

**FUNCTIONAL FITNESS AND FALLS
IN OLDER ADULTS ON HAEMODIALYSIS**

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v. Abbreviations and Definitions

Abbreviations and Definitions

CKD **Chronic Kidney disease, previously Chronic Renal Failure**

Impaired kidney function, usually irreversible and progressive, with a variety of signs and symptoms depending on stage of disease.

AKI **Acute Kidney Injury**

Impaired renal function, occurring over days or weeks, often reversible if recognised early enough.

ESRD **End Stage Renal Disease**

(synonymous with End Stage Renal Failure - ESRF)

The ultimate outcome of progressive chronic kidney disease – the kidneys are not providing enough function to sustain life - the patient will die if renal replacement therapy is not initiated.

GFR **Glomerular Filtration Rate**

The volume of ultrafiltrate formed in the kidney tubules from the blood passing through the glomerular capillaries divided by time of filtration. A good measure of kidney function and categorises the stage of kidney disease. GFR is reported in millilitres per minute.

K/DOQI **Kidney Disease Outcomes Quality Initiative™**

An evolving set of evidence-based clinical practice guidelines for all stages of chronic kidney disease (CKD) and related complications. The National Kidney Foundation, a United States based non-profit research and support organisation for kidney patients and professionals, has been providing these guidelines since 1997.

NHS **National Health Service**

NKF **National Kidney Foundation**

A major voluntary nonprofit health organization, based in the United States, dedicated to preventing kidney and urinary tract diseases,

improving the health and well-being of individuals and families affected by kidney disease and increasing the availability of all organs for transplantation

NSF National Service Framework

These are NHS documents which set national standards and define service models for a service or care group, put in place programmes to support implementation, and establish performance measures against which progress within agreed timescales would be measured.

pmp per million population

RCT Randomised Controlled Trial

RRT Renal Replacement Therapy

Treatments used to sustain life when end stage renal disease has occurred, includes all forms of renal dialysis and renal transplant.

Other Definitions

The definitions proposed by Caspersen et al. in 1985 provide a useful framework for discussions of physical activity, exercise, and functional fitness (Caspersen et al., 1985).

Physical activity is defined as “any voluntary movement produced by the skeletal muscles that results in increased energy expenditure”. This is in contrast to **exercise** which is described as “a subcategory of physical activity, which is planned, structured, and repetitive, with the intent of improving or maintaining one or more facets of physical fitness or function”. **Fitness** is then defined as the ability to achieve certain performance criteria i.e. **functional** performance. Physical activity and exercise are therefore behaviours, which translate into performance i.e. fitness.

vi. Abstract

The number of older adults with end stage renal failure is rapidly increasing. Over the last 30 years, attitudes, technologies, resources and the premorbid health status of older adults have evolved and dialysis is now being offered routinely to this group. Dialysis is a life maintaining treatment but is demanding physically and psychologically and these burdens interplay with the normal consequences of aging. To ensure length of life is not preserved at the expense of quality requires focus on the interactions of end stage renal disease (ESRD), renal replacement therapy (RRT) and ageing-related problems, such as immobility and falls. However, despite these considerations being specifically referenced in national policy and recognised amongst dialysis groups internationally, there is limited literature regarding the specific and specialised needs of this patient group or guidance on focussed service development within the United Kingdom.

This work describes the extent and impact of the problems at a local level, explores the depth and impact of these concerns for patients and staff. An extensive literature review was performed. The changing demographics of the renal patient population are described and current services set in the context of local and national planning and policy. The topics of kidney physiology, renal disease, physical fitness, falls, bone metabolism and rehabilitation in non-uraemic and dialysed older adults were studied.

To respond to the patients' reports and falls events, a study was proposed to assess measures of postural stability before and after a single haemodialysis session in older adults on maintenance haemodialysis. A small-scale exploratory study and feasibility pilot was problematic and prompted review of the research plans. Preliminary data must be interpreted with caution, but suggested that older haemodialysis patients might be weaker and less posturally stable than comparable

non-dialysed older adults but that there was no significant effect of a haemodialysis session on the parameters measured. Reports of this initial study have been published in a peer-reviewed journal and presented locally and internationally.

To evaluate fitness limitations from the patients' perspective, a questionnaire study was administered to 66 older adult maintenance haemodialysis patients and 66 non-uraemic controls. The study revealed higher levels of inactivity, immobility, and dependency, less positive perception of life quality, lower mood, and fewer leisure and pleasure activities in the dialysis group. However, it did not reveal a significantly different falls incidence. This work is being prepared for publication.

A third original project examined staff perceptions of patient fitness and exercise encouragement practices within our local unit. This demonstrated that staff members know of the benefits of encouraging exercise, accept it as part of their role and responsibility and want to promote exercise. Many are already doing so. However, some staff members lack knowledge and confidence. It is encouraging that staff members feel that patients are able and keen to improve their physical fitness and that they would take part in structured programs with regular encouragement and feedback. This work is submitted for national poster presentation and is being prepared for publication.

The optimum design and implementation of exercise regimens for older haemodialysis patients is debated. The thesis concludes with a discussion of the findings and the implications both for service development and for future research. At the time of submission, a project scoping group is meeting to discuss the introduction of a lifestyle program involving exercise interventions, as recommended in this thesis, with the original data supporting a case of need. This group will seek funding for an exercise and lifestyle intervention project through the East Midlands Regional Innovation Fund.

vii. Research Aims

1. To consider possible pathophysiological mechanisms underlying physical fitness limitations in older adults on haemodialysis in order to open avenues for research and possible intervention strategies.
2. To define the nature of physical fitness limitations in older adults with ESRD on RRT in Nottingham, encompassing the clinical, functional and psychosocial issues raised. In particular to examine the impact of haemodialysis itself.
3. To identify appropriate strategies for intervention, and to plan targeted and pragmatic exercise and lifestyle interventions with consideration of the known local resource situation as well as staff and patient factors.

This thesis offers original data and discourse which advances knowledge in each of these areas.

This work is offered for the degree of Master of Philosophy.

viii. Thesis Structure

Chapter One is comprised of background information gathered from literature review.

After an introduction and description of the research methods used, the changing demographics of the renal patient population are described within the context of local and national policy and planning.

A brief outline of the physiology of the ageing kidney, renal disease and renal replacement therapy in older adults, and the impact of uraemia is given. The next section focuses on reduced physical fitness and limitations of function in older adults, and in those with renal disease. The literature on falls in older patients in health and with renal disease is reviewed. Bone mineral metabolism in health and in renal disease is described with particular reference to the possible fractures sustained by falls in renal patients. The potential role of haemodialysis as an independent risk factor for falls and fractures is acknowledged, along with possible intervention pathways. There is a small but rapidly increasing body of literature on rehabilitation strategies for CKD and dialysis patients and this is reviewed.

Chapter Two reports three original studies, in Sections 2.2, 2.3 and 2.4.

A short introduction in Section 2.1 describes the evolution of the research story.

The study described in **Section 2.2** was a small scale exploratory and pilot study designed to assess the feasibility of assessing postural stability and performance assessments before and after a single haemodialysis session and to collect preliminary data examining the immediate effect of a single haemodialysis session on functional mobility and balance. The data has been widely presented and published in a peer-reviewed journal.

Section 2.3 presents a study to define the extent of the problem of reduced physical fitness, postural instability and falls risk in older haemodialysis patients, as perceived by patients in Nottingham. A questionnaire study explored physical health and physical functionality including falls and falls risk. It was administered to all older adults on maintenance haemodialysis in Nottingham and to an age matched group of older adults outside the renal unit. This study recruited 66 dialysis patients and 66 controls. The findings are discussed, along with recognised flaws and limitations of the study.

A second questionnaire study, described in **Section 2.4**, explored the understanding, attitudes, opinions and behaviours of Nottingham Haemodialysis Unit staff members towards older adult patients and their physical fitness, benefits of exercise for this group, and current exercise encouragement practices.

Chapter Three draws together the literature and original research, summarises the current knowledge, and discusses implications for current practice and future service development. The data generated by this project has already contributed to local service development and a project-scoping group is currently meeting to discuss the lifestyle and exercise interventions proposed. The final section of this chapter explores possibilities for further study.

The thesis is closed with appendices containing documentation to support the studies presented in Section 2.3 and 2.4. A presentation list and publication list are offered. References are listed in the final section.

ix. Introduction

The demographics of both the general and the renal patient populations are changing rapidly and the median age of patients on renal replacement therapy (RRT) is rising year by year (Ansell et al., 2009)(see section 2.3). Health professionals involved in renal medicine are therefore seeing more patients in whom the problems of ageing are interacting with the pathologies and implications of chronic kidney disease (CKD), end stage renal failure (ESRD) and RRT.

The author has been involved in the care of renal patients since 2002 and observed that older adults on haemodialysis with mobility and stability problems formed a subgroup of older adults less likely to thrive on RRT. The author found older haemodialysis patients and their carers and nurses were worried about rapidly deteriorating physical functioning after commencing haemodialysis. Concerns were being raised about the physical fitness levels, activity levels and consequent quality of life in this group of patients.

Many patients reported suffering falls and sustaining subsequent injury. In 2003, over the course of six months, the author was involved in the care of seven older haemodialysis patients who had suffered falls and had been injured. This represented 11% of the haemodialysis population over 65 years old at this time. Six required hospital admission. Four sustained fractures; three with isolated hip fractures, one with hip and wrist fractures. Three patients died during the hospital admissions. The author was interested to observe that those sustaining fractures had fallen in the six hours after a haemodialysis session. Indeed, one patient sustained serious injury in the car park whilst on the way towards their taxi transport.

On informally questioning Haemodialysis Unit staff, the author was concerned to discover that six of the seven fallers were known to have fallen previously, some more than once. Unit staff or the general practitioners had referred none of these fallers for medical or physiotherapy review. None had been referred to the local falls prevention program. Referral for assessment or falls prevention intervention is accepted practice for older adults in the general population. Reduced physical fitness is a common problem in older adults and contributes to the development of instability and falls, which have devastating psychosocial and physical consequences. It is of concern that uraemic older adults may not be receiving the same level of care for their non-uraemic problems as the general population. There is a tendency for patients adopted into intensive programs (such as maintenance dialysis) to have their non-specialty needs subsumed. It is well recognised that maintenance haemodialysis patients tend to consult dialysis unit doctors for problems which may be more appropriately managed in primary care (Holley, 1998) and this may mean that they miss out on a generalist's valuable overview of their problems.

Hip fracture is one of the most feared outcomes of falls. Patients with ESRD are at around 4.4 times greater risk of hip fracture than the general population (Alem et al., 2000b) and that those who do suffer from hip fracture have an increased all cause mortality when compared to the general population (Mittalhenkle et al., 2004). The reason for this increased fracture risk has not been elucidated. Fractures may be a function of multiple factors such as reduced bone strength, or any predisposition to causative events such as falls.

It is believed that over 90% of the hip fractures sustained in the older adult general population are the result of falls, often of relatively low trauma, and it has been suggested that the same factors predict hip fracture in the general and dialysis populations (Stehman-Breen et al., 2000). Some dialysis patients may suffer from renal bone disease with increased bone fragility. However, this author suggests that

there may be additional risk factors specifically predisposing dialysis patients to falls. These factors might include myopathy, vascular disease and autonomic dysfunction, vitamin D insufficiency, lack of exercise, poly-pharmacy, and depression. Additionally, undergoing a session of haemodialysis treatment may also be an independent risk factor for falls. This might be due to the rapid fluid and electrolyte shifts during dialysis, orthostatic hypotension or as yet undefined factors.

Whilst dialysis may often extend length of life, this should not be at an unacceptable quality cost to the patient. Older adults on dialysis represent a rapidly expanding patient group who are now receiving the benefits of advances in renal medicine and resources. However, this project was borne out of concern that the impact of these interventions on overall health and well being has not been adequately explored and that services are not adequately addressing the holistic care of these patients.

CHAPTER ONE

1.1 Chapter Overview

This chapter comprises information from an extensive literature review and is intended to summarise what is known thus far about relevant topics and themes underpinning this research area, and identify the “gap” in current knowledge to which this work aims to contribute. This chapter describes renal patient demographics, the pathophysiology of renal disease and relevant clinical considerations in older adults with renal disease. It includes bone mineral metabolism and vitamin D as relevant to muscle strength and fracture risk.

This chapter offers a review of the current literature relevant to physical functioning and functional impairment and falls in older adults both in health and renal disease. The paucity of data regarding falls and reduced functional capacity in renal patients is highlighted. Subsequent sections explore exercise rehabilitation and falls prevention strategies in older adults, both in health and with renal disease on dialysis. This chapter identifies the need to define the burden of reduced physical fitness and falls risk in dialysis patients, particularly older adults. It highlights the need for research to explore whether dialysis may be an independent risk factor for postural instability and therefore falls. It also shows a need to examine whether reduced functional fitness is a real and relevant problem for local patients, and explore the barriers and limitations that may prevent these problems being addressed.

The aim of this chapter is to demonstrate the relevance and need for the subsequently presented body of original research by presenting relevant literature and an evolving research theme.

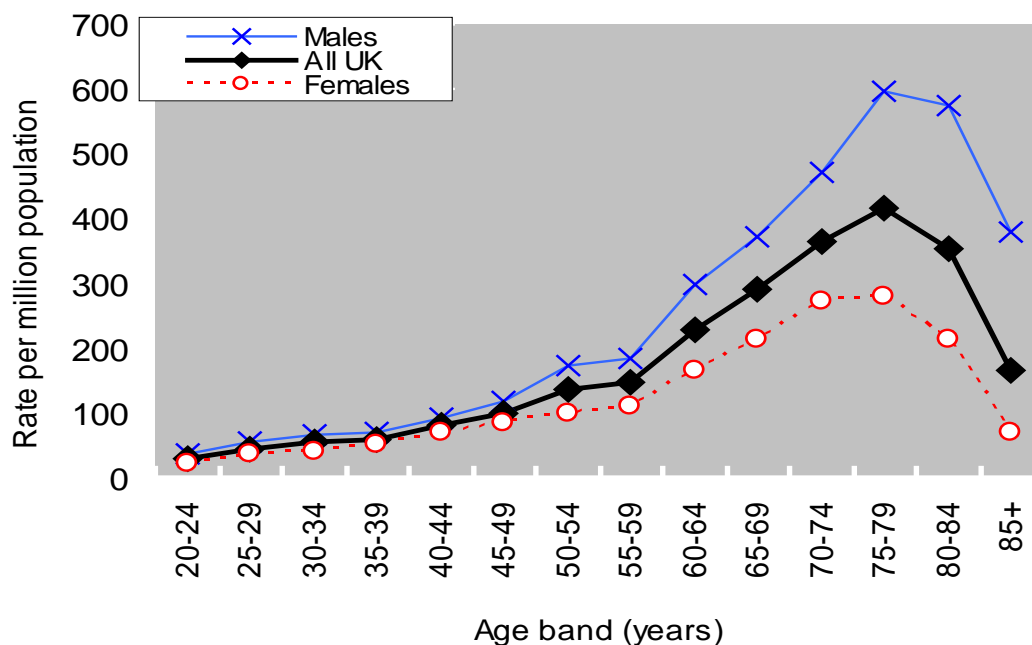
1.2 Literature Review Methods

This systematic literature review covered original research and reviews and was updated regularly throughout the research period. The Pubmed, Medline, Embase and Cinahl databases were searched, with the latter three searches combined. A further search was made using the Internet search engine "Google" to look for unpublished or discussion forum material. Searches were narrowed to human subjects, availability in English and between 1986 and 2009. Duplicates were eradicated. From both searches, review of abstracts was undertaken and relevant work was selected manually. Over 300 works have been referenced, with around four times this number considered.

1.3 The Changing Demographics of the Renal Patient Population: Statistics, Planning and Policy

The 2009 United Kingdom Renal Registry Report provides the most up to date data on the UK renal patient population (Farrington et al., 2009). There were 47,525 adult patients receiving RRT in the UK on 31/12/2008, equating to a UK prevalence of 774 pmp. This represents an annual increase in prevalence of approximately 4.4%. The median age of prevalent patients on all RRT was 57.3 years and on haemodialysis was 65.7 years. The dialysis acceptance rate for patients over 65 is approaching 300 pmp, compared to 72 pmp in those aged 18-64 years (see Figure 1.3.i below). 67% of patients over 65 years commencing RRT are on haemodialysis. These trends are being seen across the Western world. Worldwide, of the one million chronic dialysis patients, more than half are now over 65 years, as are approximately ten percent of patients waiting for cadaveric transplants (Registry, 2008).

Figure 1.3.i. Prevalence Rate by UK Country and Age band of Patients on RRT as of 31.12.2008 (Ansell D et al., 2006) (non copyright public access slideset)



This pattern is in sharp contrast to the patterns seen in the early years of dialysis therapy in the 1970s and 1980s when older patients were not routinely offered dialysis. This ageist practice was partly a resource issue but may have also been based on the presumption that older patients would not benefit from renal replacement therapy. It is now clear that age alone should be no contraindication to dialysis, and that good outcomes can be achieved in many older adults (Mandigers et al., 1996, Chandra et al., 1999, Ronsberg et al., 2005).

The National Health Service is committed to improving services for both older adults and for renal patients, and has recently published National Service Frameworks (NSFs) in both these of areas (2001, 2004a, 2005). NSFs are strategy documents published since 1998 by the UK Department of Health to address areas of major clinical need. They set measurable goals to be achieved

within set time frames. They are designed to set national standards and identify key interventions for defined groups and act as drivers towards delivering the NHS Modernisation Agenda. The NSFs are not guideline documents and there has been concern that without specific targets and ring-fenced funding the NSFs are somewhat soft. However, they do ensure that there is a nationally agreed direction for service development, and that areas of major clinical need must be addressed at all service levels. NSFs have been published for Older People (March 2001) and for Renal Services, Part One: Dialysis and Transplantation (January 2004) and Part Two: Chronic Kidney Disease, Acute Renal Failure and End of Life Care (February 2005).

Relevant to this work, The National Service Framework for Older People includes a standard on falls (Chapter 2, Standard 6), stipulating that action should be taken to prevent falls and reduce resultant fractures and other injuries in older people and that those who have fallen receive effective treatment and rehabilitation and advice on preventing further falls through a specialised falls service. The NSF has been backed up by clinical guidelines from The National Institute for Health and Clinical Excellence (NICE)(NICE, 2004). This evidence based guideline document covers older people who live in the community, either at home, in a retirement complex, or in a residential or nursing home and specifies that older people coming into contact with health professionals should be assessed as to their falls risk and evidence based interventions should be provided if appropriate. This is a guideline document and health professionals would be expected to justify deviating from these guidelines.

The Renal National Service Framework, Part Two, Chapter One, Section 21 specifically acknowledges the need for integration of the fields of renal services and older persons' care. Additionally, "Guidelines for the identification, management and referral of adults with chronic kidney disease" (Tomson et al.,

2005) have being developed to provide advice on managing CKD in primary care and on appropriate referral to specialist renal services, much of which is directly relevant to older people. The guidelines are authored by the Joint Specialty Committee on Renal Disease of the Royal College of Physicians of London and the Renal Association with the Royal College of General Practitioners, and have been developed in conjunction with the British Geriatric Society (as well as the Association of Clinical Biochemists, the Society for District General Hospital Nephrologists, the, the Professionals Advisory Council of Diabetes UK, and the National Kidney Federation).

There is clearly acknowledgement that national service development must address the needs of older patients with co-morbidities such as renal disease. There is, however, limited evidence to guide the direction of further investigation, data collection and resources. This work is therefore timely and relevant to UK national health policy.

In the United States, evolution of renal services has been guided by the National Kidney Foundation's Dialysis Outcomes Quality Initiative (NKF-DOQI or KDOQI) Clinical Practice Guidelines. First published in 1997, and updated again in 2000 and 2006, these guidelines are an attempt to offer evidence-based guidance to clinical teams, to standardise practice in over 3,100 US dialysis facilities. The guidelines also aimed to develop plans that could have a measurable positive impact on quality of life for dialysis patients. The KDOQI guidelines are well respected, have been widely adopted in the US and abroad and are the basis for many audit, research and service development programs.

Of relevance to this work is "Guideline 14: Smoking, Physical Activity, and Psychological Factors" presented in Section II. Guidelines on management of cardiovascular risk factors within the KDOQI Clinical Practice Guidelines for

Cardiovascular Disease in Dialysis Patients. Specifically this recommends that all dialysis patients should be counselled and regularly encouraged by nephrology and dialysis staff to increase their level of physical activity and that the "unique challenges" to exercise in dialysis patients need to be identified, with patients receiving appropriate referrals e.g. to physiotherapy. The guidelines recommend that regular evaluation of physical functioning and of the recommended physical activity program should be done at least every 6 months, and barriers to participation should be identified. The guidelines suggest that the goal for activity should be "cardiovascular exercise at a moderate intensity for 30 minutes most, if not all, days per week", with deconditioned patients building up to this very gradually. Of relevance, the guidelines highlight the importance of a culture that promotes exercise and reviews this regularly.

However, the KDOQI guidelines recognise that the evidence for these guidelines is "weak". In particular these guidelines recommend that randomised clinical trials are needed to study the effects of exercise training on cardiovascular risk in dialysis patients and to determine the optimal exercise prescription and practical ways of incorporating physical activity and assessment of physical functioning into the routine care of dialysis patients. The guidelines suggest that studies are needed to define the barriers to exercise in dialysis patients and incorporate physical activity into the routine care of dialysis patients.

This demonstrates that the focus of this work is timely and relevant to the international nephrology community and addresses areas of knowledge that are incompletely explored.

1.4 Ageing and the Kidney

1.4.1. Normal renal function in older adults

Functional nephron mass declines with age (Baracskay et al., 1997). This is accompanied by limitations of sodium conservation, electrolyte management, and acid-base homeostasis. Even so, despite losing up to 25% of the original kidney volume, older individuals maintain body fluid and electrolyte homeostasis under most circumstances. However, the renal “reserve” or ability to withstand environmental, disease-related, or iatrogenic stresses becomes progressively limited.

Early studies assessed the effects of aging on the kidney by using cross-sectional studies and institutionalized elderly subjects, with the attendant scientific drawbacks of limited population selection and multiple potential confounding factors. Later, an appreciation of this prompted some reappraisal of these established concepts. Newer longitudinal studies, in the latter part of the 20th century, utilized appropriate patient cohorts selected for lack of renal disease, including potential kidney transplant donors (Lindeman et al., 1985, Lindeman RD et al., 1984). These studies confirm the morphological and functional decline with aging, but suggest that it tends to be less marked than previously thought, and may be associated predominantly prolonged exposure to other renal insults, rather than ageing per se.

Renal excretory function is measured by glomerular filtration rate (GFR), a calculated estimate or measurement of the volume of water filtered out of the plasma through glomerular capillary walls into the urinary collecting system per unit of time, (ml/minute). In one study, the fall in GFR was absent or minimal in healthy subjects and most pronounced in those with coexisting cardiovascular disease (Lindeman RD et al., 1984). This suggests that the reduction in renal function in the elderly occurs predominantly secondary to hypertension, ischaemia

or impaired glucose tolerance and that specific age-related effects may be less important (Lindeman RD et al., 1984, Ribstein et al., 2001). However, the common denominator of these functional changes is still an attenuation of renal reserve and limitations on ability for renal homeostasis. Data from cross-sectional studies have suggested that GFR falls by about half between the ages of 30 to 80 years in both men and women (J Kampmann et al., 1974). The ability to conserve and excrete sodium and potassium, and to concentrate and dilute the urine, is also impaired in the elderly (Rowe JW et al., 1976, Murray and DC, 1993). These defects may have important clinical consequences, such as increased susceptibility to develop dehydration, water intoxication, sodium retention, hypokalaemia and hyperkalaemia. Although these alterations are not of major consequence under everyday conditions, they become significant when residual renal function is challenged by the superimposition of an insult such as an acute illness, environmental or medication change. All of these are, of course, very common in older adults.

In any exposition of renal pathophysiology in the elderly, it is worth noting that serum creatinine concentration is an insensitive indicator of renal function because, with the age-related loss of creatinine-producing muscle mass, creatinine can remain in the normal range whilst GFR declines. However, in practical terms, the calculated creatinine clearance offers an accepted approximation of the GFR without the need for invasive testing, often referred to as estimated (e)GFR.

1.4.2 Renal Disease in Older Adults

The incidence of CKD in patients over the age of 65 years is ten times greater than in young and middle-aged adults (UK Renal Registry, 2004). In this population, the causes of both acute and chronic kidney disease differs from those in younger patients, with renal vascular disease, diabetes mellitus (Type II),

obstructive uropathy, myeloma and systemic vasculitis all more common in older patients (UK Renal Registry et al., 2002). The table below shows the diagnoses submitted to the UK Renal Registry for older adults commencing renal replacement therapy. Data collected by the UK Renal Registry does not allow discrimination between or description of some of the diagnoses more commonly seen in older adults, particularly if patients have not undergone renal biopsy (these will be classified as “uncertain aetiology”). However, UK data do confirm a higher proportion of incident older adults commencing RRT have renal vascular disease as their primary renal diagnosis (Ansell et al., 2009). The comparative diagnoses of primary renal disease in patients under 65 years and patients over 65 years of age is shown below.

Table 1.4.2. Percentage Distribution of Primary Renal Disease by Age in UK Patients Commencing RRT 2007. Data from UK Renal Registry (Ansell et al., 2009)

Note; not all incident starts have an attached diagnosis submitted to the Registry therefore there is a proportion of patients with ESRD due to uncertain aetiology and also a proportion of Data not available.

Diagnosis	Aged < 65 years	Age ≥ 65 years
Uncertain aetiology	18.5	27
Glomerulonephritis	12.7	6.3
Pyelonephritis	6.8	6.0
Diabetes	21.2	18.3
Renal vascular disease	2.3	11.4
Hypertension	5.5	4.9
Polycystic kidney	10.0	2.5
Other	14.4	12.7
Data not available	8.7	10.8

It is important to appreciate the more common conditions bringing older patients to RRT as this allows an understanding of the likely co morbidities and associated disabilities in this group.

1.4.3 Chronic Kidney Disease in Older Adults

Chronic kidney disease (CKD), (previously described as chronic renal failure) is characterized by progressive loss of functioning renal mass over a period of months to years. It is a clinical entity, independent of the precipitating primary renal disease.

In each healthy kidney, there are approximately 1 million nephrons, each contributing to the total GFR. In chronic kidney disease there is irreversible sclerosis and progressive loss of functioning nephrons (the functional "filtration units" within the kidney). Glomerular filtration rate (GFR) declines with nephron loss. The rate varies depending on the underlying aetiology. The kidney attempts to maintain GFR by hyperfiltration and compensatory hypertrophy of the remaining healthy nephrons so that measured substances, such as urea and creatinine, only start to show significant increases in plasma levels once the GFR has decreased to less than 50% of normal (i.e. when the renal reserve has been exhausted). With a 50% reduction in GFR, the plasma creatinine value might be expected to approximately double from the previous "healthy" level, but may still be within laboratory reference ranges. Hyperfiltration and hypertrophy by the remaining nephrons, although initially functionally beneficial, ultimately contributes to progressive renal dysfunction. In other words, once kidney damage is established, it almost inevitably deteriorates. Other factors may cause progressive renal injury including hypertension, acute insults from nephrotoxins or altered mineral metabolism.

Signs and symptoms of uraemia can develop once GFR falls below 30ml/min, and increment as GFR declines. End-stage renal disease (or end stage renal failure) is irreversible kidney impairment that cannot be controlled by medical management alone and requires RRT to maintain life. This is usually seen in patients whose GFR has declined to levels of less than 10 mls /min. Survival is rarely for longer than

days or weeks. If appropriate, renal replacement therapy is instigated as patients reach end stage and become symptomatic.

In 2002, the American Kidney Disease Outcomes Quality Initiative (KDOQI) proposed a new classification system for CKD . This initiative provides evidence-based clinical practice guidelines for all stages of chronic kidney disease and related complications, from diagnosis to monitoring and management. KDOQI expands the Dialysis Outcomes Quality Initiative or DOQI, a project begun by the National Kidney Foundation in 1997 and recognised throughout the world for improving the care of dialysis patients. The classification has been well received and is widely used (see Table 1.4.3 below).

Table 1.4.3.i KDOQI Chronic Kidney Disease Classification

(<http://www.kidney.org/professionals/kdoqi/guidelines>)

CKD Stage	GFR (ml/min)	Clinical Implications
1	>90	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease Observation, control of blood pressure.
2	60-89	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease Observation, control of blood pressure and risk factors.
3	30-59	Moderately reduced kidney function Observation, control of blood pressure and risk factors
4	15-29	Severely reduced kidney function Planning for end stage renal failure.
5	<15	Very severe, or end stage kidney failure, ultimately requiring dialysis or leading to death.

The signs and symptoms of chronic kidney disease depend to some extent on the degree of impairment but also vary between individuals with the same degree of measured biochemical derangement. The reasons for this variation are incompletely understood. The most commonly experienced effects are summarised below in Table 1.4.3.ii.

Table 1.4.3.ii. Features of Chronic Kidney Disease

GFR (mls/min) CKD Stage	Feature	Cause	Consequence
< 60 Stage 3	Normochromic normocytic anaemia	Decreased renal synthesis of erythropoietin decreased RBC survival, tendency of bleeding from uraemia-induced platelet dysfunction.	"Renal" anaemia. Fatigue.
< 60 Stage 3	Secondary hyper-parathyroidism	Hyperphosphatemia decreased renal synthesis of 1,25-dihydroxycholecalciferol and hypocalcaemia.	Renal osteodystrophy, bone pain, fatigue.
30-60 Stage 3	Phosphate Retention	Inability of the kidneys to excrete the excess dietary intake.	Hyperphosphatemia suppresses the renal hydroxylation of inactive 25-hydroxyvitamin D to calcitriol.
30-60 Stage 3	Vitamin D deficiency	Reduced functioning nephron mass for activation of vitamin D.	Hypocalcaemia, hyperphosphatemia
20-25 Stage 4	Hyperkalaemia	Decreased ability of the kidneys to excrete potassium.	Cardiac arrhythmia (may be fatal).
< 15 Stage 5	Metabolic acidosis	Kidneys are unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium.	Cardiac dysfunction, Muscle dysfunction, seizure.
< 15 Stage 5	Extra cellular volume expansion and fluid overload	Failure of sodium and free water excretion.	Peripheral and pulmonary oedema and hypertension.
< 10 Stage 5	Uraemia	Inability of kidney to excrete poorly defined "middle molecules".	Coma, seizure, death.

1.4.4. Dialysis in Older Adults

Before 1980, few patients over the age of 65 years started chronic dialysis in the UK. The shortage of hospital haemodialysis facilities in the UK in the 1970s, the intensity and exhausting nature of dialysis with the earliest equipment and techniques, and the perception of a hopeless prognosis were the principal reasons why most middle-aged and elderly patients with ESRD were denied treatment. As outlined in Section 1.3, since then the number of elderly patients starting renal

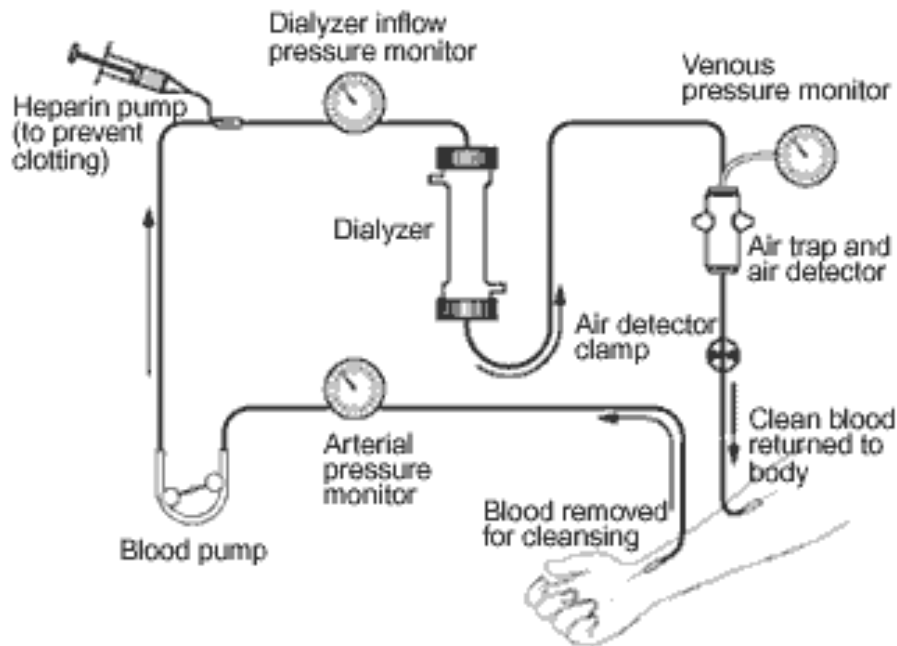
replacement has increased year on year (Ansell et al., 2009) and currently accounts for between a third and a half of all new dialysis patients (UK Renal Registry et al., 2008).

The widespread introduction of continuous ambulatory peritoneal dialysis was largely responsible for the change in this policy in the 1980s. Peritoneal dialysis was shown to be an acceptable and effective treatment for many elderly patients. This modality was perceived as a less invasive or “gentler” option and could be learned quickly, allowing older adults to remain independent at home (Nicholls et al., 1984). Use of peritoneal dialysis precipitated a positive shift in attitude, although in fact it is now recognised that peritoneal dialysis can have significant complications in the elderly and it is being used much more selectively. It has been suggested that older patients are more likely to develop severe Gram-negative peritonitis, perhaps due to associated diverticular disease, although this is disputed in some studies (De Vecchi et al., 1998, Suh et al., 1993). Increased intra-abdominal pressure from the constant presence of intra-peritoneal fluid can precipitate abdominal herniae and this is more likely to occur in the elderly due to weaker abdominal wall musculature. In the long-term, waste product removal may be inadequate with peritoneal dialysis, leading to muscle wasting and malnutrition. Malnutrition, which often develops insidiously, is a significant problem in the elderly dialysis patient and is difficult to recognize and reverse.

For these and other reasons, the majority of chronic dialysis patients over 65 years old now opt for hospital haemodialysis (Ansell et al., 2009).

To understand the impacts the physiological impacts of haemodialysis requires an appreciation of the theory and mechanism underlying this treatment. Haemodialysis involves diffusion of solutes across a semi-permeable membrane and uses counter current flow. A specially prepared fluid called dialysate is flowing in the opposite direction to blood flow in an extra-corporeal circuit.

Figure 1.4.4. The Extra Corporeal Haemodialysis Circuit



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Blood is removed and returned to the body via a point of vascular access, either an indwelling central venous catheter (often called a "vascath" or "permcath"), or an arterio-venous fistula or shunt created from the patient own vasculature. The counter-current flow of blood and dialysate maintains the concentration gradient across the membrane, allowing the dialysis to be so efficient that, in contrast to peritoneal dialysis, haemodialysis can be performed intermittently (usually for four and a half hours, three times a week). Fluid removal (ultrafiltration) is achieved by altering the hydrostatic pressure, causing free water to move across the membrane down a pressure gradient. The dialysis solution consists of a sterilized solution of mineral ions. Urea, potassium and phosphate and other "uraemic toxins" diffuse down a concentration gradient into the dialysis solution, but concentrations of most mineral ions are similar to those of normal plasma to achieve homeostasis.

Hospital haemodialysis has the potential for many serious problems. In the UK, in 2006, 12% of adults over 65 years commencing renal replacement therapy died within 90 days (Ansell et al., 2009). The most common cause of death in older adults on RRT is cardiac disease (28%), with infection causing 19% of deaths.

Morbidity levels are also high. For, example, vascular access is more difficult to maintain in older patients because of generalized atherosclerosis, and attempts to create fistulae, the most reliable form of access, may be unsuccessful. Permanent central venous catheters are increasingly used for dialysis access but should be avoided where possible, as they are prone to infection and thrombosis, and often provide sub-optimal blood flow for efficient dialysis.

To offer older patients the best renal replacement therapy option, nephrologists need to understand the medical problems that can become more significant in later life, such as immobility, instability, incontinence, intellectual impairment, iatrogenic disease and immunosenescence. Not all older patients face these difficulties, but for those that do these issues can have implications for renal replacement treatment choices, treatment tolerance and quality of life.

Each patient must be individually and comprehensively assessed, including consideration of functional psychological and social issues, to ensure their renal replacement modality is suitable. The table below highlights some of the advantages and disadvantages of each modality for older patients (see Table 1.4.4.i).

Table 1.4.4.i. Advantages and disadvantages of Haemodialysis and Peritoneal Dialysis modalities for older patients.

	Haemodialysis	Peritoneal Dialysis
Advantages	<p>Does not rely on patient input so better for frail or confused patients.</p> <p>Does not place a burden on family or carer.</p> <p>Dialysis unit provide a social structure.</p> <p>Dialysis unit provides regular opportunity for nursing and medical review.</p>	<p>Can be carried out at home.</p> <p>Access usually easier to achieve and maintain.</p> <p>Access infections usually less severe.</p> <p>Anaemia usually less severe.</p> <p>Safer for patients with cardiovascular disease.</p> <p>Visit hospital only for clinics/reviews.</p>
Disadvantages	<p>May precipitate angina, myocardial ischaemia or stroke.</p> <p>Access may be more difficult. Complications of line sepsis may be particularly severe due to immunosenescence.</p> <p>Intradialytic problems (e.g. arrhythmias, hypotension, leg cramps) less well tolerated in older patients.</p> <p>Anaemia may be more severe.</p> <p>Repeated hospital visits disruptive and unsettling.</p> <p>Hospital transport difficult to arrange. Lengthy waits can mean missed meals, deranged diabetes, leaving a dependant partner at home etc.</p>	<p>Difficult for patients with impaired functional mobility, muscle weakness, reduced manual dexterity or confusion etc.</p> <p>Can place a huge burden on family or carer.</p>

Psychological and social aspects

Consideration of psychological and social aspects is of utmost importance when selecting a dialysis modality. Dialysis is an intensive intervention with inevitable discomforts and high risk for potential problems. Whilst life is maintained it is essential that the patient views the quality of life achieved positively. This is a priority in the author's clinical practice and is emphasised repeatedly in this thesis.

Preserving social structures is particularly important in patients who may already be at risk of becoming socially isolated. Some older patients may find the environment of the dialysis unit socially rewarding. Others are may be disinclined to thrive in this enforced semi-institutionalisation. Regular hospital attendance for haemodialysis may mean giving up daytime activities such as work, volunteer activities or day centres. Peritoneal dialysis does offer flexibility and freedom from frequent visits to the hospital, but means patients have more responsibility for their treatment and do not receive such regular positive re-enforcement of their treatment benefits from dialysis unit staff. If a patient is being assisted in having dialysis at home then their carer, who is often a family member, can find both the practical and emotional issues to be a heavy burden. There is a risk is that an arrangement like this can "medicalise" the patient's central relationships and result in loss of normality of family structure.

An experienced multidisciplinary team should monitor the patient and their family and be prepared to suggest changes if appropriate. Depression is common both in older adulthood and in patients with end stage renal failure(Livesley, 1982) and may be overlooked in the complicated balance of managing dialysis therapy. Regular review with this in mind will help to identify patients who are not coping well.

Ethical Issues

Complex ethical problems will increasingly arise. For example, difficult situations are encountered when making renal replacement therapy decisions with patients who have advanced or unstable co-morbidities, such as critical heart disease or cancer. Challenges also occur if older patients have questionable capacity, for example patients who have memory dysfunction and cannot understand the demands and implications of treatment.

Several countries have now published guidelines and recommendations that deal with withholding and withdrawing life supporting treatments. The UK National Service Framework and the American Society of Nephrology give guidance that addresses these issues specifically in end-stage renal failure (2005, 2000). These emphasise the importance of transparency and good planning with full involvement of the nephrologist, multidisciplinary team, primary care, patient and their family.

1.4.5. Renal Transplantation in Older Adults – Older Recipients, Older Donors

Renal transplantation offers clear advantages over dialysis for many patients with ESRD. However, in older patients the benefits must be weighed against the risks, which include increased likelihood of surgical complications, and problems with immunosuppression, including long-term steroid use, e.g. mitotic disease, infection, diabetes and cataracts. The proportion of patients aged over 60 years in Europe receiving renal transplants therefore remains small (FC et al., 1996). Older patients are more likely to be unsuitable for renal transplantation because of an increased prevalence of co-morbidity such as cardiovascular disease or malignancy. Whilst there is no absolute age related cut off, most UK units suggest

age over 65 years is a relative contraindication. The British Transplantation Society currently suggests that one of the absolute contraindications for listing for renal transplantation is any condition with a life expectancy < 5 years, and this may include overall co morbidity effect in older adults. For this reason it is important to concentrate resources on optimising RRT for older patients.

