialysis patients. *J Ren Nutr*, **15**(2), pp. 244-252.


CROOK, S., GILBERTBÜSCHING, SCHULTZ, K., LEHBERT, N., JELUSIC, D.,
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