

CKMAPPS

A national study of practice patterns in UK renal units in the use of dialysis and conservative kidney management to treat people aged 75 years and over with chronic kidney failure (stage 5 chronic kidney disease, CKD5)

PROTOCOL

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GLOSSARY

CKD5	Stage 5 chronic kidney disease
CKM	Conservative Kidney management
RRT	Renal replacement Therapy
ERF	Established renal failure
PAM	Professionals allied to medicine
PS	Propensity score
IV	Instrumental variable
DH	Department of Health
RAG	Renal Advisory Group
HSR	Health Services Research
BOLDE	Broadening Options for long term dialysis in the elderly
PD	Peritoneal dialysis
HD	Haemo dialysis
EPO	Erythropoietin

Lay summary

An estimated 50,000 people in the UK have lost more than 85% of their kidney function (stage 5 Chronic Kidney Disease, CKD5). The majority of these people are elderly and their numbers are increasing as the population of older people grows. Many have disabling diseases in addition to kidney disease. Some patients remain stable and asymptomatic but in others kidney function declines and symptoms arise, raising the issue of whether to consider renal replacement therapy (RRT). Most are not able to have a kidney transplant and the main decision they have to make is when and whether to start long term kidney dialysis treatment.

Dialysis is an effective but invasive treatment, usually requiring frequent hospital attendances and expensive specialist care. 1-2% of the NHS budget is spent on dialysis and as the pressure on NHS funding intensifies, it is essential that dialysis is offered to those patients who will benefit from it and not to those who will gain little improvement in length or quality of life.

Many older people with CKD5 and their doctors are uncertain whether starting dialysis is, on balance, the right thing for them to do. Currently there is limited evidence to guide patients and doctors when making this important decision. Whilst national policy has encouraged renal units to establish conservative kidney management (CKM) programmes, there is a wide range of clinical practice and service provision across the country in the balance of dialysis and conservative care without dialysis. Better evidence is needed of the comparison between dialysis and conservative care in terms of how long people live with CKD5 and their quality of life (and that of their principal carers), for which types of patient conservative care might be most appropriate, and the comparative costs of CKM and dialysis. Such evidence would inform decision making between patients carers and clinicians, and service planning.

The strongest level of evidence for comparing these treatments would be a randomised controlled trial (RCT) in which patients give informed consent to receive either dialysis or CKM. The choice between these treatments would be made by random allocation. Such a trial could be justified in patients with advanced CKD for whom one treatment is not proven to be better than the other. However patient and carer preferences are very important to guide options in CKD5. Nor is it clear how many clinicians would be willing to consider entering their patients into such a trial. To try and address this we will therefore explore the opinions of clinicians who manage patients with advanced CKD about their willingness to take part in a trial.

The next best level of evidence would be a large study which compares what happens to patients with kidney failure receiving dialysis compared to conservative care in several renal units (a prospective multicentre observational study). We aim to undertake such a national study in future, but first we need to understand better how renal units are developing conservative care, how this varies between units in extent and content, how decisions about whether to refer patients and/or start dialysis are made by clinicians (both GPs and kidney specialists), patients and their families, and the quality of the information about this process and the outcomes that are routinely collected by renal units.

This proposed study will therefore select 9 renal units with a range of proportions of older people aged 75 or over with CKD5 under nephrological care starting CKM, including some units known to have pioneered active conservative care programmes. The first phase will be based on interviews with key clinical staff in the renal units who deliver dialysis and CKM and local conservative care teams, in whom we will also explore the issue of an RCT. Based on the findings from these interviews a postal questionnaire will be developed and sent to all 72 UK renal units to determine the extent and nature of their conservative care programmes. Data that are routinely collected on patients with CKD5 in the units will be collated in order to identify what additional information would be needed to be collected in any future study. We will also explore in a sample of units what proportion of patients with CKD5 are looked after by their GPs in primary care rather than by renal units, and explore why GPs choose this course of action.