Interestingly, those older patients who are fit for transplantation have graft survival rates comparable with younger recipients (Oniscu et al., 2004). In fact, it is now recognized that the immunosenescence of older patients may be a favourable phenomenon, translating into less frequent and less severe rejection than in younger patients. The dose of immunosuppressants required to prevent rejection may be less than in younger patients, which may to some extent balance the increased susceptibility of older recipients to adverse effects from immunosuppression (FC et al., 1996, Kappes et al., 2001, Palomar et al., 2001).

Increasing recipient age does not appear to influence graft outcome but is a strong predictor of subsequent patient survival. This is not surprising, as cardiovascular disease rather than infection now accounts for the majority of deaths in renal-transplant recipients in the UK. The average life of a transplanted cadaver kidney is now 7–10 years and so patients whose life expectancy is much less than this may be considered unsuitable for renal transplantation, taking into account the serious shortage of donor kidneys. In Europe, 5-year patient survival in patients transplanted between 1985 and 1992 was 67% for those aged over 60, compared with 91% for those adults aged less than 40 years (FC et al., 1996). The survival of older patients is better in renal transplant recipients than in those remaining on long-term dialysis, but it is likely that this apparent benefit is mainly due to differences in co-morbidity between these patient populations. However, it is notable that older transplant recipients seem to have a significantly better

quality of life when compared to older dialysis patients or younger adults using any form of renal replacement therapy (Rebollo et al., 2001).

Most kidneys transplanted in the UK are from cadaveric donors, with <10% of the total being accounted for by live-related or unrelated donors. This shortfall in the availability of organs has led to the use of kidneys from older donors for transplantation. The decline in renal function in the ageing kidney has particular significance in this situation. In about a third of cadaveric transplants in the UK, acute tubular necrosis occurs around the time of organ retrieval and re-implantation and kidneys from older donors are less likely to recover fully from this. The older donor kidney may also be more vulnerable to damage from acute rejection. It has been suggested that it may be more appropriate for it to be allocated to an older recipient who may be less likely than a younger recipient to develop acute rejection. For this reason, age-matching in addition to tissue-type matching between recipients and donors has been advocated (Kasiske and Snyder, 2002, Donnelly et al., 1990). Both acute and chronic nephrotoxicity from nephrotoxic agents such as cyclosporin and tacrolimus are more likely in the older donor kidney.

1.4.6 Impact of Renal Disease on the problems of ageing

In our society, ageing is perceived as a negative process, bringing unwanted changes (see Table **1.4.6.a**). In physiological terms, ageing is a complex interaction of biological processes occurring normally within an adult over time. These changes usually render the adult less functionally robust and inevitably nearer to the point of death.

Table 1.4.6.i Perceived Negative Changes of Ageing

Reduced body function
Ill health
Cognitive decline
Uncertain social status due to retirement and disabilities
Fall in income, poverty, Lower living standards
Bereavement and loneliness
Social Isolation
Unhappiness, grief, depression
Increased risk of accident
Greater vulnerability to abuse and security violations (robberies, attacks)
Dependency

The ageing process brings many implications for medical care of patients. These are summarised in Table 1.4.6.ii, below.

Table 1.4.6.ii Medical Aspects of Ageing

Multiple diseases, with possible cascade effect.
Multiple causes of the same symptom. Such symptoms include intellectual impairment, incontinence, instability (and falls), and immobility . These have been called the Geriatric Giants(1992).
Late presentation because of low health expectations by the patient, or fear of treatment or hospitalisation. This leads to possible poorer outcomes.
"Social problems" (e.g. inability to self care in own home) may obscure an underlying disease or complicate its management.
Multiple drug use may complicate management or cause pathology.
Cognitive impairment may complicate history taking and management.

Intellectual impairment

Cognitive decline in older age is common but by no means inevitable. Studies suggest a general population incidence of age-associated memory impairment of around 30-40% in adults over 60 old (Hanninen et al., 1996). The cause is thought to be multifactorial (see Table 1.4.6.iii), but a large proportion of the decline probably represents small vessel cerebrovascular disease, particularly in renal patients (Lass et al., 1999). Risk factors for this are, in general, the same risk factors as for other vascular pathology, including renal vascular disease (Peters, 2006).

Table 1.4.6.iii Causes of Intellectual Impairment in Older Adults

Lack of mental activity
Smoking
Illicit drugs
Alcohol
Lack of physical exercise
Malnutrition
High blood pressure
Diabetes
Uraemia
High cholesterol and atherosclerosis
Depression
Chronic renal impairment
Multiple medications
Impairment in vision and hearing
Head trauma
Sleep disorders
Lack of involvement in social activities

Chronic kidney disease is associated with intellectual impairment, and the cognitive impairment is greater in more advanced chronic kidney disease (Kurella et al., 2004). In patients reaching ESRD, post mortem examinations confirm histological abnormalities of brain tissue (Pereira et al., 2005). There is limited data on cognitive function in older dialysis patients. The limited data available suggest the incidence of cognitive impairment is again around 30–40%, although this does not quantify the degree of dysfunction (Tyrrell et al., 2005). It is suggested that the cognitive impairment of advanced renal disease is improved once dialysis is instigated and mechanism of this is postulated to be multifactorial, probably because of improvements in anaemia and reduction of chronic uraemia (Pickett et al., 1999). The intellectual impairment of ageing or of progressive chronic renal disease has implications for the education and understanding of this patient group, who may struggle to process and retain important advice regarding medications, diet, fluid restriction etc. There are also serious implications for patients' capacity when making decisions regarding treatment options.

Incontinence

There is minimal direct link between incontinence and renal disease. Pathological incontinence is more often associated with urological or neurological disease. Some forms of urological disease can cause both incontinence and renal failure e.g. prostate cancer or prostatic hypertrophy.

In some forms of renal disease there may be loss of the urine concentrating ability. This can lead to polyuria, which may aggravate pre-existing incontinence. However, in many cases, urine volume diminishes in advanced and end stage renal failure. In renal disease, diuretics are often used to balance fluid intake with output and avoid fluid overload. Diuretics do not cause incontinence but may again aggravate pre-existing continence problems.

Instability and Immobility are discussed in Section 1.5

1.5 Reduced Physical Function with Aging and in Uraemic Older Adults

1.5.1 Changes of Ageing; Immobility, Instability

Whilst it is well recognised that older adults often suffer from reduced mobility and instability, the underlying physiology and pathophysiology is not fully elucidated. Some factors are clear but much of the physiology of cellular senescence is poorly understood.

Well-recognised physiological and pathophysiological changes are summarised below.

Table 1.5.1.i

Factors Contributing to Immobility and Instability in Older Adults in the General Population

Sarcopenic myopathy - Reduction in number and CSA of muscle fibres
Reduction in metabolic efficiency – cellular senescence – reducing muscle strength potential
Reduction in water content of tendons and of cartilage reducing joint strength and stability
Impairment of sensory cue – visual impairment, auditory impairment, peripheral neuropathy
Atherosclerotic and other vascular disease contributing to impaired blood pressure homeostasis and baroreflex insensitivity
Cognitive impairment – impairing safe interpretation of environmental and other risk
Negative cycle of inactivity - deconditioning
Acute intercurrent illnesses – more common in older adults – with illness and recovery implications
Disease of ageing e.g. Parkinson's
Malnutrition
Polypharmacy
Psychological factor – self isolation and lack of motivation may be triggered by low mood

1.5.2 Reduced Physical function in Uraemic Older Adults

Fitness declines rapidly over time in established dialysis patients. Significant evidence of adverse changes in body composition, physical activity, function, and performance can be observed in haemodialysis patients over just one year (Johansen et al., 2003b). Promoting strategies to preserve physical capabilities should therefore begin in the pre-dialysis phase (Klang et al., 1998, Clyne, 2004).

Uraemic patients and chronic dialysis patients have lower physical work capacities than average when compared with healthy control subjects (Barnea et al., 1980, Beasley et al., 1986, Bonzel et al., 1991). Patients on haemodialysis are less active than healthy sedentary controls, and this difference is more pronounced among older individuals (Johansen et al., 2000). In one study, only 17/54 (31%) patients achieved physical performance assessments within a normal range when compared to healthy controls (Bullock et al., 1984). Low levels of physical activity are related to high levels of fatigue (Brunier and Graydon, 1993). This is recognized by both health professionals (Heiwe et al., 2003) and patients (Cade, 1995) as contributing to a poorer quality of life. Impairment in exercise capacity does not appear to be explained by the type or quality of renal replacement therapy (Bullock et al., 1984).

Muscle Metabolism in Uraemia

There are rationales for both central cardio respiratory and peripheral skeletal muscular phenomenon to explain impaired exercise tolerance in uraemic patients (Diesel et al., 1990). The concept of "uraemic myopathy" remains controversial. However, significant changes are found in biopsy samples of uraemic patient muscle (Diesel et al., 1993). Biopsy studies show marked muscular atrophy in all types of fibres with type II fast twitch fibres worse affected (Kouidi et al., 1998). Ultrastructural study shows severe degenerative changes in the skeletal muscle

fibres, mitochondria, and capillaries and electron microscopy reveals a large variety of additional nonspecific abnormalities, including mitochondrial changes. This confirms "uraemic myopathy" as a histopathological entity but does not confirm causation. Perhaps unsurprisingly, the changes seen in dialysis patients are more pronounced than those seen in CKD patients (McIntyre et al., 2006).

A prevalent hypothesis is that much of the reduced performance and the structural injury in uraemic muscle can be attributed to reduced muscle blood flow (Bradley et al., 1990). A supportive study showed that, in the calf muscle of haemodialysis patients, energy production via oxidative metabolism is impaired and compensated for by an increase in anaerobic glycolysis (Durozard et al., 1993). The pathogenesis is probably multifactorial and occurs at many levels of vasculature, affected by hypertension, mineral derangements and other vasculopathic processes.

There may also be local vasoadaptive impairments. Beta-adrenoceptors modulate local vasodilatation in skeletal muscles during exercise. Activation of these receptors results in increased heart rate and force of contraction of cardiac muscle, vasodilatation in skeletal muscle, and bronchodilatation. In one study, in patients on maintenance haemodialysis, the number of lymphocyte beta 2-adrenoceptors was not different from that in healthy controls but lymphocyte cyclic AMP responses were significantly reduced (Daul et al., 1985). Exercise caused a fourfold increase in plasma catecholamines in healthy volunteers and at the same time lymphocyte beta 2-adrenoceptor number increased by about 55 per cent. In haemodialysis patients, exercise induced only a twofold increase in plasma catecholamines and did not increase beta 2-adrenoceptor number i.e. in chronic uraemia, regulation and responsiveness of beta-adrenoceptors is impaired, reducing blood supply to muscles.

Functional Limitations

Studies suggest that haemodialysis patients are significantly lower functioning than healthy patients as judged by physical impairment measures (DePaul et al., 2002). Functional capacity is an important concern in this patient group as data indicate that impaired physical functioning, whether assessed by objective laboratory measures or self reported, are independently predictive of mortality (DeOreo, 1997, Sietsema et al., 2004). It is not known whether increasing physical activity and improving exercise capacity would result in improved outcomes.

However, the number of studies focusing on functional fitness in haemodialysis patients is small and there are even fewer examining this from the patients' perspective. At the time of submission, there was no such literature focusing on older adults on maintenance haemodialysis. The patients' view is important because haemodialysis is an aggressive and very expensive therapy that maintains life, but may not improve quality of life, and may reduce it considerably. Research findings may be significant, but not clinically relevant i.e. may not impact on quality of life or outcomes experienced by the patients. If more is known about the specific difficulties patients' are experiencing then patient therapy satisfaction can be improved.

The need for consideration of functional fitness in all dialysis patients was highlighted in 1999 by Painter *et al* (Painter et al., 1999, Johansen, 1999). In 2003, Heiwe *et al* studied patients experiences of their physical fitness (Heiwe et al., 2003) and in the same year Johansen *et al* identified subtle objective changes in activity function and performance in a longitudinal study (Johansen et al., 2003b). These studies did not focus on older adults. In 2008, Cook *et al* made objective assessments of dependence and disability in patients 65 years and older

undergoing chronic outpatient haemodialysis by the Barthel and Lawton Scales (Cook and Jassal, 2008). This study showed that disability in self-care is common and identified risk factors of multiple prescription drug needs, poor timing in 'up-and-go' mobility performance, and education level with basic dependency. However, Cook did not describe functional limitations or patients view points.

Assessing functional fitness in uraemic patients

The most widely used assessment tool for functional health and well being is the "SF-36", which is a multi-purpose, short-form health survey with 36 questions. It is a generic measure yielding psychometrically based physical and mental health summary measures. It is very well validated and data has been documented in thousands of patient groups, including renal patients (Acaray and Pinar, 2005, Hayashinoetal.,2009).

However, its generic applicability whilst advantageous in comparative literature, can mean it is a less sensitive tool in groups with unique health needs. The Kidney Disease Quality of Life Instrument (KDQOL) was developed to provide a comprehensive assessment of domains of health-related quality of life (HRQOL) in patients on haemodialysis. The KDQOL is validated and correlates with the 36-Item Short-Form Health Survey(Rao et al., 2000) but provides more renal specific measures.

Both of these scales are quite lengthy and may not be easily utilised in clinical practice. The SF-36 is a research tool and demands a licence fee.

In 1997, Saito *et al* devised and piloted the 'Sit-to-Scale' score an easily applied score to follow functional status in elderly dialysis patients. Essentially a gait speed measure, the Sit-to-Scale test is measure of the time taken to walk the distance between the dialysis chair and the weighing scale with the rationale that

this would be similar each day; would vary with functional status and could be used to predict the acute onset of functional disability. The pilot study suggested this was a feasible, quick and reliable functional measurement that can be taken, on a daily basis, in a dialysis unit. The test had high intra-rater, inter-rater reliability, was responsive and was feasible. This suggests that the STS is a good surrogate measure for changes in functional status over time.

1.6 Falls in Older Adults

1.6.1. Falls Pathophysiology

A fall is defined as *"a loss of postural stability leading to inadvertent descent from one level to a level below"*. Maintenance of static postural stability involves the ability to control the position of the body, or more specifically the centre of body mass, within specific boundaries of space without changing the base of support. If the centre of body mass is not kept within the support base, a fall will occur.

Postural control requires the integration of sensory information to assess the position and motion of the body in space and the ability to generate forces for controlling body position. This is relatively straightforward in a static posture but become much more complex during movement. There is activation of synergistic groups of muscles to maintain stability during any perturbation of stance. These groups of muscles are known as neuromuscular synergies and work as units; examples are the ankle strategy when the feet are displaced, hip strategy and, when the centre of mass is displaced, the stepping strategy. Falls may occur if any step in these sequences is impaired.

Normally, peripheral inputs from visual somatosensory and vestibular systems detect the body's frame of reference for postural control. Visual inputs report motion of the head and provide a reference for positioning but those with other systems intact can keep their balance when the eyes are closed. The somatosensory system includes joint and muscle proprioceptors, cutaneous and pressure receptors and provides information about the body's position with reference to supporting surfaces. These somatosensory receptors are less reliable when the supporting surfaces are moving. Finally, the vestibular system contributes two other categories of information. The semicircular canals sense acceleration of the head, particularly fast head movements occurring during gait or imbalance e.g. slips, trips or stumbles. The otoliths distinguish linear position head position with respect to gravity.

1.6.2. Risk Factors for Falls

There is vast literature on falls risk factors, the majority exploring falls risk in older adults. Increasing age is associated with increasing falls risk and the subsequent morbidity and mortality of associated fractures, other injuries and psychosocial sequelae. On average, 33% of elderly people experience at least one fall per year with approximately 7% of the fallers experience a fracture as a result (Tinetti et al., 1988).

Falls risk factors can be categorised as can being internal or external, and further subdivided into sensory, neuromuscular, psychosocial and environmental. Relevant falls risk factors for older adults with renal disease are summarised below in Table 1.5.2.1.

Table 1.6.2.i Relevant Risk Factors For Falls in Older Adults with Renal Disease

	Example	Reference
Sensory		
Impaired vision	Diabetic retinopathy	Black and Wood, 2005
Impaired hearing	Presbycusis	Tinetti et al, 1988
Sensory Neuropathy	Diabetic neuropathy, uraemic neuropathy	Tilling et al 2006
Over stimulation	Busy environment	
Neuromuscular		
Reduced strength	Muscle Disuse atrophy, uraemic myopathy, vitamin D insufficiency	Tinetti et al, 1988
Joint Pathology	Osteoarthritis	Pandya et al, 2005
Reflex blunting	Cerebrovascular disease, neurological disease	Stolze et al, 2004
Intercurrent Illness	Recurrent hospital admissions	
Co-morbidity	Cardiovascular disease, cerebrovascular disease	Aronow and Ahn, 1997
Anaemia	Pathological anaemia	Dharmarajan and Norkus, 2004
Postural hypotension	Reduced baroreflex sensitivity	Graafmans et al, 1996
Malnutrition	Chronic disease, living alone	Heaney, 1992
Environmental		
Polypharmacy	Especially sedatives	Weiner et al, 1998
Use of sedatives	Sleeping tablets	Allain et al, 2005
Poor lighting	Inadequate home adaptation	Kooijman and Comelissen, 2005
Over stimulation	Busy shopping centre, hospital	
Psychosocial		
Lack of appreciation of limitations	Over stretching, overloading	
Cognitive impairment	Dementia, cerebrovascular disease	Tinetti et al, 1998
Low mood	Depression, bereavement	Biderman et al, 2002
Alcohol use	Alcohol dependence	Guse and Porinsky, 2003

1.6.3. Morbidity and Mortality

Falls are a major cause of disability and the leading cause of mortality due to injury in older people aged in the UK (Gryfe et al., 1977). Although many are minor falls without physical injury, as above, it is estimated that between 5-10 percent of older adults who fall each year do sustain serious pathology, such as fracture, head trauma, or serious soft tissue damage. Additionally some fallers will not be able to rise and may sustain pressure damage such as sores, rhabdomyolysis or compartment syndromes. Infections following falls are common, probably because of a combination of immobility, dehydration, malnutrition, subsequent surgery, and hospital acquired illness.

Approximately 15 percent of older adult fallers require hospital admission (French et al., 1995, HEA, 1999b). The UK Royal Society for the Prevention of Accidents reported that more than 600,000 people aged over 65 were admitted to hospital as a result of falls in 2002. Of those, 48,000 had fractures of the hip and around 30% of this group (14,000 older adults) die each year in the UK as a direct or indirect result of an hip fracture (Melton, 1988, Richmond et al., 2003).

Hip fractures are the most serious fall-related injury and it is estimated that 95% of hip fractures are due to falls. Sustaining a hip fracture appears to at least double the risk of death (Richmond et al., 2003, Empana et al., 2004). Worldwide, there were approximately 740,000 hip fracture associated deaths in 1990. Hip fractures account for approximately 20% of orthopaedic bed occupancies in the UK (Johnell et al., 1992) . There were 1.75 million disability adjusted life-years lost, representing 0.1% of the global burden of disease world-wide (Johnell and Kanis, 2004).

Psychological

Even without injury, falls often lead to mobility limitations resulting from a fear of falling or injury. These are usually self-imposed. The incidence of fear of falling is 22.5% in adults over 65 years and increases with age (Lach, 2005). Having two or more falls, feeling unsteady, and reporting fair or poor health status were independent risk factors for developing fear of falling (Lach, 2005). Fear of falling can lead to severe curtailments in activity level, functional capability and independence. Fear of falling is associated with functional decline, increasing depression, decreased quality of life, and further falls risk (Jorstad et al., 2005, Cumming et al., 2000).

Fear of falling can be assessed by the Tinetti Falls Efficacy Scale, based on the operational definition of this fear as "low perceived self-efficacy at avoiding falls during essential, non-hazardous activities of daily living." It is a well-validated and very useful research tool. It has shown correlation with functional limitation and with balance performance (Chamberlin et al., 2005, Tinetti et al., 1990, Tinetti et al., 1994b).

Immobility

Any restrictions of mobility occurring as a result of injury or psychological trauma from falls increases the risk of complications such as pressure sores, contractures, muscle weakness, decalcification of bone, and depression. Mobility restrictions can precipitate further functional decline, which may contribute to increased risk of falls (see Section 1.5.1 and 1.5.2).

Carer Burden

Many fallers do not regain their previous level of independent activity, and about half of those who fall will need some help with everyday activities. Dependency can precipitate caregiver burden and are often a prompt for institutional placement.

Financial Costs

Falls are associated with a rise in health care costs and these increase with more severe and frequent falls. The average health care cost of a fall injury in people aged 72 and older requiring hospital admission was £10,750 and is projected to rise further as dependency levels increase (Rizzo et al., 1998, Englander et al., 1996).

It is known that falls prevalence is correlated with fracture prevalence in the general elderly population (Grisso et al., 1991, Lauritzen, 1997, Parkkiari et al., 1999). The cost of hip fracture care averages £25,424 per patient (French et al., 1995). The total estimated cost of UK hip fractures to UK society is almost £726 million per annum, without including any loss of earning for carers who would otherwise be employed.

1.6.4 Falls Prevention

In an ideal scenario, to provide optimum use of resources, patients would be screened and stratified by falls risk (e.g. high, medium, low). Those who are highest risk of falling would be identified and could then benefit from effective targeted falls prevention strategies. Unfortunately, this approach is still limited by the lack of useful validated screening tools, and, to a lesser extent, by some continued uncertainty as to what constitutes effective falls prevention strategies.

To be useful, a falls prediction tool should have predictive validity i.e. high sensitivity and positive predictive value (a high 'true positive' rate), high specificity and negative predictive value (a high 'true negative' rate). This would allow good total predictive accuracy of classifying fallers versus non-fallers. In addition, tools should have easy and fast to use, have good inter-rater reliability (different staff will usually reach the same score), require minimal need training or specialist equipment. These factors will also promote high adherence from

users. Tools should also be validated on comparable health groups and in comparable settings to the one in which they are to be used and should perform better than the judgement of ward staff in predicting risk.

At the commencement of this study, many units offering falls prevention strategies to the general elderly population were using “home-made” risk assessments, or taking referrals on the basis of previous falls. There was limited consensus on the best screening tools and limited rollout of these to other areas such as acute and general inpatient wards and the community. As this work has progressed, numerical risk prediction tools have become more widely used e.g. FallScreen© (Lord et al., 2003), STRATIFY(Oliver et al., 1997) and Morse Falls Scale (Haines et al, 2007).

Successful interventions to prevent falls often use checklists to prompt action on risk factors. The York falls care plan (Healey et al., 2004) uses a falls risk-factor checklist. These tools focus on factors that can be treated or managed, and suggest interventions for each one. A range of trials and initiatives using such checklists has reduced falls (Fonda et al., 2006, Von Renteln-Kruse, 2007) suggesting that they can play an important role in falls prevention programmes. Unfortunately, few of them have been validated in multiple settings or patient cohorts, although the STRATIFY score (Oliver, 2008a) and the Morse Falls Scale (Morse et al, 1989) are exceptions.

The STRATIFY score was the fastest and easiest to complete and the most widely validated of all risk assessment tools for falls in hospital (Vassallo et al., 2005). However, it still performs only moderately well overall. In a systematic review of nine validation studies of STRATIFY in various countries (Oliver et al., 2008) it was found to be most useful in excluding lower risk patients but poor at identifying high risk patients.

What has been shown to work in falls prevention is the systematic identification of common risk factors and meaningful plans to do something about each one (Oliver, 2008a; Von Renteln-Kruse et al, 2007; Fonda et al, 2006). Some of the most successful fall prevention programmes in hospitals did not use risk prediction tools at all.

Some falls prevention interventions are likely to benefit all patients. For example, patients with unsafe footwear need safer footwear, patients on medication with central sedative effects need assessment of whether the benefits outweigh the risks of falling, and patients with acute confusion or behavioural disturbance need to be assessed and managed.

With the recent publication of the National Service Framework for Older People(2001), falls reduction programs have come under renewed focus. The NSF advocates a community-wide strategy at population level focused particularly on adults who have had more than one fall using specialist multidisciplinary and multi-agency falls services (Leveille et al., 1998).

Population strategies which are evidence based include encouraging appropriate weight-bearing and strength-enhancing physical activity (Hillsdon et al., 1995, Munro and al., 1997) and promoting healthy eating (particularly adequate intake of calcium and vitamin D)(Bischoff et al., 2003).

A community strategy to prevent falls should also include measures such as keeping pavements in good repair, adequate street lighting and making property safer.

The NSF suggests guidelines for those who should be offered referral to specialist falls services (see Table 1.6.4.i. below).

Table 1.6.4.i High Risk Markers For Targeted Falls Reduction Strategies

Older adults should be considered for falls risk reduction interventions if they: -
Have had previous fragility fractures
Attend A&E having fallen
Called an emergency ambulance having fallen
Have two or more intrinsic risk factors in the context of any fall
Have frequent unexplained falls
Fall in hospital or in a nursing or residential care home 254
Live in unsafe housing conditions
Are very afraid of falling

Specialist assessment is then suggested to identify risk factors associated with an individual older person's health and their environment, particularly those likely to respond to intervention and to enhance strategies for coping with a fall in the future. Additionally the service should identify any psychological consequences of the fall that might lead to self-imposed restriction of activity.

Table 1.6.4.ii Individual Interventions Recommended by The NSF for Older People (Section Six).

Diagnosis and treatment of underlying medical problems e.g. postural hypotension or cardiac rhythm abnormality, inappropriate or excessive medication.
Rehabilitation (HEA, 1999a) including physiotherapy to improve confidence in mobility, occupational therapy to identify home and environmental hazards.
Equipment, repairs or adaptations to the home.
Social care support.
Tailored exercise programs.

1.6. 5 Falls in Patients with Kidney Disease

There are few studies focussing on falls in older maintenance dialysis patients, and in fact at the start of this work in 2003 there were none. During the course of this thesis, five such studies were published.

In 2003, Roberts *et al* hypothesised that older adults on haemodialysis may be vulnerable to falls due to interdialytic postural hypotension. They collected self-reported falls history, self reported history of symptomatic hypotension and pre and post haemodialysis blood pressure readings from 47 haemodialysis patients over 70. Whilst causality could not be assumed, these patients reported high rates of interdialytic hypotensive symptoms, recalled falls in the previous year and suffered significant post dialytic postural hypotension(Roberts et al., 2003).

In 2005 Cook *et al* undertook a cross sectional interview based study to determine one year falls prevalence in this group and found it to be 27%(Cook and Jassal, 2005). In the same year, Desmet *et al* undertook an eight week prospective study of falls incidence in this group and found it to be 12% (Desmet et al., 2005).

In 2006, the same group lead by Cook et al (Cook et al., 2006) undertook a prospective cohort study to examine falls rate and falls risk factors in older maintenance haemodialysis patients and found a falls rate of 1.6 falls/patient-year (compared with 0.6-0.8 falls/patient-year in published data for non uraemic community dwelling older adults). Risk factors included age, comorbidity, mean predialysis systolic blood pressure and history of falls.

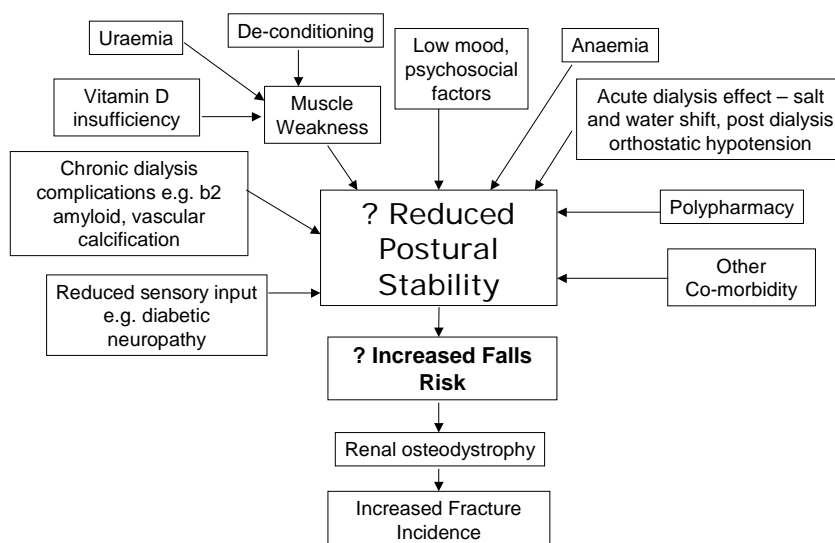
Most recently, and most alarmingly, in 2008 Li *et al* (Li et al., 2008) published the results of prospective, cohort study of 162 haemodialysis patients aged over 65 years. Patients were followed biweekly, and falls occurring within the first year

were recorded. Outcome data were collected until death, study end transplantation or transfer to another dialysis centre. Survival was worse amongst fallers compared to non-fallers (HR 2.13, 95% CI 1.32-3.45; P = 0.002) even after adjustment for age, dialysis vintage, co morbidity and laboratory variables. They concluded that the occurrence of more than one fall was associated with an independent increased risk of death. This brings new impetus to the search for effective rehabilitation and falls reduction studies in this patient group.

Risk factors

Potentially modifiable risk factors for falling have been identified within the general elderly population, including muscle weakness and polypharmacy, clinical and psychosocial aspects etc (Nevitt et al., 1989, Campbell et al., 1989, Tinetti et al., 1988). It is possible that the dialysis population have particular characteristics within these categories that may have special implications for their falls risk. Figure 1.6.5., summarises the postulated risk factors for falls in uraemic dialysis patients. Some of these factors are discussed in further detail below.

Figure 1.6.5. Postulated Risk Factors for Falls in Uraemic Patients



Anaemia

Anaemia is universal in ESRD, usually developing as the GFR falls below 35ml/min and worsening with declining GFR. Other contributing factors include shortened red blood cell survival, uraemic and cytokine inhibition of erythropoiesis (especially during infections or other inflammatory conditions), iron deficiency, hypothyroidism, active blood loss (including haemodialysis circuits, GI bleeding), haemolysis, haemoglobinopathies, aluminium overload, hyperparathyroid osteitis fibrosa, folic acid or vitamin B12 deficiency. Improving haemoglobin can give major improvements in quality of life, exercise capacity, cognitive function, sexual function, nutrition, sleep patterns and cardiac status (Muirhead, 2002), (although caution should be exercised in those patients with pre-existing severe cardiac disease as in these patients an increased mortality with normalised haematocrit has been shown (Macdougall and Ritz, 1998)). Anaemia has been suggested as an independent risk factor for falls in the general population (Plati et al., 1992), and it would seem rational and intuitive that anaemic patients functioning at a depressed physical level may have reduced control of postural stability and thus an increased falls risk. There is, as yet, no reported data addressing this specifically.

Vitamin D Insufficiency (see also Section 1.7)

In ESRD, there is decreased production of 1,25 vitamin D by the failing kidney and vitamin D insufficiency occurs. Vitamin D insufficiency causes a myopathy, particularly of the proximal limb muscles, and has been linked with increased falls risk in the general elderly population (Janssen et al., 2002, Dhesi et al., 2002). Correcting vitamin D insufficiency has been shown to reduce falls rate in the general elderly population, and it has been suggested that careful treatment with calcitriol (i.e. activated Vitamin D, 1,25-(OH)₂D₃) therapy can diminish muscle weakness in uraemic patients (Wanic-Kossowska et al., 1995, Verhaar et al., 2000). There has been some concern that treatment with calcitriol therapy

worsens renal function as a rise in creatinine has been observed after commencement of vitamin D therapy(HEA, 1999a), but it may be that the increased creatinine seen can be explained by augmented release from improving muscular tissue. It has been shown that the inulin clearance during vitamin D therapy remains stable and that creatinine levels return to baseline if the vitamin D is stopped(et al., 1990).

Polypharmacy

It is well recognised that polypharmacy is a risk factor for falls in the elderly (Caramel et al., 1998, Ebly et al., 1997, Weiner et al., 1998). Many dialysis patients are on multiple medications for hypertension, bone disease, other aspects of the uraemic syndrome or for co-morbidities or concurrent illnesses. The association recognised in the general population is likely to be maintained in dialysis patients.

Cardiovascular

Dysfunction of the cardiovascular autonomic nervous system is a common complication in end-stage renal disease(Jassal et al., 1998). Patients may have diabetic autonomic neuropathy, poor left ventricular reserve and/or be on antihypertensive therapy. Abnormal haemodynamic responses coupled with large volume salt and fluid shifts contribute to intradialytic hypotensive episodes which occur in 15-50% of treatment sessions (Stojceva-Taneva et al., 1991). These factors may increase vulnerability to orthostatic hypotension between dialysis sessions, which could pre-dispose to falls.

The autonomic nervous system dynamically controls the response of the body to a range of external and internal stimuli in order to maintain physiological stability. Heart rate variability (HRV) is the standard deviation of the R-R interval representing beat-to-beat duration on the standard electrocardiograph (ECG)

trace. HRV is an index of parasympathetic tone of the cardiovascular system (Pumpria et al., 2002). The likely range of values for HRV is on the order of approximately 30-60 milliseconds. A higher HRV indicates increased parasympathetic tone. HRV tends to be higher in younger, fitter subjects and can be increased by exercise training. Overall, haemodialysis patients have a lower HRV than non-uraemic patients. Reduced HRV predicts arrhythmia and sudden cardiac death (Carpeggiani et al., 2004). Arrhythmia is a cause of collapse or falls in older adults and may reasonably be expected to be contributing to falls risk in dialysis patients. Interestingly, exercise training can increase heart rate variability in ESRD and also reduce the incidence of arrhythmias (Deligiannis et al., 1999b).

Psychological

Depression is a further risk factor for falls in the elderly (Biderman et al., 2002). End stage renal failure is a chronic disease with huge impact on the patients lifestyle and haemodialysis patients have been shown to have a lower level of mood than amongst non-dialysed patients (Livesley, 1982). Patients who are receiving treatment for depression have also been shown to be at increased risk of falls (Joo et al., 2002), thought to be an effect of polypharmacy, treatment-induced orthostatic hypotension, or residual depression. It would be reasonable to suggest that the association recognised in the general population is likely to be maintained in dialysis patients.

Sensory impairment or neuropathy

Amongst the home-dwelling older population, those with a sensory neuropathy have an increased risk of falls (odds ratio of 2.5) (Koki et al., 1998). All patients reaching ESRD after a duration of CKD will have some degree of neuropathy (Krishnan and Kieran, 2009). Around 30 – 40% of the incident dialysis patients have a diagnosis of diabetes mellitus (Ansell et al., 2004) and diabetic neuropathy may be seen. Neuropathy may also be seen as a result of uraemia,

altered bone mineral metabolism, pharmacological effects and other systemic primary renal diseases. Again, it would be reasonable to suggest that the association between neuropathy and falls recognised in the general population is likely to be maintained in dialysis patients.

Dialysis Related Arthropathy

B2-microglobulin is a non-glycosylated single chain protein that, over time, accumulates in soft tissues in dialysis patients. It is not clear whether this is due to decreased glomerular filtration or increased production in uraemia. B2-microglobulin has a predilection for bone and collagen and can cause a disabling and painful arthropathy which may limit mobility and reduce stability, and may be a contributory factor in falls.

Failure of Clinical Focus

Unfortunately, the gravity and impact of ESRD is such that patients can find that issues such as functional mobility and falls risk are subsumed. This patient group can be thought of as selected to tolerate a high intensity life-maintaining programme and therefore would be a group which might benefit greatly from other interventions to enhance quality of life.

Bone disease (see also Section 1.7)

All patients with CKD progressive to ESRD will have renal bone disease of varying degrees of severity by the time they require renal replacement therapy. Dialysis does not cure but merely prolongs the state of renal failure, and therefore renal bone disease does not improve but continues to progress on dialysis. Histologically, renal bone disease is an extremely heterogeneous entity. Low vitamin D levels and subsequent hypocalcaemia causing hyperparathyroidism underlies the basic pathogenesis of hyperparathyroid bone disease (osteitis fibrosa). Osteomalacia and adynamic bone disease are also seen. Many patients

have mixed lesions. However, it seems that all histological diagnoses can cause increased bone fragility and thus theoretically increase fracture risk for any degree of trauma sustained. Therefore whilst bone disease may not contribute directly to falls risk, certainly it increases concern about the possible injuries received.

The pathogenesis and progression of renal bone disease will be discussed in greater detail and in relation to fracture risk in Sections 1.7.

1.7 Bone Mineral Metabolism, Vitamin D, Fracture Risk

1.7.1 Normal Physiology

In this section, the bone mineral metabolism pathways in health are explored in detail. This is relevant as background to the pathophysiology of the abnormal bone mineral metabolism that occurs in renal disease, and its implications for overall physical health as discussed in Section 2.8. The author has taken particular interest in the role of vitamin D abnormalities in these problems as an emerging area for potential relevant future research and intervention.

Under influence of ultraviolet radiation, 7-dehydrocholesterol is photoconverted to pre-vitamin D₃ in the skin, which is converted to vitamin D₃ (cholecalciferol). In the serum, bound to a vitamin D binding protein (DIP), vitamin D₃ is transported to the liver, where it is hydroxylated to 25(OH) D₃.

In the kidneys, 25(OH) D₃ is further metabolised to 1 α , 25-dihydroxyvitamin D₃ [1,25(OH) D₃]. This is the biologically active form of vitamin D (Disso and Brown, 1998). Activated Vitamin D, 1,25(OH)D₃, exerts its influence on distant target tissue, mediated by a vitamin D receptor (and so it is actually a hormone rather than a vitamin). Its metabolism is under tight control by various feedback systems.

In addition to being photoconverted in the skin, vitamin D can be obtained from diet through ingestion of vitamin D₃-containing foods (e.g.fatty fish, liver, egg yolk), vitamin D-fortified foods (e.g. milk, margarine and cereals) or from supplements (which contain combinations of vitamin D₃ (cholecalciferol) and vitamin D₂ (ergocalciferol)). The vitamin D ingested via these routes is metabolised in the same manner as endogenously produced vitamin D.

Function of Vitamin D

The major target organs for vitamin D for maintaining body calcium homeostasis are well described; intestine, kidney, bone, and parathyroid gland.

Table 1.7.1. Target Organs and Actions of Vitamin D

Organ	Actions
Intestine	Enhances calcium and phosphate absorption
Kidneys	<ul style="list-style-type: none">- Enhances calcium resorption from the tubule- Inhibits the synthesis of 1α-hydroxylase- Stimulates the synthesis of 24-hydroxylase
Bone	<ul style="list-style-type: none">- Stimulates osteoblasts to produce alkaline phosphatase and osteocalcin, and less collagen, favouring bone formation- Stimulates mononuclear cells to differentiate into macrophages which fuse with osteoclasts and increase calcium mobilisation
Parathyroid glands	Inhibits PTH secretion
Lymphomedullary system	Stimulates immunogenic and anti tumour activity

Other target sites for vitamin D metabolites continue to be defined (e.g. skin, muscle, pancreas, immune system, hematopoietic system, and reproductive organs). New actions have been discovered and these areas are still under research (Dusso and Brown, 1998). In December 2005, there was huge resurgence of public interest after the publication of a meta-analysis looking at studies investigating the possible role of Vitamin D in reducing cancer risk (Garland et al., 2005). Many of these additional roles are in very early stages of investigation.

Measuring Vitamin D

The serum concentration of “precursor” 25(OH)D₃ (calcifidiol) is 1000 times that of “active” serum 1,25(OH)D₃(calcitriol). In effect, 25(OH)D₃ represents a hormone storage capability and is a much more stable and representative indicator of overall vitamin D status. In health, an elevated serum parathyroid hormone concentration is commonly used as a preliminary indicator of vitamin D insufficiency.

The “normal range” for vitamin D is debated. Different concentrations of 25(OH)D₃ have been proposed as the minimum required to prevent secondary hyperparathyroidism (MK Thomas et al., 1998, Malabanan et al., 1998). Alternatively, a gradual scale was proposed in which hypovitaminosis D is defined as a 25(OH)D₃ concentration <100 nmol/L (40 ng/mL), vitamin D insufficiency as a 25(OH)D₃ concentration <50 nmol/L (20 ng/mL), and vitamin D deficiency as a 25(OH)D₃ concentration <25 nmol/L (10 ng/mL)(McKenna and Freaney, 1998).

