PAAlliative Care in chronic Kidney disease study

(PACKS study)

Quality of life, decision making, costs and impact on carers in people managed without dialysis

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| Chief Investigator: | Dr Helen Noble  
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<table>
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<tr>
<th>Full Protocol Title:</th>
<th>PAlliative Care in chronic Kidney diSease (PACKS) Study: Quality of life, decision making, costs and impact on carers in people managed without dialysis</th>
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A review of the protocol has been completed and is understood and approved by the following:

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<th>Chief Investigator Name</th>
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<td>Dr Helen Noble</td>
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<td>Clíona McDowell</td>
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Statistician

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Protocol Number v4.0 22/07/2015>
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<tr>
<td>AE</td>
<td>Adverse Event</td>
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<td>AR</td>
<td>Adverse Reaction</td>
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<tr>
<td>CI</td>
<td>Chief Investigator</td>
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<tr>
<td>CNS</td>
<td>Clinical Nurse Specialist</td>
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<tr>
<td>CRF</td>
<td>Case Report Form</td>
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<tr>
<td>CTA</td>
<td>Clinical Trial Authorisations</td>
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<tr>
<td>CTU</td>
<td>Clinical Trials Unit</td>
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<tr>
<td>DCS</td>
<td>Decisional Conflict Scale</td>
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<tr>
<td>eGFR</td>
<td>Estimated glomerular filtration rate</td>
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<tr>
<td>ESKD</td>
<td>End stage kidney disease</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>HSC</td>
<td>Health and Social Care</td>
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<tr>
<td>ICH</td>
<td>International Conference of Harmonisation</td>
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<tr>
<td>KDQOL</td>
<td>Kidney Disease Quality of Life</td>
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<tr>
<td>KREI</td>
<td>Kidney Research and Education Initiative</td>
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<tr>
<td>MREC</td>
<td>Multi-Centre Research Ethics Committee</td>
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<tr>
<td>NICTU</td>
<td>Northern Ireland Clinical Trials Unit</td>
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<tr>
<td>NIKPA</td>
<td>Northern Ireland Kidney Patient Association</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>POS-S</td>
<td>Palliative Outcome Scale - Symptoms</td>
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<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>QALYS</td>
<td>Quality-adjusted life years</td>
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<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
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<tr>
<td>SAR</td>
<td>Serious Adverse Reaction</td>
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<tr>
<td>SOPs</td>
<td>Standard Operating Procedures</td>
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<tr>
<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
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<tr>
<td>TMF</td>
<td>Trial Management File</td>
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<tr>
<td>TMG</td>
<td>Trial Management Group</td>
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<tr>
<td>6CIT</td>
<td>Six item cognitive impairment test</td>
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# 1 STUDY SUMMARY

<table>
<thead>
<tr>
<th>Study Design:</th>
<th>Mixed methods</th>
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| **Study Aims and Objectives:** | • To measure and describe longitudinally patient reported outcomes including quality of life (QOL), symptoms, satisfaction with decision-making and costs in patients receiving conservative kidney management (palliative care).  
• To measure and describe longitudinally changes in cognition, frailty and performance in patients receiving conservative kidney management  
• To measure and describe longitudinally QOL for carers of patients receiving conservative kidney management.  
• To explore the decision making process that precedes referral to conservative kidney management.  
• To measure and describe the associated health and social care costs of patients receiving conservative kidney management.  
• To measure and describe the subjective and objective burden of providing informal care in carers, loss of earnings and the opportunity costs of providing informal care.  
• To document blood parameters over 12 months once a patient makes a decision not to embark on dialysis  
• To collect patient demographic and clinical characteristic data. |
| **Primary Outcome:** | Quality of life of patients at 3 months from baseline measured using the EQ-5D-5L visual analogue scale. |
| **Secondary Outcomes:** | • Changes in QOL and symptoms (including anxiety and depression) in patients receiving conservative kidney management measured 3-monthly over 12 months.  
• Changes in cognition, frailty and performance in patients receiving conservative kidney management measured 3-monthly over 12 months.  
• Understanding of the decision making process that precedes referral to conservative kidney management with renal physicians/Clinical Nurse Specialists (CNS).  
• Patient satisfaction with decision-making with patients measured at baseline, 6 and 12 months. |
| | • Associated health and social care costs of patients receiving conservative kidney management using a Patient Service Use Log.  
• Changes in QOL for carers of patients receiving conservative kidney management measured 3-monthly over 12 months using the EQ-5D-5L  
• Subjective and objective burden of providing informal care in carers, loss of earnings and the opportunity costs of providing informal care measured 3 monthly using Carer questionnaires  
• Calculation of the number(%) of deaths at 3, 6, 9 and 12 months and time to death  
• Changes in blood parameters over course of study  
• Report of patient demographic and clinical characteristics |
|---|---|
| Study Setting: | The study takes place in the UK across ten sites;  
**Belfast Health & Social Care Trust; Northern Health & Social Care Trust (Belfast City Hospital);**  
**Northern Health & Social Care Trust (Antrim Hospital);**  
**Southern Health & Social Care Trust (Daisy Hill Hospital);**  
**Western Health & Social Care Trust (Altnagelvin Area Hospital);**  
**South Eastern Health & Social Care Trust Ulster Hospital);**  
**Barts Health NHS Trust (The Royal London Hospital);**  
**The Royal Free London NHS Foundation Trust (The Royal Free Hospital);**  
**St George’s University Hospitals NHS Foundation Trust (St. George’s Hospital);**  
**NHS Greater Glasgow & Clyde (South Glasgow University Hospital);**  
**East and North Hertfordshire NHS Trust (The Lister Hospital).**  
Patient and carer data will be collected either in the clinic setting in a private room or over the telephone. Interviews with renal physicians/CNS will be carried out individually in a private room. |
| Sample Size: | Full sample (patients 112, carers 112, renal physicians/CNS 15-20) |
| Study Duration: | 24 months |
## 2 STUDY TEAM

<table>
<thead>
<tr>
<th>Role</th>
<th>Details</th>
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<tbody>
<tr>
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3 BACKGROUND AND RATIONALE