We will:

- i) disseminate the findings to health care commissioners and providers of renal services to help them develop conservative care programmes and
- ii) use the findings to design a subsequent prospective study in several renal units to compare the impact of conservative care on patients opting for this treatment with similar patients opting for dialysis.

Aim

The overall aim of this study is to determine the practice patterns for conservative kidney management (CKM) of older patients with CKD5. This will inform service development and the design of a future prospective multicentre study to evaluate the effectiveness, cost effectiveness and appropriateness of CKM compared to dialysis for treating elderly patients.

Objectives

- i) To describe the variation between renal units in the extent and nature of CKM, its relative scale compared to dialysis, the factors influencing service developments and future plans.
- ii) To explore how and when decisions are made in renal units about the main treatment options for older patients with CKD5, and what are the main clinical and patient factors that influence decisions to opt for CKM.
- iii) To explore clinicians willingness to randomise patients with CKD5 to CKM versus dialysis and to assess the feasibility of a subsequent prospective study (e.g. clinicians' and patients' willingness to participate, availability of key data in renal units, factors for a propensity score and instrumental variable approaches).
- iv) To describe the interface between renal units and primary care in managing CKD5 patients.
- v) To identify the resources involved and potential costs of CKM.

Research questions

Primary

How does conservative kidney management for patients with CKD5 vary in extent and nature?

Secondary

Would clinicians consider randomising patients to CKM versus dialysis? Is a national prospective study feasible?

Background

Current international guidelines (1), endorsed by NICE (2), categorise chronic kidney disease into 5 stages, where stage 5 CKD (CKD5) is an estimated glomerular filtration rate of $<15\text{ml/min}/1.73\text{m}^2$. This is termed chronic kidney failure. The symptoms of chronic kidney failure are largely due to the failure of erythropoietin production and consequent anaemia, accumulation of toxic metabolites ('uraemia'), acid base imbalance, and fluid retention. Although the relationship between symptoms and eGFR is inverse, it is variable at the individual patient level.

Moreover the progression rate within CKD5 to a lower eGFR is also variable. Clinicians and patients are faced with complex decisions about whether RRT should be started (and if so when to establish access, e.g. fistula for haemodialysis) and then when to start dialysis. These decisions are especially difficult in older patients who often have additional co morbidities. 'Established renal failure' (ERF) is a term coined by the Renal National Service Framework to indicate a state where dialysis or transplantation is needed for survival. This is hard to define objectively so this study will use the term CKD5 which can at least be defined by the eGFR level.

The incidence of CKD5 and the need for renal replacement therapy (RRT) is increasing steadily, (3,4) in part because of the ageing population, the epidemic of diabetes and a decline in competing mortality risk from cardiovascular disease (4). This increase in RRT is highest among those over 75 years old, with disproportionate numbers who are frail and have other co-morbid conditions (5,6). In 2009 there were over 1500 patients aged 75 and over who started RRT in the UK (3). Several small retrospective or prospective cohort studies have raised the possibility that the balance of benefit versus burden in this older frail group may, in contrast to current perception, favour non-dialysis (conservative) management (5-9), especially when the patient has a strong preference for this pathway. Those 75 years and over who have dialysis do have a survival advantage, but this advantage may be small in those with co-morbidity (6), especially when the effects of establishing access for dialysis, time spent travelling and receiving dialysis three times a week, and complications of dialysis per se which often result in hospitalisation are also considered (8). For these selected patients, and in the context of increasing frailty and loss of independence (10,11), RRT may therefore be an intervention both costly for patients (in terms of quality of life and treatment burden) and costly to the NHS (in terms of resource usage). This is highly pertinent given concern over public sector finances and the NHS budget.