Vitamin D and Muscle Physiology

A direct influence of vitamin D on muscle function was first demonstrated in the mid-1970s (Birge and Haddad, 1975). Since then, it has been extensively verified that vitamin D metabolites affect muscle cell metabolism through various pathways (Birge and Haddad, 1975, Boland, 1986).

Although 1,25(OH)D₃ is traditionally considered to be the “active” form of vitamin D, clinical studies reported a correlation between serum levels of the precursor 25(OH)D₃, muscle strength (Mowe et al., 1999, Stein et al., 1999) and functional ability (Gloth et al., 1995b). This may be explained by the discovery that muscle tissues express 1 α -hydroxylase which can activate 25(OH)D₃ locally in target tissues (Helicon et al., 2000, Zehnder et al., 2001).

Vitamin D has been found to affect muscle metabolism in 3 ways:

- 1) by mediating gene transcription,
- 2) through rapid pathways not involving DNA synthesis,
- 3) By the allelic variant of the vitamin D receptor.

1. Mediating gene transcription

A vitamin D receptor has been found in both in animals and human skeletal muscle cells that specifically binds $1,25(\text{OH})\text{D}_3$ (Boland et al., 1995, Boland et al., 1985). $1,25(\text{OH})\text{D}_3$ binds to the receptor and this ligand-receptor complex is transported to the cell nucleus. Here it is modulated by various transcription factors and biochemical processes (Dusso and Brown, 1998). The final transcription complex mediates cell proliferation and maturation and influences muscle cell calcium uptake, phosphate transport across the muscle cell membrane, and phospholipid metabolism (Boland et al., 1995, Bischoff et al., 2001, EM et al., 1986).

2. Rapid pathways

Supplementing with Vitamin D induces rapid changes in calcium metabolism of the muscle cell that cannot be explained by a slow genetic pathway. $1,25(\text{OH})\text{D}_3$ acts directly on the muscle cell membrane possibly through a vitamin D membrane receptor, activating several second-messenger pathways and resulting in enhanced calcium uptake within minutes (RU et al., 1985, Nemere I et al., 1998). The calcium uptake allows enhanced muscle contraction.

3. Allelic variants of the vitamin D receptor

Finally, muscle strength appears to be influenced by the genotype of the vitamin D receptor in the muscle cell. Several vitamin D receptor polymorphisms have been determined. The variants appear to confer different muscle properties. In elderly women, a 23% difference in quadriceps strength and a 7% difference in grip

strength between the 2 homozygote types of a restriction site were found (V et al., 1992).

Vitamin D and Muscle Function

Vitamin D deficiency has long been known to be associated with muscle weakness, originally described as “osteomalacic myopathy” (P et al., 1997). The weakness is predominantly of the proximal muscle groups, mainly affecting the weight-bearing anti-gravity muscles of the lower limb, which are necessary for postural balance and walking (Glerup et al., 2000). It is therefore manifested by difficulty in activities such as climbing stairs and rising from a chair, and patients sometimes complain of tiring easily or a feeling of heaviness in the legs. Muscle atrophy has been described histopathologically (Schott GD and MR, 1976, Ziambaras K and S., 1997, Smith R and G, 1969).

The deficiency is reversible with supplementation, and results can be quite dramatic. This is supported by numerous case reports in the recent literature in which both young and elderly adults have been described with severe vitamin D associated muscle weakness, often leading to marked disability, and improving with vitamin D supplementation (JA, 1994, G et al., 1999, A et al., 2000, Rimaniol et al., 1994, Ziambaras and Dagogo-Jack, 1997).

Vitamin D in Older Adults

Ageing is inevitably accompanied by a reduction in muscle mass and muscle strength, even in older people with no recognised co-morbidity (Smith and G, 1969, Lexell, 1995, BF, 1995). As discussed previously, this results in functional impairment (Aniansson et al., 1986, Bassey et al., 1992, Samson et al., 2000), the need for assistance in the performance of daily activities (Hyatt et al., 1990), and an increased risk of falling and non-vertebral fractures (Wolfson et al., 1995).

Developing understanding the role of vitamin D in muscle physiology has inevitably lead to interest in the vitamin D status of older adults and the potential contribution to treating the problems of declining muscle strength. Vitamin D deficiency is common in older people (Gloth et al., 1995a). The cause is suggested to be multifactorial, including reduced dietary intake, diminished sunlight exposure, skin thinning, impaired intestinal absorption, and impaired hydroxylation in the liver and kidneys (Omdahl et al., 1982, McKenna, 1992, Holick, 1995). In a European study of 824 older adults, 36% of men and 47% of women were vitamin D deficient (wintertime serum 25-hydroxyvitamin D₃ [25(OH)D₃] concentrations <30 nmol/L) (van der Wielen et al., 1995). In the Women's Health and Ageing Study (Semba et al., 2000), amongst the least disabled group, the frequency of severe vitamin D deficiency was 8.3% in those aged 65-74, 14.5% at ages 75-84, and 17.4% at 85 and over.

There are a limited number of studies that examine the relationship between muscle strength and vitamin D status in older adults. In an mature population (65–95 years), 12% of women and 18% of men had a serum 25(OH)D₃ concentration <30 nmol/L and a significant correlation was found between vitamin D metabolites and leg extensor power (Bischoff et al., 1999). In 349 elderly people (≥ 70 years of age), serum 25(OH)D₃ concentrations were significantly lower in those with reduced handgrip strength, inability to climb stairs, not participating in any outdoor activity, and who had fallen in the previous month (Mowe et al., 1999). In addition, a low serum 25(OH)D₃ concentration (<40 nmol/L) was associated with reduced handgrip strength and walking distance in 63 community-dwelling older adults (82.5 ± 5.4 years of age) (Mets, 1994).

A causal relation cannot be concluded from these cross-sectional studies, but data from interventional studies does support the hypothesis of causality.

In a small study, muscle strength and mobility were measured in older women who were vitamin D deficient. They were then treated for 6 months with 0.5 µg alfalcidol daily (active vitamin D, i.e. 1,25(OH)₂D₃) (Verhaar et al., 2000). Both knee extension strength and walking distance improved significantly, whilst no improvement was seen in an untreated vitamin D replete control group. In other study, supplementation of "frail elderly" adults with pre-vitamin D (ergocalciferol, vitamin D₂) and calcium significantly improved the "time taken to dress" and functional ability as measured with the Frail Elderly Functional Assessment Questionnaire (Sorensen et al., 1979, Gloth et al., 1995b). Vitamin D supplementation has also been demonstrated to improve balance as measured by body sway (Pfeifer et al., 2000). In 148 older women, with serum 25(OH)D₃ concentration <50 nmol/L, pre-vitamin D (cholecalciferol) and calcium supplementation for just 8 weeks resulted in a decrease in body sway (as compared with calcium monotherapy (9%; *P* < 0.05)).

Not all interventional studies have been supportive. In one study, patients admitted to a geriatric ward for a longer period received supplementation with 225 µg (9000 U) vitamin D₂ (ergocalciferol) but this did not significantly improve performance in activities of daily living as compared with placebo treatment (Corless et al., 1985). Explanations for this are suggested as inadequate dose, or other independent factors affecting performance. Additionally, being vitamin D replete or supplementing with vitamin D does not prevent age-related decline in muscle strength. Even in healthy, vitamin D-replete, elderly people, muscle strength declined with age (Boonen et al., 1997), which was not prevented by vitamin D supplementation (Grady et al., 1991, Johnson et al., 1980).

Vitamin D, Falls and Fractures

In one study showing that more than a third of people aged over 65 fell each year, the main risk factor was muscle weakness (Blake et al., 1988). As described

above, there is evidence that vitamin D supplementation in this population improved muscle strength, walking distance, functional ability (Gloth et al., 1995b, Sorensen et al., 1979, Verhaar et al., 2000), and body sway (Pfeifer et al., 2000). These findings and the observed improvements in bone density after vitamin D supplementation (Glerup et al., 2000, Ooms et al., 1995, Dawson-Hughes et al., 1997) provide an explanation for the association between vitamin D supplementation and fewer falls and non-vertebral fractures in elderly people (Bischoff et al., 2003, Bischoff-Ferrari et al., 2004).

Lower serum 25(OH)D₃ concentration is also associated with a higher occurrence of falls in elderly people (Stein et al., 1999, Mowe et al., 1999, Pfeifer et al., 2000). In 148 vitamin D deplete older women (25(OH)D₃ <50 nmol/L), supplementation for 8 weeks with pre-vitamin D and calcium resulted in fewer falls per subject over 1 year of follow-up, when compared with calcium monotherapy (0.24 compared with 0.45; $P < 0.05$) (Pfeifer et al., 2000).

In a female nursing home population, Vitamin D and calcium supplementation resulted in 43% fewer hip fractures than in a placebo group ($P = 0.043$) (Chapuy et al., 1992). In addition, bone mineral density improved significantly (by 2.7%; $P < 0.001$) in the supplemented group but decreased (by 4.6%) in the placebo group. A recent meta-analysis examining the role of vitamin D in fracture prevention included 12 randomised controlled trials (RCTs); 5 for hip fracture ($n = 9294$) and 7 for non-vertebral fracture risk ($n = 9820$) (Bischoff-Ferrari et al., 2005). All trials used oral cholecalciferol ("pre"-Vitamin D₃). Heterogeneity among studies for both hip and non-vertebral fracture prevention was observed, which disappeared after combining RCTs with low-dose (400 IU/d) and higher-dose vitamin D (700-800 IU/d), separately. A vitamin D dose of 700 to 800 IU/d reduced the relative risk (RR) of hip fracture by 26% (3 RCTs, total $n=5572$; pooled RR, 0.74; 95% confidence interval [CI], 0.61-0.88) and any non-vertebral

fracture by 23% (5 RCTs, total n= 6098; pooled RR, 0.77; 95% CI, 0.68-0.87) versus calcium or placebo. No significant benefit was observed for trials with lower dose 400 IU/d vitamin D (2 RCTs, total n=3722; pooled RR for hip fracture, 1.15; 95% CI, 0.88-1.50; and pooled RR for any non-vertebral fracture, 1.03; 95% CI, 0.86-1.24). The meta analysis concluded oral vitamin D supplementation was effective only in the higher doses of between 700 to 800 IU/d. These doses appear to reduce the risk of hip and any non-vertebral fractures in ambulatory or institutionalised elderly persons.

These studies support the use of vitamin D as both a falls prevention and fracture prevention intervention. The mechanisms of action for each role and the possible overlaps are not clear. The NICE Falls guidelines do not yet consider the evidence strong enough to recommend the use of Vitamin D in falls prevention strategies, (but do state that use of Vitamin D for fracture prevention will be recommended in the forthcoming NICE Osteoporosis Guidelines which are in development).

In summary, Vitamin D and the specific roles of its metabolite subgroups is the focus of great interest and ongoing research. There is emerging evidence that vitamin D plays a part in muscle strength, balance regulation and falls prevention, but the precise metabolite actions have not been elucidated.

In populations that are vitamin D deplete and have an altered vitamin D metabolism, such as in renal patients, the impact of vitamin D insufficiency on falls and fractures is not known. The next section considers what is known about abnormal bone mineral metabolism and the implications for physical fitness in kidney disease.

1.7.2 Bone Mineral Metabolism in Kidney Disease

There are two major relevant abnormalities in bone mineral metabolism in chronic and end stage kidney disease.

Firstly, hyperphosphatemia develops due to reduction in filtered phosphate load. Secondly, there is reduced activation of vitamin D with subsequent hypocalcemia. The kidney's ability to convert vitamin D to its active metabolite, $1,25(\text{OH})_2\text{D}_3$ or calcitriol, is impaired because of reduced functioning nephron mass. Active vitamin D synthesis begins to decline significantly at GFR 60 mL/min/1.73 m². The eventual outcome of both of these is hyperparathyroidism. Both hyperparathyroidism and high phosphate levels have pathological implications.

Hypersecretion of PTH is initially appropriate from the viewpoint of calcium and phosphate homeostasis. By increasing calcium and phosphate release from bone and enhancing urinary phosphate excretion (via a decrease in proximal tubular reabsorption), PTH acts to correct both hypocalcemia and hyperphosphatemia. However, once ESRD approaches and excretory capability is lost, there can be little or no urinary excretion of excess phosphate and the hyperparathyroidism thus begins to contribute to the hyperphosphatemia by continuing to enhance the release of calcium and phosphate from bone.

Even at a relatively late stage, dietary phosphate restriction reduces the serum concentration of both phosphate and PTH, although not usually to normal (Delmez and Slatopolsky, 1992). As a result, the addition of oral "phosphate binders" is often required. These are drugs, taken with meals or snacks, which bind phosphate to enhance its excretion via the gastrointestinal tract. Calcium-containing salts are cheap and effective and widely used as binders. The combination of marked hyperphosphatemia and a normal or low-normal serum calcium concentration results in an elevated calcium-phosphate product (calculated by multiplying the serum concentrations of calcium and phosphate in units of mg/dL), which is associated with increased mortality (Stevens et al., 2004). The calcium-phosphate product is further elevated if there is increased

intake of calcium [via calcium-based phosphate binders]. There is then a tendency for calcium-phosphate to precipitate in arteries, joints, soft tissues, and the viscera. This process is called metastatic calcification. There is a spectrum of metastatic calcification. At its most severe, calciphylaxis may occur which leads to tissue ischaemia by affecting dermal arterioles (Delmez and Slatopolsky, 1992). The pathogenesis is again multifactorial, with local tissue injury and altered acid-base status favouring metastatic calcification in the context of elevated calcium-phosphate product. The implications of soft tissue calcification are discussed further below.

Vitamin D Treatment in Chronic Kidney disease

As outlined above, there are several primary sources of vitamin D. Ergocalciferol (vitamin D₂) is occurs in plant sources (such as yeast and fungi) whilst cholecalciferol (vitamin D₃) is found in animal sources (such as oily fish, meat and eggs), supplements, or formed from the photo-conversion of 7-dehydrocholesterol via pre-vitamin D₃ to vitamin D₃. Both of these agents have equal biologic activity but both require metabolism in the liver to calcifediol (25-hydroxycholecalciferol) and then hydroxylation in the kidney to calcitriol (1,25-dihydroxycholecalciferol). Without functional renal tissue, this final step cannot occur i.e. patients with chronic renal disease cannot convert calcifediol to calcitriol in the kidney. Even in the very early stages of CKD, conversion is reduced. In these patients, alfacalcidol (1-hydroxyvitamin D₃), a synthetic analogue of calcitriol, can be used as it is rapidly converted in the liver to calcitriol, bypassing the renal conversion step.

Vitamin D therapy is primarily used in CKD to control secondary and tertiary hyperparathyroidism. Active vitamin D suppresses parathyroid hormone release via the feedback mechanisms. The pre-cursor forms of vitamin D are used in the earlier stages. UK guidelines for management of bone mineral metabolism in CKD

published in September 2005 (Tomson et al., 2005) recommend that vitamin D replacement should be initiated in patients with an elevated PTH level and suggests that this treatment is likely to be of most benefit for those at increased risk of falls.

The rationale for doing this is to prevent the bone disease and cardiovascular complications of hyperparathyroidism. It has also been suggested that treatment of vitamin D insufficiency improves clinical manifestations of uraemic myopathy in dialysis patients (Wanic-Kossowska et al., 1995).

Vitamin D Treatment in Renal Replacement Therapy

Since the majority of patients with advanced chronic kidney disease suffer from altered bone mineral metabolism, it is self evident that the majority of patients reaching ESRD and requiring RRT will also have established bone mineral metabolism abnormalities and secondary or tertiary hyperparathyroidism. Commencing dialysis does not reverse this pathology because it does not correct the underlying defect and patients remain unable to convert calcifidiol to active vitamin D (calcitriol). Additionally, the parathyroid glands have usually become hypertrophied by this stage and continue to release PTH even if the underlying mineral disorder is corrected (tertiary hyperparathyroidism). Dialysis patients are vulnerable to the complications of hyperparathyroidism seen in chronic kidney disease, perhaps even more so as they have other factors contributing to their cardiovascular risk. For these reasons, patients on dialysis continue to require active management of their hyperparathyroidism.

Vitamin D is used in dialysis patients to suppress parathyroid hormone release. As above, Vitamin D can be delivered orally or intravenously and in a variety of different formulations. Obviously any route or formulation used in ESRD will be

required to bypass hydroxylation in the kidney i.e. vitamin D must be given in its activated form.

The United States Kidney Disease Outcomes and Quality Initiative (KDOQI) Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease 2004 guidelines are widely used in the absence of UK specific guidelines (2003). These suggest that all dialysis patients with serum levels of intact PTH levels >300 pg/mL should receive an active vitamin D to reduce the serum levels of PTH to a target range of 150 to 300 pg/mL. Active vitamin D sterols (such as calcitriol, alfacalcidol, or paricalcitol) are available both oral and intravenous forms. There is some evidence that pulsed high dose oral therapy is more effective than low dose daily therapy (Gu et al., 2005) and that intravenous therapy is more effective than pulsed oral therapy (Indridason and Quarles, 2000, Fischer and Harris, 1993), although some researchers have shown little difference (Peng et al., 1997). In practice, most UK units use a daily oral form in peritoneal dialysis patients but are moving towards pulsed oral or intravenous delivery in haemodialysis patients as it can be given easily on dialysis days.

As well as controlling parathyroid hormone levels, there appear to be additional benefits to using vitamin D in dialysis patients. Elevated plasma phosphorus and Ca x P product concentrations increased all-cause mortality risk in haemodialysis and peritoneal dialysis patients (Noordzij et al., 2005). A large historical cohort study appears to support a significant survival advantage of active injectable vitamin D in haemodialysis patients (Teng et al., 2005).

Renal Bone Disease

Renal bone disease, also called renal osteodystrophy, is a heterogeneous spectrum of conditions that combine features of secondary hyperparathyroidism,

rickets, osteomalacia, and osteoporosis. The clinical and radiographic findings in renal osteodystrophy may be a manifestation of any of these effects.

Osteomalacia results from hypomineralization of bones of completed growth and is seen in hypocalcaemia. Hyperphosphatemia also decreases the efficacy of 1-hydroxylase, which decreases the levels of 1-25(OH)₂D₃, thus the ability of the gut to absorb calcium. The converse phenomenon, osteosclerosis, also occurs in renal osteodystrophy. The pathophysiology is incompletely understood. Histological evaluations of patients with renal osteodystrophy typically reveal evidence of abnormally increased bone turnover. Additionally, an abnormally increased proportion of cancellous (spongy internal layer) bone often exists. There is abnormal calcium deposition in this cancellous bone, with deposits forming as amorphous calcium phosphate rather than the usual hydroxyapatite mineralisation. Hyperparathyroidism triggers abnormal bone resorption. This may normalize serum calcium levels by releasing the osseous storage of calcium, but de-mineralises the bone. Characteristically, sites of bone resorption include the sub periosteal region of the phalanges, the phalangeal tufts, proximal femur, proximal tibia, proximal humerus, and the clavicle.

Finally, although less frequent nowadays, aluminium-induced bone disease is an additional cause of osteomalacia. Aluminium may be introduced from dialysate solutions, antacids, or aluminium-containing phosphate-binding agents. Aluminium through inhibits osteoblast activity and hydroxyapatite crystal formation and thus negatively effects bone formation.

Renal osteodystrophy be asymptomatic or may present with non-specific signs and symptoms, including weakness, bone pain, and skeletal deformity. The most common complication of renal osteodystrophy is fracture, which may be insufficiency fractures through osteomalacic bone or pathologic fractures through brown tumours or amyloid deposits.

1.8 Rehabilitation in Kidney Disease and Dialysis

There is no one universal definition of rehabilitation. The King's Fund uses the following definition: *"A process aiming to restore personal autonomy in those aspects of daily living considered most relevant by patients or service users and their family carers"* (Sinclair and Dickinson, 1998). Rehabilitation is concerned largely with physical functioning, although other aspects of care are addressed, including psychological wellbeing and social functioning.

The National Service Framework for Older People voices the UK Government's stated aim to promote independence through effective rehabilitation services and to provide a cohesive service between the acute and community areas. There are well-resourced and researched rehabilitation strategies for older adults in the general population, but programs focusing on older adults with kidney disease are in their infancy. The known benefits of rehabilitation programs are related to areas of specific concern for patients with ESRD; particularly reduction in cardiovascular mortality, improvement in blood pressure control, better diabetes control, reduction of depression and promotion of psychosocial well being.

As outlined in Section 1.3, the Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines on management of cardiovascular disease state that, "all dialysis patients should be counselled and regularly encouraged by nephrology and dialysis staff to increase their level of physical activity" (guideline 14.2).

In 1993, the US pharmaceutical company Amgen provided grant support to the non-profit Medical Education Institute to create "Life Options", a program dedicated to "helping people live long and live well with kidney disease". Life Options recruited an extensive multidisciplinary panel of doctors, patients, nurses, social workers, researchers, physiotherapists, dieticians, administrators, rehabilitation specialists, and industry representatives to form the Life Options

Rehabilitation Advisory Council (LORAC). This group identified core principles of rehab called the "5 Es"—encouragement, education, exercise, employment, and evaluation, and in 1994, published a white paper, *Renal Rehabilitation: Bridging the Barriers* (Life Options Rehabilitation Advisory Council, 1997). *Bridging the Barriers* recommendations formed the basis of the NKF-DOQI Guidelines.

This section focuses on exercise intervention in detail but also presents data for the use of erythropoietin and carnitine which are strategies used predominantly in rehabilitation in kidney disease.

Benefits of Exercise in Pre-dialysis patients

As outlined above, patients with pre-dialytic uraemia have a reduced maximal working capacity, due to several possible factors (Clyne et al., 1987). Exercise training improves maximal exercise capacity, muscle strength and endurance in young, middle-aged and elderly pre-dialysis patients. Disappointingly, there does not appear to be a stabilizing effect on GFR decline (Boyce et al., 1997). Despite initially having lower muscle function and mobility compared with elderly healthy subjects, after 12 weeks of exercise training elderly pre-dialysis patients were able to improve both to the same extent as elderly healthy subjects (Heiwe et al., 2001).

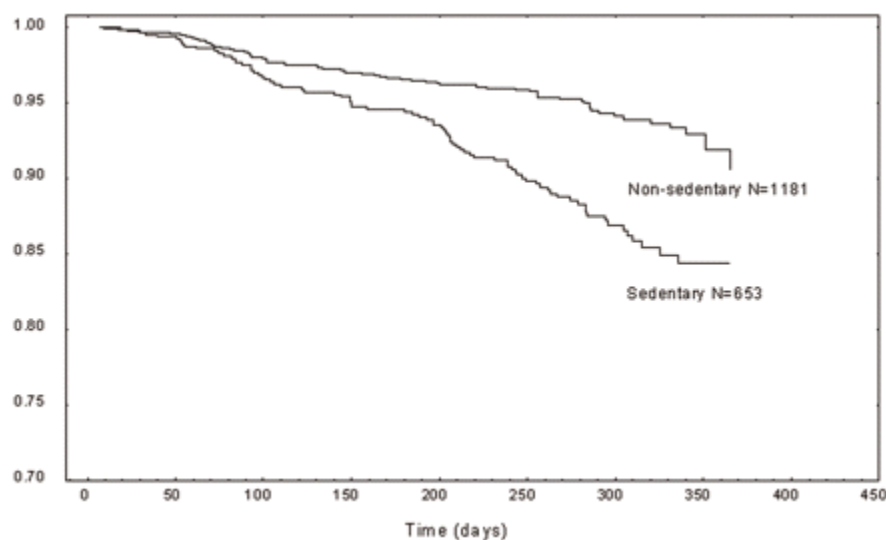
Exercise has a preventative effect on muscle catabolism and counteracts weight loss and malnutrition. Moreover, exercise training has positive effects on functional capacity and health-related quality of life (Clyne, 2004, Clyne et al., 1991). It is recognized that encouraging patients to maintain beneficial levels of physical exercise, especially in the pre-dialysis phase, has multiple benefits, not least socio-economic (Blagg, 1994). In fact, it has been suggested that rehabilitation services are more beneficial before patients commence dialysis (Fitts et al., 1999).

Benefits of Exercise for Haemodialysis Patients

Cardiovascular

The number one cause of death in dialysis patients is cardiovascular events (Ansell et al., 2009). Patients with CKD or on dialysis are at increased risk of cardiovascular disease due to a higher prevalence of established atherosclerotic risk factors, including diabetes mellitus, hypertension, dyslipidaemia, physical inactivity, as well as to unique CKD-related risk factors. Cardio-respiratory insufficiency, left ventricular dysfunction, atherosclerosis and ischaemic cardiomyopathy contribute to exercise intolerance. The corollary is that diminished exercise tolerance in patients receiving renal replacement therapy is strongly associated with cardiac abnormalities (Bullock et al., 1984). There is significantly increased cardiovascular mortality amongst sedentary dialysis patients when compared with their non sedentary peers (O'Hare et al., 2003, Sietsema et al., 2004).

Figure 1.9. Reduced Survival in Sedentary Patients vs Non Sedentary patients on Haemodialysis (O'Hare et al., 2003, Sietsema et al., 2004)



It is thus remarkable that, to date, no randomised clinical trials have been performed to assess the effects of physical activity on cardiovascular risk in

uraemic patients. However, the evidence and existing guidelines for physical activity for other populations at high risk for cardiovascular disease suggest that similar implementation of physical activity for patients with renal failure is likely to be beneficial.

Exercise training during HD significantly improves both interdialytic blood pressure and treatment-related blood pressure (Anderson et al., 2004), and in some patients reduces the number of anti-hypertensive agents necessary (Goldberg et al., 1986, Goldberg et al., 1983, Hagberg et al., 1983). Exercise also leads to a decrease in plasma triglyceride, an increase in high-density lipoprotein cholesterol levels, and an increase in glucose disappearance rates (suggesting that insulin sensitivity improved)(Goldberg et al., 1986, Goldberg et al., 1980b). However, whether these outcomes do actually reduce the incidence of cardiac morbidity and mortality rate remains to be determined. There has been a suggestion that the cardiovascular risk factors in dialysis patients may in fact be partly attributable to a sedentary lifestyle and that exercise therefore offers a potent weapon in the reduction of cardiovascular risk (Goldberg et al., 1986). By reducing coronary risk factors in haemodialysis patients, exercise training may decrease morbidity and mortality from atherosclerotic complications.

Dysfunction of the cardiac autonomic nervous system is a known complication of end-stage renal disease. Heart rate variability index (HRV) refers to the beat-to-beat alterations in heart rate. Reduced HRV is used as a marker of reduced vagal activity and is predictive of cardiovascular mortality (in non-uraemic, CKD and dialysis patients) (Deligiannis et al., 1999b, Carpeggiani et al., 2004, La Rovere et al., 2003). HRV is significantly reduced in haemodialysis patients compared with non-dialysed controls (Deligiannis et al., 1999b). Haemodialysis patients with a more depressed HRV index have a higher incidence of arrhythmias and are

significantly more likely than controls to suffer arrhythmias (40% cf 16) (Deligiannis et al., 1999b).

Exercise training programs are effective in improving cardio-respiratory capacity, left ventricular systolic function at rest, as well as in exertion (Deligiannis, 2004, Deligiannis et al., 1999a, Goldberg, 1984). Both intense and moderate exercise training improves cardiac performance during supine sub-maximal exercise (Deligiannis et al., 1999a). There is correlation between improved HRV index and better maximal oxygen consumption, a surrogate of physical fitness. This demonstrates that physical training in haemodialysis patients improves cardiac vagal activity and reduces the risk of arrhythmias (Deligiannis et al., 1999b).

Myopathy

Biopsy study has shown that exercise training improves muscular atrophy, increasing the proportion of type II fibres and mean muscle fibre area (Kouidi et al., 1998). Improvements were also seen in the structure and number of capillaries and mitochondria, confirmed by increases in VO₂ peak and exercise time, as well as muscle strength and nerve conduction velocity. In another biopsy study, a six month aerobic exercise program exercise reduced the proportion atrophic fibres, increased the cross-section fibre area and improved the capillarisation in the skeletal muscle of renal failure patients (Sakkas et al., 2003). Resistance training increases muscle strength and functional capacity in stable haemodialysis patients (Headley et al., 2002).

Chronic Inflammatory Response

Chronically uraemic patients suffer a low-grade systemic inflammation that reflects an unbalanced production of pro-inflammatory and anti-inflammatory cytokines. Elevations in C-reactive protein (CRP) and depressions of serum albumin below 40mg/dL are found in more than 50% of ESRD patients undergoing dialysis (Don and Kaysen, 2000). This phenomenon of chronic inflammation

contributes to the progression of atherosclerotic vascular disease and malnutrition (Zoccali et al., 2005, Perunicic-Pekovic et al., 2008). The inflammatory response predicts morbidity and mortality. There is conflicting evidence regarding the effect of exercise on systemic inflammation with some studies suggesting that regular exercise can reduce the systemic inflammation (Guarnieri et al., 2005) and others refuting this (Hung et al., 2002).

Psychological

Many studies have suggested a beneficial effect of exercise in improving mood and quality of life in haemodialysis patients (Goldberg et al., 1980a, Carney et al., 1983, Kouidi, 2004). In a study to assess the psychological effects of exercise training in haemodialysis patients, 8 dialysis patients (4 trained subjects, 4 controls) participated in a 6-month period of exercise training (Carney et al., 1983). The trained patients had a 28% improvement in graded exercise treadmill stress test duration and a 13% improvement in aerobic capacity and this was associated with a reduction in anxiety and depression, although not reaching statistical significance ($p < 0.06$). Other studies have shown that exercise training reduces depression and increases the performance of pleasant activities in haemodialysis patients (Carney et al., 1987).

Nutrition

There is some suggestion that patients participating in intradialytic exercise programs have improved appetite and calorie intake (Frey et al., 1999). This would be an important benefit and malnourished dialysis patients have significantly increased morbidity and mortality compared to well nourished peers (Lacquaniti et al., 2009).

Dialysis

In another study, 16 patients participated in 12 month program of progressive, self-paced exercise cycling or walking on a treadmill before or during haemodialysis (Cappy et al., 1999). Performance tests included 60-second sit-stand, 28-ft slow and brisk walk, 60-second stair climb, and 60-second leg lifts. All patients showed improvement in measures of physical performance at 3, 6, and 12 months. Mean phosphorus by 26% at 12 months ($P < 0.02$). Increases were seen in Kt/V (a measure of dialysis waste product clearance), estimated dry weight, and serum albumin; however, these were not statistically significant. Decreases were noted in mean pre-dialysis and post dialysis blood pressures and average interdialytic weight gains at 3, 6, and 12 months. Exercise improved phosphate clearance and some patients are able to reduce their phosphate binders (Goldberg et al., 1980a).

Exercise increased the efficiency of dialysis by reducing the rebound of solutes such as potassium, urea and creatinine due to increased perfusion of the skeletal muscles (Kong et al., 1999) . Clearances of these solutes increase significantly as a result.

Designing an Exercise Program

Any intervention should ideally be evidence based i.e. proven benefit. Programs should have defined goals with capacity for monitoring and auditing outcomes and adverse events. It is vitally important that programs are safe for patients and staff and are adequately resourced in terms of equipment, specialist staff and data support. Programs should be accessible to patients and enjoyable to sustain motivation. Patients and staff should be educated in the benefits of the programs and regularly supported and supervised. Exercise interventions should ideally be started in the pre-dialysis phase, as above, but otherwise as soon as possible after establishing on dialysis. A correlation, accentuated in men, was found

between muscular deterioration and the years on haemodialysis (Iborra Molto et al., 2000).

Safety of Exercise for patients with CKD and ESRD

In the general population, the most common risk of exercise participation is musculoskeletal injury but most serious risks are of cardiac origin, including arrhythmia, ischaemia and sudden death. The risk any adverse event is higher with high-intensity exercise than with sub maximal exercise (Copley and Lindberg, 1999).

Since 1995, intra-dialytic exercise training has been implemented in about 200 German dialysis centres and up to now no serious adverse effects or complications have been reported (Daul et al., 2004). Thus far, none of the published controlled exercise studies have demonstrated any serious adverse effect of exercise for haemodialysis patients.

There are no studies specifically assessing the risk of exercise among patients with CKD. The available information is from case reports and from adverse effects reported in exercise studies. Spontaneous quadriceps tendon ruptures have been reported (Shah, 2002, Jones and Kjellstrand, 1996), Risk of musculoskeletal injury may be increased in patients with CKD as a result of hyperparathyroidism and bone disease and they are at higher risk for fracture(Alem et al., 2000a). Risks for injury can be minimized by including a warm-up period in exercise sessions, and by beginning training programs at lower intensity and progressing gradually avoiding high-impact activities.

The risk for cardiac events during maximal exercise testing is low, on the order of 0.5 per 10,000 tests for death and 3.6 per 10,000 tests for myocardial infarction, estimates that are based on tests that were conducted in healthy and diseased populations (Copley and Lindberg, 1999) . No data specifically address the

absolute cardiovascular risks in patients with kidney disease. There has been concern that intradialytic exercise may compromise cardiovascular stability. The acute effects of exercise on relative blood volume (RBV) and other haemodynamic parameters have been studied. The haemodynamic response to exercise during haemodialysis is comparable with that in normal individuals. The rapid reduction in RBV on exercise occurs in spite of a significant increase in cardiac output, mainly as a consequence of fluid shifts from the microvasculature to the interstitium (Banerjee et al., 2004). A level of 60% of the maximal heart rate has been suggested as a safe starting point for a program of physical retraining in dialysis patients (Capodaglio et al., 1998).

In healthy subjects, serum potassium levels rise substantially during vigorous exercise as a result of the release of potassium from contracting muscle cells. This does not normally cause clinically hyperkalaemia in healthy subjects. There have been concerns that exercise in dialysis patients may contribute to unsafe hyperkalaemia. However, despite higher basal potassium, dialysis patients have normal potassium responses to maximal exercise (Clark et al., 1996). More vigorous insulin, catecholamine, and aldosterone levels may contribute to the maintenance of extra-renal potassium homeostasis in ESRD.

In the absence of specific data for guidance, this author suggests that it is sensible to complete medical screening before exercise participation, as ⁱⁿ all populations at high risk of cardiovascular disease. The absolute necessity for testing and the extent of investigation required should be related to the proposed intensity of training and the patient's individual medical history. Patients with symptoms suggestive of cardiac disease or with known disease should undergo exercise testing before participation in vigorous training programs (Medicine, 1995). A minimum requirement would be an electrocardiograph, but ideally

exercise electrocardiography should be undertaken. In addition to this, patients' volume status and blood pressure control should be optimised.

There are also practical and Health and Safety issues, particularly when using equipment within the haemodialysis unit. Exercise equipment must not present a risk to staff or patients moving and handling it, the equipment must not obstruct emergency access routes, or impede urgent clinical interventions.

Type and Timing of Exercise; aerobic vs. resistance, intradialytic vs. non-dialysis days

There are several studies that examine the effects of aerobic exercise in haemodialysis patients. Many of these were before the routine use of erythropoetin and included young adults, with a generally younger dialysed cohort. Few of the studies were controlled and predicted age adjusted VO₂ levels are not always used. There is also very limited assessment of functional improvements. The total number of patients studied remains small. However, although all the programs varied in length and duration of exercise session, most consisted of at least 30 minutes of aerobic exercise three times per week (usually 3-6 months). On average VO₂ peak was improved by 17%, but there is considerable variation. Despite the limitations, this is important because it indicates that patients with kidney disease can respond to exercise training.

Resistance training promotes muscle strength which is an important determinant of functional fitness in older adults (Guralnick et al., 1994). Muscle strength is a predictor of gait speed in patients on dialysis (Johansen et al., 2003a) and isokinetic muscle strength is a determinant of VO₂ max in this group (Diesel et al., 1990). It therefore makes sense that older haemodialysis patients might benefit from resistance training, but in fact there are few studies that examine the effects in this group. Headley *et al* enrolled 10 haemodialysis patients in a 12-

week twice-weekly resistance-training program. At the end of the program patients improved in 6 minute walk test, normal and maximum gait speed and sit-to-stand testing (Headley et al., 2002). Johansen *et al* completed a 2x2 factorial trial of resistance training with out without anabolic steroid administration in 79 maintenance haemodialysis patients (Johansen et al., 2006). Amongst the 68 patient who completed the study, suggested that exercise did not result in increase in lean body mass although exercise combined with steroids did. Exercisers improved self-reported physical functioning but not objective functional tests.

There are also few studies of mixed aerobic and resistance programs. Kaudi *et al* enrolled 7 patients into a 6 month program of mixed exercise three times per week on non dialysis days, with a resultant increase in VO₂ max of 48% an increase in exercise time of 29%, an improvement in muscle atrophy of around 25% for both type 1 and 2 fibres, and an increase in heart rate variability(Kouidi et al., 1998). However, this was a very small, uncontrolled study with relatively poorly defined resistance component. De Paul *et al* studied a high functioning group of dialysis patient undertaking a mixed exercise program and found significant functional improvements at the end of the 12 week study period, although these were not sustained at 5 months(DePaul et al., 2002). Mercer *et al* (Mercer et al., 2002) studied low volume mixed program exercise rehabilitation and found improvements in daily living related functional capacity and self reported functional living status. In these latter studies anaemia was fully optimized prior to exercise.

The question of when exercise should be undertaken is even less clear. In one study comparing intradialytic and non dialysis day programs, Kouidi *et al* found that whilst fitness improvements were marginally better with outpatient programs, the drop out rate was much higher(Kouidi et al., 2004). Another study

show that that measurable cardiovascular benefits were greater with a intradialytic exercise program than a home based program(Deligiannis et al., 1999a).

At the time of submission, Koh *et al* are undertaking a randomised controlled trial of intradialytic versus home based exercise training in hemodialysis patients (Koh et al., 2009) to compare the effects of six months supervised intradialytic with unsupervised home-based exercise training on physical function and arterial stiffness. Primary outcome measures are six-minute walk distance and aortic pulse wave velocity. Secondary outcome measures include augmentation index, peripheral and central blood pressures, physical activity and self-reported health. This trial is in progress at the time of submission.

Practicalities and barriers to the introduction of exercise and rehabilitation programs to haemodialysis units

The experience of many centres is that few patients are able or willing to participate in an exercise training, which is organised on an outpatient basis. It seems likely that the participation rate in intra-dialytic exercise programs would be higher than in supervised or unsupervised outpatient rehabilitation programs because older patients and patients with severe additional medical problems participate.

At the time of submission, there was very limited literature on rehabilitation specifically in the older age group on maintenance dialysis. In the only older adult focussed study, published in 2007, Jassal *et al* reported on the first three years of a rehabilitation program aim of restoring personal independence in elderly hemodialysis patients with new-onset disability from prolonged illness or an acute event rendering them incapable of living independently(Jassal et al., 2008).

Jassal used a multifaceted approach with preferential admission of elderly dialysis patients; short daily dialysis sessions; integrated multidisciplinary care by experts in rehabilitation, geriatric medicine, and nephrology; and reciprocal continued medical education among staff. Of those completing therapy, 82% met some or all of their rehabilitation goals. This is encouraging as it demonstrates older dialysis patients are able to make rehabilitation progress.

Based upon the data available, it seems likely that the best approach is to develop exercise programs consisting of low intensity endurance training, resistance training, flexibility and co-ordination and relaxation techniques, all of which can be performed during haemodialysis (Daul et al., 2004). These programs are likely to be best adhered to if offered as supervised intradialytic programs. In most studies offering intradialytic programs, seated bicycles have been used. The training starts with an initial warm-up, then building up to 60–80% of the maximal heart rate and maintaining this for increasing durations as fitness improves. Sessions can include maintenance for up to 45 minutes and then finally a cool-down phase (Fuhrmann and Krause, 2004, Frey et al., 1999).

With this in mind, and considering the multiple studies reporting experience of the beneficial effects of introducing exercise programs to adult haemodialysis facilities (Death, 1999, Daul et al., 2004, Forgeron and Valeriote, 2001, Harter and Goldberg, 1985, Curtin et al., 2002) the question remains as to why more centres and patients are not developing exercise programs. Lack of motivation, as opposed to health-related impairment, appears to one of the factors impeding dialysis patient exercise practices (Goodman and Ballou, 2004). However, almost all patients can do some form and level of exercise during dialysis.