3.1 Background Information

The number of people living with end-stage kidney disease (ESKD) has increased in part due to improved access of an aging population but also due to a higher prevalence of risk factors for chronic kidney disease such as diabetes and hypertension (Coresh et al. 2007, Levey et al. 2009). In the UK there were 53,207 adult patients receiving renal replacement therapy on 31st December 2011, an increase of 4% from 2010 (Shaw et al. 2013). Provision of treatment for ESKD is predicted to consume approximately 2% of the annual National Health Service budget (Steencamp et al. 2010) influenced by disproportionate numbers of older, frailer, dependent patients. Older people with advanced chronic kidney disease have increasing prevalence of co-morbidities (Ashby et al. 2005) and high mortality with a median of only five life years remaining for a 70-year old (Ansell et al. 2010). Evidence is emerging that dialysis may be of little benefit, in terms of survival benefit and quality of life, to some frailer patients with multiple co-morbid conditions and poor functional status (Murtagh et al. 2011, Smith et al. 2003). This has led to questioning of the suitability of renal replacement therapy for ESKD in this population (Baboolal et al. 2008) and an awareness that dialysis might be of little benefit to this group, may not improve survival and may impact considerably on quality of life (NHS Kidney Care and the NHS National End of Life Care Programme 2009). ESKD includes those patients who have reached stage 5 with estimated glomerular filtration rate ≤ 15 mL/minute as measured using the Modification of Diet in Renal Disease equation (MDRD) formula (Levey et al 1999), who are approaching the point where dialysis would normally be initiated to maintain life.

ESKD is a life-limiting condition associated with substantially increased morbidity and premature mortality. In some countries strategies to provide a ‘good quality death’ in those who are dying have been developed (Quality End-of-Life Care Coalition of Canada, 2010; American Medical Association, 2012; Department of Health, Social Services and Public Safety (DHSSPS), 2010; National End of Life Care Programme, 2012). In a number of renal units in the UK, patients are offered an alternative treatment to dialysis or transplantation known as conservative kidney management where a palliative care approach is adopted and supportive care provided by the multidisciplinary team often in liaison with the community team and GP. Deciding when to withhold treatment in this population and provide conservative kidney management as an alternative requires thorough ethical deliberation and complex decision-making but there is limited evidence to guide patients, carers and staff when making this important decision. The experience of living without dialysis and the subsequent impact on quality of life over time warrants investigation as does the effects on carers and the associated costs of this palliative approach. Although it is accepted that some patients with advanced chronic kidney disease will decide not to embark on dialysis there are few service models designed to support this group and little known about how they can be best managed. Ultimately clinicians should distinguish a patient who will do well on dialysis from a patient who will do poorly; however, any attempt to define such a population has been largely unsuccessful (Jassal & Watson 2009). Some studies have explored age (Smith et al 2003),
functional status (Murtagh et al 2011), and comorbidity burden (Murtagh et al 2007) as predictors of survival but the development of a criterion score to select people for dialysis has not been developed and individualized assessment is necessary (Vassal & Watson 2008). Informing that assessment with good quality research centred on patient and carer experience is still required as when these complex decisions are made, the way in which conclusions are met are difficult to extract, teach and embed in practice.

Prospective, randomised trials of dialysis versus conservative kidney management are neither ethically justifiable nor practical and therefore only observational studies are available to inform practice (Germain 2007). A recent study by Da Silva-Gane et al (2012) attempted to compare QOL in patients with advanced chronic kidney disease in those opting for dialysis versus conservative kidney management. This small study, which only included 30 patients receiving conservative management, did not investigate clinical decision making, resource use or impact of conservative kidney management on carers. The authors concluded that those opting for conservative kidney management may maintain a better QOL compared to dialysis but higher levels of anxiety were seen in the conservative kidney management patients. There were major demographic and clinical differences between individuals and the modality groups.

3.2 Rationale for the Study

To facilitate improved patient decision making, accurate information on expected quality of life is needed. Staff also require an understanding of the potential impact a decision not to dialyse may have on the quality of life of carers; resource use and costs and issues that influence decision making from a patient/carer and health care practitioner perspective. This is important as renal services are developed nationally to support those receiving conservative kidney management and will help to inform clinicians internationally beginning to explore this population (Brown & Masterson, 2011, Werb 2011, Davison 2011, Chan et al. 2007), recognising the dearth of research in this area. The present study makes no attempt to carry out a direct comparison of those managed with and without dialysis, acknowledging the inherent heterogeneity of these populations. Rather the present study aims to describe experiences of QOL and resource use in those receiving conservative kidney management across Northern Ireland and two hospital trusts in London, UK. It aims to add to Da Silva-Gane et al’s work by studying not only the patients’ trajectory but also the experiences of carers and also measure and describe health and social care costs to patients and carers.

This study, across ten UK sites, is designed to capture patient and carer profiles when conservative kidney management is implemented and understand trajectories of care-receiving and care-giving. It will explore the interactions that lead to clinical care decisions and the impact of these decisions on informal carers with the intention of improving clinical outcomes for patients and the care giver experience. The economic analysis of conservative kidney management will facilitate greater transparency of resource allocation processes for persons with chronic kidney disease.
4 STUDY AIMS AND OBJECTIVES

4.1 Study Aim

The aim of the study is to measure and describe longitudinally quality of life (QOL), satisfaction with decision-making, costs, cognition, frailty and performance in patients with advanced chronic kidney disease managed without dialysis. The impact on carers will also be studied.

4.2 Study Objectives

- To measure and describe longitudinally patient reported outcomes including QOL, satisfaction with decision-making and costs in patients receiving conservative kidney management (palliative care).
- To measure and describe longitudinally changes in cognition, frailty and performance in patients receiving conservative kidney management.
- To measure and describe longitudinally QOL for carers of patients receiving conservative kidney management.
- To explore the decision making process that precedes referral to conservative kidney management.
- To measure and describe the associated health and social care costs of patients receiving conservative kidney management.
- To measure and describe the subjective and objective burden of providing informal care in carers, loss of earnings and the opportunity costs of providing informal care.
- To document blood parameters over 12 months once a patient makes a decision not to embark on dialysis.
- To collect patient demographic and clinical characteristic data.

5 STUDY DESIGN

5.1 Study Design

This multiple method study will include quantitative and qualitative components (Cresswell & Plano Clark 2011). In the quantitative component longitudinal survey of QOL, satisfaction with decision-making, costs, cognition, frailty and performance in patients and QOL in carers and associated costs will be explored. In the qualitative component of the study, we will explore, with renal physicians/Clinical Nurse Specialists (CNS), the decision making process with patients and carers that precedes referral to conservative kidney management. The longitudinal nature of the study will be explained to participants. Some people may change their mind regarding their selected treatment option and commence dialysis although this is unusual in clinical practice. If this happens the patient and carer data will continue to be collected in order to examine how QOL might increase/decrease with a switch of modality.
5.2 Study Schematic Diagram

Figure 1.0: CONSORT diagram showing the flow of participants through each stage of study.