Expansion of conservative kidney management (CKM) might be a cost effective strategy for managing the rising number of older people with CKD5. However it is important to distinguish a rational and appropriate use of therapies from rationing. Rationing refers to the limiting of access to expensive medical interventions from which patients would benefit in order to control resource utilisation. A rational or appropriate approach refers to the foregoing of a therapy in circumstances in which its use is likely to be futile or to prove detrimental to patient well-being. Historically the UK RRT programme was viewed internationally as rationing care, and even now CKM is much less accepted in many other developed countries despite facing similar pressures on their RRT programmes. The UK is therefore in a key position to provide the evidence base for the appropriate and cost effective development of CKM.

In recognition of the gap in provision of high quality care for those dying with kidney failure, there have been a number of initiatives to raise the profile of care for kidney patients in the last year of life. The 2005 National Service Framework for Renal Services (Part 2) recommended that people with kidney failure receive timely evaluation of prognosis, information about their choices, and for those near the end of life, a jointly agreed palliative care plan, built around individual needs and preferences (12). The Liverpool Care pathway (designed to deliver excellent care in the last 48 hours of life) has been adapted for kidney patients (13). The Department of Health has introduced policies to improve end of life care across conditions, through initiatives such as the End of Life Care Strategy (14,15), and, in primary care, the Gold Standards Framework (16,17). To consolidate and help embed these policies, the Framework for End of Life Care in Advanced Kidney Disease was recently published (18), and is being piloted across the UK.

CKM is now recognised as an alternative to dialysis but is not a 'no dialysis' option (7). Maximum care to slow disease progression (19), management of other co-morbidities, assessment and active management of symptoms (e.g. by correcting anaemia and acidosis, maintaining fluid balance, and treating troublesome symptoms with drugs) (20;21), optimising communication and advance care planning (22), and improving care at the end of life (23), are all recommended. Services have increasingly been developed to focus on optimizing conservative care (24;25).

Potentially the delivery of such care can be undertaken by renal unit led teams in outpatients or community outreach or both, with varying input from specialist palliative care expertise and from primary care (26). There may be cross-over from intended CKM to dialysis and vice versa. Some patients with CKD5 may not be referred at all to renal units or may be referred back to primary care, so receiving all their CKM outside of specialist renal services. The physical health of patients and the attitudes of patients and physicians towards the added value of attending kidney clinics for CKM are likely to influence the decision to be referred and then remain in

secondary care. Variation at centre level in the spectrum of older patients with CKD5 referred to renal units and managed by dialysis or CKM needs to be taken into account when examining outcomes of CKM, for example when using a centre level instrumental variable approach (see below).

Major questions remain unanswered about how to deliver CKM. Data from recent UK Renal Registry Reports suggest there is significant variation between renal units in the rate of mortality during the first year of RRT (3,27). This may indicate marked variation in the decision to use RRT or conservative care, as well as referral patterns. There are no recent data on practice patterns for CKM. The last survey, conducted over five years ago before the Renal NSF Part 2, suggested that only half of units even recorded the pathway choice for conservatively managed patients, and only 5 units had nursing or professions allied to medicine (PAM) staff devoting over 12 hours per week to CKM (26). Yet it has been reported that, if late referrals are excluded (patients referred with ERF who start RRT within 3 months of referral), about 15% of elderly patients in managed nephrology care with CKD5 opt for CKM (5,7). Decisions regarding these choices are based upon clinical consensus and experience, supported by a very limited number of UK studies (6,8;28). These studies have focused predominantly on survival, and have not captured evidence on other outcomes (such as patient preference, symptom burden, quality of life, or quality of death) nor clarified which patients in the older cohort would or would not benefit from RRT. Given the cost to patients (in terms of quality of life and dialysis treatment burden) and the cost to the NHS (in terms of resource usage), addressing this question has become imperative. The outcomes and costs of different models of care may vary substantially. Currently there is no financial payment for CKM under the Payment by Results tariff scheme and a better understanding of the resources and costs of CKM is needed.