In 2005, Johansen opined that, based on available data, uraemic patients “should be encouraged to participate in moderate physical activity to meet the US Surgeon General's recommendations”(Johansen, 2005). Johansen recommended

that low intensity resistance and aerobic exercise programs should be initiated in patients with CKD and that for maximum participation and tolerance of exercise, patients should have exercise incorporated into the dialysis sessions.

As yet, there no UK national guidance as to how to introduce exercise programs into the dialysis routine. Units who are already running programs are sharing their experiences and passing advice to their nephrology community colleagues and the body of literature is expanding (Macdonald, 2006) . However, at the time of submission resources to guide development of exercise interventions within the Renal Unit remained very limited. Nephrologists are slowly gaining familiarity with the need to promote this topic, but it is unlikely that patients consistently receive counseling from clinicians. In one survey, nephrologists cited lack of time, lack of confidence in their ability to counsel patients, lack of conviction that patients would respond to advice and belief that other medical issues were more important than exercise as reasons why they did not broach these issues with their patients(Johansen et al., 2003c).

Local Programs at Nottingham City Hospital Haemodialysis Unit

In our local unit, stationary pedal cycles and resistance bands are freely available for haemodialysis patients to use during dialysis. However, there is no physiotherapy input for the unit and the exercise sessions are informally encouraged and supervised by nurses who have many other clinical responsibilities. Initial uptake of the exercise equipment was encouraging, but the lack of a structured supervised program means that many patients have stopped regular use. These events have not been formally audited.

Anecdotally, the biggest demand now is in the subgroup of patients who suffer leg cramps on dialysis and find that use of stationary cycles prevents or relieves this. The pattern of use and benefits has not yet been formally studied.

In recent months, the unit has benefited from a physiotherapist who has developed a specific interest in renal patients. This has allowed some individualized input for a small number of patients, but there are no dedicated sessions or resources for unit input as a whole.

In the pre-dialysis sessions, nurses and dieticians anecdotally report a higher awareness of the importance of exercise than the doctors. All health professionals questioned on an informal basis admit that sometimes promotion of exercise is subsumed by other concerns in their pre-dialysis consultations. There is no written departmental guidance on the benefits of exercise available for pre-dialysis patients at this time nor is there any service to promote exercise in this group.

Summary

Patients with CKD show a decline in maximal exercise capacity and muscle strength as renal function decreases. Renal anaemia, skeletal muscle dysfunction, tiredness and increasing inactivity are the major causes of this deterioration. Exercise training improves maximal exercise capacity, muscle strength and endurance in all patients at all stages of CKD. Exercise training should be preferably started during the pre dialysis stage. Nonetheless, it is effective in dialysis patients and after renal transplantation. It has a positive effect on muscle metabolism and counteracts weight loss and malnutrition. Moreover, exercise training has positive effects on functional capacity and health related quality of life. Exercise training should be prescribed by a nephrologist and their multidisciplinary team and administered by a trained nephrological physiotherapist. Exercise training is an integral part of care of the CKD patient. It not only reduces suffering but also costs, resulting in major potential benefits for the patient, the health care system and society.

CHAPTER TWO ORIGINAL RESEARCH

2.1 Introduction

This chapter presents three original studies.

The first study, Section 2.2, was undertaken as a small-scale exploratory study and feasibility pilot to explore the immediate effect of a single haemodialysis session on objective assessments of performance and postural stability. This study was logistically challenging with many limitations. These preliminary results did not support the alternative hypothesis but did guide future study direction.

The second project, presented in Section 2.3, aimed to define the extent of the problem of reduced physical fitness, postural instability and falls risk, as perceived by older haemodialysis patients themselves and by non dialysed older adults attending hospital outpatients. A questionnaire exploring fitness, functioning and falls was administered to 66 older adults on maintenance haemodialysis in Nottingham and to an age-matched group of older adults outside the renal unit. This study recruited 132 patients. It is the largest study of its kind and the only UK study to explore the limitations perceived by this patient group.

Section 2.3. provides invaluable information to justify further work on maintaining and improving functional capabilities in this patient group. This is supported by national guidelines and policy (see Chapter 1). It is vital to plan targeted and pragmatic exercise interventions with consideration of the known local resource situation and local staff and patient factors. Thus the final original study focussed on one of the major potential barriers to instigation of exercise intervention. The understanding, attitudes, opinions and behaviours of the multidisciplinary team of Nottingham haemodialysis unit staff towards older adult patients and their physical fitness needs was investigated with a self administered questionnaire study, presented in Section 2.4.

2.2 Feasibility Pilot and Small scale Exploratory Study Exploring the Effect of a Single Maintenance Haemodialysis Session on Older Adults Performance in Falls Predictive Physical Assessments

This study begins an exploration of the hypothesis that a single session of haemodialysis has an acute detrimental effect on physical function and postural stability in older adults on maintenance haemodialysis. This study was prompted by the observations that local maintenance haemodialysis patients had fallen within 60 minutes after dialysis sessions (See Introduction section ix). As stated previously, in a six-month period in 2003, all of the four haemodialysis patients sustaining fractures from falls had fallen in the hour after a haemodialysis session.

The rationale was that if a single session effect was found, interventions to improve postural stability could be targeted to post dialysis periods, extra care could be taken during this time, and remediable factors could be further investigated. The study involved balance assessments and performance tests of older haemodialysis patients immediately before and after a single routine haemodialysis session. The study was devised as a pilot study to test the feasibility of carrying out objective performance assessments in the setting of a busy haemodialysis service. There is extremely limited data in the literature to power investigations of this type, with no reports in the literature of these assessments having been carried out on older haemodialysis patients although the assessments have been widely used and validated in older adults in the general population. This was therefore also a small-scale exploratory study to collect preliminary data to support power calculations from other methods if a larger scale study was thought possible. As such a control group was not appropriate.

It was anticipated that there may be logistical problems as the service is overstretched, allowing very little flexibility to fit in research assessments around

times on and off the dialysis machine and hospital transport arrangements. Additionally, with a minimum of 4 hours prescribed dialysis and transport and waiting times either side, patients tend to regard their haemodialysis sessions as already too lengthy. It was felt they might be understandably unwilling to extend times beyond the minimum possible. Haemodialysis sessions are not always of a predictable length (patients “come off” early for a variety of reasons) and also cycled through the day from 6.30am to midnight, which provides a challenge for single researcher availability.

METHODS

Local ethical committee approval was gained for the study. It was carried out in a hospital Haemodialysis Unit at Nottingham City Hospital (estimated population served 1.16 million).

Patients aged 60 years or more at the start of the study, established on haemodialysis for more than 90 days, not inappropriately limited by disability (e.g. amputation, dementia) were invited by letter to take part. Fifty-four patients were invited. Twenty-two patients gave written informed consent.

Patient age, gender and use of mobility aid were recorded. Sitting and standing blood pressure was recorded in millimetres of mercury (mmHg) for each patient pre and post dialysis using an automated Omron cuff, and weight reduction (fluid removal) in kilograms was measured using the dialysis unit integral footplate scale. Nursing staff reported any intra-dialytic adverse events (symptomatic hypotension, nausea, vomiting, cramps).

Postural sway, leg extensor power and timed three metre “Up and Go” were measured by a single researcher, the author. These tests were chosen as simple, quick and portable, requiring little additional equipment. They were chosen to

represent functional capability, and have been shown to predict falls risk in non-dialysed older adults (although not in dialysis patients).

The location was in a clinic room on the haemodialysis unit. Subjects were assessed immediately prior to dialysis and underwent the same assessments within ten minutes of dialysis completion (time allowing for safe disconnection of dialysis access). Patients remained seated throughout the disconnection time.

Leg extensor power was measured using the Nottingham Leg Rig (Bassegy and Short, 1990). This measures explosive power of a single seated leg extension in Watts. The dominant leg was assessed. Three attempts were made and the highest score was used. This assessment was chosen as explosive leg power is a more sensitive indicator of falls risk than traditional assessments of muscle strength (Koski et al., 1998).

Postural sway was measured using the Balance Performance Monitor (SMS Technologies Ltd) (Haas and Burden, 2000, Haas and Whitmarsh, 1998) incorporates "foot plates" above load sensors connected to a feedback unit measuring anterolateral sway (as a sway number on an arbitrary scale) and sway path (mm), amongst other parameters. Postural sway was assessed in bipedal unsupported stand with the patient's eyes open and with eyes shut. Measurements were made with eyes shut to remove any bias from variable visual cues.

Timed "Up and Go" Test assesses functional mobility (Mathias et al., 1986, Podsiadlo and Richardson, 1991) and is a sensitive and specific predictor of falls risk (Shumway-Cook et al., 2000). The patient is seated in a standard armchair with customary walking aid, then is timed walking at a comfortable pace to a line on the floor three metres away, and returning. If the patient is unable to complete the test or needs assistance, this is a fail.

All assessments were recorded as the mean of three attempts.

Statistical Analysis

Data were analysed using SPSS version 12.01.1 for Windows. Median and Interquartile ranges are given for performance outcomes because the data were not normally distributed, as assessed by skew and kurtosis in SPSS. Differences in scores before and after dialysis were assessed using the Wilcoxon signed rank test for non-parametric data.

RESULTS

Twenty-two patients consented to take part in the study.

Complete data were available on 14 subjects (11 men and 3 women), median age 77 (range 62- 85 years). All patients were independently mobile, with none reporting use of a mobility aid (stick, frame or chair).

Table 2.2.i Participant Characteristics (I=Independently mobile)

N	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Gender	M	M	M	M	M	M	M	M	M	M	M	F	F	F
Age yrs	71	73	85	81	79	78	70	62	64	62	67	79	63	80
Mobility	I	I	I	I	I	I	I	I	I	I	I	I	I	I

All dialysis sessions were without adverse event. Mean weight reduction was 1.94 kg (range 0.4 kg – 3.4kg). Mean pre-dialysis blood pressure was 155/75mmHg sitting and 144/73mmHg standing, and mean post-dialysis blood pressures were 156/81 mmHg sitting and 144/73 mmHg standing. Seven patients had orthostatic hypotension (Neurology., 1996) pre-dialysis and ten patients post-dialysis (see Table 2.2.ii).

Table 2.2.ii. Weight Reduction and Pre and Post Haemodialysis Sitting and Standing Blood Pressure Measurements

Note

*Orthostatic hypotension is a physical finding defined by the American Autonomic Society and the American Academy of Neurology as a systolic blood pressure decrease of at least 20 mm Hg or a diastolic blood pressure decrease of at least 10 mm Hg within three minutes of standing.

Patient	Weight reduction (kg)	Mean Pre dialysis blood pressure (mmHg)		Mean Post dialysis blood pressure (mmHg)	
		Sitting	Standing	Sitting	Standing
	0.4	136/78	148/85	146/76	140/82
	1.6	172/95	170/84*	176/86	155/78*
	1.9	156/85	135/72*	157/89	163/75*
	1.2	145/72	152/80	145/86	146/70*
	2.2	134/57	125/64	122/58	127/59
	1.7	110/46	112/60	120/61	110/56
	3.1	191/87	169/90*	196/96	141/88*
	2.5	132/61	134/66	147/78	135/61*
	2.6	178/99	151/74*	188/102	191/90*
	0.9	189/50	165/56*	176/73	167/61*
	3.4	166/78	133/75*	177/90	131/77*
	1.7	142/80	142/79	124/78	125/72
	2.0	161/82	140/76*	156/83	139/71*
	2.0	152/80	147/76	151/82	138/69*
Mean	1.94	155/75	144/73	156/81	144/73

Table 2.2.iii. Results of Postural Sway, Leg Extensor Power and Timed Up and Go Tests before and After Haemodialysis

The results before and after haemodialysis dialysis compared by Wilcoxon signed ranks test for non-parametric data.

Note: A lower sway number and/or a shorter sway path indicate superior postural stability. A higher leg extensor power score indicates superior power. Superior functional mobility is indicated by a lower (faster) timed up and go test score.

	Before Dialysis	After Dialysis		
	Median (IQR)	Median (IQR)	Z	p
Postural Sway – eyes open (Sway number)	2.88 (1.48,6.41)	3.13 (1.98,6.33)	-0.565	0. 572
Postural sway – eyes shut (Sway number)	2.60 (1.14, 6.01)	3.20 (1.98, 6.33)	-0.351	0. 177
	Z = -0.031, p= 0.779	Z= -0.565, p= 0.572		
Postural Sway – eyes open (Sway path mm)	383 (297.25, 446.50)	398.5 (299.25, 604.13)	-1.601	0. 109
Postural sway – eyes shut (Sway path mm)	466.50 (337.00, 1214.25)	501.50 (387.75, 862.25)	-0.031	0. 975
	Z = 2.417 p =0.016	Z = -0.1.351, P= 0.177		
Leg Extensor Power (Watts)	81.3 (43.03, 91.63)	73.8 (46.65, 97.48)	-2. 83	0. 778
Timed Up and Go Test (secs)	9.34 (7.94, 10.72)	9.11 (8.15, 11.29)	-0.157	0. 875

The results for leg extensor power and for the timed "up and go" test are shown in Table 2.2.iii, above, and Figures 2.2.i and 2.2.ii, below. Seven of the patients scored increased leg extensor power after dialysis whilst seven showed reduced leg extensor power. Changes in leg extensor power ranged from -30 to +30 watts, but the range achieved before and after dialysis stayed almost the same. There was no significant difference for leg extensor power before and after dialysis ($Z = -0.283$, $p=0.778$). Eight of the patients completed the timed "Up and go" test more quickly after dialysis, but six patients took longer to complete the test. Overall, there was no significant change in timed "Up and go" test before and after dialysis ($Z=-0.157$, $p=0.875$).

Before dialysis, there was no significant difference in sway number whether the eyes were open or shut ($Z = -0.031$, $p=0.975$), but the sway path was significantly greater with eyes shut ($Z = 2.417$, $p = 0.016$), as might be expected. After dialysis, having the eyes open or shut made no significant difference to sway number or path ($Z = -0.565$, $p=0.572$ and $Z=-0.1351$, $p=0.177$). When comparing pre-dialysis and post-dialysis session balance assessments, there was no significant difference in sway number with eyes open and with eyes shut, or in sway path with eyes open and with eyes shut ($p=0.572$, 0.177 , $p=0.109$, $p=0.975$, respectively). Results for the assessment of balance are shown in the tables and figures below.

Figure 2.2.i Leg Extensor Power (watts) before and after Haemodialysis

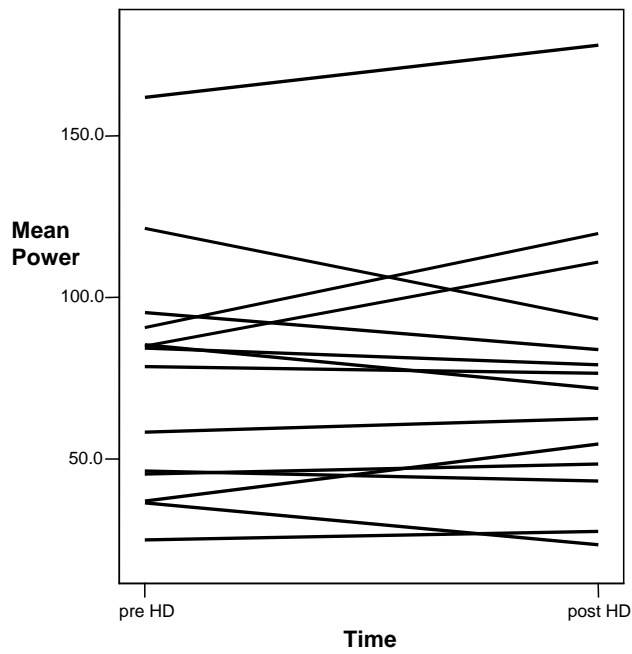


Figure 2.2.ii Timed Up and Go test (seconds) before and after Haemodialysis

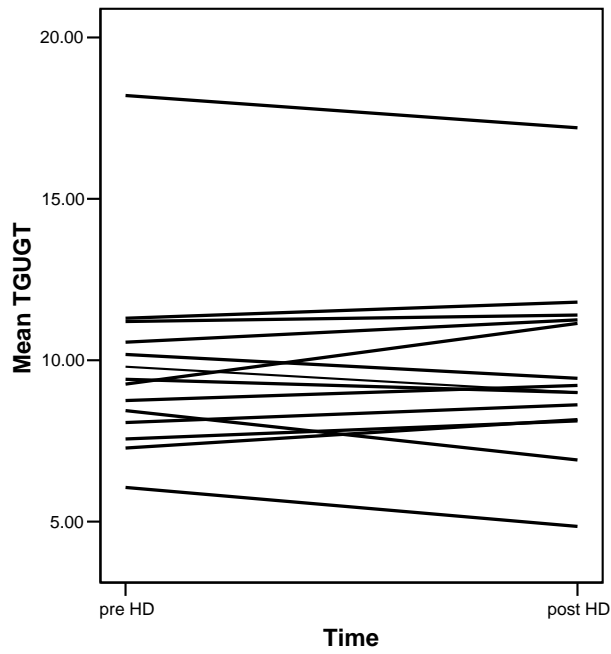
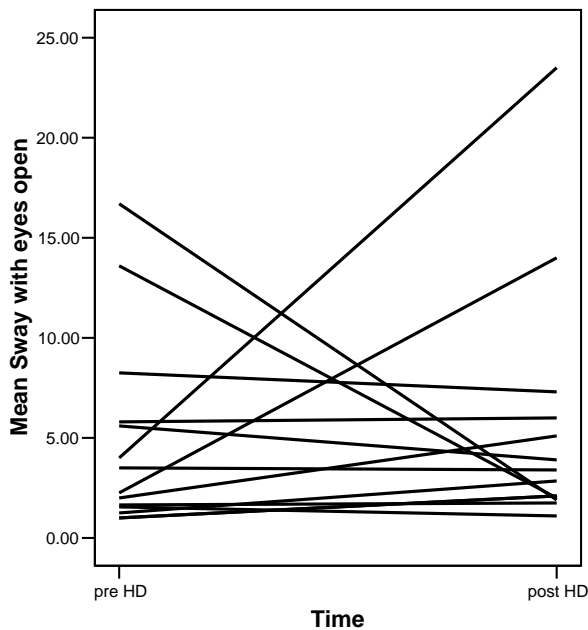


Figure 2.3.iii Sway Number (as an example of postural stability trend) Before and After Haemodialysis



DISCUSSION

This was a small exploratory study intended for preliminary data collection and feasibility assessment. The absence of statistical or clinical difference in the results before and after dialysis was not consistent with the intended subsequent hypothesis (see first line) of an acute single session effect. An exploratory and feasibility study of this type cannot be used to test such a hypothesis. Findings may be the effect of the small numbers, bias and the significant difficulties encountered during the study, as discussed below. The logistics and practicalities of performing this study in the setting of a busy haemodialysis service were such that future similar studies would not be feasible and alternative approaches or settings would be needed to explore this further. However, the enthusiasm with which both patients and dialysis unit staff embraced attempts to explore these themes was encouraging and suggested real concerns about functional fitness and stability in older dialysis patients.

Results in Context

The results did not support the hypothesis that a single session of haemodialysis has an acute effect on function and postural stability in older adults on maintenance haemodialysis, but this small-scale exploratory study was not designed for this purpose.

To develop a picture of how this group of patients compared to similar dialysed and non-dialysed patients of a similar age, we considered the results in the context of published historical data. To the best of our knowledge, there has only been one previous study investigating an acute effect of a single haemodialysis session on postural stability in older maintenance haemodialysis patients. Roberts et. al focussed on the possibility of autonomic failure and significant fluid shifts causing postural hypotension as a risk factor for falls in older haemodialysis patients (Roberts et al., 2003). This study did not undertake functional assessments. Of twenty-three haemodialysis patients aged 70, 8/23 had orthostatic hypotension pre-dialysis and 16/23 post-dialysis. These are similar proportions to those seen in our study. Roberts and concluded that elderly haemodialysis patients have a high incidence of hypotensive symptoms between dialysis sessions, recalled falls in the previous year and had significant postural hypotension post-dialysis.

Hassan, Mockett, and Doherty (Hassan et al., 2001) published general population older adult control data obtained using the same postural stability assessment methods. Their data suggests that in a control population of older adults with no reported major health problems, the comparable postural sway is less than in than in older haemodialysis patients (median sway number in historical controls 2.3, cf median comparable sway number 2.88 in dialysis patients – eyes open pre-dialysis). Timed “up and go” test scores appeared to be in the same range as

similar aged healthy subjects in previously published data (Podsiadlo and Richardson, 1991).

This inference is supported by work from other groups who consistently show reduced muscular strength in uraemic patients (see Section 1.5.2).

Clearly there are many limitations when considering our work in the context of previously published data, but the early inferences support the need for more robust and specific data in this particular patient group.

Strengths and Limitations

This is the first and only study to undertake balance and performance assessments in older adults before and after maintenance haemodialysis, and thus provides a unique and original approach to exploring the physical limitations suffered by this patient group. The study is directly relevant to our local older adult maintenance haemodialysis population. Patients and dialysis unit staff were enthusiastic about the aims of the study and keen to contribute to this body of work.

The findings were preliminary but did not support the original hypothesis. However, as well as being underpowered, the findings may have been distorted by practical and methodological difficulties introducing multiple possible sources of bias. These sources of bias would have to be addressed if the study was expanded.

Sources of bias may include selection bias (i.e. only those fitter patients who were confident in their stability agreed to take part). This is supported by the fact that none of the patients used mobility aids and the zero rate of adverse intradialytic

events, suggesting a healthier and more active group of patients. This is difficult to counter but could be addressed in recruitment stage, ensuring patients with limitations are not discouraged.

There was also potential attrition bias as many patients withdrew from the study. This could be addressed through redesigning the study to ensure assessments were more easily achievable. There was a high non-completion rate and the number completing the study was small. Eight patients did not complete the study. The reasons for this were the unpredictable and often antisocial timings of dialysis slots because the dialysis unit was working over capacity. Patients already delayed in getting onto dialysis were reluctant to add additional time to their visits and the investigator could not always be available for testing when slots were rearranged. Four completed the pre-dialysis testing but declined the post-dialysis testing. The main reason for this was the extra time that the study would add to a dialysis session. Assessments of the other four patients could not be completed because of logistical problems of limited space and hospital transport restrictions. Additionally, very early or late night dialysis "slots" limited accessibility.

Dialysis sessions "slots" offered were often changed without notice depending on clinical need of the patient or of others and it was not possible to anticipate some of these changes. Priority use of the clinic room had to be given over to any clinical emergencies and this prevented completion in one case. It would not be possible to address all these issues with current resources. The logistical problems were extremely frustrating and wasted considerable time and resources.

Those patients not completing the study said they would be willing to participate in further research projects on this topic if the logistical problems could be addressed.

All performance-based tests may be affected by a training effect and patients inevitably understood the test requirements better after dialysis because they had

completed the initial pre-dialysis assessments. This is performance bias i.e. exposure to other factors apart from the intervention of interest. Patients were also, of course, aware of the reasons for testing and, for individual reasons, may have been motivated to over or under perform during the tests. Repeating the tests around two or three dialysis sessions would go some way to addressing this.

This study did not use a control group. This was because the study was designed as a small exploratory and pilot feasibility study. If a larger scale study were possible, selection of a control group would be challenging. As the research question is on the acute effect of a single haemodialysis session, a comparable group might include patients with established end stage renal failure on dialysis and with high level waste products and fluid gain (i.e. approaching the next dialysis session). This patient group would be unlikely to want to attend the hospital for additional sessions above and beyond their dialysis appointments. It would have been useful to consider performing the assessments on the same group on non-dialysis days, but again it was felt that this would be extremely difficult to recruit to, as patients would not wish to attend additional hospital visits.

Implications for Clinicians, Services, and Future Research

In the setting of a busy working haemodialysis unit, pre and post single haemodialysis session data was extremely difficult to achieve. If possible, to assess a single session effect the assessments should be performed before and after dialysis by the same patients on repeated dialysis sessions. However, this is unlikely to be possible unless dedicated research sessions and facilities are available. Otherwise, further research into a single session effect would need preplanning to be much more sympathetic to the demands of the haemodialysis schedule, both in terms of the practical arrangements of the assessments and in

terms of patient acceptability. In particular, whilst happy in principal to aid this type of research, patients are understandably reluctant to extend the hours spent at the hospital.

With the benefit of this experience, it may be more productive to assess the “everyday” balance performance of patients rather than assessing a single session effect. It would be sensible to recruit only patients over 65 years of age (rather than 60 years), as this is a conventional cut-off point and used widely in other data. It is also absolutely necessary to recruits more inclusive sample, including patients less confident in their abilities. Utilising more functionally relevant assessments, such as the functional reach test, and including assessments of daily activity levels and fear of falling may also be more revealing. In practical terms, and to offer a greater motivation to the patient participants, these assessments may be best carried out as part of a protected physical fitness session. This could be offered away from the dialysis unit or on non-dialysis day, perhaps in a physiotherapy or domestic setting. This would also resolve the difficulty of early morning or late night dialysis slots where circadian rhythms may influence assessments (Ward and Kenny, 1996).

This study revealed a gap in the literature for a validated and reproducible falls risk screening tool for older haemodialysis patients. During the course of this study, various commercially available falls screening tools were being developed. For example, a physiological profile approach to falls risk assessment and prevention was developed by the Falls and Balance Research Group of the Prince of Wales Medical Research Institute, Sydney, Australia (Lord et al., 2003). The Physiological Profile Assessment, now copyrighted as the FallScreen Tool©, involves a series of simple tests of vision, peripheral sensation, muscle force, reaction time, and postural sway. The tests can be administered quickly, and all equipment needed is portable. The results can be used to differentiate people who

are at risk for falls ("fallers") from people who are not at risk for falls ("nonfallers"). A computer program using data from the PPA can be used to assess an individual's performance in relation to a normative database so that deficits can be targeted for intervention. FallScreen© is not validated in haemodialysis patients but in other health groups provides valid and reliable measurements that can be used for assessing falls risk and evaluating the effectiveness of interventions. It would be valuable to consider validating such a tool in haemodialysis patients.

CONCLUSION

There are many limitations to the study meaning that these preliminary results must be interpreted with caution and are intrinsically inconclusive. If the study could be performed on a larger scale, reviewing and improving the study design to avoid or reduce systematic error could address many of these limitations. However, this feasibility study concludes that it is not reasonable to carry out a larger study of this kind in the same setting.

It is possible to make a cautious inference that older haemodialysis patients may be less posturally stable than non-dialysed older adults based on comparison to historical data. Patients in our unit express that they are keen to be involved in activities and research that moves towards addressing their medical, well-being and lifestyle requirements in more integrated ways. However, in the context of a busy working haemodialysis unit, other methods are needed to explore the physical and functional limitations of this patient group. This formed the prompt for the study in Section 2.3.

2.3 A questionnaire study

Patient Perceptions of Physical Health, Falls and Falls Risk in Older Adult Maintenance Haemodialysis Patients And Non-dialysed Hospital Attending Older Adults

BACKGROUND

In the community, 30% of persons over the age of 65 years have at least one fall each year but the rate in the haemodialysis population is not known (Salva et al., 2004). Chapter One establishes that increasing age is associated with reduced physical fitness, reduced activity levels, functional limitations, increased falls risk and the subsequent morbidity and mortality of fractures, other injuries and psychosocial sequelae. These issues are all relevant to older patients who require RRT. However, there are very few studies examining physical fitness and functioning in older adults on maintenance haemodialysis considering this from the older patients' perspective (see Section 1.5.2). It is not clearly established whether or not older haemodialysis patients have a different profile of physical and functional limitations, reduced activity levels, and falls compared to the non-uraemic older adult population. Establishing this is important because it will allow better understanding of the extent of the limitations in the older haemodialysis patient group. This will advance understanding, focus interventions, and support a statement of need for service development.

Purpose of the Study

1. To describe the nature of physical fitness and functional limitations in older adults on haemodialysis in Nottingham, as perceived by patients, including social and psychological aspects.

To compare this with the same in local non-dialysed hospital attending older adults.

2. To investigate the falls pattern in this population and compare with the same in local non-dialysed older adults.
3. To prioritise appropriate goals for intervention

METHODS

Ethical approval was gained for this study from the Trust Research and Development Ethics Committee.

All haemodialysis patients fitting the criteria were invited by letter (see Appendix) to participate in this study. After giving informed consent, all eligible patients were asked to complete a structured questionnaire administered in interview form by an investigator. The questionnaire was administered during a single haemodialysis session.

The questionnaire was also administered to a control group of older adult hospital attenders at a General Geriatric Outpatient clinic during the same period. This is an unselected clinic, usually seeing older adults for one or two visits following an admission. This control group were chosen as non-dialysed hospital attending older adults with co-morbidities not including end stage renal failure. However, their current level of renal function was not known. These patients were given the same written information and allowed time to read it and consider participating. Consenting patients were then asked to complete a structured questionnaire administered in interview form by the same investigator. There was no follow up.

Questionnaire Design

The questionnaire included basic demographic information. There was a section which applied only to dialysis patients, which assessed physical wellbeing and symptoms directly related to dialysis sessions. These questions assessed recognised symptoms of haemodialysis and also asked about patients' perceptions of the effect of haemodialysis on their balance. All patients were questioned

regarding their co-morbidities, including previous fractures, and current medications. Questions covered alcohol and tobacco use, pet (see ref) ownership, all of which are relevant directly and indirectly to falls (Mukamal et al., 2004).

All patients were asked regarding level of physical activity. A standardized tool was not suitable for this purpose, so questions were operator set in order to cover the specific areas of concern. All patients were asked regarding recall of falls over six months and the previous two weeks, and regarding details of their most recent fall and any injuries sustained.

Fear of falling was assessed by the Tinetti Falls Efficacy Scale, based on the definition of this fear as "low perceived self-efficacy at avoiding falls during essential, non-hazardous activities of daily living." It is a well-validated and very useful research tool. It has shown correlation with functional limitation and with balance performance (Chamberlin et al., 2005, Tinetti et al., 1990, Tinetti et al., 1994b). The score is a 10-item rating scale to assess confidence in performing daily activities without falling. Each activity item is rated by the patient; from 1 if they have extreme confidence to 10 as no confidence at all. Participants who report avoiding activities because of fear of falling have higher FES scores, representing lower self-efficacy or confidence. The independent predictors of FES score are usual walking pace (a measure of physical ability), anxiety, and depression. The test-retest reliability score is high at $r=0.71$ (four to seven days) (Tinetti et al., 1990).

Mood was assessed using the Geriatric Depression Scale. This is a well recognized older-adult mood assessment tool which has been validated in older dialysis patients (Giordano et al., 2007). It does not require a license.

For invitation letter, consent form, information sheet and questionnaire, see appendix 4.1.

Inclusion and Exclusion Criteria

Inclusion Criteria: Male or female patients over 60 years of age able to give informed consent and to complete the questionnaire with assistance.

Exclusion Criteria: Patients unable to give informed consent or who have never been independently mobile.

Analysis

Data were analysed using SPSS Version 12.0.1.

Normal distributions were verified using Kolmogorov-Smirnov statistic with a Lilliefors significance level (>50 cases) or the Shapiro-Wilk test (<50 cases) as appropriate (*normal distribution if $p > 0.05$*).

Continuous data were analysed using the Independent t test or ANOVA if normally distributed, and the Mann Whitney U test or Kruskal-Wallis if not normally distributed.

Nominal or categorical data were analysed using the Chi-squared test.

Significance is indicated at * $p < .05$, ** $p < .005$.

RESULTS

A total of 132 subjects were recruited and all fully completed questionnaires. Sixty-six dialysis patients and 66 controls participated.

Sample Demographics

All participants were over sixty years old with a median age of 74 years, (interquartile range 67.0, 79.8). In the dialysis group there were 40 males (60.6%) and 26 females (39.4%), whilst in the control group there were 32 males (48.5%) and 34 females (51.5%). There were more male dialysis patients than female, which is consistent with the national proportions of older dialysis patients (UK Renal Registry, 2004), whereas the control group was almost exactly

evenly split. The differences in gender distribution in each group did not reach significance ($\chi^2 = 1.956$, $p = .162$).

There were no significant differences between the ages, gender distribution, heights, weights or body mass indices (BMIs) of the dialysis and control groups.

Age, height, weight and BMI data are shown below. Both groups had a median BMI just below the upper limits of the World Health Organisation recommended healthy range of 20 - 25.

Table 2.3.i Age, Height, Weight and BMI characteristics of Dialysis Patients and Controls

	Dialysis patients	Controls	Comparative tests
Median Age Years	74 (IQR = 66.7,79)	74 (IQR = 68.0,74.4)	Z = -.711 P = .477
Median height metres	1.68 (IQR = 1.60,1.77)	1.65 (IQR = 1.58,1.65)	Z = -.870 p = .384
Median weight Kg	69.5 (IQR = 58.0, 80.5)	69.5 (IQR = 63.8,82.)	Z = -.257 P = .797
Median BMI Kg.m ²	24.51 (IQR = 21.6,26.9)	24.99 (IQR=22.4,28.2)	Z = -.919 P= .358

Note: Age normally distributed in Gp 1 Lilliefors significance correlation = 0.43, but not in Gp 2 = .100 therefore displayed median and used Mann Whitney u

Height not normally distributed in group 2; Kolmogorov-Smirnov sig Gp1 = .200, Gp 2 = .024 median, used Mann Whitney u

Weight not normally distributed; Kolmogorov-Smirnov sig Gp1 = .200 Gp 2 = .200 given median and analysed with Mann Whitney u

BMI not normally distributed; Kolmogorov-Smirnov sig Gp 1 = .062 Gp 2 = .200 given median and analysed with Mann whitney u

For dialysis patients, median time on dialysis at recruitment was 31.5 months (IQR = 11.8,51.3) (*not normally distributed – Kolmogorov Smirnov = 0.24*).

Social data

There was no significant difference between the smoking patterns of dialysis patients and controls ($\chi^2=1.308$, $p=.502$), or between the median pack years smoked by the smokers in each group ($z = -1.114$, $p = .265$).

Table 2.3.ii Smoking Status of Dialysis Patients and Controls

	Smokers	Non-smokers	Ex smokers	Median pack-years of current smokers
Dialysis	7 (11%)	27 (41%)	32 (48%)	12.09 (IQR = 0 – 37.5)
Controls	10 (15%)	30 (46%)	26 (39%)	8.08 (IQR = 0 –30.0)

More of the control group used alcohol than the dialysis patients ($\chi^2 = 8.49$, $p = .014$). The median number of alcohol units per week was significantly higher in the control group ($z = -3.16$, $p=.002$).

Table 2.3.iii Alcohol use by Dialysis Patients and Controls

	Alcohol users	Never take alcohol	Median alcohol units per week
Dialysis Patients	29 (44%)	37 (56%)	0 (IQR 0-2)
Controls	45 (68%)	21 (32%)	3 (IQR 0-6)

More of the dialysis patients lived alone, and more dialysis patients lived in a house with stairs. The numbers of respondents owning pet cats or dogs was very similar in both groups. This was assessed as mobile pets are a recognised falls risk factor (Stevens et al., 2010).

Table 2.3.iv Household characteristics of Dialysis Patients and Controls

	Dialysis Group	Controls	Comparative tests
Living alone	25 (37.9%)	16 (24.2%)	$\chi^2 = 2.866, p = .09$
Live in a house with stairs	40 (60.6%)	26 (39.4%)	$\chi^2 = .292, p = .589$
Pet cat or dog	17 (25.8%)	18 (27.3%)	$\chi^2 = .039, p = .844$

Physical well-being related to dialysis

Of the 66 dialysis patients, thirty (45.5 %) reported feeling that overall they were generally less fit then before beginning to have haemodialysis treatment. 22 patients (33.3%) perceived themselves as having the same fitness, and 14 patients (21.2%) felt their physical fitness was better since starting haemodialysis. There was no significant relationship between perceived change in fitness and time on haemodialysis.

A majority of 61 (92.4%) of the 66 dialysis patients reported always or usually feeling "fine" during the haemodialysis treatment session, with only 5 patients (7.6%) always or usually feeling unwell during treatment.

30 patients (43.9%) felt worse overall after the haemodialysis treatment session than before the session. 26 (39.4%) said they felt "the same" after a haemodialysis session and only 11(16.7%) patients felt better after haemodialysis.

When asked regarding balance specifically, 35 patients (53%) felt their balance to be the same or better after haemodialysis, and 31 patients (46.9%) felt their balance was worse after haemodialysis. Of those who felt their balance was worse after haemodialysis, 21(68%) felt their balance recovered within one hour, whilst 10 (32%) patients felt their balance took more than 1 hour to recover.

Table 2.3.v Symptoms experienced by Dialysis Patients after Haemodialysis

Symptom	Experienced after haemodialysis N (%)		
	Always	Sometimes	Never
Symptomatic low blood pressure	12 (18.2%)	36 (54.5%)	18 (27.3%)
Blackouts	0	6 (9.1%)	60 (90.9%)
Cramps	7 (10.6%)	36 (54.5%)	23 (34%)
Headache	0	12 (18.2%)	54 (81.8%)
Nausea	1 (1.5%)	13 (19.7%)	52 (78.8%)
Chest pain	0	8 (12.1%)	58 (87.9%)
Itch	17 (25.8%)	17 (25.8%)	32 (48.5%)

Only 2 of 66 patients reported never experiencing any adverse symptoms on haemodialysis. Fifty one percent of patients reported always or sometimes experiencing 2 (20%), 3 (20%) or 4 symptoms (11%).

Sample Co-Morbidity

In the dialysis group, 60 (91%) patients reported at least one co-morbidity, compared to 56 (84.8%) in the non-dialysed group. The median number of co-morbidities reported was 3 (IQR 1-4) in the dialysis group and 2 (IQR 1-3.25) in the control group (p=.136). Both groups reported considerable co-morbidity. In both the dialysis and non-dialysis patients the most common co-morbid conditions reported were the same: arthritis, mobility problems, visual problems and hearing problems.

A higher proportion of the non-dialysis group reported visual problems, arthritis, angina, myocardial infarction, and osteoporosis, whilst the reverse was true for hearing problems mobility problems, diabetes and cancer. However, there were no significant differences between the numbers of subjects reporting each co-

morbidity in each group (see table), with the exception of osteoporosis which was reported by one dialysis patient, compared to 11 controls ($\chi^2 = 11.75$, $p = .008^*$).

Table 2.3.vi Medical conditions in Dialysis Patients and Controls

Patient reported medical condition	Dialysis patients N (%)	Controls N(%)	Significance Testing χ^2
Visual problems	22 (33.3%)	27 (40.9%)	$\chi^2 = .811$, $p = .368$
hearing problems	20 (30.3%)	17 (28.5%)	$\chi^2 = .338$, $p = .561$
Mobility problems	34 (51.5%)	24 (36.4%)	$\chi^2 = 3.075$, $p = .79$
Arthritis	31 (47%)	34 (51.5%)	$\chi^2 = .273$, $p = .601$
Angina	15 (22.7%)	16 (24.2%)	$\chi^2 = 1.032$, $p = .597$
Myocardial infarction	11 (16.7%)	14 (21.2%)	$\chi^2 = 1.398$, $p = .497$
Cerebrovascular disease	9 (13.6%)	9 (13.6%)	$\chi^2 = 1.009$, $p = .604$
Diabetes	16 (24.2%)	9 (13.6%)	$\chi^2 = 3.564$, $p = .168$
Cancer	13 (19.7%)	11 (16.7%)	$\chi^2 = 1.251$, $p = .535$
Osteoporosis	1 (1.5 %)	11 (16.7%)	$\chi^2 = 11.75$, $p = .008^*$

Medications

The majority of the subjects were taking prescribed medication. Only 5/66 (7.6%) of the dialysis patients were taking no prescribed medication, compared to 10/66 (15.2%) of the controls. Twice as many dialysis patients were taking more than four medications, compared with the non-dialysed controls (42 patients, 64%, 21 controls, 32%), ($\chi^2 = 13.39$, $p = <.001$).

Table 2.3.vii Medication use by Dialysis Patients and Controls

	Dialysis n (%)	Controls n (%)	Significance Testing
On medications	61 (92.4%)	56 (84.8%)	$\chi^2 = 1.88$, $p = .170$
No medications	5 (7.6%)	10 (15.2%)	$\chi^2 = 1.88$, $p = .170$
>4 medications	42 (63.6%)	21 (31.8%)	$\chi^2 =$, $p = <0.001$

A significantly higher number of the dialysis patients were prescribed diuretics, sedatives, erythropoietin and calcium supplements, but there was no significant difference in the numbers taking antihypertensive agents, bisphosphonates or steroids. Of those patients taking antihypertensive agents, the dialysis patients took significantly more agents than the control group ($\chi^2 = 21.2$, $p = <0.001$).