**Assessed for eligibility**
- Patients (n=112)
- Carers (n= up to 112)
- Renal physicians (n=15-20)

**Inclusion criteria**

**Patients:**
- Stage 5 chronic kidney disease with estimated glomerular filtration rate ≤ 15 mL/minute as measured by the Modification of Diet in Renal Disease (MDRD) formula.
- A confirmed decision for conservative management, i.e. management without dialysis or other renal replacement therapy. The decision for conservative kidney management will be confirmed with the nephrologist responsible for each patient.
- Aged over 18 years.
- Able to speak English

**Carers:**
- Primary carer for patient with stage 5 chronic kidney disease who has made a confirmed decision for conservative kidney management as agreed with clinicians.
- Aged over 18 years.
- Patient has agreed that the carer can be approached to participate.
- Able to speak English
- ‘Opted in’ to study

**Renal physicians/CNS**
- Experience of managing clinical consultations of patients with stage 5 chronic kidney disease who opt for conservative kidney management.
- Employed in the renal specialty.

**Patients over 12 months**
- 3-monthly KDQOL-36™ Survey
- EQ-5D-5L
- POS-S Renal
- DCS
- Ongoing
- Patient Service Use Log

**Carers over 12 months**
- 3-monthly
- EQ-5D-5L
- EQ-5D-5L by proxy
- Carer questionnaire
- 6-monthly
- DCS by proxy

**Renal Physicians/CNS**
- One exploratory qualitative interview with PI
5.3 Outcome Measures and tools

5.3.1 Primary Outcome Measure

The primary outcome of the study is QOL of patients at 3 months measured using the visual analogue scale from the EQ-5D-5L (EuroQOL Group 1990).

5.3.2 Secondary Outcome Measures

- Changes in QOL, symptoms, anxiety and depression in patients using the Kidney Disease QOL (KDQOL) tool, EQ-5D-5L and Palliative Outcome Scale - Symptoms (POS-S) Renal, 3-monthly over 12 months
- Changes in cognition and frailty status using the 6 Item Cognitive Impairment Test (6CIT) and the 9-point Clinical Frailty Scale 3-monthly over 12 months
- Changes in Performance using the Palliative Performance Scale (PPS) 3-monthly over 12 months
- Patient Satisfaction in Decision Making using the Decisional Conflict Scale (DCS) 6-monthly over 12 months
- Carer observation of patient’s Satisfaction in Decision Making using the Decisional Conflict Scale (DCS) 6-monthly over 12 months
- Identification of health and social care costs of patients receiving conservative kidney management using a Patient Service Use Log over 12 months of study
- Changes in QOL for carers using the EQ-5D-5L 3-monthly over 12 months
- Carers assessment of patient QOL using the EQ-5D-5L by proxy 3-monthly over 12 months
- Subjective and objective burden of providing informal care in carers, loss of earnings and the opportunity costs of providing informal care using a Carer questionnaire at baseline and another at 3, 6, 9 and 12 months of study
- Exploration of decision making process that precedes referral to conservative kidney management with renal physicians/CNS via exploratory qualitative interviews
- Calculation of the number (%) of deaths at 3, 6, 9 and 12 months and time to death

Quantitative: Tools for use with patient - 
Kidney Disease QOL-36™

Quality of life of patients will be measured using the Kidney Disease QOL-36™ Survey (KDQOL) (Hays et al 1994), a well validated tool in kidney disease which has demonstrated good test-retest reliability on most dimensions (includes general health, activity limits, ability to accomplish desired tasks, energy level, and social activities). Symptoms and problems will also be assessed (questions 17-28) and include items about how bothered a respondent feels by sore muscles, chest pain, cramps, itchy or dry skin, shortness of breath, faintness/dizziness, lack of appetite, feeling washed out or drained, numbness in the hands or feet and nausea. Anxiety
and depression will also be assessed using the KDQOL-36™ and is measured within the mental component of the tool (questions 1-12).

**EQ-5D-5L**
The EQ-5D (EuroQOL Group 1990) is the National Institute of Health and Care Excellence's (NICE) preferred method of measuring health effects in economic evaluations and it has shown to be a valid instrument for the measurement of health status in renal patients. The use of the new 5 level version, EQ-5D-5L (Herdman et al 2011), is also advocated by NICE. It consists of a descriptive system and a visual analogue scale (VAS). The EQ-5D-5L will be self-completed by the patients or with the assistance of the Research Nurse and also completed for the patient by the carer (i.e. by proxy). The inter-rater agreement can then be assessed.

**POS-S Renal**
The POS-S Renal was developed in 2011 and is used as a tool to monitor progress in individual symptoms. It is a brief tool, primarily aimed at patients with advanced disease (Murtagh & Weisbord, 2010)

**6 Item Cognitive Impairment Test (6CIT)**
The 6 Item Cognitive Impairment Test (6CIT) Kingshill Version 2000® was developed in 1983 (Brooke & Bullet 1999) and is a useful dementia screening tool in Primary Care. The tool will be used to identify cognitive impairment and changes over time during the course of the study.

**9-point Clinical Frailty Scale**
Frailty will be studied using the 9-point Clinical Frailty Scale (Rockwood et al 2005). The Clinical Frailty Scale© has performed better than measures of cognition, function or comorbidity in assessing risk for death.

**Palliative Performance Scale (PPS)**
The Palliative Performance Scale (Anderson 1996) uses five observer-rated domains correlated to the Karnofsky Performance Scale (100-0). The PPS is a reliable and valid tool and correlates well with actual survival and median survival. It has been found useful for purposes of identifying and tracking potential care needs of palliative care patients, particularly as these needs change with disease progression.

**Decisional Conflict Scale (DCS)**
This will be used to explore satisfaction with decision making from a patient perspective. The scale measures uncertainty and difficulties in the decision making process. The 16 item version measures four domains: a) uncertainty in choosing options; b) unsupported in decision making; c) feeling informed; d) decision is consistent with values. The instrument demonstrates satisfactory reliability and good construct validity (O’Connor 2010). It has been used extensively in the United Kingdom. It will be used with patients at baseline, 6 and 12 months.

**Patient Service Use Logs**
These will measure healthcare service use by patients over the study period.
Tools for use with carer - EQ-5D-5L
Carer QOL will be measured using the EQ-5D-5L detailed above. Carers will also use the EQ-5D-5L to assess the patient’s QOL.

Decisional Conflict Scale (DCS)
Carers views on the patient’s Satisfaction with Decision Making will also be explored using the DCS. It will be used with patients and carers at baseline, at 6 months and at 12 months.