The current study follows the guidance on developing and evaluating complex interventions (29). CKM is clearly a complex intervention with multiple components and outcomes, and variable patterns of delivery. We first need to understand the intervention, and to explore how it can be evaluated (whether by randomisation or not). The comparison of CKM with dialysis is not straightforward. As CKM will tend to be offered to (and we presume preferred by) patients with other co morbidities, and/or frailty and dependence, the outcome of CKM will appear unfavourable when compared to all those starting RRT, even in older patients. Adjusting for such confounding using traditional methods can be problematic for several reasons: i) knowing which confounders to measure; if some are missed residual confounding will occur; ii) modelling can be unstable especially in small studies and when there are multiple confounders; iii) there are problems if there is little overlap of confounders between the exposures/interventions, which is likely when there are strong selection effects (30). This issue will arise for CKM because a significant proportion of older patients receiving RRT would not be candidates for CKM because of their more favourable prognosis.

Two approaches can be used to address this: i) instrumental variable (31) and ii) two stage propensity score (PS) method (32). An instrumental variable (IV) is a variable that is associated (ideally strongly) with the interventions of interest (here CKM and dialysis) and that only affects relevant outcomes through this pathway. Mendelian randomisation is an example of the IV approach and IV has been used in the renal field using renal unit level variables by the DOPPS team (33). However the second assumption cannot be directly confirmed. For CKM one has to define the IV, and one can then address the general question does 'more CKM' or 'more of a certain type of CKM' influence outcome of elderly CKD5 patients. Propensity scoring is a 2-stage process which first models which factors jointly predict which treatment group patients fall into i.e. what factors are related to being in either the CKM or dialysis groups. Thus for each patient a probability or propensity of being in either group is derived. In the second stage, this propensity score is used to adjust for confounders in comparing outcomes of CKM and dialysis. This can be done in several possible ways depending on the data available; one way being to stratify the propensity score and then to compare outcomes within strata in which patients have a similar profile for the confounding variables i.e. they are 'matched'. PS has been used in the

renal field for comparing dialysis and transplantation for older people and palliative care (34, 35). Better understanding of CKM patterns of care and the factors influencing the use of such care is needed to inform the application of both of these approaches in our proposed follow-on prospective study.

Another methodological issue is to define a start time for comparative analysis of survival and other outcomes between CKM and dialysis to avoid lead time biases. Ideally this would be a point on the care pathway where intention to opt for CKM and dialysis is made but we need to explore the feasibility of such an assumption given the variability of the clinical course and complexity of decision making.

Need

There is an urgent need nationally and internationally for evidence on the effectiveness, cost effectiveness and appropriateness of conservative care as an option for elderly patients with CKD5. As a first stage we need to understand the different patterns of delivery of CKM, in terms of their extent and nature, and how decisions to opt for CKM are made. This information would have two purposes: it would guide commissioners and providers of renal services in the development of CKM and it would inform the design of a multicentre prospective (potentially randomised) study to compare outcomes and costs between CKM and dialysis.

Expressed need

Developing 'Alternatives to dialysis' was a novel and important component of the 2005 Renal National Services Framework Part 2. Subsequently the Department of Health (DH) have supported expansion of CKM and further development is one of the ongoing priorities of the Renal team at the Department of Health led by Dr Donal O'Donoghue and NHS Kidney Care led by Beverley Matthews. Any results will be fed back to the Department of Health's Renal Advisory Group (RAG), of which DO'D is the Chair and PR a member. The Kidney Alliance (see below for details) has highlighted the importance of good End of Life Care.

Sustained interest and intent

The incidence of CKD5 is likely to rise over the next decade or more given the ageing population, increase in the underlying determinants of CKD such as diabetes, and decline in competing mortality risk from cardiovascular disease. Appropriate management of older people with CKD5 will remain a key policy and service delivery consideration. Our group has the expertise and commitment to utilise the findings from this study and design and seek funding for a multicentre prospective study to evaluate the effectiveness and cost effectiveness of CKM versus dialysis. This would be a groundbreaking study of international relevance.