Table 2.3.viii Medication categories for Dialysis Patients and Controls

Significance: * $p < .05$, ** $p < .005$

Medication Type	Dialysis N (%)	Controls N (%)	Significance Testing
Antihypertensive(s)	37 (56.1%)	26 (39.4%)	$\chi^2 = 5.02$, $p = 0.81$
Diuretic(s)	5 (7.6%)	16 (24.2%)	$\chi^2 = 11.1$, $p = <.001$ **
Sedative(s)	16 (24.2%)	5 (7.6%)	$\chi^2 = 6.85$, $p = .009$ *

Erythropoietin	45 (68.2%)	1 (1.5%)	$\chi^2 = 64.59,$ $p = <.001$ **
Bisphosphonate	1 (1.5%)	7 (10.6%)	$\chi^2 = 4.79,$ $p = 0.29$
Calcium supplement(s)	35 (53%)	10 (15.2%)	$\chi^2 = 21.07,$ $p = <.001$ **
Steroid(s)	6 (9.1%)	5 (7.6%)	$\chi^2 = .099,$ $p = 0.753$

Figure 2.3.i Comparison of Number of Antihypertensives

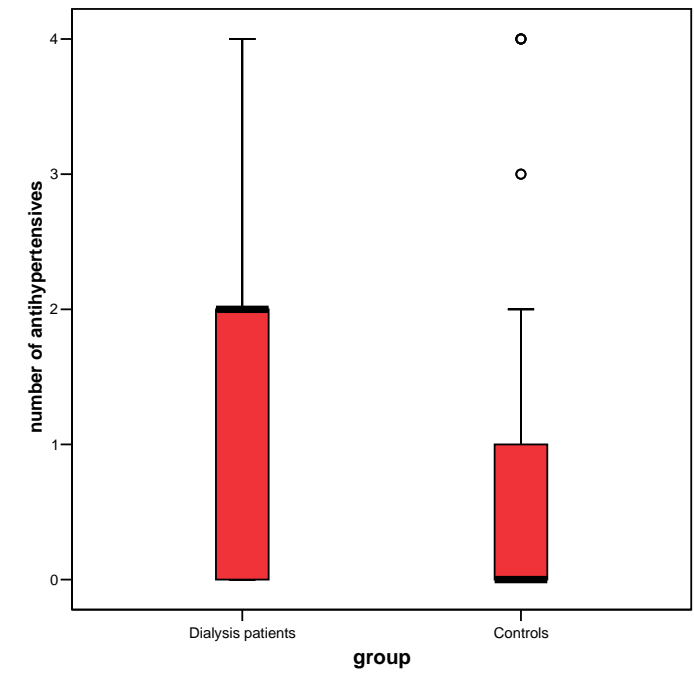
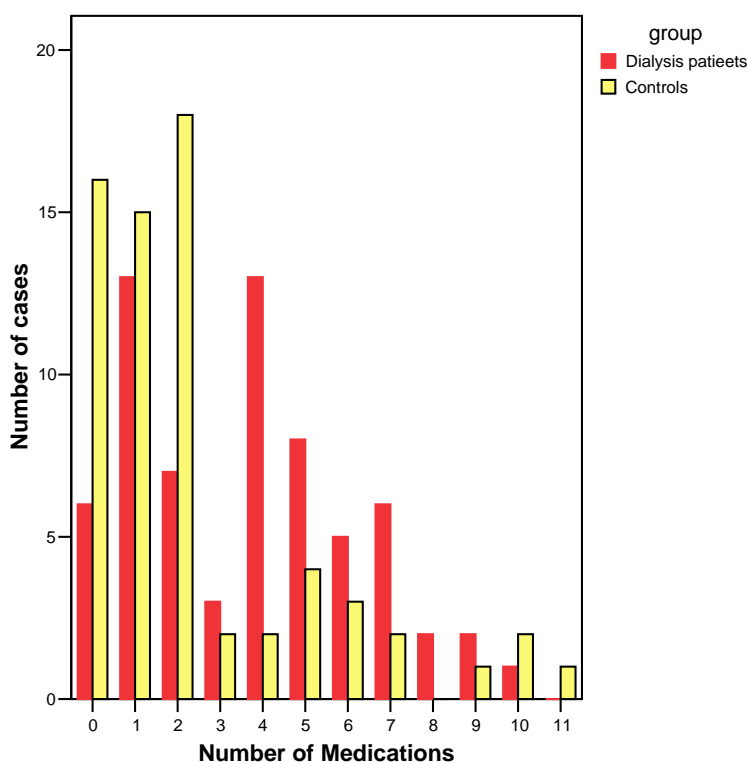


Figure 2.3.ii Comparison of total number of medications



Mobility Aids

Dialysis patients were more reliant on mobility aids than the control group, and used higher-level aids. There was a significant relationship between maintenance haemodialysis and use of any mobility aid ($\chi^2 = 13.768$, $p = .003^{**}$).

Table 2.3.ix Mobility Aids used by Dialysis Patients and Controls

	No aid N(%)	Aid N(%)		
		Stick	Frame	Wheelchair
Dialysis patients	28 (42.4%)	20 (30.3%)	2 (3%)	16 (24.2%)
Controls	45 (68.2%)	15 (22.7%)	3 (4.5%)	2 (4.5%)

Unaided Activity Level

Dialysis patients report more limitation in most of the unassisted activities of daily living and mobility levels. This was significant for every activity except walking ten yards on the flat and light intensity activity (examples given as reading or knitting). The dialysis group also engaged in significantly less physical affection or

lovemaking compared to the control group ($p < .001$), used here as a marker for risk of social isolation.

Table 2.3.x Unaided Activity Level in Dialysis Patients and Controls

Activity	Unassisted ability N (%)		Comparative tests Significance: * $p < .05$, ** $p < .005$
	Dialysis Pts	Controls	
Take a bath	53 (80.3%)	64 (97.0%)	$\chi^2 = 9.10$, $p = .003$ **
Bend, kneel or stoop	28 (42.4%)	53 (80.3%)	$\chi^2 = 19.97$, $p < 0.001$ **
Do own grocery shopping	34 (51.5%)	48 (72.7%)	$\chi^2 = 6.31$, $p = 0.012^*$
Do own cooking	38 (57.6%)	59 (89.3%)	$\chi^2 = 17.14$, $p = < .001$ **
Walk 10 yards on the flat	59 (89.4%)	63 (95.5%)	$\chi^2 = 1.731$, $p = .188$
Walk 100 yards on flat	39 (59.1%)	55 (83.3%)	$\chi^2 = 9.46$, $p = .002$ **
Walk half a mile or more	17 (25.8%)	38 (57.6%)	$\chi^2 = 13.745$, $p = .002$ **
Walk for 20 minutes on the flat	16 (24.2%)	36 (54.5%)	$\chi^2 = 12.69$, $p = < .001$ **
Climb a flight of stairs	42 (63.6%)	55 (83.3%)	$\chi^2 = 6.571$, $p = .010$ *
Climb several flights of stairs	20 (30.3%)	35 (53.0%)	$\chi^2 = 7.013$, $p = .008$ *
Exercise or sport as a hobby	14 (21.2%)	25 (37.9%)	$\chi^2 = 4.404$, $p = .036$ *
Light intensity activity	64 (97%)	64 (97%)	$\chi^2 = 00$, $p = 1.00$
Moderate activity	27 (40.9%)	46 (69.7%)	$\chi^2 = 11.064$, $p = < .001$ **
Vigorous activity	7 (10.6%)	16 (24.2%)	$\chi^2 = 4.265$, $p = .039$ *
Physical affection/lovemaking	7 (10.6%)	23 (34.8%)	$\chi^2 = 11.043$, $p = < .001$ **

Dependency/Self Care

Subjects were categorised according to whether or not their level of reported activity equipped them for independent self-caring or not. For the purposes of this analysis, subjects reporting ability to bathe themselves, put themselves to bed, prepare a simple meal and mobilise 10 yards were assessed as able to self care, whilst those unable to achieve one or more of these were considered likely to be unable to self care. The table 2.3.xi below shows that fewer dialysis patients were able to self-care than the controls. This reached statistical significance ($\chi^2 = 22.22$, $p < .001$).

Table 2.3.xi Activities of Basic Self Care in Dialysis Patients and Controls

	Bathe and prepare self for bed, mobilise 10 yards and prepare a simple meal	
	Able	Unable
Dialysis Patients	22 (33.3%)	44 (66.6%)
Controls	49 (74.2%)	17 (25.7%)

Holidays

As shown in table 2.3.xii, fewer dialysis patients report taking holidays than the control group, with only 26 (39.4%) dialysis patients taking any holidays compared to 43 (65.2%) of the control group. This reached statistical significance ($\chi^2 = 8.77$, $p = .003$). Of those taking holidays, the dialysis group also took significantly fewer than the dialysis patients ($\chi^2 = 19.38$, $p = .013$).

Table 2.3.xii Holidays in Dialysis Patients and Controls

Number of holidays taken in the previous year									
	0	1	2	3	4	6	7	10	20
Dialysis Patients	38 (57.5%)	12 (18%)	5 (7.5%)	4 (6%)	3 (4.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)
Controls	23 (34.8%)	10 (15%)	23 (34.8%)	6 (9%)	2 (3%)	2 (3%)	0	0	0

Exercise/Non-exercise Physical Activity

The dialysis patient group reported exercising less frequently than the control group. Around half of each group reported never undertaking physical activity sessions (36 dialysis patients, 30 controls). This was not significant.

Dialysis patients reported less frequent exercising and this trend was significant ($\chi^2=13.65$, $p=.008$).

Table 2.3.xiii Physical Activity Level in Dialysis Patients and Controls

	Physical activity sessions				
	Never	Less than once a month	Less than weekly	At least once per week	Five times per week
Dialysis Patients	36 (54.5%)	21 (31.8%)	1 (1.5%)	7 (10.6%)	1 (1.5%)
Controls	30 (45.5%)	11 (16.7%)	11 (16.7%)	12 (18.2%)	2 (3%)

Falls

The control groups reported more falls than the dialysis patients in the 6 months prior to the questionnaire. 24 (36.4%) of the control group reported falling (giving an approximate falls rate of 0.72 falls per person per year), compared to 21(31.8%) of the dialysis patients (approximate falls rate of 0.63 falls per person per year). In both groups a similar number of patients reported worries about falling and equal numbers reported limiting their activities due to worries about falling, but this did not reach statistical significance.

Table 2.3.xiv Reported Falls in Dialysis Patients and Controls

	Dialysis Patients N (%)	Controls N (%)	Comparative Tests
Reported any Falls (6 months)	21 (31.8%)	24 (36.4%)	P = .582 (chi squared)

Worry about falling	13 (19.7%)	16 (24.2%)	P = .528
Limit activity	20 (30.3%)	20 (30.3%)	P = 1.0

In the preceding two weeks, more dialysis patients reported falls, 8 falls versus 5 falls in the control group, suggesting falls rates of 2.45 falls per person per year in the dialysis patients and 1.96 falls per person per year in the control group. However, there were no statistical differences between groups.

Of the dialysis patients reporting falls, 15% had fallen after a dialysis session, 85% on a non-dialysis day.

Recurrent Falls

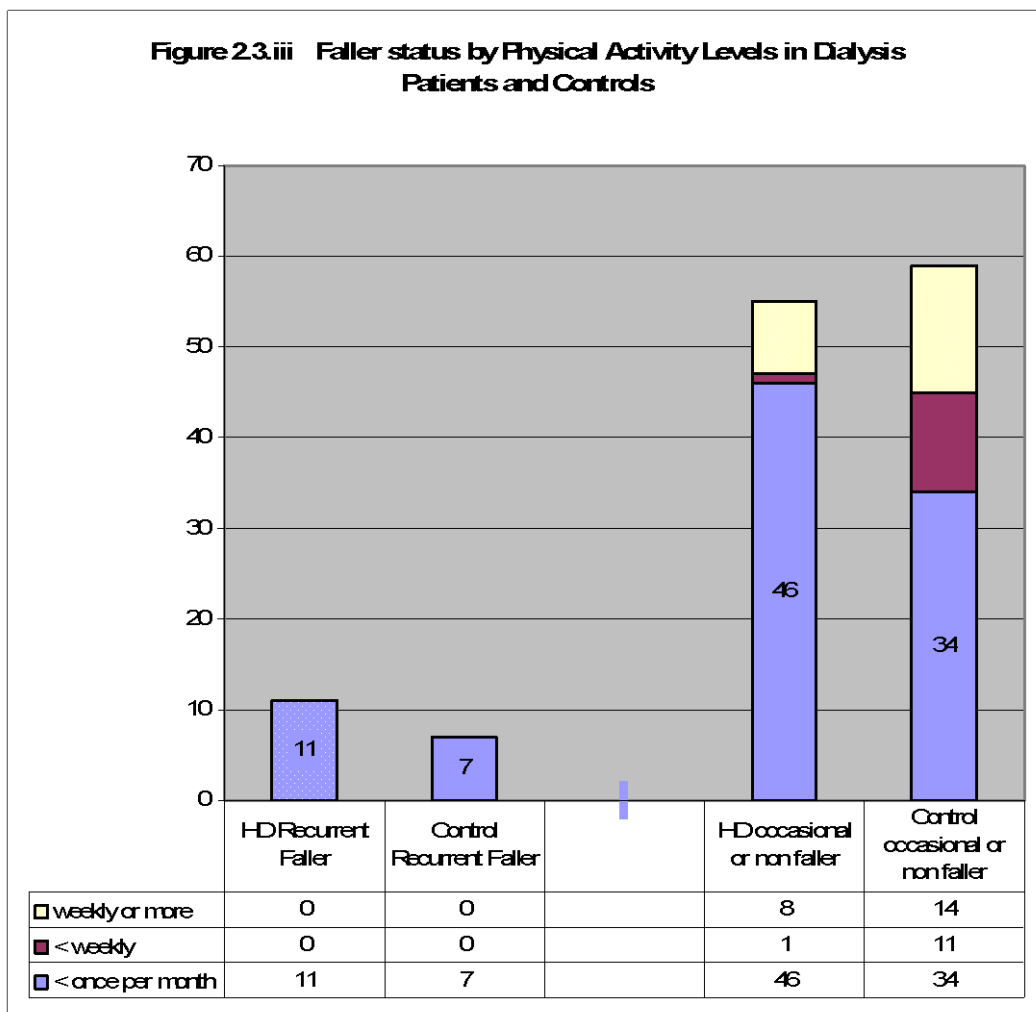
A subject reporting falls twice or more in the sixth month period was classed as a "recurrent faller". More dialysis patients than controls were recurrent fallers, but this was not significant either as a proportion of the whole group or of fallers (p= .310 and p=.113 respectively).

Table 2.3.xv Recurrent Falls in Dialysis Patients and Controls

	Recurrent faller	Non faller or occasional	Proportion of all fallers having recurrent falls
Dialysis patients	11 (17%)	55 (83%)	11/21 (52%)
Controls	7 (11%)	59 (89%)	7/24 (29%)

Activity Levels

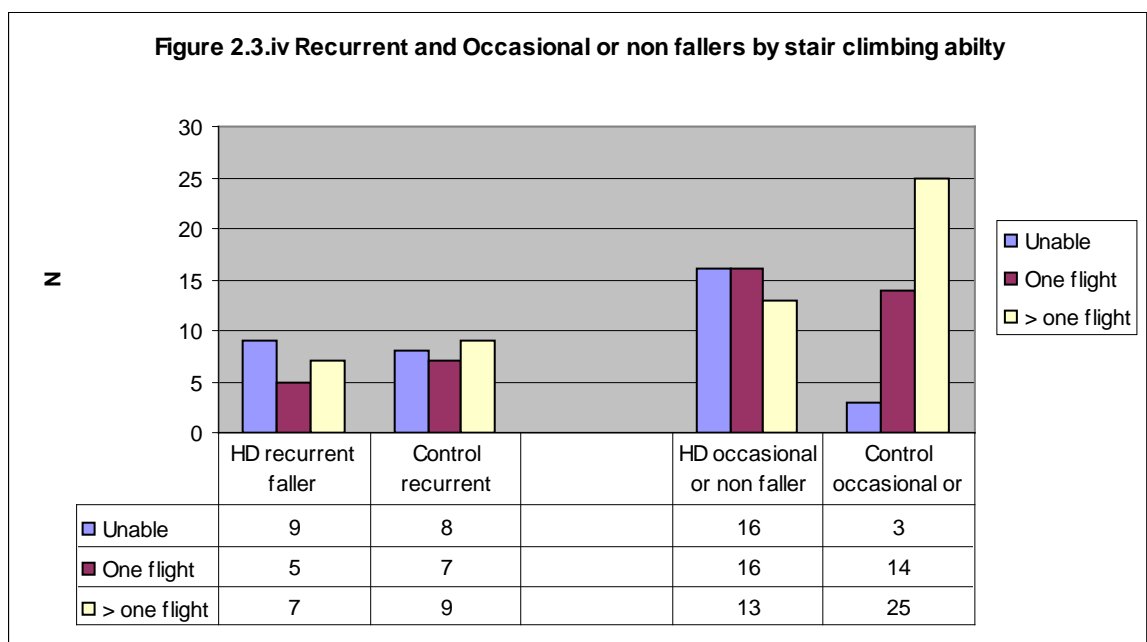
Subjects were asked how often they did “physical activity or exercise for at least half an hour that makes you feel out of breath or warmer?”. In the control group there was a significant association between lower number of exercise sessions and faller status ($\chi^2 = 10.12$, $p = .038$). The relationship was maintained but not to significance between exercise sessions and recurrent falling ($\chi^2 = 9.397$, $p = .052$). There was no significant relationship between exercise sessions and faller status or recurrent falls in the dialysis patients. Despite the relationship not reaching significance, it was noted that in both groups all of the recurrent fallers reported physical activity session less than once a month.



Stair climbing

Subjects were divided into three activity levels by ability to stair climb; 1) unable to climb stairs 2) able to climb one flight of stairs only 3) able to climb more than one flight.

There was a significant inverse relationship between stair climbing and recurrent faller status in the controls, with 6 of the 7 recurrent fallers unable to stair climb ($\chi^2 = 26.998, p=000$), but this relationship did not exist in the dialysis group ($\chi^2 = 3.014, p = .222$).



Dependency/Self Care

Ability to self care was significantly associated with faller status in the dialysis patients but not the controls ($p=.025, p=.632$). In both groups, being a recurrent faller was significantly associated with inability to self care ($p=.010$ in the dialysis patients, $p=.045$ in the controls (T test)).

Table 2.3.xvi Ability to self-care and Faller Status in Dialysis Patients and Controls

		Faller	Non-faller
Dialysis Patients	Able to self care	3 (5%)	19 (29%)
	Unable	18 (27%)	26 (39%)
Controls	Able to self care	17 (24%)	32 (48%)
	Unable	7 (3%)	10 (15%)

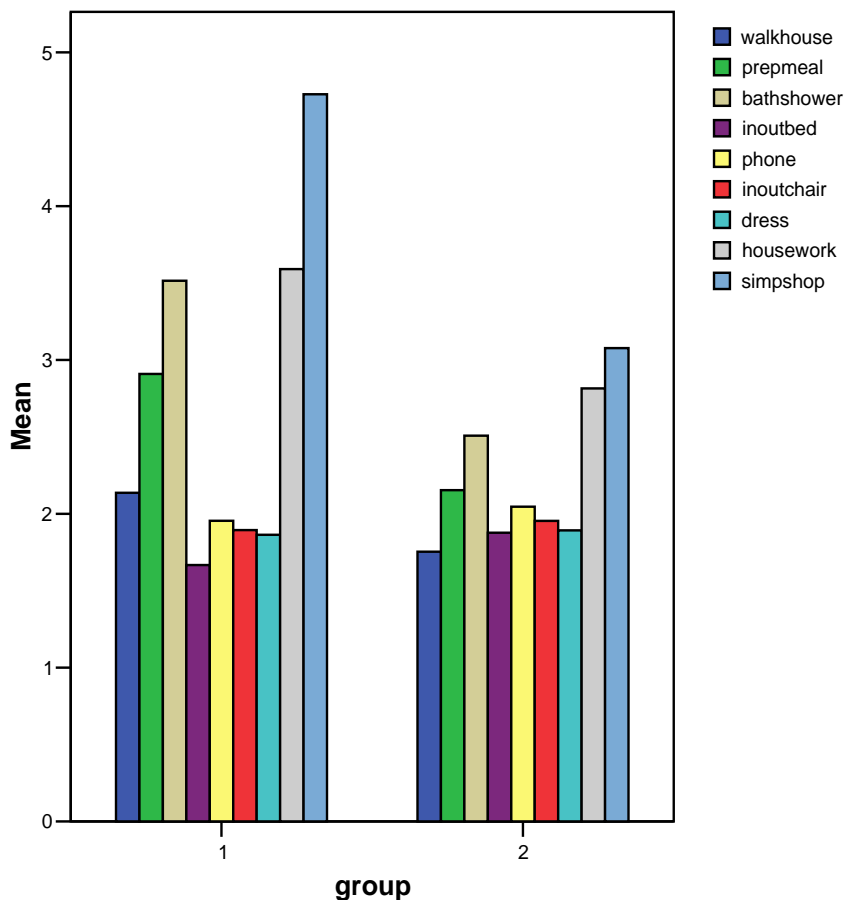
		Recurrent Faller	Non-faller occasional faller
Dialysis Patients	Able to self care	0	22 (33%)
	Unable	11 (16%)	33 (50%)
Controls	Able to self care	3 (4.5%)	46 (35%)
	Unable	4 (6%)	13 (20%)

Fear of falling

The mean fear number for the dialysis patients was 26.89 (range 10 – 100, higher scores indicating more concern about falling) and for the control group 22.2 (range 10 – 78) with no significant difference between the means (p 0.197).

Figure 2.3.v. Falls Efficacy Scores for Dialysis Patients and Controls

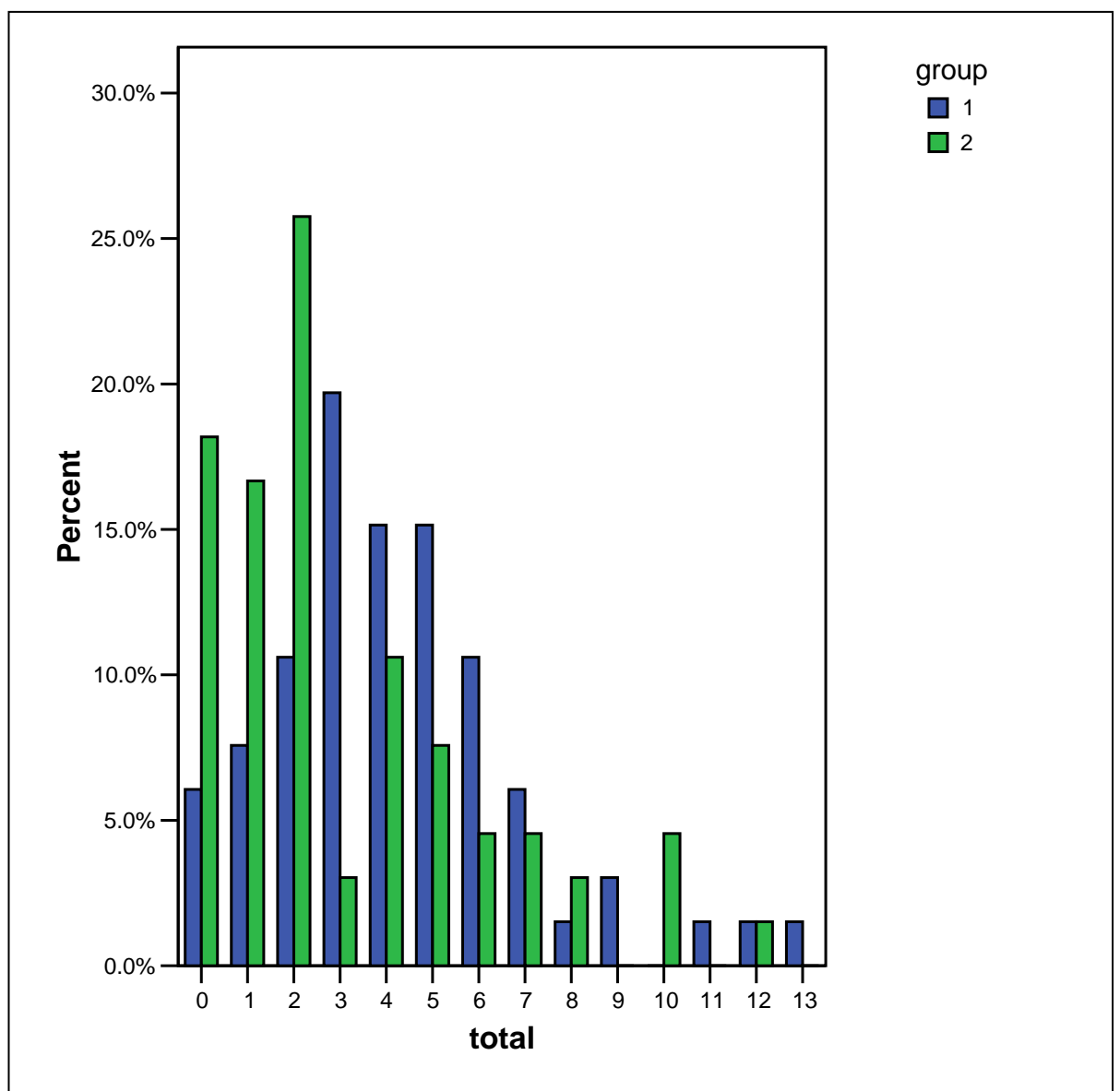
* Group 1 Dialysis Patients, Group 2 controls



Depression

The dialysis patients scored higher on the GDS than the control group (mean GDS 4.24 compared to 3.05, $p = .016$). The GDS is validated for use with a cut off of 5 or more indicating clinical depression. Of the dialysis patients, 27 (41%) scored 5 or more, and of the controls 17 (26%) scored 5 or more ($p=0.05$).

Figure 2.3.vi Comparison of distribution of GDS results



* Group 1 Dialysis Patients, Group 2 controls

DISCUSSION

Main Findings

The patients and controls were well matched for age, height, weight and BMI characteristics. Smoking patterns and household characteristics were also well matched.

Both groups reported considerable co-morbidity and there were no significant differences between the number of subjects reporting each co-morbidity between the dialysis patients and the controls, with the exception of osteoporosis 16.7% in the controls vs 1.5% in the dialysis group ($p=.008$), suggesting the controls may have been selected from generalist clinics with special interest or sessions in osteoporosis. This is likely to have implications for other findings, discussed below. Co morbidity is a determinant of outcome in patients on dialysis and has negative and statistically significant correlation with parameters of health related quality of life (Stojanovic et al., 2006).

There were significant differences in medication use with twice as many dialysis patients taking more than four medications. Whilst dialysis patients were prescribed diuretics, sedatives, erythropoietin and calcium supplements, there was no significant difference in the numbers taking antihypertensive agents, bisphosphonates or steroids. Dialysis patients took significantly more agents than the control group which is of interest as antihypertensive agents and the use of more than four prescription medications are implicated in falls risk (Tinetti et al., 1994a).

Dialysis patients were more reliant on mobility aids than the control group, and used higher-level aids. This is interesting as use of a mobility aid predicts poorer

performance in the Timed “up and go” test which may be used to predict falls risk(Kristensen et al., 2009).

The unaided activity abilities of dialysis patients and controls were significantly different. If unassisted, dialysis patients were significantly less likely to be able to take a bath, cook a meal or do their own shopping. In terms of mobility, dialysis patients reported being less able to bend, kneel or stoop, walk 100 yards on the flat, walk half a mile or more or for 20 minutes on the flat. Dialysis patients were significantly more limited in terms of stair climbing and less able to climb one or more flights of stairs. Dialysis patients were significantly less likely to undertake exercise or sport as a hobby or engage in moderate or vigorous activity. Fewer dialysis patients than controls report taking holidays. Finally, dialysis patients were less able to partake in physical affection/lovmaking activities. Many studies have reported low levels of sexual activity and libido in patients with ESRD (Fryckstedt and Hylander, 2008). Peng *et al* found that sexual dysfunction is frequent in the female haemodialysis population and is strongly associated with increasing age, and depression and poorer quality of life (Peng et al., 2005).

On the basis of ability to bathe themselves, put themselves to bed, prepare a simple meal and mobilise 10 yards, significantly fewer dialysis patients were considered potentially able to self care than controls. This has implications not only for patients’ quality of life but also for carers and social services.

Regarding depression, the mean GDS score of dialysis patients was significantly higher than in the control group and a greater proportion of the dialysis patients reported a score indicating clinical depression. This is supported by findings from other studies and is important because interventions such as exercise have been shown to reduce depression in this patient group (Kouidi et al., 2009).

In regard to falls, there were no statistically significant differences in either the six-month or two-week self-reported falls rate. The control group reported an approximate six-month falls rate of 0.72 falls per person per year, compared to 0.63 falls per person per year in the dialysis patients. In the dialysis group, this is a lower falls rate than in other literature e.g. Cook et al report a falls rate of 1.6 falls per person per year in maintenance dialysis patients over 65 years old (Cook et al., 2006). The control group falls rates is comparable with previous general older adult falls rates. Whilst the six month falls history suggested the control group were falling more frequently, in the preceding two weeks, more dialysis patients reported falls, suggesting falls rates of 2.45 falls per person per year in the dialysis patients and 1.96 falls per person per year in the control group. The reporting of a higher number of more recent falls in dialysis patients suggests a possible recall bias. This would certainly be possible in the dialysis group who are prone to small vessel cerebrovascular disease, which can lead to recall problems. Additionally, the hospital attending controls reported having had conditions that may be associated with falls. This is suggested by the high proportion of osteoporosis sufferers. An alternative control group, or the addition of another control group who were not hospital attenders, may have avoided this problem.

In some studies, the difference in the risk profile between one-time and recurrent fallers is emphasised (Campbell et al., 1981, Nevitt et al., 1989). More dialysis patients than controls were recurrent fallers. However, again this difference was not significant.

Of interest, amongst the dialysis patients reporting falls, only 15% had fallen after a dialysis session. This does not rule out the possibility that dialysis has an acute effect on postural stability (see "The effect of a single haemodialysis session on functional mobility and physical impairments in older maintenance dialysis

patients in Section 2.2). However, falls are also occurring in the interdialytic period.

In both groups, a similar number of patients reported worries about falling (not scale assessed) and equal numbers reported limiting their activities due to worries about falling. There were no statistical differences between groups. The Falls Efficacy Scale scores supported this finding. The mean Fear Number for the dialysis patients was 26.89 (range 10 – 100) and for the control group 22.2 (range 10 – 78). There was no significant difference between the means (p 0.197). This tallies with the lack of divergence in falls rate seen in the two groups.

Some falls and function studies categorise subjects by ability to stair climb; i.e. unable to climb stairs/ able to climb one flight of stairs only/ able to climb more than one flight. However, in these groups, this did not yield any significant relationships. However, inability to self-care was associated with faller status in the dialysis patients but not the controls. In both groups, being a recurrent faller was significantly associated with inability to self-care. This is an interesting finding that may allow rapid identification of those who would benefit most from falls prevention strategies.

The association found in the control group between lower number of exercise sessions and more frequent faller status might be expected, as individuals exercising regularly should reap a falls protection benefit{Wolf, 2003 #556}. The lack of this relationship in the dialysis patients may actually reflect the more limited exercise done by this group, rather than its lack of protective effect.

As discussed in section 1.6.5, there are few studies focussing on falls in older maintenance dialysis patients and in fact at the start of this work in 2003 there were none. During the course of this thesis, five such studies were published.

In 2003, Roberts *et al* hypothesised that older adults on haemodialysis may be vulnerable to falls due to interdialytic postural hypotension. They collected self-reported falls histories, self-reported history of symptomatic hypotension, and pre and post haemodialysis blood pressure readings from 47 haemodialysis patients over 70. Whilst causality could not be assumed, these patients reported high rates of interdialytic hypotensive symptoms, recalled falls in the previous year and suffered significant post dialytic postural hypotension (Roberts et al., 2003).

In 2005 Cook *et al* undertook a cross sectional interview based study to determine one year falls prevalence in this group and found it to be 27% (Cook and Jassal, 2005). In the same year, Desmet *et al* undertook an eight week prospective study of falls incidence in this group and found it to be 12% (Desmet et al., 2005).

In 2006, the same group lead by Cook (Cook et al., 2006) undertook a prospective cohort study to examine falls rate and falls risk factors in older maintenance haemodialysis patients and found a falls rate of 1.6 falls/patient-year. Risk factors included age co morbidity, mean pre dialysis systolic blood pressure and history of falls.

Most recently, and most alarmingly, in 2008 Li *et al* (Li et al., 2008) published the results of prospective, cohort study of 162 haemodialysis patients aged over 65 years. Patients were followed biweekly, and falls occurring within the first year were recorded. Outcome data were collected until death, study end, transplantation or transfer to another dialysis centre. Survival was worse amongst fallers compared to non-fallers (HR 2.13, 95% CI 1.32-3.45; P = 0.002) even after adjustment for age, dialysis vintage, co morbidity and laboratory variables. They concluded that the occurrence of more than one fall was associated with an

independent increased risk of death. This brings new impetus to the search for effective rehabilitation and falls reduction studies in this patient group.

Strengths and Limitations of the Study

This is an original study offering the first data of its kind in the UK. It is the first and only work to attempt to establish the functional fitness and falls profile of older adult haemodialysis patients compared with local non-dialysed older adults.

These findings of this study are supported by the work of other authors and are below set in the context of the current literature.

It is important because, whilst each disability aspect brings its own concerns, it is now recognised that self reported impairment in physical functioning is a predictor of mortality in dialysis patients (Curtin et al., 1999, DeOreo, 1997). At a local level, this data allows recognition of patients' perceptions of their functional limitations and falls risk, and helps to define outstanding clinical and holistic needs for this patient group.

This study aimed to provide a holistic picture of many aspects of dialysis patients lives and provide a comparison with local non-uraemic older adults and has been successful in achieving this. However, the author recognises the study limitations.

The high rate of certain co morbidities within the control group suggests that this group may not have been as widely representative of the non-uraemic population as intended. It was elected to interview older adults attending a general outpatient clinic (rather than non hospital attenders) to remove some of the confounding influence of dialysis patients being "semi-institutionalised" as regular hospital site attenders. However, it seems likely that a hospital-attending group may have over represented elders suffering with conditions leading to immobility or instability, as these are common geriatric problems. This would explain the

higher prevalence of osteoporosis in this group. It may also explain the greater six-month falls prevalence in this group. However, another possibility is that because the control group are more mobile, they have greater opportunity to suffer falls. If this study were repeated, the author would suggest matching cases and controls by mobility levels, or selecting two control groups; one of non-hospital attending elders with no hospital-attending geriatric pathology, and another of older adults with established CKD not reaching ESRD. This would allow a more useful comparison between non-uraemic general population, uraemic hospital attenders and dialysis patients.

On considering collected data, it seems that some of the scales used within the questionnaire may not have been the optimal choice. This has partly been revealed as the literature evolves and certain tests are favoured, making it more difficult to set in the context of current knowledge. For example it may have been easier to compare this data with other work if the SF-36 had been used to assess functional health and well being from the patient's point of view. The SF-36 is a practical, reliable, and valid measure of physical and mental health that can be completed in five to ten minutes. However, it requires a licence and has a cost implication that would have been beyond the scope of the very limited funding available for this study.

Recently the Falling Efficacy Scale (FES) has been compared with the Activities-Specific Balance Confidence Scale (ABC) and the Geriatric Fear of Falling Measurement (GFFM) and all three scales demonstrated strong internal consistency reliability (Huang and Wang, 2009). However, the GFFM had stronger associations with physical and psychosocial functioning and may be more appropriate for studies focused on improving all aspects of fear of falling, however this test was not developed at the time of the study (Huang, 2006).

Construction of the questionnaire could have been much improved.

In retrospect, attempting to describe functional ability and limitations as well as falls pattern probably meant that neither construct could be fully explored in a valid and reliable way. It is likely that in attempting to create a holistic picture, this study tried to explore too many aspects of patients' lives. More focussed study would be more valuable.

The content of the questionnaire was, as far as possible, based on previously validated questionnaires. However, used in combination, revalidation was required. The questionnaire was not adequately piloted and nor was construct, content or criterion validity tested. Content validity would have been the most difficult aspect of this questionnaire to assess as the scope was too wide ranging to define and distil the construct with adequate clarity. Criterion validity (whether the questionnaire truly measured functional ability and measured falls pattern and fear of falling) could have been checked by measuring against a benchmark or previously validated test. In this case, administering each validated part of the whole separately and ensuring that the answers given were the same in a pilot group. In retrospect, the overly broad scope threatened construct validity as attempting to combine too many ideas is likely to have allowed multiple possible confounding variables. It is necessary to be very cautious when interpreting the collected data as multiple possible confounding factors limit the ability to make conclusions of causality or direct association e.g. activity level may confound the relationship between dialysis and falls. Testing a much narrower set of ideas would have allowed better construct validity. In other words, this questionnaire set out to measure, amongst other things, functional ability but may instead have been measuring other well-being aspects such as anxiety or stress. It would have been preferable to reduce the scope of the study and improve validity.

The questionnaire was administered by a single investigator, which has advantages and disadvantages in terms of bias. The advantages are that the

same questions are likely to have been asked in the same way, with the same interpretation of the answers given i.e. improving consistency. However, there is the risk of introducing investigator bias. It would have been preferable to blind the investigator to whether or not patients were dialysis patients or non-dialysis patients, but was not possible with this questionnaire design. Administering the test in different methods e.g. face to face with another researcher or over the telephone might have supported reliability.

The author recognises that all of these limitations increase the risk of both type I and type II errors having been made. In type I errors, the null hypothesis is rejected when it is in fact true – for example if dialysis patients were found to have fallen less frequently than controls when in fact they actually fall more frequently but simply do not recall this. Type II errors consist of the null hypothesis is being accepted despite being false. Improving the study design, as discussed above, could reduce both of these error types and improve the quality of the data collected.

CONCLUSION

Compared to age and gender matched controls, with similar social profile and co-morbidity burden, older maintenance haemodialysis patients in Nottingham are significantly less physically active, partake in fewer leisure activities, take fewer holidays and have significantly lower mood. Dialysis patients use more and higher levels of mobility aid. No significant difference of falls profile between older haemodialysis patients and controls was shown. The need for a more holistic approach to patient care is identified.

Implications for Clinicians, Services and Future Research

This data obtained show that older adult maintenance haemodialysis patients in Nottingham report a reduced physical fitness and functioning compared to non dialysed controls, but that this is part of a wider and multilevel set of impairments and reductions in quality of life. Each aspect is important in its own right, but also because studies show that self reported impairments in physical functioning are a predictor for mortality and morbidity in this patient group. These data provide support to state a case of need within the Nottingham Renal Unit for a more holistic approach encompassing all aspects of patients well being, which may include exercise interventions.

2.4 Haemodialysis Unit Staff Perceptions of Physical Fitness, Exercise Benefits, and Current Exercise Encouragement Practices for Older Patients

BACKGROUND

The questionnaire study presented in Section 2.3 identified higher levels of inactivity, immobility, and dependency amongst older haemodialysis patients than in the older adult population attending general medical outpatient at the same hospital in Nottingham. The dialysis patients also participated in fewer active leisure and pleasure activities. Low levels of physical functioning and physical activity are a consistent finding in other dialysis patient group studies, both nationally and internationally. It is widely documented that exercise training of these patients does result in improvements in physical functioning (Painter, 2003, Painter and Johansen, 1999). Although data are thus far only available from formal exercise programs, the nephrology community is now promoting likely benefit from all exercise encouragement practices (Cheema and Singh, 2005). It is recognised that brief interventions of verbal encouragement and education show positive benefit, both in promoting exercise and in other areas of healthy lifestyle promotion (Lancaster and Stead, 2004, Lawlor and Hanratty, 2001).

This is supported by specific recommendations in the 2004 National Service Framework Part One: Dialysis and Transplantation (DOH, 2004b). Standard 1,A states "Patients [approaching end stage renal failure] will need information on the nature and consequences of renal failure including advice on nutrition, anaemia, hypertension and lipid control, bone disease, **exercise** and smoking cessation."