Carer questionnaires
Adapted from the iMTA Valuation of Informal Care Questionnaire (iVICQ; Hoefman et al 2011), the baseline and follow up carer questionnaires will gather information on background characteristics of informal caregiver (including employment status), background characteristics of the care recipient, subjective and objective burden, QOL and questions which will allow monetary valuation of informal care using the opportunity cost method.

Qualitative
Qualitative interviews
Individual semi-structured interviews with renal physicians/CNS will focus on the decision making process with patients and carers that precedes referral to conservative kidney management. Experiences of physicians related to counselling a patient who makes the decision not to commence dialysis will be captured.

5.4 Study Duration

24 months

5.5 End of Study

End of study will be declared when all patients have been recruited and followed up.
PARTICIPANT SELECTION CRITERIA

6.1 Inclusion/exclusion Criteria

**Inclusion criteria patients:**
- Stage 5 chronic kidney disease with estimated glomerular filtration rate ≤ 15 mL/minute as measured by the Modification of Diet in Renal Disease (MDRD) formula (Levey et al 1999).
- A confirmed decision for conservative management, i.e. management without dialysis or other renal replacement therapy. The decision for conservative kidney management will be confirmed with the nephrologist responsible for each patient.
- Aged over 18 years.

**Exclusion criteria patients**
- Patients lacking capacity to give consent to participate will be excluded. Capacity for consent to participate will be assessed in collaboration with the clinicians.
- Stage 1-4 chronic kidney disease
- Hasn't made a confirmed decision for conservative management
- Under the age of 18
- Non-English speaking patients or those who do not adequately understand verbal or written information unless an interpreter is available

**Inclusion criteria carers:**
- Primary carer for patient with stage 5 chronic kidney disease who has made a confirmed decision for conservative kidney management as agreed with clinicians.
- Aged over 18 years.
- Patient has agreed that the carer can be approached to participate.
- Carer has ‘opted in’ to study by making contact with the Research Nurse

**Exclusion criteria carers:**
- Carers who lack capacity to give consent to participate in the study will be excluded.
- Under the age of 18
- Patient has not agreed that the carer can be approached to participate
- Non-English speaking patients or those who do not adequately understand verbal or written information unless an interpreter is available

**Inclusion criteria – renal physicians/CNS**
- Experience of managing clinical consultations of patients with stage 5 chronic kidney disease who opt for conservative kidney management.
- Employed in the renal specialty.

**Exclusion criteria – renal physicians/CNS**
- No experience of managing clinical consultations of patients who opt for conservative kidney management
- Not employed in the renal specialty
7 PATIENT SCREENING AND CONSENT

7.1 Screening Procedure

Recruitment will take place from January 2015 to December 2015 and data collection continue for another 12 months or until death. The Chief Investigator (CI) will initially make contact with Clinical Nurse Specialists/ Research Nurses at the ten study sites. These staff will be provided with training by the CI.

Patients
All patients across the ten study sites who have made a decision not to dialyse and meet the study inclusion criteria will be invited to participate. The initial treatment decision is made in clinic with a renal physician or a CNS. The study will be mentioned at this consultation to patients by the renal physician or CNS so that the patient is aware that they may be approached and receive information on the study in the post.

Once the patient has made a decision not to embark on dialysis, a letter of referral is sent to the Conservative Management / Supportive Care service on each site. Research Nurses at each site will liaise with renal physicians or CNS and use the inclusion/exclusion criteria to identify potential participants.

Patients who have already made the decision not to embark on dialysis up to three months prior to the start of the study, who have not yet had their first clinic visit and fit the inclusion/exclusion criteria will also be invited to participate in the study

Carers
Carers will be supplied with information about the study from the patient. With the patient's agreement and if the patient is happy for the carer to participate in the study, the information will be sent to the patient to give to the carer. An ‘opt-in' method will be employed, whereby patients pass information to the carer who then makes contact with the Research Nurse if they wish to hear more about the study. This will prevent patients from passing carers’ personal contact details to the Research Nurse without consent.

The Research Nurse will use the inclusion/exclusion criteria to assess the suitability of each carer for the study.

Renal physicians/CNS
Renal physicians/CNS from each of the ten study sites who fulfil the inclusion criteria will be identified through the lead nephrologists/Senior Renal Managers for each study site and invited to take part in a semi-structured qualitative interview, conducted to explore the experience of counselling a patient who ultimately declines dialysis. Recruitment will continue until data are saturated (Creswell 1998).

7.2 Informed Consent Procedure

Patients
Research Nurses will identify with nephrologists/CNS, any patients who have made the decision not to embark on dialysis and who fit the inclusion criteria of the study. These patients will be asked if they might be interested in receiving more information about participating in the study. If a patient agrees to receive further information, the Research Nurse will provide them with an information pack containing the following:

- A letter inviting them to take part in the study
- An information sheet on the study

Patients will also be asked if they would be happy for their main carer to participate in the study. If they agree to this they will be asked if information on the study can be sent to the patient to share with their carer. With the patient's agreement the nurse will add to the patient's pack, information for the carer containing the following:

- A letter inviting them to take part in the study
- An information sheet on the study

Patients will then be contacted by the Research Nurse by telephone once they have at least 24 hours to think about participating. They will be asked if they have received the information in the post, if they have any questions and if they would like to participate in the study. If a patient agrees to participate they will be asked if they are happy for their carer to ‘opt-in’ and participate in the study and if they have shared the study information with them. If the patient is opposed to this carers will not be approached.

The Research Nurse will make arrangements to see the patient at their next clinic visit which should take place within three months and two weeks after making the decision not to embark on dialysis. This will be the baseline visit. At the appointment informed consent will be obtained and baseline data collection carried out. If a patient is unable to attend a clinic appointment in the hospital (e.g. due to frailty, ill-health), they will be posted a consent form and asked to send this back signed in the stamped addressed envelope provided to the Research Nurse once they are fully informed of the study and if they wish to participate. Research data will then be collected over the telephone by the Research Nurse. Patient logs to capture health and social care costs will be sent directly to the patient and the Research Nurse will give an explanation of the log and how it should be used over the telephone. The logs can be collected at home where possible by any CNS who carries out home visits for patients unable to attend hospital.

If patients wish they can complete the tools themselves, with the nurses or with their carers. The way in which the data are captured (self-completion or help from staff member or carer) will be noted on the front sheet of the questionnaires.