Capacity to generate new knowledge

The research proposed here is the first stage in a process that aims to address the gap in knowledge on the effectiveness and cost effectiveness of CKD and to generate more robust information for decision making for patients, carers, clinicians and commissioners. The design of this first stage is the most comprehensive to date, with integration of qualitative and quantitative methods and its national scope, as most prior research has been single centre. New knowledge will be gained on the diversity of CKM provision, inequities of CKM care and the feasibility of a RCT (albeit from a clinician perspective, subsequent research would be needed with patients). Any subsequent national prospective study, whether randomised or not, would be entirely novel. Information on the benefits and risks of CKM versus dialysis would contribute to informed decision making which would be an important advance for individual patients and their families, and nephrologists. We have discussed this with Dr Steven Laitner, National Clinical Director for Informed Decision Making.

Organisational focus consistent with HSR mission

The findings of this research process will inform all three dimensions of health care quality: patient experience, effectiveness of care and, to a lesser extent, patient safety. It will address

equity of provision of CKM, and explore its appropriateness to the needs of different individuals and carers, all key objectives of the HSR programme.

Generalisable findings and prospects for change

Better understanding of existing patterns of care in CKM and identification and sharing of practice would assist other NHS organisations, both providers and commissioners, in establishing and improving CKM services.

Any second stage prospective study which evaluates the relative benefits and costs of RRT and CKM will assist NHS organisations in planning future CKM and dialysis services, including workforce and clinical facilities. The findings would inform the development of national quality indicators for CKM which are being proposed.

Building on existing work

Whilst there has been a prior survey of CKM in the UK this was over 5 years ago and it did not have the detailed qualitative work to inform the survey design. Nevertheless we will be able to compare changes over time for consistent questions.

There are several ongoing studies on the NIHR portfolio that are complementary to our proposed study.

i) BOLDE (Broadening Options for Long-term Dialysis in the Elderly) is a multicentre study funded by Kidney Research UK through a grant from Baxter Healthcare (UK). (Professor Ken Farrington is a co-applicant). Two of the sub-studies are of relevance. (BOLDE 2) is a questionnaire-based study to determine how older patients perceive their involvement in decision making concerning the choice of modality. Results showed significant centre variation in approaches to modality selection in relation to older people. About half of the participants reported having problems remembering and a similar proportion had mobility problems. Results highlighted that patients wanted to be involved with decision making regarding dialysis modality. BOLDE 3 is a qualitative study of older patients 6 months after starting PD or HD to determine how dialysis affected their lives and factors determining modality choice. It will seek to understand how these patients have ended up on their current dialysis modality as well as providing a greater understanding of the issues faced by older people on or nearing dialysis.

ii) Dr Joseph Low at the Royal Free Hospital is undertaking qualitative research in four London renal units to identify the perspectives of carers of people with CKD5 on CKM programmes about the decision making process and support they receive from the programme (British Renal Society funded). He is also interviewing patients about their experiences of CKM in one of the units in a separate study (Kidney Research UK funded).

NHS Kidney Care has funded pilot work to implement the recommendations in the Kidney Care National End of Life Programme (18). This work aims to improve the quality of care for advanced kidney disease patients through identification of patients approaching the last year of life, implementation of a Gold Standards register for these patients, and use of this register to introduce advance care planning, exploration of preferred place of care, and detailed end of life care planning. This work may influence the evolution of conservative care pathways in some of those centres taking part; members of the project team will therefore liaise closely with these projects as they progress, and are well placed to do so (FC and FM are actively involved in the Bristol and Kings service development work, respectively, and DO'D is part of the Board overseeing this work).

Methods

We will primarily achieve our five objectives by a two stage mixed methods design with qualitative semi-structured interviews with clinical staff and patients (stage 1), then a national questionnaire survey of all renal units (stage 2). In addition we will address: i) the use of routine

databases to explore non-referral of CKD5 patients to renal units supplemented by structured phone interviews with their GPs (Objective 4) ii) explore the feasibility of renal unit databases for capturing key data on CKM including survival estimates (Objective 3) iii) identify the key drivers to costs of CKM (Objective 5).