Standard 2, in Preparation and Choice states [Interventions for those who are likely to progress to RRT may include] "advice on lifestyle changes such as smoking cessation and **exercise**. **Older patients, in particular, may benefit**

from therapy/advice to maintain their functional abilities and promote active lives”.

In spite of this, interventions to improve physical functioning and activity levels are still not a routine part of UK renal replacement therapy practice. On the UK Renal Association website, only 3 of the 76 UK dialysis hubs present exercise interventions as part of their unit program. Locally, in Nottingham, exercise interventions are not resourced. Additionally, education on the benefits of physical activity and training in skills for recommending, motivating, and encouraging patients to increase their levels of physical fitness are still not part of the routine programs for renal physicians or nurses. The topics of physical fitness and exercise do not appear on the syllabus for trainee renal physicians as described in the two nephrology training curricula offered by the UK Joint Royal College of Post Graduate Training Board. Nurse training programs are lead locally. Nottingham School of Nursing runs the Renal Program, a training course for nurses employed by the Renal Unit. In the Renal Program, a single session led by a physiotherapist has been introduced on a trial basis as of January 2009. However, as yet only two such sessions have been delivered and this is reliant on the enthusiasm of the individual staff involved rather than yet being recognised as a routine requirement of renal training.

Similar concerns have been raised in other programs. In the ESRD Network of Texas, USA, Curtin *et al* reported rehabilitation activities in 169 dialysis facilities (Curtin et al., 2002). Exercise related rehabilitation activities were infrequently practiced, with only 21% of the units offering any provision. A survey of US nephrologists reported that only 38% “almost always” or “often” assess patient activity levels and provide counselling to inactive patients to increase activity (Johansen et al., 2003c) The reason for this lack of focussed exercise encouragement in renal programs is unclear.

In the USA, as part of the Renal Exercise Demonstration Project, Painter *et al.* surveyed dialysis patient care staff with the stated goals to (a) determine their level of knowledge and perceived skills for assessing physical functioning and encouraging exercise, (b) assess their attitudes and practice related to assessment of physical functioning and exercise counselling for their patients and (c) identify factors that predict encouragement of exercise by staff (Painter *et al.*, 2004). In Toronto, Canada, Kontos *et al.* used focus groups to examine factors influencing exercise participation by older adults requiring chronic haemodialysis (Kontos *et al.*, 2007).

This chapter reports the first UK data exploring NHS Haemodialysis Unit staff perceptions of exercise encouragement practices, examines these with corresponding international data, and informs possible interventional approaches. Particularly, this chapter explores staff understanding, attitudes, perceptions and beliefs, which may act either as gateways or as barriers to the introduction of exercise encouragement practices within the Nottingham City Hospital Haemodialysis Unit and across the UK.

METHODS

A questionnaire was developed, adapting the core questions used in Determinants of Exercise Encouragement Practices in Haemodialysis Staff, as above (Painter *et al.*, 2004) (See Appendix 6.5). This questionnaire was cross sectional and qualitative in design. The questionnaire was adapted from the original format to the specific concerns of this thesis and to the colloquialisms of UK staff. There was no copyright restriction on this questionnaire format. It was not an externally validated questionnaire, thus adaptations could be made. No validated questionnaires exist to explore this topic.

The questions were intended to assess staff perceptions of their own awareness and acceptance of the benefits of considering physical functioning and physical fitness and encouraging exercise for their haemodialysis patients. Additionally they aimed to assess staff attitudes towards their own role and responsibility in this and the patient factors important in promoting these themes. Finally, questions were devised to discover staff opinions on factors such as time, opportunity, skills, training, current practice and program planning.

34 "question statements" were selected covering six subtopics; -

1. Appreciation of known exercise benefits for patients.
2. Perceptions of patient factors
3. Current practice of exercise encouragement of the haemodialysis unit
4. Role, responsibility, time and opportunity
5. Opinion on suitable encouragement methods and exercise programs
6. Skills and training in methods of encouraging exercise.

Care was taken to keep statements short and avoid profession specific technical terms. Groupings were loose as there is some overlap between the themes in each subtopic. Grouped items were distributed at random through the survey. Additionally, an item was designed to identify those clinicians already practicing exercise encouragement behaviours, and thus to try and define identifying characteristics of this group.

To simplify completion, all responses were on a Likert –type scale with 5 possible responses (i.e. strongly agree, agree, don't know, disagree, strongly disagree).

A free text response box was included to invite comments.

The questionnaire was piloted on an informal basis to six representative respondents (2 doctors, 4 nurses) to ensure that the questions were easily

interpretable and that time taken to complete the survey was less than five minutes. There were no concerns or revisions made during this informal pilot.

A multidisciplinary team including nurses, Consultants and Registrars in renal medicine and dieticians, cares for the patients in the Haemodialysis Unit at Nottingham City Hospital. The questionnaire was offered to all of the of haemodialysis staff with direct and regular patient contact. The investigator presented the questionnaire to staff members during several shifts, with the pattern of shifts selected designed to allow paper copies to be given to the vast majority of staff (69/75). Staff filled in the questionnaire during rest periods. Those staff members not responding during this cycle were left copies of the survey in the communal areas and pigeonholes. Questionnaires were emailed to those staff not available on the initial visits. The questionnaire could be completed and returned electronically.

As the purpose of the survey was to inform service development, and as it surveyed only staff members, we were advised that formal ethical approval was not required for this study.

Statistical Analysis

Frequencies of responses to each item were determined. All statistical analysis was completed using SPSS version 12.0.1.

Questions were grouped by category and trends visualised through observation and graphical interpretation. Responses were considered as ordered-categorical data rather than interval data.

Comments provided in free text were used to highlight points made in the discussion.

RESULTS

Of a possible 75 respondents, 54 completed surveys were obtained, representing a 73% response rate. Four replies were received electronically.

Respondent Characteristics

Table 2.4.i Respondent Characteristics by Profession

Profession	Possible respondents	Number of Respondents	Response rate
Doctor	16	15	94%
Nurse	54	34	63%
Dietician	3	3	100%
Physiotherapist	2	2	100%
Total	75	54	72%

Table 2.4.ii Respondent Characteristics by Time Spent Working on the Haemodialysis Unit

Profession	Mean time working on dialysis Unit
All	40.2 months
Doctor	30 months
Nurse	85.2 months
Dietician	39.3 months
Physiotherapist	6.5 months

For the primary analysis, responses from all 54 professionals were pooled because the main aim was to examine the attitude of the multiprofessional team as a whole, rather than the effect of profession on attitude. Results are described in the text and displayed graphically for a representative selection of responses.

However, as a secondary analysis, responses of each professional group were considered. These secondary findings are briefly described in the results and discussion. Full responses by profession are shown in the results tables. The question statements appear in the order they were asked in the questionnaire.

Staff appreciation of patient benefit from exercise.

All doctors, dieticians and physiotherapists agreed or strongly agreed with the statement "I am aware of the benefits of exercise for haemodialysis patients. 70% (24/34) nurses agreed with this statement, but 12% (4/34) disagreed and 18% (6/34) were unsure.

The majority of staff, 80% (43/54), disagreed or strongly disagreed with the statement "I do not believe encouraging exercise would alter my patients' quality of life". However, 4 nurses agreed with this statement and 7 respondents replied, "don't know". The majority of staff, 85% (46/54), including all doctors, physiotherapists and dieticians, agreed or strongly agreed with the corollary statement "I believe my patients would have a better quality of life if they were encouraged to undertake regular exercise." Whilst nobody disagreed with this statement, 24% (8/34) nurses were unsure.

96% (52/54) disagreed with the statement that it was harmful for dialysis patients to exercise moderately (i.e. walking, stationary cycling.) 2 nurses agreed with this statement. Opinions were more varied regarding dialysis patients exercising vigorously with only 55% (30/54) disagreeing, which included all dieticians and physiotherapists. 11% (6/54) agreed or strongly agreed that it is harmful for dialysis patients to exercise vigorously (5 nurses, one doctor) and 33% (18/54) were unsure.

All dieticians and physiotherapists agreed that "the staff I work with believe that exercise is important for our patients". Whilst 4 doctors and 16 nurse also agreed with this, 9 doctors and 15 nurses did not know and 2 doctors and 3 nurses disagreed.

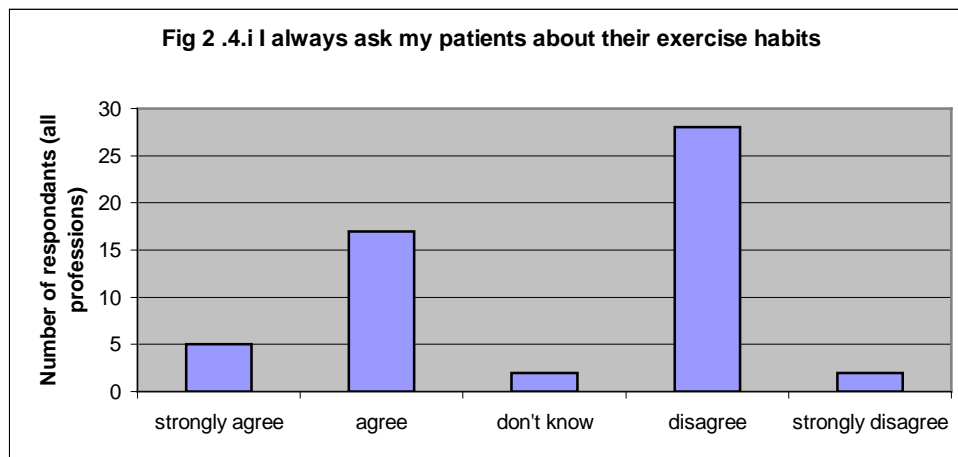
Table 2.4.iii. Staff Appreciation of patient benefit from exercise

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
It is harmful for dialysis patients to exercise moderately (i.e. walking, stationary cycling.)					
All n=54		2 (4%)	7 (13%)	36 (66%)	9 (16%)
Doctors n=15				11 (73%)	4 (27%)
Nurses n=34		2 (6%)	7 (21%)	22 (65%)	3 (8%)
Dieticians n=3				2 (66%)	1 (33%)
Physiotherapists n=2				1 (50%)	1 (50%)
It is harmful for dialysis patients to exercise vigorously (i.e. sports like running, bicycling.)					
All n=54	1 (2%)	5 (9%)	18 (33%)	26 (48%)	4 (7%)
Doctors n=15		1 (6%)	3 (20%)	10 (66%)	1 (6%)
Nurses n=34	1 (3%)	4 (12%)	15 (44%)	12 (35%)	2 (6%)
Dieticians n=3				2 (66%)	1 (33%)
Physiotherapists n=2				2 (100%)	
The staff I work with believe that exercise is important for our patients.					
All n=54	2 (3%)	12 (22%)	24 (54%)	16 (30%)	
Doctors n=15		4 (27%)	9 (60%)	2 (13%)	
Nurses n=34		16 (47%)	15 (44%)	3 (8%)	
Dieticians n=3		3 (100%)			
Physiotherapists n=2	2 (100%)				
I am aware of the benefits of exercise for haemodialysis patients.					
All n=54	13 (24%)	31 (57%)	6 (11%)	4 (7%)	
Doctors n=15	3 (20%)	12 (80%)			
Nurses n=34	6 (17%)	18 (52%)	6 (17%)	4 (12%)	
Dieticians n=3	2	1			
Physiotherapists n=2	2				
I do not believe encouraging exercise would alter my patients' quality of life.					
All n=54		4 (7%)	7 (13%)	34 (63%)	9 (17%)
Doctors n=15			1 (7%)	12 (80%)	2 (13%)
Nurses n=34		4 (12%)	6 (18%)	21 (62%)	3 (8%)
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
I believe my patients would have a better quality of life if they were encouraged to undertake regular exercise.					
All n=54	19 (35%)	27 (50%)	8 (14%)		
Doctors n=15	7 (46%)	8 (54%)			
Nurses n=34	8 (24%)	18 (53%)	8 (24%)		
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				

Current practice of exercise encouragement

All dietitians, physiotherapists and 73% (11/15) of doctors and 68% (23/34) of nurses disagreed or strongly disagreed with the statement "I do not usually assess the physical functioning of my dialysis patients". Of those who agreed with this, 12 were nurses and 3 were doctors.

41% (22/54) agreed or strongly agreed that "I always ask my patients about their exercise habits". This included all dietitians and physiotherapists, but only 4 doctors and 13 nurses. **See Fig 2.4.i.**



Around half of responders (52%, 28/54) agreed or strongly agreed "As part of my job, I often talk to patients about the benefits of exercise and encourage and advise them on ways to improve their physical fitness". This included all physiotherapists and dietitians, 6/15 doctors and 19/34 nurses.

Many respondents were unsure whether or not "The staff I work with regularly encourage patients to exercise", with 40% (24/54) replying, "Don't know". Whilst all physiotherapy and dietetic staff agreed with this, 30% (16/54, 8 doctors and 8 nurses) disagreed.

There were mixed views regarding the statement "This dialysis unit places a high level of importance on assessing physical functioning of patients". 41% (22/54) agreed or strongly agreed and 48% (26/54) disagreed or strongly disagreed. 6 respondents (3 doctors, 2 nurses, one dietician" replied "don't know" to this question.

Table 2. 4. iv Current Practice of Exercise Encouragement

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
I do not usually assess the physical functioning of my dialysis patients.					
All n=54		15 (27%)	1 (2%)	32 (50%)	6 (11%)
Doctors n=15		3 (20%)	1 (7%)	8 (53%)	3 (20%)
Nurses n=34		12 (35%)		22 (65%)	
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
I always ask my patients about their exercise habits.					
All n=54	5 (9%)	17 (31%)	2 (4%)	28 (52%)	2 (4%)
Doctors n=15		4 (27%)	2 (13%)	8 (53%)	1 (7%)
Nurses n=34	1 (3%)	12 (35%)		20 (59%)	2 (6%)
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
As part of my job, I often talk to patients about the benefits of exercise and encourage and advise them on ways to improve their physical fitness.					
All n=54	4 (7%)	24 (44%)		25 (42%)	1 (2%)
Doctors n=15		6 (40%)		9 (60%)	
Nurses n=34		19 (56%)		16 (30%)	1 (29%)
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
The staff I work with regularly encourage patients to exercise.					
All n=54	2 (4%)	12 (22%)	24 (44%)	16 (29%)	
Doctors n=15			7 (47%)	8 (53%)	
Nurses n=34		9 (17%)	17 (50%)	8 (24%)	
Dieticians n=3		3 (100%)			
Physiotherapists n=2	2 (100%)				
This dialysis unit places a high level of importance on assessing physical functioning of patients.					
All n=54	2 (4%)	20 (37%)	6 (11%)	24 (44%)	2 (4%)
Doctors n=15		4 (26%)	3 (20%)	7 (47%)	1 (&%)
Nurses n=34	1 (29%)	14 (41%)	2 (59%)	26 (48%)	1
Dieticians n=3		1 (33%)	1 (33%)	1 (33%)	
Physiotherapists n=2	1 (50%)	1 (50%)			

Perceptions of patient factors

Perceptions of patient satisfaction with their levels of physical functioning and the care given to any problems they may have with physical functioning were very variable. However only 14% (7/49) of doctors or nurses agreed that patients were satisfied with their levels of physical functioning and only 29% (14/49) thought that patients were satisfied with the level of care given to any problems they had with physical functioning. There were 22% (12/54) respondents who did not know whether or not patients were satisfied with their levels of physical functioning and 31% (17/54) who did not know if patients were satisfied with the care given to any problems they may have with physical functioning respectively.

Opinions were divided on the question of patients have too many other problems for them to want to participate in exercise with 49% (24/49) disagreeing with this statement, 27% (13/49) agreeing and 29% (14/49) unsure. Around half (25/49) of doctors and nurses thought patients would exercise more if they felt better, 37% (18/49) did not know and 12% (6/49) disagreed.

Seven respondents thought dialysis patients did not want to participate in regular exercise. 44% (24/54) either disagreed with this and 44% (24/54) did not know. 15% (8/54), including one physiotherapist, agreed that dialysis patients lack the motivation to stick with an exercise program. 46% (25/54) of respondents did not know, whilst 39% (21/54) disagreed or strongly disagreed.

Most respondents, 74%(40/54), disagreed or strongly disagreed that "Dialysis patients are too ill to exercise" , although 11% (6/54) agreed and 15% (8/54), including one physiotherapist, answered "Don't know". One respondent, a dialysis unit nurse, commented, ***"Some of my patients are very frail but there is a big group of older people who are still very active. They get quite bored***

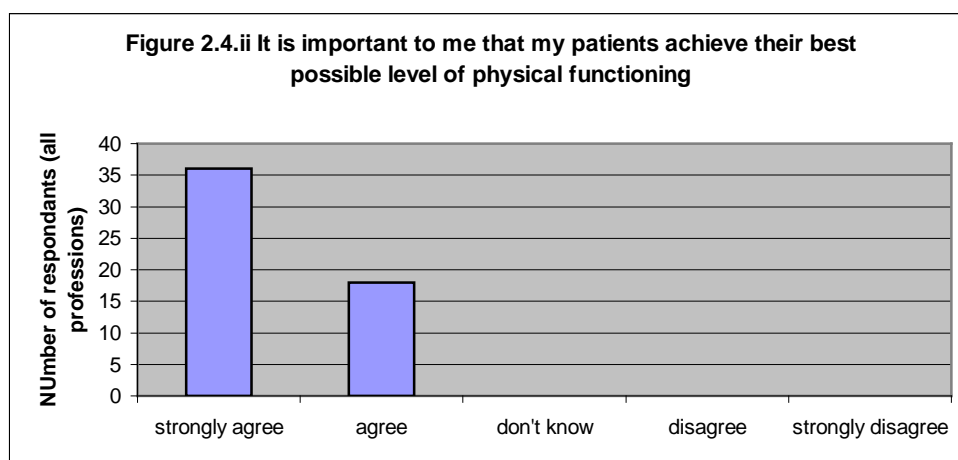
on dialysis. I think they would enjoy doing something to keep fit and it would stop them feeling that dialysis was wasted time”.

Table 2.4.v. Perceptions of patient factors

		Strongly agree	Agree	Don't know	Disagree	Strongly disagree
My patients are satisfied with their levels of physical functioning.						
All	n=54		7 (13%)	12 (22%)	25 (46%)	10 (19%)
Doctors	n=15		1 (7%)	4 (27%)	8 (53%)	2 (14%)
Nurses	n=34		6 (18%)	8 (24%)	14 (41%)	6 (18%)
Dieticians	n=3				1 (33%)	2 (66%)
Physiotherapists	n=2				2 (100%)	
Dialysis patients are too ill to exercise.						
All	n=54		6 (11%)	8 (15%)	37 (69%)	3 (6%)
Doctors	n=15		1 (7%)	2 (13%)	10 (66%)	2 (13%)
Nurses	n=34		5 (15%)	5 (15%)	24 (71%)	
Dieticians	n=3				2 (66%)	1 (33%)
Physiotherapists	n=2			1 (50%)	1 (50%)	
My patients are satisfied with the level of care given to any problems they may have with physical functioning.						
All	n=54	1 (2%)	15 (28%)	17 (31%)	18 (33%)	3 (6%)
Doctors	n=15	1 (7%)	2 (13%)	6 (40%)	4 (27%)	2 (13%)
Nurses	n=34		12 (35%)	9 (26%)	12 (35%)	1 (3%)
Dieticians	n=3			1 (33%)	2 (66%)	
Physiotherapists	n=2		1 (50%)	1 (50%)		
My patients have too many other problems for them to want to participate in exercise.						
All	n=54		13 (24%)	12 (22%)	28 (52%)	1(2%)
Doctors	n=15		4 (27%)	1 (7%)	10 (66%)	
Nurses	n=34		9 (26%)	11 (2%)	14 (41%)	
Dieticians	n=3				2 (66%)	1 (33%)
Physiotherapists	n=2				2 (100%)	
Dialysis patients would exercise more if they felt better.						
All	n=54	6 (11%)	24 (44%)	18 (33%)	6 (11%)	
Doctors	n=15	1 (7%)	4 (27%)	6 (40%)	4 (27%)	
Nurses	n=34	3(9%)	17 (50%)	12 (35%)	2 (6%)	
Dieticians	n=3	1 (33%)	2 (66%)			
Physiotherapists	n=2	1 (50%)	1 (50%)			
Dialysis patients don't want to participate in regular exercise						
All	n=54		7 (13%)	24 (44%)	22 (33%)	1 (2%)
Doctors	n=15		3(20%)	6 (40%)	6 (40%)	
Nurses	n=34		3 (9%)	18 (53%)	13 (38%)	
Dieticians	n=3		1 (33%)		1 (33%)	1 (33%)
Physiotherapists	n=2				2 (100%)	
Dialysis patients lack the motivation to stick with an exercise program.						
All	n=54		8 (15%)	25 (46%)	20 (37%)	1 (2%)
Doctors	n=15		2 (4%)	8 (15%)	5 (33%)	
Nurses	n=34		5 (15%)	16(47%)	13 (38%)	
Dieticians	n=3			1 (33%)	1 (33%)	1 (33%)
Physiotherapists	n=2		1 (50%)		1 (50%)	

Staff factors: Attitudes, role, responsibility, time and opportunity

All of the doctors, dieticians and physiotherapists and three quarters of the nurses (76%, 26/34) expressed concerns about the physical functioning of their patients. Without exception, all responders agreed or strongly agreed that it was important to them that their patients achieved their best possible level of physical functioning. See Fig 2.4.ii.



Only 9% (5/54) respondents, all nurses, disagreed with the statement that it was their responsibility to help patients increase their physical functioning. 18% (10/54) respondents replied "don't know" to this question. All physiotherapists and dieticians, and 87% (13/15) of doctors disagreed or strongly disagreed that "It is not my role to discuss or encourage exercise for my patients". 41% (14/34) of nurses agreed with this. Of the 9 respondents replying "don't know", 8 were nurses.

Replies were split on the subject of time and opportunity to address issues of physical functioning with 43%(23/54) and 37%(20/54) agreeing with the statements "There is no time in my daily work schedule to discuss exercise with my patients" and "There is no opportunity in my daily routine to encourage patients to exercise". 55% (30/54) and 59%(32/54) respondents disagreed or

strongly disagreed with this. As might also be expected, physiotherapists and dieticians affirmed that they had time and opportunity in their working day to achieve this. Around two thirds of doctors agreed that they had both time and opportunity to promote exercise, 66%(10/15) agreeing they had time, and 73%(11/15) opportunity. Nurses also seem less able to fit these activities into their working days, with only 47% (16/34) feeling they had opportunity and only 44%(15/34) feeling they had time to discuss or encourage exercise.

Two nurses commented specifically on this in the free text section; “ ***Some days we hardly have time to do the tinzaparins*** [anticoagulant drug administered during dialysis] ***let alone anything else,***” and “ ***I would love to be able to do more for the patients especially things like exercise but first we need more staff just to do the dialysis.***”

Table 2.4.vi. Staff Factors: attitudes, roles, responsibility, time and opportunity

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
It is important to me that my patients achieve their best possible level of physical functioning.					
All n=54	36 (67%)	18 (33%)			
Doctors n=15	11 (73%)	4 (27%)			
Nurses n=34	20 (59%)	14 (41%)			
Dieticians n=3	3 (100%)				
Physiotherapists n=2	2 (100%)				
I have no concerns about the physical functioning of any the dialysis patients I look after.					
All n=54		4 (7%)	4 (7%)	24 (44%)	22 (41%)
Doctors n=15				8 (53%)	7 (47%)
Nurses n=34		4 (12%)	4 (12%)	14 (41%)	12 (41%)
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2				1 (50%)	1 (50%)
It is my responsibility to help patients increase their physical functioning.					
All n=54	10 (19%)	29 (54%)	10 (19%)	5 (10%)	
Doctors n=15	3 (20%)	10 (66%)	2 (13%)		
Nurses n=34	3 (9%)	18 (53%)	8 (24%)	5 (15%)	
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
It is not my role to discuss or encourage exercise for my patients.					
All n=54	1 (2%)	14 (26%)	9 (17%)	25 (46%)	5 (9%)
Doctors n=15		1 (7%)	1 (7%)	12 (80%)	1 (7%)
Nurses n=34	1 (3%)	13 (38%)	8 (24%)	12 (35%)	
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
There is no time in my daily work schedule to discuss exercise with my patients.					
All n=54		23 (43%)	1 (2%)	26 (48%)	4 (7%)
Doctors n=15		5 (33%)		10 (66%)	
Nurses n=34		18 (53%)	1 (3%)	15 (44%)	
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
There is no opportunity in my daily routine to encourage patients to exercise.					
All n=54		20 (37%)	2 (4%)	28 (52%)	4 (7%)
Doctors n=15		4 (27%)		11 (73%)	
Nurses n=34		16 (47%)	2 (6%)	16 (47%)	
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)

Staff factors: Skills and training

39% (21/54) respondents agreed with the statement “I don't know how to motivate patients to exercise”, and 43% (23/54) with the statement “I don't know how to counsel patients on how to improve physical functioning” whilst 44% (24/54) and 46% (25/54) disagreed or strongly disagreed respectively.

All of the dieticians and physiotherapists agreed or strongly agreed that their training had included information on the benefits of exercise for haemodialysis patients and included practical measures to assess and encourage exercise for my patients. Of the doctors and nurses, 84% (41/49) disagreed or strongly disagreed with these statements. One nurse commented; ***“I would like to know more. At the moment I'm afraid I would tell them something wrong”.***

Table 2.4.vii. Staff factors: skills and training

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
I don't know how to motivate patients to exercise.					
All n=54		21 (39%)	9 (17%)	19 (35%)	5 (9%)
Doctors n=15		5 (33%)	3 (20%)	7 (47%)	
Nurses n=34		16 (47%)	6 (18%)	11 (32%)	1 (3%)
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
I don't know how to counsel patients on how to improve physical functioning.					
All n=54		23 (43%)	6 (11%)	20 (37%)	5 (9%)
Doctors n=15		4 (27%)	1 (7%)	10 (66%)	
Nurses n=34		19 (56%)	5 (15%)	9 (26%)	1 (3%)
Dieticians n=3				1 (33%)	2 (66%)
Physiotherapists n=2					2 (100%)
My training included information on the benefits of exercise for haemodialysis patients.					
All n=54	6 (11%)	15 (28%)	3 (6%)	28 (52%)	2 (4%)
Doctors n=15	1 (7%)	5 (33%)		8 (53%)	1 (7%)
Nurses n=34	1 (3%)	9 (26%)	3 (9%)	20 (59%)	1 (3%)
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
My training included practical measures to assess and encourage exercise for my patients.					
All n=54	4 (7%)	7 (13%)	2 (4%)	38 (70%)	3 (6%)
Doctors n=15		2 (13%)		11 (73%)	2 (13%)
Nurses n=34		4 (12%)	2 (6%)	27 (79%)	1 (3%)
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				

Opinion on suitable encouragement methods and exercise programs

A high proportion of respondents (38/54, 70%) agreed or strongly agreed that dialysis patients would exercise regularly if given structured programs with regular review. Of those who did not agree, only 3 disagreed (3 nurses), whilst the remainder did not know (24%, 13/54, 3 doctors, 10 nurses). All dietitians and physiotherapists agreed or strongly agreed that dialysis patients would exercise regularly if given encouragement and information. Although 31/49 (63%) doctors and nurses also gave a positive response, they were less sure of this with 18/49 (37%) answering "Don't know" and 5/49 (10.2%) disagreeing.

Most respondents 70% (31/54) agreed or strongly agreed 28% (15/54) with the statement "I believe the Haemodialysis unit should do more to encourage patients to maintain or improve their physical functioning". This included all dietitians and physiotherapists.

More than two thirds, 70% (38/54), of respondents agreed or strongly agreed that dialysis patients would exercise regularly if given encouragement and information. Only 6% (3) respondents disagreed with this and only 24% (13/54, 10 nurses, 3 doctors) answered "Don't know".

In terms of which program might be most suitable, many were unsure with 37% (20/54) and 50% (27/54) answering "Don't know" to "My patients would be more likely to participate in exercise programs on the dialysis unit", and "My patients would be more likely to undertake a home exercise program" respectively. Of those favouring one type of program, more supported exercise programs on the dialysis unit 48%, 26/54, agreed or strongly agreed the patients would be more likely to participate in Unit based programs). Those favouring unit-based programs included the physiotherapists. Whilst 26% (14/54) agreed that patients would be more likely to undertake a home exercise program, roughly the same number 24% (13/54) disagreed or strongly disagreed with this statement. Of

those who did not, 7% (4) responded, "don't know" and 7% (4) disagreed or strongly disagreed.

There were no responses disagreeing with the statement "I believe that patients would benefit from having dedicated staff (e.g. a Renal Physiotherapist) to assess physical fitness and encourage exercise". 37% (20/54) respondents strongly agreed with this, 57% (31/54) agreed although 5% (3 nurses) were unsure.

Table 2.4.viii. Opinion on appropriate encouragement methods and exercise programs.

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
<i>Dialysis patients would exercise regularly if given encouragement and information.</i>					
All n=54	5 (9%)	26(48%)	18(33%)	5 (9%)	
Doctors n=15	1 (7%)	7 (47%)	5 (33%)	2 (13%)	
Nurses n=34	2 (6%)	16(47%)	13(38%)	3 (9%)	
Dieticians n=3	1 (33%)	2 (66%)			
Physiotherapists n=2	1 (50%)	1 (50%)			
I believe the Haemodialysis unit should do more to encourage patients to maintain or improve their physical functioning.					
All n=54	15 (28%)	31(57%)	4 (7%)	3 (6%)	1 (2%)
Doctors n=15	2 (13%)	9 (60%)	2 (12%)	1 (6%)	1 (6%)
Nurses n=34	9 (26%)	21(62%)	2 (6%)	2 (6%)	
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
Dialysis patients would exercise regularly if given structured programs with regular review					
All n=54	11 (20%)	27(50%)	13(23%)	3 (6%)	
Doctors n=15	1 (7%)	11(73%)	3 (20%)		
Nurses n=34	6 (18%)	15(44%)	10(29%)	3 (9%)	
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				
My patients would be more likely to undertake a home exercise program.					
All n=54	2 (4%)	12(22%)	27(50%)	11(20%)	2 (4%)
Doctors n=15		5 (33%)	7 (47%)	2 (6%)	1 (7%)
Nurses n=34	1 (3%)	7 (20%)	18(33%)	7 (21%)	1 (3%)
Dieticians n=3	1 (33%)		1 (33%)	1 (33%)	
Physiotherapists n=2			1 (50%)	1 (50%)	
My patients would be more likely to participate in exercise programs on the dialysis unit.					
All n=54	5 (9%)	21(39%)	20(37%)	8 (15%)	
Doctors n=15	1 (7%)	5(33%)	6 (40%)	3 (20%)	
Nurses n=34	3 (9%)	14(41%)	12(35%)	5 (15%)	
Dieticians n=3		1 (33%)	2 (66%)		
Physiotherapists n=2	1 (50%)	1 (50%)			
I believe that patients would benefit from having dedicated staff (e.g. a Renal Physiotherapist) to assess physical fitness and encourage exercise					
All n=54	20 (37%)	31(57%)	3 (6%)		
Doctors n=15	6 (40%)	9 (60%)			
Nurses n=34	10 (29%)	21(62%)	3 (9%)		
Dieticians n=3	2 (66%)	1 (33%)			
Physiotherapists n=2	2 (100%)				

DISCUSSION

In summary, staff members at the haemodialysis unit are aware of the benefits to patients of encouraging exercise, and have a positive attitude towards the prospect of patients partaking in exercise activities. Staff would like to promote exercise practices and most feel that it is part of their responsibility and accept it as part of their role. Many staff are already talking to patients about the benefits of exercise and encouraging and advising them on ways to improve their physical fitness. However, many also feel that they lack time and skills in how to do this, probably because it is not a routine part of their training. Staff members envisage that patients would take part in structured programs with regular encouragement and feedback, probably based on the Haemodialysis unit and ideally under supervision of a specialist such as a physiotherapist.

Results in Context

In Nottingham, there is strong evidence that haemodialysis unit staff members are aware of the benefits of exercise and feel that encouraging exercise would improve their patients' quality of life. This shows a higher level of awareness of the benefits of exercise than the US group surveyed by Painter *et al.* In Painter's study only 45% of staff believed that the majority of their patients would benefit from exercise training, compared to around 80% of the Nottingham group. Our survey was completed two years later than Painter's and it may be that time has allowed increased dissemination of this information amongst the international nephrology community. Painter surveyed a mixed group of nursing professionals and dieticians, whilst in Nottingham respondents also included doctors and physiotherapists who may be more likely to appreciate the benefits of exercise. Also, this study included no patient profile data. It may be that the patients cared for by staff in Painter's study and by the Nottingham staff differ in some respect that affects the staff perception of their patients likelihood of benefit from exercise

e.g. the patients in the US may be generally more frail. Additionally, in Nottingham, there may be a higher local level of awareness due to the profile of fitness investigations within the unit and enthusiasm of individuals locally.

In terms of more specific understanding, 96% of Nottingham respondents were aware that it was not harmful for dialysis patients to exercise moderately and 55% thought that vigorous activity for dialysis patients was not harmful, compared to 85% and 70% in Painter's group. In Nottingham, 33% were unsure if vigorous exercise was harmful for their patients. Of this 33%, most were nursing staff who have a more hands-on involvement in the dialysis process, but less involvement in the overview of a patients' general medical management.

One of the comments submitted on the survey form submitted by a senior dialysis nurse stated ***"I would be worried that patients might overdo it on the exercise equipment and have a heart attack or stroke or something on dialysis"***. This suggests a recognition of the more common co-morbidities suffered by older dialysis patients and an anxiety regarding possible harmful effects of more energetic exercise in this patient group. This concern would need to be explored further, but might be addressed by more detailed education, training in monitoring during assessment, and exercise programs recommended on an individual basis after medical and physiotherapy assessments.

Around half of staff in Nottingham often talk to patients about the benefits of exercise and encourage and advise them on ways to improve their physical fitness, including all physiotherapists and dieticians. This is a lower proportion than in Painter's group, where 74% of staff sometimes or regularly encourage their patients to exercise. The size of the interventions that our haemodialysis staff are making was not assessed and may be very brief and informal; one nurse said ***"It is not always appropriate as some of our patients are very ill, and***

you know they can't do much anyway, but with the more active ones it often comes up in conversation". However, even small interventions are important. Kontos *et al* (Kontos et al., 2007) found that a significant barrier to exercise was nurses lack of encouragement to exercise. One Nottingham doctor commented ***"It is on a checklist in the back of my mind when I see patients in Haemodialysis clinic. I don't always remember, but when I talk about smoking habits and alcohol ,I try to mention exercise as part of healthy lifestyle advice."***

Painter determined the optimum predictor variables for encouragement practice by multiple regression analysis, explaining 33.2% of the variance. Painter found four significant positive predictor variables; 1) profession, i.e. trained nurse or social worker compared to patient care technician, 2) acceptance of responsibility to help patients increase their physical functioning, 3) perception of having skills to motivate patients, and 4) perceiving that dialysis patients have the motivation to exercise. Selecting those agreeing or strongly agreeing that they often talk to patients about the benefits of exercise and encourage and advise them on ways to improve their physical fitness, a subset of 24/54 (48.9%) respondents were identified as "exercise encouragers". It was felt that it would not be valid to repeat this with the Nottingham data because the discriminator question used to select "exercise encouragers" was not robust, as discussed.

Encouragingly, in Nottingham, just 15% thought that dialysis patients lack the motivation to stick with an exercise program, although 36% agreed with this in Painter's group. Only a small proportion in Nottingham (13%) thought that dialysis patients did not want to participate in regular exercise (14% in Painters's group). This is important as in Toronto, Kontos et al found that one of the motivators to exercise included patients aspirations to exercise(Kontos et al.,

2007). The Nottingham findings are very encouraging, implying that staff feel positive towards the likelihood of dialysis patients embracing exercise programs.

In Nottingham, only 24% thought patients had too many other problems for them to want to participate in exercise and only 11% thought patients were too ill to exercise, compared to 27% and 12% in Painter's group. However, in Nottingham, 55% thought dialysis patients would exercise more if they felt better (79% in Painter's group). The Nottingham findings appear contradictory but suggest a perception that it is the way patients feel in themselves that may act as a barrier to exercise, rather than specific physical limitations of their conditions. This is supported by the finding that 67% of respondents agreed that dialysis patients would exercise regularly if given encouragement and information (compared with 25% in Painter's group).

Positive expectation is recognised to be an important factor in the promotion of positive behaviours. Expectation are guided by self and by "authority figures", in this case dialysis unit staff, by local society (other patients) and wider society. Thus the attitudes of staff towards patients' exercising is very important (Kontos et al., 2007). This is again supported by the finding that, in Nottingham, agreement with the statement that "Staff I work with regularly encourage dialysis patients to exercise" is a positive predictor of exercise encouragement practice. Staff in Nottingham appear to appreciate the importance of a positive culture within the unit as a whole, with 86% agreeing that the unit should do more to encourage patients to maintain or improve their physical functioning.

Acceptance of responsibility was the most important positive predictor in Painter's group, but this was not found in Nottingham. In Painter's study, 72% accepted that it is their responsibility to help patients improve their physical functioning. The percentage was the same in Nottingham. Whilst staff members in Nottingham

accept this responsibility, it seems that there is some barrier to translating this into action. Painter found that perception of own skills was an important positive predictor variable in exercise encouragement practice i.e. those feeling that they lack the skills are less likely to encourage patients to exercise. Whilst this was not found in Nottingham, skills confidence may still be an issue. In our staff group, around 40% said that they knew how to motivate patients to exercise or how to counsel patients on how to improve physical functioning. In Painter's study, 68% stated that they knew how to motivate and counsel patients about exercise.

The Nottingham findings may be a reflection of the topics covered in training. As should be expected, all of the dieticians and physiotherapists had training that included information on the benefits of exercise for haemodialysis patients and practical measures to assess and encourage exercise. Of the doctors and nurses, 43% had training that included information on the benefits of exercise for haemodialysis patients, but only 16% had any training in practical measures to assess and encourage exercise. Training issues were not explored in Painter's group.

It is very encouraging that Nottingham Haemodialysis Unit staff appear to be supportive of the idea of exercise encouragement practice. A high proportion of respondents (70%) agreed that dialysis patients would exercise regularly if given structured programs with regular review.

There was no strong consensus on what type of exercise program might be best, although unit based seemed to be favoured, including by the physiotherapists. This is supported by the finding of Kontos *et al* that motivators to exercise include formal incorporation of exercise into the overall dialysis treatment plan. Almost 50% agreed the patients would be more likely to participate in Unit based programs, whilst only 25% thought that patients would be more likely to undertake a home exercise program. These are projected opinions, but taken in

combination with thoughts on patient motivation and preferences seems to suggest that staff feel patients would be most likely to adhere to a supervised unit-based program. In the small number of UK Haemodialysis units which report formally offering exercise to their older patients (4/72 Hub units), all provide unit-based intradialytic programs(website, 2009), although here is currently no available literature reporting the outcomes of these routine interventions. These programs are supervised either by physiotherapists or by specially trained dialysis nurses. This is an approach supported by Nottingham staff, where almost all respondents thought that patients would benefit from having dedicated staff (e.g. a Renal Physiotherapist) to assess physical fitness and encourage exercise.

Strengths and Limitations of the Study

The major problem identified in the analysis of this work has been that the response scale offered has not been appropriate for some of the statement questions. On reviewing the responses it became apparent, that the middle option of "Don't know" has not offered a point of neutrality, necessary in the classic Likert scale. Particularly in those questions asking respondents to provide their opinion or assessment of another group's thoughts feelings of behaviour (either patients or other staff), there is inherent ambiguity in the "don't know" response. It also meant that, unless there were no "don't know" responses, it was not possible to analyse yes/no subgroups e.g. to select staff members already practicing exercise encouragement behaviours (encourages vs. non encouragers), and thus to try and compare and define identifying characteristics of the groups. Using a central scale point of "Neither agree nor disagree" and offering quantitative responses to certain items would allow greater clarity. This problem was not identified in the small pilot study, but it is possible that a larger pilot with formal feedback and with pilot analysis may have identified this issue.

The questionnaire would have benefited from fewer questions in each category as the lengthy appearance and small print may have been off putting. The survey should be introduced through both written, face to face presentation and email means. The delivery of the questionnaire at training day or meeting would reduce the time spent reminding people and re-issuing emails.