**Carers**

If a patient is happy for the carer to participate in the study they will share information with their carer. Carers will be asked to ‘opt-in’ to the study by making contact with the Research Nurse to express their interest in participating. Carers should be recruited to the study within three months, similar to patients. If they are interested in participating they will be asked to attend the patient's clinic appointment so that informed consent can be obtained and baseline data collected. If they are unable to
make this visit the Research Nurse will send a consent form and baseline data
collection tools to their home with their agreement. They will be asked to return the
consent form to the hospital. Information on how to complete the tools will be given
over the telephone. Carers can either complete the tools themselves or with the
Research Nurse. They can be posted back to the Research Nurse or collected by
any CNS who carries out home visits for patients unable to attend hospital or by the
Research Nurse via the patient at clinic.

Carers may request to complete tools with staff and this will be documented although
it is expected that most carers will self-complete.

Renal doctors

The renal physicians/CNS taking part in the qualitative interviews will be approached
by the CI via email and an explanation of the study given. If they agree to take part
they will be emailed:

- An information sheet on the study

They will be asked to contact the CI by email if they would like to take part in the
study. Consent will be taken prior to the interview taking place.

Consent procedure for patients, carers and renal physicians/CNS

All potential participants should be given information about the study prior to
inclusion in the study. The dignity of the potential participant should be taken into
consideration, and a private area used for the consent process if required.
A verbal explanation of the study must be given to the potential participant (and
friends and family where appropriate). Time for questions throughout the discussion
must be given and questions adequately addressed. When describing the study the
person seeking consent should explain:

- What the purpose of the study is and any background information that may be
  relevant.

- Why the patient/carer/renal physicians/CNS has been approached and that
  confidentiality will be maintained throughout the study, should they decide to
  participate.

- Details of the study design

- The number of people taking part in the study.

- The duration of the study and the number of study visits involved. It should be
  explained where the patient/carer/health care professional will be seen and by
  whom.

- All procedures, such as questionnaires that are required as part of the study
  must be discussed.
• The potential benefits and risks of participation in the study should be discussed.

• That the patient/carer/renal physician/CNS enters the study voluntarily and can withdraw at any time without any prejudice to them or their future care.

• The responsibilities of the patient/carer/renal physician/CNS if they choose to take part

The subject should be given adequate time to discuss with any family and friends (if applicable), prior to agreeing to participate. The subject should not be coerced to participate, and should be reassured that refusing to enter the study will not affect their care.

Once the subject has had time to read the information sheet and has had any questions regarding their participation answered satisfactorily, then they should be asked to sign the written informed consent form relating to the study. The informed consent form must be personally signed and dated in ink easily visible on photocopies (e.g. black) by the person seeking consent, and the participant. Each should also clearly print their name by their signature. Once all parties have signed the written informed consent form, the participant should receive a signed and dated copy. A copy of the above must be placed in the participant’s medical notes and a copy kept by the study team.

7.3 Withdrawal of Consent

Patients, carers and renal physicians have the right to withdraw from the study at any time. Should a participant decide to withdraw, an off study form should be filled in and sent to the CTU within one week of the event.
8 STUDY ASSESSMENTS

8.1 Study Visits and Procedures

8.1.1 Screening / Baseline Visit and Procedures

The first/baseline visit (for patients and carers) and routine bloods should take place within three months and two weeks of making the decision not to embark on dialysis. Subsequent visits and routine blood tests should take place at three months, with two weeks leeway either side of the three months.

It may be decided to discontinue blood tests for some patients and this should be documented on the CRF at Section 10 – Additional Comments.

Please note: Many blood results will be out of range. Bloods are only being documented to monitor changes over time and are part of routine care. Abnormalities will not be reported or acted upon as part of the study.

At baseline several tools will be used:

**Patient**

**Completed by patient at baseline (or where required carer or Research Nurse)**
- KDQOL-36™
- POS-S Renal
- EQ-5D-5L
- DCS
- Patient Service Use Log ongoing between 3-month appointments (patient keeps at home)

**Completed by nurse at baseline**
- Patient demographics through a review of clinical records at study entry on: age, gender, ethnicity (using UK Office for National Statistics categories), marital status, disease severity (as measured by eGFR) and primary renal disease.
- Comorbidity using the Davies Comorbidity Score
- Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level
- Blood Urea (mmol/L) **OR** Blood Urea Nitrogen (BUN) (mmol/L)
- Urine protein creatinine ratio
- Liver function tests including:
  - Alanine transaminase
  - Aspartate aminotransferase.
  - Alkaline phosphatase
  - Albumin Total protein
  - Bilirubin.
- Smoking habits of patient
- Yes / No / previous smoker and when stopped
- Smoking habits of other people living in household
- Yes / No / previous smoker and when stopped
- Diabetes + or if + then diabetic comorbidity i.e. retinopathy (blindness), amputations, neuropathy.
- Ischemic heart disease, angina, myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.
- Document answer to question ‘Would you be surprised if patient dies within 6 months?’ with an answer of ‘Yes’ or ‘No’.
- 9-point Clinical Frailty Scale
- 6CIT
- Functional performance using the PPS
- Detail from patient's hospital notes on who made decision to accept conservative management
  a) Patient (alone)
  b) Family/carer (alone)
  c) Patient and doctor
  d) Patient, family/carer and doctor
  e) Doctor (alone)

**Carer**
**At baseline**

- EQ-5D-5L whilst patient included in study or three months after death of patient or study end
- EQ-5D-5L for patient by proxy.
- Baseline Carer questionnaire
- DCS

**Renal Physicians/CNS**
Exploratory semi structured qualitative interviews with renal physicians/CNS will be undertaken by the CI over the period of the study to explore the decision making process with patients and carers that precedes referral to conservative kidney management.

**8.1.2 Study Visit and Procedures**

**Visit 1 – at 3 months**

**Patients**
- KDQOL-36™
- EQ-5D-5L
- POS-S Renal
- Patient Service Use Log ongoing between 3-month appointments (patient keeps at home)
**Completed by nurse**
- Disease severity (as measured by eGFR)
- Comorbidity using the Davies comorbidity Score
- Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level
- Blood Urea (mmol/L) **OR** Blood Urea Nitrogen (BUN) (mmol/L)
- Urine protein creatinine ratio
- Liver function tests including:
  - Alanine transaminase
  - Aspartate aminotransferase.
  - Alkaline phosphatase
  - Albumin Total protein
  - Bilirubin.
- Smoking habits of patient
  - Yes / No / previous smoker and when stopped
- Smoking habits of other people living in household
  - Yes / No / previous smoker and when stopped
- Diabetes + or if + then diabetic comorbidity i.e. retinopathy (blindness), amputations, neuropathy etc.
- Ischemic heart disease, angina, Myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.
- Document answer to question ‘Would you be surprised if patient dies within 6 months?’ with an answer of ‘Yes’ or ‘No’.
- 9-point Clinical Frailty Scale
- 6CIT
- Functional performance using the PPS