Stage 1 Qualitative study

This is a major component of our research. We will interview both staff and patients.

1.1 Staff

We will conduct approximately 45-55 semi-structured interviews in a maximum variation purposive sample of 9 renal units with a range of CKM practices for people aged 75 years and above. We will include units known to have been at the forefront of developing CKM (Lister, Bristol, East Birmingham, King's, and identify others with less developed CKM through available UK Renal Registry data (e.g. 1 year mortality on dialysis as proxy for use of CKM, and a UK Renal Registry survey of renal units which will be conducted in July 2010 and which will have 1 or 2 questions on CKM activity). A minimum of five/six members of the multidisciplinary team will be interviewed per unit (clinical director, another nephrologist, dialysis nurse, unit manager, social worker, and palliative care consultant). Sampling will be iterative and other team members (e.g. renal pharmacist, palliative care nurse) will be interviewed if early findings suggest their relevance to the research question/aims. Informed consent will be obtained.

Interview topic guides will be designed by the research team (who provide considerable methodological and substantive topic-specific expertise) with input from the wider Advisory Group members and updated literature review to ensure important topics are explored, while leaving adequate flexibility to permit interviewees to raise issues not covered in the topic guide as the interviews progress. Interviews will be conducted by an experienced researcher, who will first pilot the topic guide to ensure its relevance, acceptability and validity.

Topics that will be explored are likely to include perspectives on:

- the development of CKM in their unit
- components of the service
- how decisions are made about CKM, including who is involved, which are key factors influencing decisions (such as social support, frailty, extent and severity of co morbidities, cognitive function, use of the 'surprise' question, patient or carer preference) and the degree to which care decisions are made by particular individual clinicians. Narratives will be elicited from interviewees relating to care decisions, either "typical" or "individual". Accounts from individual respondents within a unit will be integrated, and points of difference highlighted for further investigation.
- when decisions are made
- the value of CKM generally and their unit's own service
- liaison with other specialist services for managing co morbidities
- how end of life and bereavement care are managed
- the role of primary care and of specialist palliative care services
- barriers and facilitators to implementation of CKM
- training in palliative care
- perceptions of which are key components of CKM really make the difference to outcome.
- major dilemmas e.g. for which types of patient is CKM most appropriate

We will identify the staff involved in CKM (e.g. renal consultant, specialist nurse, occupational therapist, social worker, dietician, pharmacist, psychologist, administrative support, psychology, specialist palliative care). We will explore the type of activities undertaken (including clinic consultations, blood result review, multidisciplinary meetings, writing letters to GPs, telephone support and consultations with patients and carers, home visits and liaison with other non-renal palliative care workers). We will gather information on the types of high cost resource use such as erythropoietin (EPO) for renal anaemia from clinical records. We will explore with the renal

clinicians (nephrologists, senior nurse) their willingness to consider randomising patients to dialysis and CKM and questions of treatment equipoise, and if they are not willing their reasons.

Differences between professionals may arise from different perceptions of what is delivered, from different priorities, and from different beliefs about healthcare provision in this context. One of the key features of the qualitative interviews will be the depth of the interviews - although semi-structured, we will explore the reasons behind differing perceptions, priorities and beliefs in order to understand the underlying meaning which professionals give for their statements. In this way, the interviews intend to provide rich data which will allow not only a descriptive approach, but also an analytic approach – addressing why there are differences, and what might underlie them, in order to both understand the reasons, and use them to refine the questionnaire (see below). We should also emphasize that in the analysis, we will particularly seek out ‘deviant’ or contrasting cases in order to refine or evolve the thematic typology. If there is divergence within or across units we will seek to understand this diversity and how it reflects the organisation of the units and their facility to develop new services.