Construct validity was not tested before administering the questionnaire. This would have been difficult, but could have been achieved by using a control group e.g. administering to non dialysis staff members, and/or by using an intervention approach or staff members before and after an exercise promotion education session. If there is a significant difference pre and post-test, usually analysed with simple statistical tests, then this proves good construct validity.

Assuring construct validity is difficult with a qualitative questionnaire study. It could be argued that the questionnaire is not testing the ideas described in the hypothesis because of a number of threats. Hypothesis guessing is virtually unavoidable in this study i.e. staff members are aware of the investigators agenda to promote exercise and, depending on their perception of this agenda, may respond differently. Evaluation apprehension and researcher bias may have clouded the responses i.e. respondents felt under pressure and picked up cues from the researcher as to the "preferred" responses. Construct confounding may also occur e.g. staff personality types and attitudes - staff members with more "paternalistic" attitudes towards their patients may answer differently to those who promote patient autonomy and independence. It would have been helpful to devise other supportive ways of evaluating staff perceptions and attitudes, for example observation, patient feedback, or knowledge testing. Dieticians and physiotherapists were included with caution for a number of reasons. Firstly, the specific remit of dieticians and physiotherapists is heavily focussed on physical fitness and healthy lifestyle. This means they are likely to give more specialty relevant answers, which may mask trends in the non-specialist responses. Also, in

Nottingham, dieticians and physiotherapists are involved in the care of dialysis patients but not assigned to the renal unit in a dedicated fashion. Thus their involvement with haemodialysis patients is less routine and regular but more formal and intensive than renal doctors and nurses. This is important, as it may not be clear if responses are referencing the brief informal interventions suitable for renal doctors and nurses or fuller prescribed strategies from physiotherapists or dieticians. Finally, the small numbers of dieticians and physiotherapists means this subgroup response may not be meaningful.

Self-reported data and attitudinal data contain several potential sources of bias, particularly if Likert scales are used. Respondents may avoid using extreme response categories (central tendency bias) or may agree with statements as presented (acquiescence bias). In this study setting, preconception and attribution bias are possibilities (i.e. attributing attitudes and actions that respondents regard as positive to one's self). This is social desirability bias and especially likely in responses submitted without anonymity when respondents may try to "impress" the researcher. It may also be that certain professional groups or individuals are more or less inclined to admit lack of knowledge or understanding of this specialist area, especially if they have chosen to provide name or contact details for further discussion. Results may also be influenced by selective or over-specific memory (allowing perceptions to be coloured by recent experiences only and not passing forward all experiences e.g. remembering a particularly frail or particularly active patient seen on the day of completing the questionnaire).

After consideration, each item was analysed separately rather than summed within groups. Responses were considered as ordered-categorical data rather than interval data. When treated as ordinal data, Likert responses can be collated into bar charts, central tendency summarised by the median or the mode, dispersion summarised by the range across quartiles, or analysed using non-parametric tests. However, these methods of description and analysis were not considered to

augment the information already attained or increase achievement of the aims of the study.

Data from Likert scales are sometimes reduced to the nominal level by combining all agree and disagree responses into two categories of "agree" and "disagree". With a non-neutral centre point, this was not possible for many items. However this did not prevent achievement of the aims of the study.

Despite the methodological limitations pointed out above, this study makes a significant contribution to the body of knowledge focussing of exercise intervention in dialysis patients, whilst responding to local level needs identified by practicing clinicians and patients. It is an original study, being the first and only exploration of staff attitudes towards exercise encouragement in a UK NHS Haemodialysis unit. This chapter achieves its original aim by advancing knowledge of staff factors, which may act either as gateways or as barriers to the introduction of exercise encouragement practices within a UK NHS Haemodialysis Unit.

This is strengthened by a very high overall response rate, particularly amongst doctors, dieticians and physiotherapists. The high response rate amongst doctors may be due to the proximity of the investigator to this group on a daily basis, allowing frequent reminders. Dieticians and Physiotherapists are invested in this topic area and keen to support the development of their own services. The lower response rate amongst nurses is likely to be due to a number of factors such as shift patterns, annual leave during the research period, irregular accessing of post and email, time pressures during busy shifts and limited involvement in or enthusiasm for the topic area. Overall, it was very encouraging to receive many statements of positive and supportive feedback from staff members appreciating the value of research into this area.

CONCLUSION

This original study has achieved its aims. It is the first UK study to provide insight into the factors that may aid or impede exercise encouragement practices by haemodialysis unit staff for older patients. The finding that staff members are in the majority receptive to these interventions is encouraging and invites proposals for the design and introduction and study of exercise intervention schemes. However, the need for a more encompassing shift in culture is recognised. Staff education and training must be revised and the importance of exercise accepted within the nephrology community.

Implications for Clinicians, Services, and Future Research

The next stage of this work should focus on a pragmatic and achievable pathway towards the local introduction of regular exercise encouragement practices. Ultimately this investigator would aim to achieve routine exercise interventions and the resourcing of dedicated trained staff to deliver this. This body of work strongly endorses exercise interventions and could be used to support applications for resources to fund this.

This investigator would suggest a multilevel approach. Firstly, all staff working within the unit should have an understanding of the potential benefits of exercise for haemodialysis patients. For nursing staff, this could be achieved through the renal program run at a local level. In Nottingham, this has in fact already been introduced on a trial basis.

For renal doctors in training, the topic of exercise does not appear on the national syllabus, and this could be queried to the Joint Specialist Committee through

trainee representatives. Meanwhile, the Deanery offers a local program and it would be possible to incorporate this topic into the sessions.

It is vital to incorporate consideration of physical functioning into the routine assessments of all dialysis patients. Within the current Nottingham haemodialysis unit service structure, all dialysis patients are reviewed by renal doctors in a formal medical clinic, at least six monthly and usually more frequently. A brief functional assessment could easily be incorporated into the haemodialysis clinic proforma. Nursing staff complete monthly update reports for all their patients and this too could incorporate simple physical functioning assessments. Triggers should be identified which prompt concern. Currently, there is no dedicated Haemodialysis unit physiotherapist, but referral can be made to hospital or community physiotherapists or to the local falls program. The investigator believes these services are currently under utilised by haemodialysis patients.

As Nottingham expands its haemodialysis programs, with the opening of further satellite facilities, consideration of these interventions could be made at a design level i.e. ensuring sufficient room for intradialytic exercise equipment to be used and stored, and space for functional assessments or exercise education. Capacity and transportation issues must also be considered.

Patient factors are also important and patient education to support these interventions can be approached by means other than staff delivery. Discussion of the importance of exercise and its benefits in CKD and ESRD can begin in the pre-dialysis phase. Written materials and reference to approved national websites and other resources may help to promote a cultural shift and positive expectation in patients and their relatives.

CHAPTER THREE

3.1 Discussion

As this work has progressed, the body of literature related to the effects of exercise among patients with ESRD has been rapidly expanding. There is now ESRD-specific literature demonstrating that exercise interventions can improve physical functioning, muscle strength, activity performance, cardiovascular health, dialysis efficacy and, and self-reported quality of life indices (e.g. Cheema et al, 2005). As yet, the data on falls profile and falls risk is much more limited, but it is now recognised as a priority area as links to mortality have been demonstrated(Li et al., 2008).

This work has therefore been timely and relevant to the focus of the nephrology community. It has contributed to knowledge by providing the first data on the single session effect of haemodialysis on functional performance assessments and balance in older haemodialysis patients. This data has been published in a peer-reviewed journal. This dissertation also presents the first UK study of patients' perceptions of their physical fitness and functioning and the first study of haemodialysis patients to use the Tinetti Falls Efficacy Scale to demonstrate the anxieties patients are suffering about their self-perceived risk of falling. This work also offers the first UK data on staff attitudes towards exercise for older haemodialysis patients and the first assessment of staff factors as a potential barrier or facilitator of exercise intervention in this setting.

The individual limitations of the original studies have been discussed in the relevant sections. In general terms, many of the limitations have been the result of designing studies that failed to anticipate some of the problems encountered in data collection and analysis. Additionally designing studies to explore an

“information-free” zone meant that as new data evolved this data was less easily comparable.

3.2 Conclusion

Chapter One provides an thorough insight into the background of this study and though examination of the literature available on older adults in the general population and those on RRT, expounds upon possible pathophysiological mechanisms which might underlie physical fitness limitations in older adults with CKD and receiving RRT.

The Feasibility Pilot and Small Scale Exploratory Study Exploring the Effect of a Single Maintenance Haemodialysis Session on Older Adults Performance in Falls Predictive Physical Assessments presented in Section 2.2 demonstrated the difficulties of carrying out clinical research in a busy and overstretched working environment. It achieved its aim of establishing whether or not undertaking a larger scale project of this nature was feasible. It did not provide useful data for subsequent research proposals or power calculations. However, these “negatives” were useful findings. The enthusiasm with which the themes were embraced by patients and staff indicate real concerns.

The original research project presented in Section 2.3, Physical Health, Falls and Falls Risk in Older Haemodialysis Patients, provides new data describing the scale and impact of physical fitness limitations in older adults on maintenance RRT in Nottingham. The data includes specific functional and psychological and social information and can be used to support a case of need for improved local services for this group. Despite the limitations, this study does contribute new knowledge to the renal community.

The final study in Section 2.4, Haemodialysis Unit Staff Perceptions of Physical Fitness, Exercise Benefits, and Current Exercise Encouragement Practices for Older Patients, is perhaps the most academically robust. It contributes important information suggesting that the barriers to staff promoting exercise are not due to negative attitudes or beliefs but are mainly practical and historical i.e. simple changes such as including exercise in the training syllabus and empowering clinical staff to promote exercise may achieve real benefits.

In terms of achieving the stated research aims, the original research has been successful, but with some limitations within each study. The research story evolves sequentially through the thesis. There was initially consideration of a study to examine the possible acute single session effect of haemodialysis on balance and performance assessments to establish whether or not haemodialysis might be an independent risk factor for falls. After a small-scale pilot, this avenue was not progressed as major logistical problems were recognised. However this first study revealed great enthusiasm from both staff to explore this neglected area. The next study then attempted to explore the impact of physical and functional limitations on quality of life and well being in older maintenance haemodialysis patients compared to non-dialysed older adults i.e. are the suspected limitations important to patients themselves? On finding that the limitations were indeed severe and significant, the final study then examined the barriers to the pragmatic intervention of exercise encouragement from unit staff.

The impetus behind this thesis has been to provide data to support service development for our rapidly expanding older adult maintenance dialysis population. The growth of this group is a positive reflection of recent developments in medical care and offers an exciting opportunity to establish links between nephrology and geriatric medicine. There is great interest in the nephrology community in developing our knowledge in this field but, in a

relatively small and over-stretched specialty, there are limits on the rate of progression. Additionally, research into the wider and more holistic aspects of geriatric nephrology may perhaps have been perceived as less urgent in an evolving and fiercely academic and technical field. Nevertheless, it is important not to lose sight of the very real problems in the day-to-day existence of this group of older dialysis patients. Ultimately this can only improve our clinical expertise and the services and benefits we offer to our patients.

Older adult haemodialysis patients, staff and carers are rightly demanding that clinicians focus not just on the technical aspects of their life-maintaining dialysis treatment, but on the other issues which impact on their overall quality of life. It becomes more and more evident that a new subspecialty of nephrology practice is developing. Embracing these changes with a positive, forward-looking attitude is opening up an important and rewarding new field of clinical practice and will yield vast numbers of further service and research possibilities.

3.3 Implications for Service Development

With the resources and patient pathways currently available, it would be possible to support many small changes to the routines and protocols, which may yield significant benefits. Initial steps should be to incorporate simple assessments of physical activity levels, fitness and functional capacity (including ability to self care) into routine clinic review, particularly at transition stages (e.g. from CKD to pre-dialysis clinic, from pre-dialysis clinic to dialysis clinic). These could be used to identify patients at highest risk, and offer as a minimum the services that are already available to other older adult. As well as specialty specific teams, there needs to be a multidisciplinary approach, involving the General Practitioner and Social Care, as many such services are currently accessed from the community. Information on the benefits of exercise, and the risks of inactivity, should be available to patients at each stage of their disease, both in consultation and in printed form. This could be done at patient information days, one on one in clinics and on the wards, and by providing written materials in the outpatient settings and in the CKD and predialysis packs. Patient information leaflets are being prepared at the time of submission.

The Renal Unit should encourage self-reporting and staff reporting of functional limitations and physical fitness concerns, especially falls. Established physiotherapy services and falls prevention programs are available within the trust but are anecdotally underused by uraemic patients.

The next step towards this will be to petition for dedicated physiotherapist time. Physiotherapy review should be accessed as routinely as dietician review, which is offered to every predialysis patient.

Ultimately, this author would hope to offer physiotherapist-supported exercise programs for the maintenance and improvement of physical fitness and functioning to every uraemic patient treated under the care of the Nottingham Renal Unit. This should be of proven efficacy, accessible to as many patients as possible, enjoyable for the patients and well supported by resources and staff. Whilst programs may have a group based or generic component, exercise prescriptions should be individualised for medical safety and motivational reasons. The programs should ideally be offered in the pre dialysis stage and continued throughout the renal patient career through dialysis and /or transplantation. Medical assessments of fitness to partake in these programs should be routine, as many of the standard review assessments already in place are relevant.

Current best evidence suggests that for patients established on RRT, supervised intradialytic programs are likely to provide the most lasting benefit (Cheema et al.). Individually tailored programs of mixed aerobic and resistance training should be offered. Advice should be sought from units already running similar programs. Despite the lack of national guidelines on how to develop a local dialysis exercise program, information can be gained from units already providing these services and sharing knowledge amongst the nephrology community will advance expertise.

Any intervention program should be subject to feedback and monitoring on a regular basis. It would be important to try to feed any data stream into our local renal database.

Staff members involved in motivating, supervising or monitoring these programs should receive training and support. They should have dedicated time available for this task. This is supported by evidence offered in Section 2.4.

This author proposes the incorporation of exercise programs into more holistic positive lifestyle packages to promote exercise as part of a strategy to enhance well being. The Renal Unit has renal dieticians, a psychologist, and predialysis and dialysis specialist nurses as well as medical and allied auxiliary staff. Working together, the multidisciplinary team could devise education and care packages that incorporate newer interventions in coordination with the extensive support already in place. This could take inspiration from approaches such as the Amgen Life Options "Five Es" model of rehabilitation, which is mentioned above in Section 1.8. The Life Options program is structured around the "5 Es". Each of these should be considered in the context of local knowledge. Education prepares the patient for participation and responsibility and, as discussed, could be relatively easily achieved locally. Emotional support (or Encouragement) encompasses trying to achieve patient acceptance of serious chronic disease burden whilst living with positive expectations. Positive attitudes from staff and carers are also important. This is in part an issue of education but also requires constant supervision, encouragement and reassessment. Locally, a dedicated renal psychologist is experienced at managing renal patients and can play a vital role in this project. Evaluation incorporates this as individualised planning and regular assessment of progress. Exercise would be a key part of any program, as discussed already, and Employment is a focus for those of an age and capability.

A Renal Lifestyle program could offer a portfolio of education, dietetic input, psychological support, exercise interventions and access to social workers to discuss benefits and financial issues. The package could be provided to individuals but with some services in a group setting. This would work well dovetailed into the patient support network and supported by national kidney groups such as the National Kidney Foundation.

Already, a multidisciplinary panel has been convened to drive this forward in Nottingham. This author led the first meeting of a project-scoping group for Positive Lifestyle Interventions for Nottingham Dialysis Patients took place on September 25th 2009. The intention is to seek funding through the East Midlands Regional Innovation Fund, but a pilot exercise is underway.

Whilst the work in this thesis has focused on older patients, many of the lessons learned could be extrapolated to other age groups. This is important as the pathophysiology of functional decline and of renal bone disease means that it is not just older dialysis patients who may have “uraemic disability” and may be vulnerable to low trauma fractures. Many younger patients with end-stage renal failure are likely to live into older adulthood with the lifelong burden of renal disease impacting on their ageing process, so it is vital to invest in these groups.

3.4 Future Research

As more literature emerges confirming the suspected increased falls risk in older maintenance haemodialysis patients, this author proposes that focus should shift to validating falls risk screening tests to identify higher risk patients within this group. Validating established single measures such as Timed Get Up and Go Test or Sit to Stand Tests would be valuable but a multifaceted test is likely to be more sensitive and specific. Validating widely used or commercially available combined tests such as the FallScreen Tool© (Lord et al., 2003) would be a preferable option. The higher risk patients can then be referred on for risk factor assessments and intervention.

Identifying risk factors is critical, as intervention here is an effective way of reducing falls occurrence. There is increasing evidence that factors associated with haemodialysis or ESRF are contributory (e.g. bone disease (Boudville et al.)). However, there is still limited research exploring haemodialysis as an independent risk factor for falls. Additionally, there is currently no published literature to explore falls in patients of all ages on other forms of RRT e.g. comparing rates in haemodialysis with those in peritoneal dialysis or with renal transplant. It would also be interesting to explore falls and functional fitness in those with a spectrum of stages of CKD.

In the longer term, there has recently been great interest in the falls literature regarding the role of vitamin D insufficiency in falls, and supporting the use of Vitamin D supplementation in effective falls reduction programs (Larsen et al., 2005). The implications for this in CKD and ESRD are particularly exciting. As functioning nephron mass declines, vitamin D production also declines so patients with ESRD or on dialysis are invariably vitamin D deplete. The relationship between Vitamin D and renal function is well accepted but both vitamin D

research and bone mineral management in CKD and ESRD have evolved significantly in recent years. There is no recent published data on the levels of the vitamin D metabolites in those patients with CKD and ESRD managed with latest guidelines. There is also no published data on the wider impact of the altered vitamin D metabolism in these patients and whether vitamin D insufficiency may play a part in reduced activity, reduced postural stability, falls burden and increased fracture rate. This potentially provides an angle from which we may be able to advance understanding of subgroup vitamin D metabolite effects in reduced muscle strength in all patients.

As discussed above, any new services must provide data for monitoring, audit and clinical governance. As well as clinical governance and audit implications, this could provide a data stream for future study. The introduction of holistic intervention and education programs incorporating exercise but also promoting positive lifestyle changes with an overall focus on quality of life would be a fascinating avenue.

APPENDICES

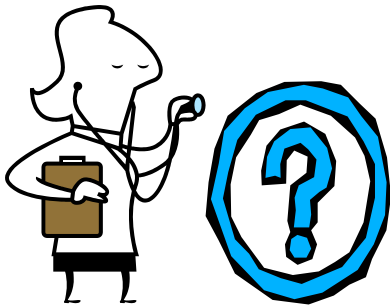
4.1 Documentation for Section 2.3

4.1.1 Questionnaire

Date _____/_____/____ Patient ID number _____

Physical Health, Falls and Falls Risk in Dialysis Patients

A retrospective cohort study by investigator administered questionnaire.



This questionnaire is part of our research into the physical fitness of dialysis patients. This questionnaire is designed to gather information about you and your health.

It focuses on how dialysis makes you feel and aspects of your health such as falls, fractures, your daily life and activities.

The information you give will be treated in the strictest confidence.

Your Personal Details

First Name _____

Surname _____

Age (years) _____

Gender Male Female

If you know your height, please fill it in...

(feet and inches) _____ OR (metres) _____

What is your target weight (kg) _____

Your dialysis

How do you feel PHYSICALLY during a dialysis session?

- I *always* feel fine.
- Most sessions I feel fine, but I occasionally I have problems.
- Most sessions I feel unwell some or all of the time.
- I *always* feel unwell or have problems.

Do you have any of the following problems whilst you are on dialysis?

- | | | | | | | |
|-----------------------------|--------|--------------------------|-----------|--------------------------|-------|--------------------------|
| • Low blood pressure | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Blackouts | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Cramps | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Headaches | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Nausea / vomiting | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Chest pain | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Itching | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |
| • Pains at the fistula site | Always | <input type="checkbox"/> | Sometimes | <input type="checkbox"/> | Never | <input type="checkbox"/> |

How do you usually feel PHYSICALLY after a haemodialysis session?

- Worse
- The same
- Better

Do you think haemodialysis affects your balance (steadiness on feet)?

- My balance is **worse** after my dialysis session.
 - ... for less than one hour.
 - ...for more than one hour.
- My balance is **the same** before and after a dialysis session.
- My balance is **better** after a dialysis session.

If you would like to make any other comments about your haemodialysis treatment and how it makes you feel, please use the space below: -

Your Medical History

In addition to your kidney failure, do you have any other medical problems? (tick any that apply)

- Visual problems
- Hearing problems
- Mobility Problems
- Arthritis
- Angina
- Heart Attack
- Stroke
- Diabetes
- Cancer
- Osteoporosis (thin bones)

Other Please state below

Your Medications (drugs or tablets from the doctor or chemist).

Do you take any medications? YES (Please indicate below)
NO (Please go onto the next section)

Do you take **four or more** different medications? YES NO

Your daily activities

These questions are designed to assess your level of physical health and what activities you can do in your daily life. We also ask how you feel about your physical fitness.

Do you ever use a wheelchair or a walking aid? (you may tick more than one).

- No.
- Yes, a frame.
- Yes, a stick.
- Yes, a wheelchair.

Do you feel your physical fitness has changed since you started haemodialysis?

- I have got worse
- I am about the same
- I feel my fitness is better

Below is a list of some activities which you may do. Please tick the boxes next to those activities which you regularly carry out unassisted (at least once a week).

LOOKING AFTER YOURSELF

- Bathing or dressing yourself.
- Bending, kneeling or stooping.
- Doing your own grocery shopping.
- Doing your own cooking.

WALKING

- Walking up to ten yards on the flat.
- Walking one hundred yards on the flat.
- Walking half a mile or more.
- Walk for twenty minutes on the flat without stopping.

STAIRS

- Climb one flight of stairs unassisted.
- Climbing several flights of stairs.

LEISURE AND RELAXATION

- Undertaking physical exercise or sport as a **hobby**
(e.g. golf, walking, bowling).
- Vigorous activities such as running, digging, lifting weights.
- Physical affection / lovemaking with a partner .

Since you started haemodialysis have you been able to take holidays or breaks in the UK or abroad?

YES NO Number -----

How often do you do physical activity or exercise for at least half an hour that makes you feel slightly breathless or warmer?

- Less than once a month
- More than once a month but less than once a week
- Once a week or more
- Five times a week or more

Falls

We define falls as any events which lead to you being unintentionally on a lower level than where you started; for example tripping over and landing on the floor, stumbling, slipping or losing your footing, blacking out or collapsing.....

Have you had any falls

- **in the past two weeks ?** YES NO Number -----

- **in the past six months?** YES NO Number -----

If you have had a fall, please fill in details of YOUR MOST RECENT FALL below;

Do you remember when it happened?

- On a dialysis day...
 - Before a dialysis session
 - After a dialysis session
- On a non-dialysis day
- Can't remember

Do you remember why it happened?

- Slip, trip or stumble
 - Collapse or "blackout"
 - Other reason
-
- I don't know why it happened
 - Can't remember

Did you hurt yourself?

- Yes, cuts, bumps or bruises
- Yes, broken bone/s
- No. I was unhurt

In general, would you say that you **worry** about having a fall?

YES NO

Do you **limit activities** that you do because of worry about falling?

YES NO

Does fear of falling affect your daily life?

The following questions are about your normal level of physical fitness and activity in relation to the confidence that you have with your balance. We want to know which activities you feel confident and safe to carry out by yourself.

Please mark the scale by placing a tick in the box to indicate how confident you are in carrying out the following activities...

1 = completely confident. 10 = No confidence.

(**For example;** if you feel *reasonably* happy walking around the house by yourself, but have had the occasional “wobble” or “stumble”, then you might decide to give yourself a score of 4/10.)

	1	2	3	4	5	6	7	8	9	10
Walking around the house				√						

MOST CONFIDENT → LEAST CONFIDENT

	1	2	3	4	5	6	7	8	9	10
Walking around the house										
Reaching into cabinets or closets										
Preparing meals (that do not require the carrying of heavy or hot objects)										
Taking a bath or shower										
Getting in and out of bed										
Answering the door or telephone										
Getting into or out of a chair										
Getting dressed or undressed										
Doing light housework (make the bed, dusting etc.)										
Doing simple shopping										

Broken Bones

Have you ever broken any bones? YES (please provide details below)
 NO (please go onto the next section)

As far as you know, has anyone **in your family** ever suffered from **osteoporosis** (thin bones), curvature of the spine, height loss or broken bones in their older age?

- Yes, my mother
- Yes, another family member
- No
- Don't know

Some General Questions

Do you **smoke**? YES NO

Given up

If you smoke or used to smoke; How many cigarettes per day? _____

For how many years? _____

Do you drink **alcohol**? YES NO

Units per week _____

(one unit is half a pint of beer, a glass of wine, or a measure of spirits)

Do you live by yourself? YES NO

Does your house have stairs? YES NO

Do you have a pet cat or dog? YES NO

How you feel today

The following questions are about your mood and spirits at this time.

Please tick the appropriate box to indicate whether or not you agree with the following statements.

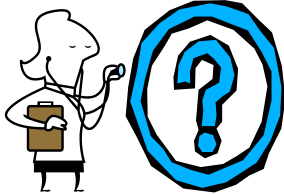
	YES	NO
Are you basically satisfied with your life?		
Have you dropped or given up many of your activities and interests?		
Do you feel your life is empty?		
Do you often get bored?		
Are you in good spirits most of the time?		
Are you afraid that something bad is going to happen to you?		
Do you feel happy most of the time?		
Do you often feel helpless?		
Do you prefer to stay at home rather than going out and doing new things?		
Do you feel that you have more problems with your memory than most?		
Do you think it is wonderful to be alive now?		
Do you feel pretty worthless the way you are now?		
Do you feel full of energy?		
Do you feel that your situation is helpless?		
Do you think most people are better off than you?		

Thank you for taking the time to complete these questions.

4.1.2 Invitation Letter

Physical Health, Falls and Falls Risk in Dialysis Patients

Investigators: Dr RJA Sims, SN Taylor, Dr MJ Cassidy, Dr T Masud, Dr S Roe



Dear Patient,

As you may be aware, we are currently carrying out some research looking into the physical health of dialysis patients such as yourself. In particular, we are interested in your mobility, muscle strength, balance and posture. We are interested in how these things affect the chances of people having falls which may cause injuries.

As part of this research, we are asking patients to help us by taking part in a questionnaire study. This questionnaire is designed to collect information about you and your health. It focuses on how dialysis makes you feel and also on aspects of your health such as falls, injuries, broken bones, your daily life and activities.

We would like to come and ask you some questions about these things during one of your dialysis sessions. The questions are likely to take about thirty minutes, although this time may vary. We would not ask you to do any of the paperwork yourself! The only thing we would ask you to do is to bring in an up-to-date list of your current medications so we can make a note of these.

We would be very grateful if you could take a few minutes to read the more detailed information sheet enclosed with this letter. Take some time to think about whether you would like to help with the study. During one of your dialysis sessions, one of our researchers will then come back and ask you if you would like to participate. If you would prefer not to participate then this will not affect your treatment in any way.

The information you give will be treated in the strictest confidence.

Many thanks.

Yours faithfully, Dr RJA Sims, SN Taylor, Dr MJ Cassidy, Dr T Masud, Dr S Roe

Contact for further information

If you would like any further information about the study, please contact Dr. Rebecca Sims or Research Nurse Rachael Taylor on 0115 8402666, or on pager via the switchboard (0115 9691169).

4.1.3 Information Sheet

Physical Health, Falls and Falls Risk in Dialysis Patients

Investigators: Dr RJA Sims, SN Taylor, Dr MJ Cassidy, Dr T Masud, Dr S Roe

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. Thank you for reading this.

What is the purpose of the study?

We already know that people on haemodialysis have an increased risk of broken bones compared to people not having haemodialysis. This is thought to be for a number of reasons. For example, weaker bones can be due to kidney disease or can occur if you need to take steroids for your illness. However, even if the bones are weak, there is usually an accident or event, which puts stress on the bone to cause the break. Sometimes broken bones are due to falls. We are interested in whether or not having dialysis treatment might affect your risk of falling.

More research is needed into this subject. We want to use a questionnaire study to find out about falls and risks for falling in patients on haemodialysis, compared to patients who have other types of dialysis or those who do not require dialysis at all. Many renal patients will be invited to take part in this study. For a variety of reasons, some people will not be able to complete the study questionnaire and so may not be eligible to take part.

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 be asked to sign a consent form. You are free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

This study will involve completing a questionnaire during your dialysis session. One of the researchers will talk you through the questionnaire. We anticipate that it will take about thirty minutes although this time may vary. It may be necessary for us to access your medical notes to check any details that are unclear. We ask you to bring a list of your normal medicines and the doses in with you if you can.

What are the possible disadvantages and risks of taking part?

None

foreseen.

What are the possible benefits of taking part?

Taking part in this study will not change the treatment you receive, and is not anticipated to have any direct benefits for yourself, but may help us improve treatments in future.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. We will not routinely inform your GP.

Contact for further information: If you would like any further information about the study, please contact Dr. Rebecca Sims or Research Nurse Rachael Taylor on 0115 8402666, or on pager via the switchboard (0115 9691169).

4.1.4 Consent Form

Physical Health, Falls and Falls Risk in Dialysis Patients

Investigators: Dr R Sims, SN Taylor, Dr M Cassidy, Dr T Masud, Dr S Roe

The patient should complete the whole of this sheet himself/herself.

Please cross out as necessary

- Have you read & understood the patient information sheet? YES/NO
- Have you had opportunity to ask questions & discuss the study? YES/NO
- Have all the questions been answered satisfactorily? YES/NO
- Have you received enough information about the study? YES/NO
- Do you understand that your GP (own doctor) will not be informed about your participation in this study (unless you specifically request that we do so)? YES/NO
- Who have you spoken to about the study? _____
- Do you understand that you are free to withdraw from the study
 - At any time? YES/NO
 - Without having to give a reason? YES/NO
 - Without affecting your future medical care? YES/NO
- Do you agree to take part in the study? YES/NO

Signature (Patient)

Date

Name (In block capitals)

I have explained the study to the above patient and he/she has indicated his/her willingness to take part.

Signature (Investigator)

Date

Name (In block capitals)

4.2 Questionnaire for Section 2.4

**Staff Perception of the Benefits of Exercise for Older Adult
Haemodialysis Patients**

Thank you for taking the time to complete this short questionnaire.

This questionnaire investigates staff perceptions and opinions about physical functioning and the benefits of exercise in older haemodialysis patients. In this study, the term "physical functioning" means ability to independently undertake the physical component of a variety of daily activities ranging from washing and dressing to work and leisure.

Once analysed, the results of the questionnaire will be used as part of a larger research thesis on physical fitness in older haemodialysis patients and may be used to support development of services in this unit and other haemodialysis units. The results will be presented to the department and can be made available to you by e-mail.

If you have any additional comments or would be willing to discuss this topic further, please indicate this in the free comments box below.

I am very grateful for your time and input.

Dr Rebecca Sims. becsims@gmail.com

<p>Name _____ (not required)</p> <p>Job Title _____</p> <p>Time working within Renal Unit _____ years _____ months</p> <p>Email address _____ (if you wish to be e-mailed with the results)</p>
--

<p>Comments</p>
--

	Strongly agree	Agree	Don't know	Disagree	Strongly disagree
It is important to me that my patients achieve their best possible level of physical functioning.					
I have no concerns about the physical functioning of any the dialysis patients I look after.					
My patients are satisfied with their levels of physical functioning.					
I do not usually assess the physical functioning of my dialysis patients.					
I always ask my patients about their exercise habits.					
My patients are satisfied with the level of care given to any problems they may have with physical functioning.					
It is my responsibility to help patients increase their physical functioning.					
It is not my role to discuss or encourage exercise for my patients.					
There is no time in my daily work schedule to discuss exercise with my patients.					
There is no opportunity in my daily routine to encourage patients to exercise.					
As part of my job, I often talk to patients about the benefits of exercise and encourage and advise them on ways to improve their physical fitness.					
I don't know how to motivate patients to exercise.					
I don't know how to counsel patients on how to improve physical functioning.					
My patients have too many other problems for them to want to participate in exercise.					
Dialysis patients would exercise more if they felt better.					
Dialysis patients don't want to participate in regular exercise.					
Dialysis patients would exercise regularly if given a chance and information.					
Dialysis patients lack the motivation to stick with an exercise program.					
Dialysis patients are too ill to exercise.					
It is harmful for dialysis patients to exercise moderately (i.e. walking, stationary cycling).					
It is harmful for dialysis patients to exercise vigorously (i.e. sports like running, bicycling).					
The staff I work with regularly encourage patients to exercise.					
The staff I work with believe that exercise is important for our patients.					
This dialysis unit places a high level of importance on assessing physical functioning of patients.					
My training included some information on the benefits of exercise for haemodialysis patients.					
I believe the Haemodialysis Unit should do more to encourage patients to maintain or improve their physical functioning.					
I believe that patients would benefit from having dedicated staff (e.g. a Renal Physiotherapist) to assess physical fitness and encourage exercise.					
I am aware of the benefits of exercise for haemodialysis patients.					
My training included information on the benefits of exercise for haemodialysis patients.					
My training included practical measures to assess and encourage exercise for my patients.					
I do not believe encouraging exercise would alter my patient's quality of life.					
I believe my patients would have a better quality of life if they were encourage to undertake regular exercise.					

4.3 Presentations of Research

- **Sims R.J.A.**, Mockett, S., Cassidy, M.J.D., Postural Stability in Haemodialysis Patients; A rationale for Physiotherapy Input. Oral Presentation. British Renal Society Symposium. May 2003.
- **Sims R.J.A.**, Mockett S., Taylor R., Masud T., Roe S., Cassidy M.J.D. A pilot study investigating the effect of haemodialysis on leg extensor power, postural sway and the timed "Up and Go" test. The Scottish Physiotherapy Research Group and Physiotherapy Research Society Joint Spring Meeting. Queen Margaret University College, Edinburgh. May 2003
- **Sims R.J.A.**, Mockett, S., Cassidy, M.J.D., Masud, T. Is haemodialysis an independent risk factor for falls? Performance based assessments of falls risk in haemodialysis patients. Poster Presentation. East Midlands and Trent Falls Symposium. July 2003.
- **Sims R.J.A.**, Mockett, S., Taylor, R., Cassidy, M.J.D., Masud,T. Is there a rationale for targeted falls prevention programs on the haemodialysis unit? Poster Presentation. The 4th International Conference on Falls and Postural Stability, September 2003.
- **Sims R.J.A**, Mockett, S., Taylor, R., Roe, S., Cassidy, M.J.D., Masud, T. The effect of a single haemodialysis session on performance based assessments of falls risk in older adults on haemodialysis. Poster with Discussion Forum. Renal Association Annual Meeting, May 2006.
- **Sims R.J.A**, Taylor R., Mockett S., Masud T. Perceptions of physical health, functional ability, falls risk and quality of life in older haemodialysis

patients compared with non-dialysed controls. 7th International Conference on Falls and Postural Stability. September 2006.

4.4 Publications of Research

- **Sims, R.J.A.**, Masud, T., Cassidy, M.J.D. The increasing number of older patients with renal disease. *BMJ*, Aug 2003; 327: 463 – 464
- **Sims, R.J.A.** Ageing patients pose a rewarding challenge. *Nephronline*. www.nephronline.org September 2003.
- **Sims R.J.A**, Cassidy M.J.D. Dialysis in the elderly, new possibilities, new problems. *Minerva Urol Nefrol*. 2004 Sep;56(3):305-17. Review.
- **Sims R.J.A**, Hosking, D.J., Ubhi, C. Hyperparathyroidism in the elderly patient. *Drugs Aging*. 2004; 21(15): 1013-24. Review.
- **Sims, R.J.A**, Taylor R., Masud T., Roe S., Cassidy M.J.D., Mockett S. The Effect of a single Haemodialysis session on Functional Mobility and Physical Impairment in Older Adults: a pilot study. *International Journal of Geriatric Urology and Nephrology*.2.7. Volume 34. Issue 4. Pages 1287-93.

REFERENCES

- A, P., R, G. and P, D. (2000) *Arch Intern Med*, **160**, 119-203.
- Acaray, A. and Pinar, R. (2005) *Edtna Erca J*, **31**, 35-8.
- Alem, A., Sherrard, D. J., Gillen, D. L., Weiss, N. S., Beresford, S. A., Heckbert, S. R., Wong, C. and Stehman-Breen, C. (2000a) *Kidney Int*, **58**, 396-9.
- Alem, A. M., Sherrard, D. J., Gillen, D. L., Weiss, N. S., Beresford, S. A., Heckbert, S. R., Wong, C. and Stehman-Breen, C. (2000b) *Kidney Int*, **58**, 396-9.
- Allain, H., Bentue-Ferrer, D., Polard, E., Akwa, Y. and Patat, A. (2005) *Drugs Aging*, **22**, 749-65.
- Anderson, J. E., Boivin, M. R., Jr. and Hatchett, L. (2004) *Ren Fail*, **26**, 539-44.
- Aniansson, A., Hedberg, M., Henning, G. and Grimby, G. (1986) *Muscle Nerve*, **9**, 585-91.
- Ansell D, Feest TG, Tomson C, Williams AJ and G, W. (2006) (*supplement*) *Nephrology Dialysis & Transplantation*.
- Ansell, D., Casula, A., Farrington, K., Feehally, J., Fluck, R., Fogarty, D., Ford, D., Hodsman, A., Tomson, C., Williams, A., Warwick, C. and Udayaraj , U. (2009) <http://www.renalreg.com/Reports/2008.html>.
- Ansell, D., Feest, T., Ahmad, A. and Rao, R. (2004) UK Renal Registry.
- Aronow, W. S. and Ahn, C. (1997) *J Am Geriatr Soc*, **45**, 1051-3.
- Banerjee, A., Kong, C. H. and Farrington, K. (2004) *Nephrol Dial Transplant*, **19**, 1528-32.
- Baracskey, D., Jarjoura, D., Cugino, A., Blend, D., Rutecki, G. W. and Whittier, F. C. (1997) *Clin Nephrol*, **47**, 222-8.
- Barnea, N., Drory, Y., Iaina, A., Lapidot, C., Reisin, E., Eliahou, H. and Kellermann, J. J. (1980) *Isr J Med Sci*, **16**, 17-21.
- Bassey, E. and Short, A. (1990) *Eur J Appl Physiol Occup Physiol*, **60**, 385-90.
- Bassey, E. J., Fiatarone, M. A., O'Neill, E. F., Kelly, M., Evans, W. J. and Lipsitz, L. A. (1992) *Clin Sci (Lond)*, **82**, 321-7.

- Beasley, C. R., Smith, D. A. and Neale, T. J. (1986) *Aust N Z J Med*, **16**, 5-10.
- Bertoli, M., Luisetto, G., Ruffatti, A., Urso, M. and Romagnoli, G. (1990) *Clin Nephrol*, **33**, 98-102.
- BF, B. H. (1995) *J Gerontol*, **50A**, 41-4.
- Biderman, A., Cwikel, J., Fried, A. V. and Galinsky, D. (2002) *J Epidemiol Community Health*, **56**, 631-6.
- Birge, S. and Haddad, J. (1975) *J Clin Invest*, **56**, 1100-7.
- Bischoff, H. A., M. B., F. G. and al, e. (2001) *Histochem J*, **33**, 19-24.
- Bischoff, H. A., Stahelin, H. B., Dick, W., Akos, R., Knecht, M., Salis, C., Nebiker, M., Theiler, R., Pfeifer, M., Begerow, B., Lew, R. A. and Conzelmann, M. (2003) *J Bone Miner Res*, **18**, 343-51.
- Bischoff, H. A., Stahelin, H. B., Urscheler, N., Ehram, R., Vonthein, R., Perrig-Chiello, P., Tyndall, A. and Theiler, R. (1999) *Arch Phys Med Rehabil*, **80**, 54-8.
- Bischoff-Ferrari, H. A., Dawson-Hughes, B., Willett, W. C., Staehelin, H. B., Bazemore, M. G., Zee, R. Y. and Wong, J. B. (2004) *Jama*, **291**, 1999-2006.
- Bischoff-Ferrari, H. A., Willett, W. C., Wong, J. B., Giovannucci, E., Dietrich, T. and Dawson-Hughes, B. (2005) *Jama*, **293**, 2257-64.
- Black, A. and Wood, J. (2005) *Clin Exp Optom*, **88**, 212-22.
- Blagg, C. R. (1994) *Am J Kidney Dis*, **24**, S17-21; discussion S31-2.
- Blake, A. J., Morgan, K., Bendall, M. J., Dallosso, H., Ebrahim, S. B., Arie, T. H., Fentem, P. H. and Basse, E. J. (1988) *Age Ageing*, **17**, 365-72.
- Boland, R. (1986) *Endocr Rev*, **7**.
- Boland, R., A. N., E. R. and W, H. (1985) *Biochem Biophys Res Commun*, **128**, 305-11.
- Boland, R., AR, d. B., MJ, M., G, S., G, V. and S, Z. (1995) *Mol Cell Endocrinol*, **114**, 1-8.