**Carers**
- EQ-5D-5L whilst patient included in study or three months after death of patient or study end
- EQ-5D-5L for patient by proxy.
- Follow up Carer questionnaire

**Visit 2 – at 6 months**

**Patients**
- KDQOL-36™
- EQ-5D-5L
- POS-S Renal
- Patient Service Use Log ongoing between 3-month appointments (patient keeps at home)
- DCS

**Completed by nurse at 6 months**
- Disease severity (as measured by eGFR)
- Comorbidity using the Davies comorbidity Score
- Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level
- Blood Urea (mmol/L) **OR** Blood Urea Nitrogen (BUN) (mmol/L)
- Urine protein creatinine ratio
- Liver function tests including:
  - Alanine transaminase
  - Aspartate aminotransferase.
  - Alkaline phosphatase
  - Albumin Total protein
  - Bilirubin.
- Smoking habits of patient
  - Yes / No / previous smoker and when stopped
- Smoking habits of other people living in household
  - Yes / No / previous smoker and when stopped
- Diabetes + or if + then diabetic comorbidity i.e. retinopathy (blindness), amputations, neuropathy etc.
- Ischemic heart disease, angina, Myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.
- Document answer to question ‘Would you be surprised if patient dies within 6 months?’ with an answer of ‘Yes’ or ‘No’.
- 9-point Clinical Frailty Scale
- 6CIT
- Functional performance using the PPS

Carer
At baseline
- EQ-5D-5L whilst patient included in study or three months after death of patient or study end
- EQ-5D-5L for patient by proxy.
- Follow up Carer questionnaire
- DCS

Visit 3 – at 9 months

Patients
- KDQOL-36™
- EQ-5D-5L.
- POS-S Renal
- Patient Service Use Log ongoing between 3-month appointments (patient keeps at home)

Completed by nurse
- Disease severity (as measured by eGFR)
- Comorbidity using the Davies comorbidity Score
- Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level
- Blood Urea (mmol/L) OR Blood Urea Nitrogen (BUN) (mmol/L)
- Urine protein creatinine ratio
- Liver function tests including:
  - Alanine transaminase
  - Aspartate aminotransferase.
- Alkaline phosphatase
- Albumin Total protein
- Bilirubin.
- Smoking habits of patient
  - Yes / No / previous smoker and when stopped
- Smoking habits of other people living in household
  - Yes / No / previous smoker and when stopped
- Diabetes + or if + then diabetic comorbidity i.e. retinopathy (blindness), amputations, neuropathy etc.
- Ischemic heart disease, angina, Myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.
- Document answer to question 'Would you be surprised if patient dies within 6 months?' with an answer of ‘Yes’ or ‘No’.
- 9-point Clinical Frailty Scale
- 6CIT
- Functional performance using the PPS

**Carers**

- EQ-5D-5L whilst patient included in study or three months after death of patient or study end
- EQ-5D-5L for patient by proxy.
- Follow up Carer

**Visit 4 at 12 months**

**Patients**

- KDQOL-36™
- EQ-5D-5L
- POS-S Renal
- Patient Service Use Log ongoing between 3-month appointments (patient keeps at home)
- DCS

**Completed by nurse at 6 months**

- Disease severity (as measured by eGFR)
- Comorbidity using the Davies comorbidity Score
- Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level
- Blood Urea (mmol/L) **OR** Blood Urea Nitrogen (BUN) (mmol/L)
- Urine protein creatinine ratio
- Liver function tests including:
  - Alanine transaminasen
  - Aspartate aminotransferease.
  - Alkaline phosphatase
  - Albumin Total protein
  - Bilirubin.
- Smoking habits of patient
- Yes / No / previous smoker and when stopped
- Smoking habits of other people living in household
- Yes / No / previous smoker and when stopped
- Diabetes + or if + then diabetic comorbidity i.e. retinopathy (blindness), amputations, neuropathy etc.
- Ischemic heart disease, angina, Myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.
- Document answer to question ‘Would you be surprised if patient dies within 6 months?’ with an answer of ‘Yes’ or ‘No’.
- 9-point Clinical Frailty Scale
- 6CIT
- Functional performance using the PPS

**Carer**

**At baseline**
- EQ-5D-5L whilst patient included in study or three months after death of patient or study end
- EQ-5D-5L for patient by proxy.
- Follow up Carer questionnaire
- DCS

8.1.2 Follow Up Visits and Procedures

If a patient deteriorates during the study and is unable to complete the tools they will remain in the study so that survival can be explored and carers can continue to rate QOL of patient using the EQ-5D-5L by proxy.

If a patient dies during the study, cause of death should be recorded on the CRF at Section 9; 9.5, under ‘Additional Comments’

If a patient dies during the study carers will be followed up 3 months later. The EQ-5D-5L will be completed
## 8.1.4 End of Study Visit and Procedures

**Table 1: Schedule of Assessments**

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Screening Baseline</th>
<th>Visit (1) 3 months</th>
<th>Visit (2) 6 months</th>
<th>Visit (3) 9 months</th>
<th>Visit (4) 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Informed Consent</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inclusion/Exclusion Criteria</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographic Data</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detail from patient's hospital notes on who made decision to accept conservative management</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Davies Comorbidity Score</td>
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<td>x</td>
</tr>
<tr>
<td>9-point Clinical Frailty Scale</td>
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<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>6 Item Cognitive Impairment Test (6CIT)</td>
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<td>Functional performance using the PPS</td>
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</tr>
<tr>
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<tr>
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<td>Serum creatinine, albumin, calcium, phosphate, parathyroid hormone, alkaline phosphate and haemoglobin level</td>
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<td>Urine protein creatinine ratio</td>
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<td>Smoking habits of other people living in household</td>
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</tr>
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<td>Diabetes and diabetic comorbidity check</td>
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<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Check for Ischemic heart disease, angina, myocardial infarction, percutaneous coronary Intervention, coronary artery bypass graft, peripheral vascular disease, strokes in all patients.</td>
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<td>x</td>
<td>x</td>
<td>x</td>
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</tr>
<tr>
<td>Answer question 'Would you be surprised if patient dies within 6 months?'</td>
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<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td><strong>CARER</strong></td>
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<td>Informed Consent</td>
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<td></td>
</tr>
<tr>
<td>Inclusion/Exclusion Criteria</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D-5L</td>
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<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>EQ-5D-5L for the patient by the carer (i.e. by proxy)</td>
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<td>x</td>
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<td>Baseline Carer questionnaire</td>
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</tr>
</tbody>
</table>
9 DATA MANAGEMENT