1.2. Patients

Inclusion criteria:

- CKD5
- Age 75+
- English speaking
- On a CKM pathway or eGFR <10 or on dialysis in the last year.

Exclusion criteria:

- Those patients who would need a translator in order to carry out the interviews.

We propose to recruit up to 5 patients (45 in total) with CKD5 in each of our nine units. This will be a purposive sample, to achieve as much diversity in the sample as possible, using the key criteria of which management pathway is chosen (CKM, dialysis planned, on dialysis); we will ensure at least two patients are on the CKM pathway. The key focus of the interviews will be their perception on how the decision was made, the information they received, what factors influenced their choice and their views on the chosen pathway.

In addition we will explore what their thoughts are on being randomized to CKM vs dialysis, for example what would they want to know before considering randomization, and their willingness to participate.

The information from these interviews will be important in its own right but will also ensure that insights gained are used to design a highly relevant survey questionnaire. We will take account of the complex, and often iterative or cumulative nature of the decision making process.

Whilst we will ensure patients from ethnic minorities are included, we will not aim specifically to detect differences in the decision-making process across different ethnic backgrounds, and do not propose to use translators for our in-depth semi-structured interviews with patients from ethnic minority backgrounds. The issue of whether different cultural beliefs influence a decision about whether or not to undertake dialysis is important but we feel is a different study.

1.3 Qualitative analysis

Digitally recorded interviews will be transcribed verbatim by a professional in-house scribe in preparation for thematic analysis (36, 37). Data will be stored and analysed using qualitative data management software (NVivo). Analysis will commence as soon as data collection begins and will draw on principles of constant comparative analysis. This will involve (vertical and horizontal) reading and line by line coding of the transcribed interviews, while also listening to

audio-recorded interviews (to detect important nuances, as well as to act as a transcription validation check). The key purpose will be to identify robust and recurring issues to help us answer key questions posed (while remaining open to emerging insights, not anticipated by the interview topic guide). Two researchers will be involved in the analysis. Rigour and credibility will be ensured by employing standard methods (e.g. multiple coding - check validity of coding and consistency of coding allocation; negative case analysis - avoid premature completion/decision on key thematic framework; audit trail and reflexive practice).

Stage 2 National survey

We will develop a questionnaire which aims to describe the factors associated with development of CKM, how CKM is currently delivered and future plans. It will be fully informed by the issues identified in the qualitative phase and a robust survey instrument will allow us to test out the relevance and texture of the issues and quantify their importance across all units. Several of the applicants are very experienced at analysing mixed methods results and organising findings to understand health related problems.

The questionnaire is likely to have several sections which may be completed by different renal unit staff depending on local circumstances. We will pilot it in a three units.

For the main survey the researcher will contact the renal unit directors of all 72 renal units to establish their willingness to engage and explain the study and seek initial consent. The questionnaire will then be sent to them by post or electronically. We expect a high response rate given previous unit surveys, the high level of interest in CKM, and the expected endorsement of the study by the National Clinical Director, the President of the British Renal Society and the Clinical Affairs Board of the Renal Association.

We have used this approach in a survey of practice patterns for phosphate control and had only one unit not participating (ongoing research work for Dr Alex Hodsman's PhD thesis at the University of Bristol, supervisors Professor Y Ben-Schlomo, Dr C Tomson, Professor P Roderick).

A telephone follow-up will be conducted after the initial mail out in cases where non-response arises. Member of the research team are experienced in survey design and the questionnaire will be designed to facilitate completion.

We will supplement the survey with follow-on phoned interviews with the Clinical Director in a sample judged to have developed significant CKM to clarify and extend the insights. Such structured data would only be recorded manually. The initial consent to the survey will include willingness to answer such subsidiary questions by phone.

It will also seek estimates of the numbers of patients with stage 5 CKD aged 75 and over seen in the last year, the proportion where the intention was to start CKM rather than dialysis, and numbers on active CKM pathways. If the qualitative phase suggests there is some willingness to consider a RCT we will include questions on this to the Clinical Director, and in any event we will ask their willingness to consider participating in a future multicentre study.