- Bonzel, K. E., Wildi, B., Weiss, M. and Scharer, K. (1991) *Pediatr Nephrol*, **5**, 22-8.
- Boonen, S., Vanderschueren, D., Geusens, P. and Bouillon, R. (1997) *Int J Androl*, **20**, 134-43.
- Boudville, N., Inderjeeth, C., Elder, G. J. and Glendenning, P. *Clin Endocrinol (Oxf)*, **73**, 299-304.
- Boyce, M. L., Robergs, R. A., Avasthi, P. S., Roldan, C., Foster, A., Montner, P., Stark, D. and Nelson, C. (1997) *Am J Kidney Dis*, **30**, 180-92.
- Bradley, J. R., Anderson, J. R., Evans, D. B. and Cowley, A. J. (1990) *Clin Sci (Lond)*, **79**, 239-45.
- Brunier, G. M. and Graydon, J. (1993) *Anna J*, **20**, 457-61; discussion 462, 521.
- Bullock, R. E., Amer, H. A., Simpson, I., Ward, M. K. and Hall, R. J. (1984) *Br Med J (Clin Res Ed)*, **289**, 1479-84.
- Cade, P. (1995) *Nephrol News Issues*, **9**, 26-8.
- Campbell, A. J., Borrie, M. J. and Spears, G. F. (1989) *J Gerontol*, **44**, M112-7.
- Campbell, A. J., Reinken, J., Allan, B. C. and Martinez, G. S. (1981) *Age Ageing*, **10**, 264-70.
- Capodaglio, E. M., Villa, G., Jurisic, D. and Salvadeo, A. (1998) *Int J Artif Organs*, **21**, 391-7.
- Cappy, C. S., Jablonka, J. and Schroeder, E. T. (1999) *J Ren Nutr*, **9**, 63-70.
- Caramel, V. M., Remarque, E. J., Knook, D. L., Lagaay, A. M. and Van den Brande, K. J. (1998) *J Am Geriatr Soc*, **46**, 1178-9.
- Carney, R. M., McKevitt, P. M., Goldberg, A. P., Hagberg, J., Delmez, J. A. and Harter, H. R. (1983) *Nephron*, **33**, 179-81.
- Carney, R. M., Templeton, B., Hong, B. A., Harter, H. R., Hagberg, J. M., Schechtman, K. B. and Goldberg, A. P. (1987) *Nephron*, **47**, 194-8.
- Carpeggiani, C., L'Abbate, A., Landi, P., Michelassi, C., Raciti, M., Macerata, A. and Emdin, M. (2004) *Int J Cardiol*, **96**, 361-8.

- Caspersen, C. J., Powell, K. E. and Christenson, G. M. (1985) *Public Health Rep*, **100**, 126-31.
- Chamberlin, M. E., Fulwider, B. D., Sanders, S. L. and Medeiros, J. M. (2005) *J Gerontol A Biol Sci Med Sci*, **60**, 1163-7.
- Chandra, S. M., Schulz, J., Lawrence, C., Greenwood, R. and Farrington, K. (1999) *BMJ*, **318**, 217-223.
- Chapuy, M. C., Arlot, M. E., Duboeuf, F., Brun, J., Crouzet, B., Arnaud, S., Delmas, P. D. and Meunier, P. J. (1992) *N Engl J Med*, **327**, 1637-42.
- Cheema, B. S. and Singh, M. A. (2005) *American Journal of Nephrology*, **25**.
- Clark, B. A., Shannon, C., Brown, R. S. and Gervino, E. V. (1996) *J Am Soc Nephrol*, **7**, 1223-7.
- Clyne, N. (2004) *Clin Nephrol*, **61 Suppl 1**, S10-3.
- Clyne, N., Ekholm, J., Jogestrand, T., Lins, L. E. and Pehrsson, S. K. (1991) *Nephron*, **59**, 84-9.
- Clyne, N., Jogestrand, T., Lins, L. E., Pehrsson, S. K. and Ekelund, L. G. (1987) *Acta Med Scand*, **222**, 183-90.
- Cook, W. L. and Jassal, S. V. (2005) *Int Urol Nephrol*, **37**, 649-52.
- Cook, W. L. and Jassal, S. V. (2008) *Kidney Int*, **73**, 1289-95.
- Cook, W. L., Tomlinson, G., Donaldson, M., Markowitz, S. N., Naglie, G., Sobolev, B. and Jassal, S. V. (2006) *Clin J Am Soc Nephrol*, **1**, 1197-204.
- Copley, J. B. and Lindberg, J. S. (1999) *Adv Ren Replace Ther*, **6**, 165-71.
- Corless, D., Dawson, E., Fraser, F., Ellis, M., Evans, S. J., Perry, J. D., Reisner, C., Silver, C. P., Beer, M., Boucher, B. J. and et al. (1985) *Age Ageing*, **14**, 76-84.
- Cumming, R. G., Salkeld, G., Thomas, M. and Szonyi, G. (2000) *J Gerontol A Biol Sci Med Sci*, **55**, M299-305.
- Curtin, R. B., Klag, M. J., Bultman, D. C. and Schatell, D. (2002) *Am J Kidney Dis*, **40**, 331-8.

- Curtin, R. B., Lowrie, E. G. and DeOreo, P. B. (1999) *Adv Ren Replace Ther*, **6**, 133-40.
- Daul, A. E., Khalifa, A. M., Graven, N. and Brodde, O. E. (1985) *Proc Eur Dial Transplant Assoc Eur Ren Assoc*, **21**, 178-84.
- Daul, A. E., Schafers, R. F., Daul, K. and Philipp, T. (2004) *Clin Nephrol*, **61 Suppl 1**, S26-30.
- Dawson-Hughes, B., Harris, S. S., Krall, E. A. and Dallal, G. E. (1997) *N Engl J Med*, **337**, 670-6.
- De Vecchi, A. F., Maccario, M., Braga, M., Scalamogna, A., Castelnovo, C. and Ponticelli, C. (1998) *Am J Kidney Dis*, **31**, 479-90.
- Death, C. (1999) *Edtna Erca J*, **25**, 13-5.
- Deligiannis, A. (2004) *Clin Nephrol*, **61 Suppl 1**, S39-45.
- Deligiannis, A., Kouidi, E., Tassoulas, E., Gigis, P., Tourkantonis, A. and Coats, A. (1999a) *Int J Cardiol*, **70**, 253-66.
- Deligiannis, A., Kouidi, E. and Tourkantonis, A. (1999b) *Am J Cardiol*, **84**, 197-202.
- Delmez, J. A. and Slatopolsky, E. (1992) *Am J Kidney Dis*, **19**, 303-17.
- DeOreo, P. B. (1997) *Am J Kidney Dis*, **30**, 204-12.
- DePaul, V., Moreland, J., Eager, T. and Clase, C. M. (2002) *Am J Kidney Dis*, **40**, 1219-29.
- Desmet, C., Beguin, C., Swine, C. and Jadoul, M. (2005) *Am J Kidney Dis*, **45**, 148-53.
- Dharmarajan, T. S. and Norkus, E. P. (2004) *J Am Med Dir Assoc*, **5**, 395-400.
- Dhesi, J. K., Moniz, C., Close, J. C., Jackson, S. H. and Allain, T. J. (2002) *Age Ageing*, **31**, 267-71.
- Diesel, W., Emms, M., Knight, B. K., Noakes, T. D., Swanepoel, C. R., van Zyl Smit, R., Kaschula, R. O. and Sinclair-Smith, C. C. (1993) *Am J Kidney Dis*, **22**, 677-84.

- Diesel, W., Noakes, T. D., Swanepoel, C. and Lambert, M. (1990) *Am J Kidney Dis*, **16**, 109-14.
- DOH (2001) *National Service Framework for Older People*, Department of Health.
- DOH (2004a) Department Of Health.
- DOH (2004b), Vol. Department of Health.
- DOH (2005) *National Service Framework for Renal Services (Part Two: Chronic Kidney Disease, Acute Renal Failure and End of Life Care)*, Department of Health.
- Don, B. R. and Kaysen, G. A. (2000) *J Nephrol*, **13**, 249-59.
- Donnelly, P. K., Simpson, A. R., Milner, A. D., Nicholson, M. L., Horsburgh, T., Veitch, P. S. and Bell, P. R. (1990) *Nephrol Dial Transplant*, **5**, 808-11.
- Durozard, D., Pimmel, P., Baretto, S., Caillette, A., Labeeuw, M., Baverel, G. and Zech, P. (1993) *Kidney Int*, **43**, 885-92.
- Dusso, A. and Brown, A. (1998) *Am J Kidney Dis*, **32(suppl)**, :S13-24.
- Ebly, E. M., Hogan, D. B. and Fung, T. S. (1997) *J Clin Epidemiol*, **50**, 857-63.
- EM, C., HM, B. and D, F. (1986) *Endocrinology*, **119**, 2214-20.
- Empana, J. P., Dargent-Molina, P. and Breart, G. (2004) *J Am Geriatr Soc*, **52**, 685-90.
- Englander, F., Hodson, T. J. and Terregrossa, R. A. (1996) *J Forensic Sci*, **41**, 733-46.
- Farrington, K., Hodsman, A., Casula, A., Ansell, D. and Feehally, J. (2009) *Nephron Clin Pract*, **111 Suppl 1**, c43-68.
- FC, B., EHP, J., O, M. and F, V. (1996) *Nephrol Dial Transplant*, **11(supple)**, 37-40.
- Fischer, E. R. and Harris, D. C. (1993) *Clin Nephrol*, **40**, 216-20.
- Fitts, S. S., Guthrie, M. R. and Blagg, C. R. (1999) *Nephron*, **82**, 115-21.
- Fonda, D., Cook, J., Sandler, V. and Bailey, M. (2006) *Med J Aust*, **184**, 379-82.
- Forgeron, S. and Valeriotte, L. (2001) *Cannt J*, **11**, 19-21.
- French, F. H., Torgerson, D. J. and Porter, R. W. (1995) *Age Ageing*, **24**, 185-9.

- Frey, S., Mir, A. R. and Lucas, M. (1999) *J Ren Nutr*, **9**, 71-7.
- Fryckstedt, J. and Hylander, B. (2008) *Scand J Urol Nephrol*, **42**, 466-71.
- Fuhrmann, I. and Krause, R. (2004) *Clin Nephrol*, **61 Suppl 1**, S14-25.
- G, M., Greco AV, M, C. and G., G. (1999) **353**, 806.
- Garland, C., Garland, F., Gorham, E., Lipkin, M., Newmark, H., Mohr, S. and Holick, M. (2005) *Am J Public Health*, doi:10.2105/AJPH.2004.045260.
- Giordano, M., Tirelli, P., Ciarambino, T., Gambardella, A., Ferrara, N., Signoriello, G., Paolisso, G. and Varricchio, M. (2007) *Nephron Clin Pract*, **106**, c187-92.
- Glerup, H., Mikkelsen, K., Poulsen, L., Hass, E., Overbeck, S., Andersen, H., Charles, P. and Eriksen, E. F. (2000) *Calcif Tissue Int*, **66**, 419-24.
- Gloth, F. M., 3rd, Gundberg, C. M., Hollis, B. W., Haddad, J. G., Jr. and Tobin, J. D. (1995a) *Jama*, **274**, 1683-6.
- Gloth, F. M., 3rd, Smith, C. E., Hollis, B. W. and Tobin, J. D. (1995b) *J Am Geriatr Soc*, **43**, 1269-71.
- Goldberg, A. P. (1984) *Am J Nephrol*, **4**, 132-3.
- Goldberg, A. P., Geltman, E. M., Gavin, J. R., 3rd, Carney, R. M., Hagberg, J. M., Delmez, J. A., Naumovich, A., Oldfield, M. H. and Harter, H. R. (1986) *Nephron*, **42**, 311-6.
- Goldberg, A. P., Geltman, E. M., Hagberg, J. M., Gavin, J. R., 3rd, Delmez, J. A., Carney, R. M., Naumowicz, A., Oldfield, M. H. and Harter, H. R. (1983) *Kidney Int Suppl*, **16**, S303-9.
- Goldberg, A. P., Hagberg, J., Delmez, J. A., Carney, R. M., McKeivitt, P. M., Ehsani, A. A. and Harter, H. R. (1980a) *Am J Clin Nutr*, **33**, 1620-8.
- Goldberg, A. P., Hagberg, J. M., Delmez, J. A., Haynes, M. E. and Harter, H. R. (1980b) *Kidney Int*, **18**, 754-61.
- Goodman, E. D. and Ballou, M. B. (2004) *Nephrol Nurs J*, **31**, 23-9.
- Graafmans, W. C., Ooms, M. E., Hofstee, H. M., Bezemer, P. D., Bouter, L. M. and Lips, P. (1996) *Am J Epidemiol*, **143**, 1129-36.

- Grady, D., Halloran, B., Cummings, S., Leveille, S., Wells, L., Black, D. and Byl, N. (1991) *J Clin Endocrinol Metab*, **73**, 1111-7.
- Grisso, J. A., Kelsey, J. L., Strom, B. L., Chiu, G. Y., Maislin, G., O'Brien, L. A., Hoffman, S. and Kaplan, F. (1991) *N Engl J Med*, **324**, 1326-31.
- Gryfe, C. I., Amies, A. and Ashley, M. J. (1977) *Age Ageing*, **6**, 201-10.
- Gu, Y., Ding, F., Chen, N., Mei, C. L., Qian, J. Q., Wang, X. Y., Shi, W., Hou, F. F., Li, X. W., Wang, M. and Chen, Y. P. (2005) *Ren Fail*, **27**, 205-12.
- Guarnieri, G., Grassi, G., Barazzoni, R., Zanetti, M. and Biolo, G. (2005) *J Ren Nutr*, **15**, 121-4.
- Guralnick, J., EM, S., L, F., RJ, G., LF, B., GD, B., PA, S. and RB, W. (1994) *J Gerontol*, **49**, M85 - M94.
- Guse, C. E. and Porinsky, R. (2003) *Wmj*, **102**, 37-42.
- Haas, B. and Burden, A. (2000) *Physiotherapy Research International*, **5**, 19-32.
- Haas, B. and Whitmarsh, T. (1998) *Physiotherapy research international*, **3**, 135-47.
- Hagberg, J. M., Goldberg, A. P., Ehsani, A. A., Heath, G. W., Delmez, J. A. and Harter, H. R. (1983) *Am J Nephrol*, **3**, 209-12.
- Hanninen, T., Koivisto, K., Reinikainen, K. J., Helkala, E. L., Soininen, H., Mykkanen, L., Laakso, M. and Riekkinen, P. J. (1996) *Age Ageing*, **25**, 201-5.
- Harter, H. R. and Goldberg, A. P. (1985) *Med Clin North Am*, **69**, 159-75.
- Hassan, B. S., Mockett, S. and Doherty, M. (2001) *Ann Rheum Dis*, **60**, 612-8.
- Hayashino, Y., Fukuhara, S., Akiba, T., Akizawa, T., Asano, Y., Saito, S. and Kurokawa, K. (2009) *Diabet Med*, **26**, 921-7.
- HEA, H. E. A. (1999a) London.
- HEA, H. E. A. U. (1999b) London.
- Headley, S., Germain, M., Mailloux, P., Mulhern, J., Ashworth, B., Burris, J., Brewer, B., Nindl, B., Coughlin, M., Welles, R. and Jones, M. (2002) *Am J Kidney Dis*, **40**, 355-64.

- Healey, F., Monro, A., Cockram, A., Adams, V. and Heseltine, D. (2004) *Age Ageing*, **33**, 390-5.
- Heaney, R. P. (1992) *Proc Soc Exp Biol Med*, **200**, 153-6.
- Heiwe, S., Clyne, N. and Dahlgren, M. A. (2003) *Physiother Res Int*, **8**, 167-77.
- Heiwe, S., Tollback, A. and Clyne, N. (2001) *Nephron*, **88**, 48-56.
- Hewison, M., Zehnder, D., Bland, R. and Stewart, P. M. (2000) *J Mol Endocrinol*, **25**, 141-8.
- Hillsdon, M., Thorogood, M., Anstiss, T. and Morris, J. (1995) *Journal of Epidemiology and Community Health*, **49**, 448- 453.
- Holick, M. F. (1995) *Am J Clin Nutr*, **61**, 638S-645S.
- Holley, J. L. (1998) *Am J Kidney Dis*, **31**, 574-83.
- Huang, T. T. (2006) *Int J Nurs Stud*, **43**, 357-65.
- Huang, T. T. and Wang, W. S. (2009) *Int J Nurs Stud*, **46**, 1313-9.
- Hung, A. M., Chertow, G. M., Young, B. S., Carey, S. and Johansen, K. L. (2002) *J Ren Nutr*, **12**, 170-6.
- Hyatt, R. H., Whitelaw, M. N., Bhat, A., Scott, S. and Maxwell, J. D. (1990) *Age Ageing*, **19**, 330-6.
- Iborra Molto, C., Pico Vicent, L., Montiel Castillo, A. and Clemente Ramon, F. (2000) *Edtna Erca J*, **26**, 38-40.
- Indridason, O. S. and Quarles, L. D. (2000) *Kidney Int*, **57**, 282-92.
- Isaacs, B. (1992) *The Challenge of Geriatric Medicine*, Oxford University Press.
- J Kampmann, K Siersback-Nielson, Kristensen, M. and al., e. (1974) *Acta Med Scand*, **196**, 517-20.
- JA, R. (1994) *Muscle Nerve*, **17:578-80**, 578-80.
- Janssen, H. C., Samson, M. M. and Verhaar, H. J. (2002) *Am J Clin Nutr*, **75**, 611-5.
- Jassal, S. V., Chiu, E. and Li, M. (2008) *Adv Chronic Kidney Dis*, **15**, 115-22.
- Jassal, S. V., Douglas, J. F. and Stout, R. W. (1998) *Nephrol Dial Transplant*, **13**, 1702-8.

- Johansen, K., PL, P., Sakkas, G. K., Gordon, P. L., J, D. and T, S. (2006) *J Am Soc Nephrol*, **17**, 2307-2314.
- Johansen, K., T, S., J, D., B, S., Sakkas, G. K. and JA, K.-B. (2003a) *Kidney Int*, **63**, 201-207.
- Johansen, K. L. (1999) *Adv Ren Replace Ther*, **6**, 141-8.
- Johansen, K. L. (2005) *Sports Med*, **35**, 485-99.
- Johansen, K. L., Chertow, G. M., Ng, A. V., Mulligan, K., Carey, S., Schoenfeld, P. Y. and Kent-Braun, J. A. (2000) *Kidney Int*, **57**, 2564-70.
- Johansen, K. L., Kaysen, G. A., Young, B. S., Hung, A. M., da Silva, M. and Chertow, G. M. (2003b) *Am J Clin Nutr*, **77**, 842-6.
- Johansen, K. L., Sakkas, G. K., Doyle, J., Shubert, T. and Dudley, R. A. (2003c) *Am J Kidney Dis*, **41**, 171-8.
- Johnell, O., Gullberg, B., Allander, J., Kanis, J. and Group, M. S. (1992) *Osteoporosis International*, **2**, 298-302.
- Johnell, O. and Kanis, J. A. (2004) *Osteoporos Int*, **15**, 897-902.
- Johnson, K. R., Jobber, J. and Stonawski, B. J. (1980) *Age Ageing*, **9**, 121-7.
- Jones, N. and Kjellstrand, C. M. (1996) *Am J Kidney Dis*, **28**, 861-6.
- Joo, J. H., Lenze, E. J., Mulsant, B. H., Begley, A. E., Weber, E. M., Stack, J. A., Mazumdar, S., Reynolds, C. F., 3rd and Pollock, B. G. (2002) *J Clin Psychiatry*, **63**, 936-41.
- Jorstad, E. C., Hauer, K., Becker, C. and Lamb, S. E. (2005) *J Am Geriatr Soc*, **53**, 501-10.
- K/DOQI (2003) *Am J Kidney Dis*, **42**, S1-201.
- Kappes, U., Schanz, G., Gerhardt, U., Matzkies, F., Suwelack, B. and Hohage, H. (2001) *Am J Nephrol*, **21**, 259-63.
- Kasiske, B. L. and Snyder, J. (2002) *J Am Soc Nephrol*, **13**, 1067-72.
- KDOQI (2002).
- Klang, B., Bjorvell, H., Berglund, J., Sundstedt, C. and Clyne, N. (1998) *J Adv Nurs*, **28**, 36-44.

- Koh, K. P., Fassett, R. G., Sharman, J. E., Coombes, J. S. and Williams, A. D. (2009) *BMC Nephrology*, **0**:doi:10.1186/1471-2369-10-2.
- Kong, C. H., Tattersall, J. E., Greenwood, R. N. and Farrington, K. (1999) *Nephrol Dial Transplant*, **14**, 2927-31.
- Kontos, P. C., Miller, K. L., Brooks, D., Jassal, S. V., Spanjevic, L., Devins, G. M., De Souza, M. J., Heck, C., Laprade, J. and Naglie, G. (2007) *Int Urol Nephrol*, **39**, 1303-11.
- Kooijman, A. C. and Cornelissen, F. W. (2005) *J Bone Miner Res*, **20**, 2061-2; author reply 2063.
- Koski, K., Luukinen, H., Laippala, P. and Kivela, S. L. (1998) *Gerontology*, **44**, 232-8.
- Kouidi, E. (2004) *Clin Nephrol*, **61 Suppl 1**, S60-71.
- Kouidi, E., Albani, M., Natsis, K., Megalopoulos, A., Gigis, P., Guiba-Tziampiri, O., Tourkantonis, A. and Deligiannis, A. (1998) *Nephrol Dial Transplant*, **13**, 685-99.
- Kouidi, E., Grekas, D., Deligiannis, A. and Tourkantonis, A. (2004) *Clin Nephrol*, **61 Suppl 1**, S31-8.
- Kouidi, E., Karagiannis, V., Grekas, D., Iakovides, A., Kaprinis, G., Tourkantonis, A. and Deligiannis, A. (2009) *Eur J Cardiovasc Prev Rehabil*.
- Krishnan, A. V. and Kiernan, M. C. (2009) *Nat Rev Neurol*.
- Kristensen, M. T., Foss, N. B. and Kehlet, H. (2009) *Physiother Res Int*, **14**, 30-41.
- Kurella, M., Chertow, G. M., Luan, J. and Yaffe, K. (2004) *J Am Geriatr Soc*, **52**, 1863-9.
- La Rovere, M. T., Pinna, G. D., Maestri, R., Mortara, A., Capomolla, S., Febo, O., Ferrari, R., Franchini, M., Gnemmi, M., Opasich, C., Riccardi, P. G., Traversi, E. and Cobelli, F. (2003) *Circulation*, **107**, 565-70.
- Lach, H. W. (2005) *Public Health Nurs*, **22**, 45-52.

- Lacquaniti, A., Bolignano, D., Campo, S., Perrone, C., Donato, V., Fazio, M. R., Buemi, A., Sturiale, A. and Buemi, M. (2009) *Ren Fail*, **31**, 239-45.
- Lancaster, T. and Stead, L. (2004) *The Cochrane Database of Systematic Reviews*.
- Larsen, E. R., Mosekilde, L. and Foldspang, A. (2005) *Aging Clin Exp Res*, **17**, 125-32.
- Lass, P., Buscombe, J. R., Harber, M., Davenport, A. and Hilson, A. J. (1999) *Clin Nucl Med*, **24**, 561-5.
- Lauritzen, J. B. (1997) *Dan Med Bull*, **44**, 155-68.
- Lawlor, D. and Hanratty, B. (2001) *Journal of Public Health Medicine*, **23**, 219-26.
- Leveille, S., Wagner, E. and Davis, C. (1998) *Journal of American Geriatric Society*, **46**, 1191-8.
- Lexell, J. (1995) *J Gerontol*, **50A**, 11-16.
- Li, M., Tomlinson, G., Naglie, G., Cook, W. L. and Jassal, S. V. (2008) *Nephrol Dial Transplant*, **23**, 1396-400.
- Life Options Rehabilitation Advisory Council, L. (1997) Medical Education Institute.
- Lindeman RD, Tobin J and NW, S. (1984) *Kidney Int*, **26**, 861-8.
- Lindeman, R. D., Tobin, J. and Shock, N. W. (1985) *J Am Geriatr Soc*, **33**, 278-85.
- Livesley, W. J. (1982) *J Psychosom Res*, **26**, 581-4.
- Lord, S. R., Menz, H. B. and Tiedemann, A. (2003) *Phys Ther*, **83**, 237-52.
- Macdonald, J. (2006) *Invited Address at the The British Renal Society & The Renal Association, The Renal Conference, Harrogate,, 03.05.2006*.
- Macdougall, I. C. and Ritz, E. (1998) *Nephrol Dial Transplant*, **13**, 3030-3.
- Malabanan, A., Veronikis, I. and Holkis, M. (1998) *Lancet*, **351**, 805-6.
- Mandigers, C. M., de Jong, W., van den Wall Bake, A. W. and Gerlag, P. G. (1996) *Neth J Med*, **49**, 135-42.
- Mathias, S., Nayak, U. S. and Isaacs, B. (1986) *Arch Phys Med Rehabil*, **67**, 387-9.

- McIntyre, C. W., Selby, N. M., Sigrist, M., Pearce, L. E., Mercer, T. H. and Naish, P. F. (2006) *Nephrol Dial Transplant*, **21**, 2210-6.
- McKenna, M. and Freaney, R. (1998) *Osteoporos Int*, **8(S)**, 3-6.
- McKenna, M. J. (1992) *Am J Med*, **93**, 69-77.
- Medicine, A. C. o. S. (1995) *Guidelines for Exercise Testing and Prescription*.
- Melton, L. (1988) In *Osteoporosis Etiology, Diagnosis and Management*(Eds, Riggs, B. and Melton, L.) New York, pp. 133-154.
- Mercer, T. H., Crawford, C., Gleeson, N. P. and Naish, P. F. (2002) *Am J Phys Med Rehabil*, **81**, 162-7.
- Mets, T. (1994) *Bmj*, **309**, 193.
- Mittalhenkle, A., Gillen, D. L. and Stehman-Breen, C. O. (2004) *Am J Kidney Dis*, **44**, 672-9.
- MK Thomas, Lloyd-Jones, D., RI, R. T. and al., e. (1998) *N Engl J Med*, **338**.
- Mowe, M., Haug, E. and Bohmer, T. (1999) *J Am Geriatr Soc*, **47**, 220-6.
- Muirhead, N. (2002) *Nephrol Dial Transplant*, **17 Suppl 6**, 2-7.
- Mukamal, K. J., Mittleman, M. A., Longstreth, W. T., Jr., Newman, A. B., Fried, L. P. and Siscovick, D. S. (2004) *J Am Geriatr Soc*, **52**, 1174-9.
- Munro, J. and al., e. (1997) *Journal of Public Health Medicine*, **19**, 397-402.
- Murray, M. and DC, B. (1993) *Ann Rev Pharmacol Toxicol*, **33**, 435-65.
- Nemere I, Z, S., H, P., VL, S., DD, D. and BD, B. (1998) *J Bone Miner Res*, **13**, 1353-9.
- Neurology., T. C. C. o. t. A. A. S. a. t. A. A. o. (1996) *Neurology*, **46**.
- Nevitt, M. C., Cummings, S. R., Kidd, S. and Black, D. (1989) *Jama*, **261**, 2663-8.
- NICE (2004) *Falls: The assessment and Prevention of Falls in Older People*, National Institute for Clinical Excellence, Guideline 21.
- Nicholls, A. J., Waldek, S., Platts, M. M., Moorhead, P. J. and Brown, C. B. (1984) *Br Med J (Clin Res Ed)*, **288**, 18-9.
- Noordzij, M., Korevaar, J. C., Boeschoten, E. W., Dekker, F. W., Bos, W. J. and Krediet, R. T. (2005) *Am J Kidney Dis*, **46**, 925-32.

- O'Hare, A. M., Tawney, K., Bacchetti, P. and Johansen, K. L. (2003) *Am J Kidney Dis*, **41**, 447-54.
- Oliver, D., Britton, M., Seed, P., Martin, F. C. and Hopper, A. H. (1997) *Bmj*, **315**, 1049-53.
- Oliver, D., Papaioannou, A., Giangregorio, L., Thabane, L., Reizgys, K. and Foster, G. (2008) *Age Ageing*, **37**, 621-7.
- Omdahl, J. L., Garry, P. J., Hunsaker, L. A., Hunt, W. C. and Goodwin, J. S. (1982) *Am J Clin Nutr*, **36**, 1225-33.
- Oniscu, G. C., Brown, H. and Forsythe, J. L. (2004) *Am J Transplant*, **4**, 2067-74.
- Ooms, M. E., Roos, J. C., Bezemer, P. D., van der Vijgh, W. J., Bouter, L. M. and Lips, P. (1995) *J Clin Endocrinol Metab*, **80**, 1052-8.
- P, G., C, V., J, V., J-J, C., Boonen S and J, R. (1997) *J Bone Miner Res*, **12**: **2082-8**.
- Painter, P. (2003) *Curr Sports Med Rep*, **2**, 173-80.
- Painter, P., Carlson, L., Carey, S., Myll, J. and Paul, S. (2004) *Nephrol Nurs J*, **31**, 67-74.
- Painter, P. and Johansen, K. (1999) *Adv Ren Replace Ther*, **6**, 107-9.
- Painter, P., Stewart, A. L. and Carey, S. (1999) *Adv Ren Replace Ther*, **6**, 110-23.
- Palomar, R., Ruiz, J. C., Cotorruelo, J. G., Zubimendi, J. A., de Francisco, A. L., Rodrigo, E., Sanz, S. and Arias, M. (2001) *Nefrologia*, **21**, 386-91.
- Pandya, N. K., Draganich, L. F., Mauer, A., Piotrowski, G. A. and Pottenger, L. (2005) *Clin Orthop Relat Res*, 150-6.
- Parkkiari, J., Kannus, P., Palvanen, M., Natri, A., Vaino, J., Aho, H., Vuorri, I. and Jarvinen, M. (1999) *Calcif Tissue Int*, **65**, 183-7.
- Peng, S. J., Yang, C. S., Ferng, S. H. and Chen, L. Y. (1997) *Miner Electrolyte Metab*, **23**, 13-8.
- Peng, Y. S., Chiang, C. K., Kao, T. W., Hung, K. Y., Lu, C. S., Chiang, S. S., Yang, C. S., Huang, Y. C., Wu, K. D., Wu, M. S., Lien, Y. R., Yang, C. C., Tsai, D.

- M., Chen, P. Y., Liao, C. S., Tsai, T. J. and Chen, W. Y. (2005) *Kidney Int*, **68**, 760-5.
- Pereira, A. A., Weiner, D. E., Scott, T. and Sarnak, M. J. (2005) *Am J Kidney Dis*, **45**, 448-62.
- Perunicic-Pekovic, G., Pljesa, S., Rasic-Milutinovic, Z., Stankovic, S., Ilic, M. and Maletic, R. (2008) *Can J Physiol Pharmacol*, **86**, 205-9.
- Peters, R. (2006) *Postgrad Med J*, **82**, 84-8.
- Pfeifer, M., Begerow, B., Minne, H. W., Abrams, C., Nachtigall, D. and Hansen, C. (2000) *J Bone Miner Res*, **15**, 1113-8.
- Pickett, J. L., Theberge, D. C., Brown, W. S., Schweitzer, S. U. and Nissenson, A. R. (1999) *Am J Kidney Dis*, **33**, 1122-30.
- Plati, C., Lanara, V. and Mantas, J. (1992) *Scand J Caring Sci*, **6**, 113-8.
- Podsiadlo, D. and Richardson, S. (1991) *J Am Geriatr Soc*, **39**, 142-148.
- Pumpria, J., Howarka, K., Groves, D., Chester, M. and Nolan, J. (2002) *International Journal of Cardiology*, **84**, 1-14.
- Rao, S., Carter, W. B., Mapes, D. L., Kallich, J. D., Kamberg, C. J., Spritzer, K. L. and Hays, R. D. (2000) *Clin Ther*, **22**, 1099-1111.
- Rebollo, P., Ortega, F., Baltar, J. M., Alvarez-Ude, F., Alvarez Navascues, R. and Alvarez-Grande, J. (2001) *Nephrol Dial Transplant*, **16**, 1675-80.
- Registry, U. R. (1998).
- Ribstein, J., Du Cailar, G. and Mimran, A. (2001) *J Hypertens*, **19**, 2257-64.
- Richmond, J., Aharonoff, G. B., Zuckerman, J. D. and Koval, K. J. (2003) *J Orthop Trauma*, **17**, 53-6.
- Rimaniol, J.-M., Authier, F.-J. and Chariot, P. (1994) *Intensive Care Med*, **20**, 591-2.
- Rizzo, J. A., Friedkin, R., Williams, C. S., Nabors, J., Acampora, D. and Tinetti, M. E. (1998) *Med Care*, **36**, 1174-88.
- Roberts, R. G., Kenny, R. A. and Brierley, E. J. (2003) *Int Urol Nephrol*, **35**, 415-21.

- Ronsberg, F., Isles, C., Simpson, K. and Prescott, G. (2005) *Age Ageing*, **34**, 148-52.
- Rowe JW, Shock MW and RA, D. (1976) *Nephron*, **17**, 270-80.
- RPA (2000) *Clin Nephrol*, **53**, 493-4.
- RU, S., GA, T. and AJ, A. (1985) *J Biol Chem*, **260**, 8882-91.
- Sakkas, G. K., Sargeant, A. J., Mercer, T. H., Ball, D., Koufaki, P., Karatzaferi, C. and Naish, P. F. (2003) *Nephrol Dial Transplant*, **18**, 1854-61.
- Salva, A., Bolibar, I., Pera, G. and Arias, C. (2004) *Med Clin (Barc)*, **122**, 172-6.
- Samson, M., Meeuwse, I., Crowe, A., Duursma, S. and Verhaar, H. (2000) *Age Ageing*, **29**, 235-42.
- Schott GD and MR, W. (1976) *Lancet*, **1**.
- Semba, R. D., Garrett, E., Johnson, B. A., Guralnik, J. M. and Fried, L. P. (2000) *Am J Clin Nutr*, **72**, 1529-34.
- Shah, M. K. (2002) *Clin Nephrol*, **58**, 118-21.
- Shumway-Cook, A., Brauer, S. and Woollacott, M. (2000) *Phys Ther*, **80**, 896-903.
- Sietsema, K. E., Amato, A., Adler, S. G. and Brass, E. P. (2004) *Kidney Int*, **65**, 719-24.
- Sinclair, A. and Dickinson, E. (1998) *London*, **King's Fund**.
- Smith R and G, S. (1969) *J Neurol Sci*, **8**, 511-20.
- Smith, R. and G, G. S. (1969) *J Neurol Sci*, **8**, 511-20.
- Sorensen, O. H., Lund, B., Saltin, B., Andersen, R. B., Hjorth, L., Melsen, F. and Mosekilde, L. (1979) *Clin Sci (Lond)*, **56**, 157-61.
- Stehman-Breen, C. O., Sherrard, D. J., Alem, A. M., Gillen, D. L., Heckbert, S. R., Wong, C. S., Ball, A. and Weiss, N. S. (2000) *Kidney Int*, **58**, 2200-5.
- Stein, M. S., Wark, J. D., Scherer, S. C., Walton, S. L., Chick, P., Di Carantonio, M., Zajac, J. D. and Flicker, L. (1999) *J Am Geriatr Soc*, **47**, 1195-201.
- Stevens, J. A., Teh, S. L. and Haileyesus, T. (2010) *J Safety Res*, **41**, 69-73.

- Stevens, L. A., Djurdjev, O., Cardew, S., Cameron, E. C. and Levin, A. (2004) *J Am Soc Nephrol*, **15**, 770-9.
- Stojanovic, M., Ilic, S. and Stefanovic, V. (2006) *Int J Artif Organs*, **29**, 1053-61.
- Stojceva-Taneva, O., Masin, G., Polenakovic, M., Stojcev, S. and Stojkovski, L. (1991) *Am J Nephrol*, **11**, 123-6.
- Stolze, H., Klebe, S., Zechlin, C., Baecker, C., Friege, L. and Deuschl, G. (2004) *J Neurol*, **251**, 79-84.
- Suh, H., Wadhwa, N. K., Cabralda, T., Sokunbi, D. and Solomon, M. (1993) *Adv Perit Dial*, **9**, 134-7.
- Teng, M., Wolf, M., Ofsthun, M. N., Lazarus, J. M., Hernan, M. A., Camargo, C. A., Jr. and Thadhani, R. (2005) *J Am Soc Nephrol*, **16**, 1115-25.
- Tilling, L. M., Darawil, K. and Britton, M. (2006) *J Diabetes Complications*, **20**, 158-62.
- Tinetti, M. E., Baker, D. I., McAvay, G., Claus, E. B., Garrett, P., Gottschalk, M., Koch, M. L., Trainor, K. and Horwitz, R. I. (1994a) *N Engl J Med*, **331**, 8217
- Tinetti, M. E., Mendes de Leon, C. F., Doucette, J. T. and Baker, D. I. (1994b) *J Gerontol*, **49**, M140-7.
- Tinetti, M. E., Richman, D. and Powell, L. (1990) *J Gerontol*, **45**, P239-43.
- Tinetti, M. E., Speechley, M. and Ginter, S. F. (1988) *N Engl J Med*, **319**, 1701-7.
- Tomson, C., Bilous, R., Blades, C., Burden, R., Cunningham, J., Dennis, J., Gilbert, D., Lamb, E., Newman, D., Nicholas, G., O'Riordan, S., Roderick, P., Stevens, P. and Vora, J. (2005) Joint Specialty Committee on Renal Disease, The Royal College of Physicians of London, The Renal Association.
- Tyrrell, J., Paturel, L., Cadec, B., Capezzali, E. and Poussin, G. (2005) *Aging Ment Health*, **9**, 374-9.
- UK Renal Registry, 2002, Ansell, E. D. and Feest, T. (2002)
- V, M., LM, F., R, B. and AR., d. B. (1992) *Mol Cell Endocrinol*, **84**, 15-22.
- van der Wielen, R. P., Lowik, M. R., van den Berg, H., de Groot, L. C., Haller, J., Moreiras, O. and van Staveren, W. A. (1995) *Lancet*, **346**, 207-10.

- Vassallo, M., Stockdale, R., Sharma, J. C., Briggs, R. and Allen, S. (2005) *J Am Geriatr Soc*, **53**, 1034-8.
- Verhaar, H. J., Samson, M. M., Jansen, P. A., de Vreede, P. L., Manten, J. W. and Duursma, S. A. (2000) *Aging (Milano)*, **12**, 455-60.
- Von Renteln-Kruse, W. (2007) *Journal of the American Geriatric Society*, **TI;55: 12**,
- Wanic-Kossowska, M., Grzegorzewska, A., Plotast, H. and Bombicki, K. (1995) *Peritoneal Dialysis International*, **16**, S305-308.
- Ward, C. and Kenny, R. A. (1996) *Am J Med*, **100**, 418-22.
- Weiner, D. K., Hanlon, J. T. and Studenski, S. A. (1998) *Gerontology*, **44**, 217-21.
- Wolfson, L., Judge, J., Whipple, R. and King, M. (1995) *J Gerontol A Biol Sci Med Sci*, **50 Spec No**, 64-7.
- Zehnder, D., Bland, R., Williams, M. C., McNinch, R. W., Howie, A. J., Stewart, P. M. and Hewison, M. (2001) *J Clin Endocrinol Metab*, **86**, 888-94.
- Ziambaras K and S., D.-J. (1997) *West J Med*, **167**, 435-9.
- Ziambaras, K. and Dagogo-Jack, S. (1997) **167**, 435-9.
- Zoccali, C., Tripepi, G. and Mallamaci, F. (2005) *Semin Nephrol*, **25**, 358-62.