9.1 Data Collection

All data required according to this protocol will be recorded on the case report form (CRF). All data will be recorded directly into the CRF. All entries on the CRF, including corrections will be made by designated staff. The CRFs will be collected as per the CRF submission schedule and forwarded to the CTU:

NI Clinical Trials Unit
1st Floor Elliott Dynes Unit
(Data Management Office)
Education and Research Centre
The Royal Hospitals
Grosvenor Road
Belfast
BT12 6BA

9.2 Data Management

The study will be supported by the Northern Ireland CTU which is a UK Clinical Research Collaboration registered clinical trials unit based within the Belfast Health and Social Care Trust. Baseline data including carer demographics will be collected using a proforma developed with the CTU. The CTU will undertake the health economics (Dr Ashley Agus) and statistical analysis (Mrs Cliona McDowell) for the study. The CTU will also undertake data management and monitoring activities. IT and data management support will be provided to develop and maintain the study database, including the development of data collection tools, the data management plan, data validation and discrepancy management to ensure data quality. Discrepancy management will be led by the data manager assigned to the study at the CTU, who will raise data queries to address where data falls outside acceptable ranges and where data are missing. Monitoring for the study will include both on site and central monitoring activities as agreed with the Sponsor, to ensure compliance with the protocol and research governance. The CTU will also provide support in relation to research management activities which will be undertaken by the Post-Doctoral Fellow and a management group will be established which will include members of the team from the CTU who will manage the study on a day to day basis.
10 Adverse Events

10.1 Identifying adverse Events

In this study adverse events may be related to the impact the study methods have on participants. When completing assessments it will be necessary to look for signs of fatigue or if the person is uncomfortable and to curtail any assessments as necessary. Thought will also need to be given to issues such as the length of assessment and time of day when it takes place. Written information will need to take into consideration cognitive abilities and participants' preferred way of taking on information. Research Nurses will adapt to needs as required. E.g. some patients may need to be spoken to very slowly. The study has the potential for misunderstanding as it may be believed that dialysis is being withheld and rationed for certain patients and supportive and palliative care offered as a cheaper option. Although not the case, patients, carers and staff need to be fully conversant with treatment options for renal disease and fully satisfied with treatment decisions. Clarity on these points will be required through the duration of the study.

Completion of questionnaires may cause participants to reflect on the nature of their disease and cause upset. If this happens participants will be advised to talk to a member of their health care team. They will also have access to a renal counsellor at the two study sites in London. In Northern Ireland the Education Nurses have counselling qualifications and offer a counselling service. Referrals can be made by the Research Nurse on each site.

11 STATISTICAL CONSIDERATIONS

11.1 Sample Size

The primary goal is to measure the true mean QOL at 3 months using the EQ-5D-5L visual analogue scale. Using a standard deviation estimate of 18 from a similar study (Nephrol Dial Transplant (2004) 19: 1594–1599), with 100 individuals in our sample we would calculate a 95% confidence interval (CI) for the true mean which would be of width 7.2 units, i.e. 95% of the time we would estimate the true mean within plus or minus 3.6 units. With an estimated death/drop out rate at 3 months of 10%, a total of 112 is required. For the exploratory qualitative interviews with renal physicians, in order to achieve data saturation when no new patterns emerge, a sample of approximately 15-20 will be recruited until data saturation reached.
11.2 Data Analysis

Baseline data: Descriptive summaries of baseline demographic data for patients and carers will be tabulated. Questionnaire data from patients and carers will be analysed using frequencies and descriptive statistics. 

Primary Outcome: The mean and 95% CI for the EQ-5D-5L visual analogue scale will be calculated. Additional exploratory analyses will be used to compare the mean EQ-5D-5L visual analogue scale at 3 months between categories of categorical variables (such as gender, marital status, comorbidity) using ANCOVA adjusting for baseline scores. The association between EQ-5D-5L visual analogue scale and other continuous variables will be investigated using simple linear regression with EQ-5D-5L visual analogue scale score at 3 months as the dependent variable. Multiple linear regression will also be used to investigate associations with comorbidities, age, gender, marital status, severity of symptoms and depression to allow adjustments for confounding. As the study is not powered to detect statistically significant differences in EQ-5D-5L visual analogue scale all results will be interpreted with caution. Statistical significance will be assumed for P values 0.05.

Secondary Outcomes: Descriptive summaries of patient and carer questionnaire data at 3, 6, 9 and 12 months will be tabulated and presented graphically where appropriate. The number (%) of deaths at 3, 6, 9 and 12 months will be tabulated. Time to death data will be investigated using KaplanMeier curves. The log rank test statistic will be used to compare categorical variables and cox proportional hazards model for continuous variables where appropriate. Rate of deterioration of renal function (eGFR) will be correlated to changes in quality of life over study period. In the exploratory qualitative aspect of the study, coding of qualitative data (patient and carer diary questionnaires and renal physician interviews) will be assisted with the use of NVivo version 10, (QSR 2011) qualitative software to organise, store and retrieve data. Physician interviews will be recorded by the researcher using a digital recorder and subsequently professionally transcribed by a transcription company previously employed to do similar work. Electronic versions of diary transcripts will be saved and imported into the software programme to enable computer-assisted coding analysis. This iterative process will be guided by an approach described by de Wet and Erasmus (2005). Their approach draws on grounded theory techniques including first level coding and pattern coding and the development of relationships in the data.

11.3 Economic evaluation.

A partial economic evaluation in the form of a cost outcome description of conservative kidney management will be performed. Each patient's healthcare service use and QOL over the 12 month study period will be collected as stated under Data Collection. Unit costs will be applied to the quantity of resource use for each patient and these will be obtained from national sources where possible. Utilities for the calculation of quality adjusted life years (QALYs) will be obtained using responses on the EQ-5D-5L. Descriptive summaries of costs and QALYs will be tabulated. Multiple regression methods will be used to examine patient/carer factors which are potentially associated with the costs and to adjust for potential confounders. Descriptive summaries of responses on
the carer questionnaire related to subjective and objective burden of providing informal care in carers, loss of earnings and the opportunity costs of providing informal care will be tabulated. Although the cost effectiveness of conservative kidney management compared with dialysis cannot be established within the current single arm study design, the estimation of the costs and outcomes of conservative kidney management will allow comparisons to be made with similar estimates for dialysis already in the literature.
12 STUDY MONITORING

12.1 Data Access

The agreement with each investigator will include permission for trial-related monitoring, audits, ethics committee review and regulatory inspections by providing direct access to source data/documents and consent forms. The patients’ confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

12.2 Monitoring Arrangements

The CI will complete a risk assessment outlining any potential hazards and a proposal on how to minimise them. The extent of monitoring for the trial is based on a risk assessment from the CI and directed by the sponsors. Monitoring for the study will include both on site and central monitoring activities as agreed with the Sponsor, to ensure compliance with the protocol and research governance. The CTU will also provide support in relation to research management activities which will be undertaken by the Research Fellow and a management group will be established which will include members of the team from the CTU who will manage the study on a day to day basis.
13 RESEARCH COMMITTEES

13.1 Trial Management Group (TMG)

A trial management group (TMG) will be established and chaired by the CI. The TMG will have representation on it from the CTU and other investigators or members of collaborating groups who are involved in the study and provide trial specific expertise. This group will have responsibility for the day to day operational management of the trial, and regular meetings of the TMG will be held to discuss and solve problems and monitor progress. The discussions of the TMG will be formally minuted and a record kept in the TMF.

13.2 Advisory Groups

The study will be overseen by mentors Professor Maxwell, Professor Yaqoob and Professor Normand. Meetings with Professor Peter Maxwell will occur 1-2 monthly, quarterly with Professor Yaqoob in London and bi-annually with Professor Normand to review the progress of the study. Regular email and telephone support will also be available.

An advisory team made up of a statistician (Mrs Cliona McDowell), 2 health economists (Dr Ashley Agus and Professor Charles Normand), mentors (Professor AP Maxwell and Professor M Yaqoob), Chairman UK Renal Registry (Dr Damian Fogarty), Consultant Nephrologist leading on renal end-of-life care (Dr Aine Burns), an expert in patient reported outcome measures (Professor Kevin Brazil), Professor of Public Health (Professor Paul Roderick) and a patient (Colin Thompson) will meet quarterly in Northern Ireland or virtually to provide expertise and a strategic view on the development of the research. They will help identify emerging issues such as those related to the ethical understanding of the work and how best to respond to them.

13.3 User Involvement

This proposal has been developed in collaboration with members of the Kidney Research and Education Initiative (KREI) and the Northern Ireland Kidney Patient Association (NIKPA). Those involved in this research proposal have personal knowledge and experience of kidney disease and offer differing perspectives to the research team. Regular feedback meetings will be arranged on the progress of the research for comment and scrutiny with a particular focus on ethics, documentation (for example in questionnaires, and information leaflets) and methodology. This shared decision-making will strengthen the partnership between patients, clinicians and researchers involved in the research.
14 REGULATIONS, ETHICS AND GOVERNANCE

14.1 Sponsorship

Queens University Belfast will act as sponsor for the study and the Chief Investigator (CI) will take overall responsibility for the conduct of the trial. Agreements will be put in place between the Sponsor and individual participating sites.

Separate agreements will be put in place between the Sponsor, CI and each organisation who will undertake delegated Sponsor duties in relation to the management of the study.

14.2 Regulatory and Ethical Approvals

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The protocol will be approved by a Multi-Centre Research Ethics Committee (MREC).

14.3 Good Clinical Practice

The research will be carried out in accordance with the principles of the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines (www.ich.org). All members of the team will be required to have completed GCP training.

14.4 Protocol Compliance

The investigators will conduct the study in compliance with the protocol given approval/favourable opinion by the Ethics Committee and the appropriate regulatory authority. Changes to the protocol will require competent authority/ethics committee approval/favourable opinion prior to implementation, except when modification is needed to eliminate an immediate hazard(s) to patients. The CI will submit all protocol modifications to the competent authority/research ethics committees for review in accordance with the governing regulations. Protocol compliance will be monitored by a research monitor from the CTU who will undertake site visits to ensure that the trial protocol is adhered to and that the necessary paperwork (e.g. CRF’s, Patient Consent) is being completed appropriately. Any deviations from the protocol will be fully documented in the source documentation and the CRF.
14.5 Patient Confidentiality

In order to maintain confidentiality, all CRF’s, questionnaires, study reports and communication regarding the study will identify the patients by the assigned unique trial identifier and initials only. Patient confidentiality will be maintained at every stage and will not be made publicly available to the extent permitted by the applicable laws and regulations.

14.6 Record Retention

Data pertaining to the study will be stored in a locked filing cabinet within the School of Nursing and Midwifery for 5 years following completion of the study.

14.7 Indemnity

Queen’s University Belfast will provide indemnity for negligent and non-negligent harm incurred as a result of taking part in the study.

14.8 Finance

Research costs will be met by a post-doctoral fellowship award from the National Institute for Health Research. Queen’s University Belfast will raise contracts with the employing organisations of members of the trial team.
15 PROPOSED STUDY MILESTONES

Grant activation - December 2013
Site recruitment starts - June 2014
Site recruitment ends - December 2015
Data collection ends - December 2016
Complete analysis - ongoing through to December 2016
Study end - December 2016

16 DISSEMINATION/PUBLICATIONS

Dissemination of the study findings will include a number of national and international presentations over the time of study and associated publications. In the proposed project dissemination of the study findings will include a number of national and international presentations over the time of study and associated publications. Year 1 will include a presentation at the 2nd Commonwealth Nurses Conference in London, May 14, of the study design; year 2 a presentation at the European Association of Palliative Care Conference 2015, on the quality of life aspects of the study and in year 3 two presentations at the European Dialysis and Transplant Nurses Association conference 2016 and the American Society of Nephrology conference 2016 to present the economic aspects of the study and the overall findings. Findings will be presented annually to staff working in renal units where the study will take place in London and Northern Ireland and to patients and carers through Kidney Patient Associations on both sites allowing for their input on strategies for wider dissemination. Publications will be prepared and submitted to high impact nephrology journals including Nephrology Dialysis Transplantation and the American Journal of Kidney Diseases.

The department of Health and Social Care (HSC), Research and Development Office in Northern Ireland have funding available to support knowledge transfer activities, which enable dissemination of important findings from studies to health care professionals. Support from this source will be sought within the period of the post-doctoral fellowship to assist in the dissemination of my research findings. Patient and carer involvement in the study will allow for and provide valuable information and direction on how best to disseminate results of this research amongst renal patients and their carers, and their expertise will be sought throughout the study. Patients and carers have already committed to helping disseminate findings from the study and explore ways to ensure changes in practice where required are implemented.
17 Appendices


EuroQol (1990) EuroQol--a new facility for the measurement of health-related quality of life. Health Policy. Dec;16(3):199-208