Questionnaire data will be extracted and double entered in SPSS and analysis will largely be using standard descriptive statistics. Key aspects will be the variation in patterns of CKM between units and whether different models of CKM can be identified.

Additional components

Information routinely collected on CKM and non-referral of CKD5 patients to specialist nephrology services.

There is a lack of information regarding the proportion of patients receiving kidney care from either or both of primary care/renal specialist services, the factors that influence the decision to refer patients with CKD5 to secondary care, and the decision to remain in primary care or return to primary care of ongoing CKM.

To address this we will define a retrospective cohort of all incident patients aged 75 and over with incident CKD5 arising from the catchment area of their local chemical pathology laboratory in our 9 stage 1 units, in liaison with the renal unit IT manager.

This will be a limited exploration of the scale and reasons for under-referral of CKD5 patients to renal units to provide better insight into selection issues and potential unmet need.

A retrospective incident cohort of CKD5 will be defined as follows:

- All patients aged 75+ with 2 eGFR results that are $<15\text{ml/min/1.73m}^2$ during the retrospective study period (months -18 to -6). These two results must be a minimum of 3 months apart with no results ≥ 15 following the index result.
- Patients will be excluded if they have existing CKD 5 at month -18 (i.e. 2 eGFR results $<15\text{ml/min/1.73m}^2$ a minimum of 3 months apart prior to month -18 OR a single eGFR $<15\text{ml/min/1.73m}^2$ prior to month -18 if no subsequent confirmatory results are available).
- Patients residing outside the "GP catchment area" of chemical pathology laboratory will also be excluded (using their postcode). This will ensure that patients from outside this catchment area who are attending specialist clinics at the hospital are not included in either the numerator (CKD 5 referred/ discharged) or denominator (all CKD 5) counts.

From the date of first measurement of eGFR <15 we will link the laboratory and hospital renal IT systems to define the location of kidney care at initial diagnosis and subsequent referral and any use of dialysis. We will also explore the feasibility of extracting data from renal unit IT systems on key parameters such as dates of first eGFR <15 indicating CKD5 and eGFR <10 indicating progression, timing of decisions to opt for dialysis or CKM, and details of receipt of CKM. The linkage of clinical biochemistry data on CKD5 patients to renal unit data has been piloted in two of our units (Bristol, East Birmingham). We are seeking to identify patients with CKD5 who are on the clinical biochemistry database but not on the renal unit system so we can estimate the degree of under-referral, and use such information to further explore reasons for under-referral with respective GPs.

In four units where applicants are based (E Birmingham, Lister, Bristol and King's) we will identify a sample of 25 patients with incident CKD 5 in the last 6 months for whom we cannot find evidence of referral to a nephrologist. A research fellow will carry out a brief structured telephone interview of the patients' GP to determine issues such as whether CKD5 had been recognised, if there had been any communication with renal specialists and if not reasons why and how palliative care needs were addressed. We recognise that this could be perceived as threatening but we will ensure that the interview is handled professionally and non-judgementally by appropriate training of the research fellow. These (100) interview schedules would have largely fixed responses with only a few open comments, and will be straightforward to enter and analyse descriptively. The sample size is pragmatic and feasible.

This phase will be undertaken during months 6-12 months so that we can incorporate any relevant issues into the national survey, and they will not involve the research fellow significantly. In these four units we will also explore whether we can estimate the survival of patients in the retrospective cohorts from the first date of CKD5 that has fallen to an eGFR <10 , whether treated by eventual dialysis or presumed CKM, using linkage to hospital electronic records or routine tracing using NHS number. Such survival data, whilst only one relevant outcome, would be useful in designing any future study.

We will investigate the ethical and governance issues raised by our research team in identifying individual patients who have not been referred and in contacting their GPs. We do not intend to seek individual patient consent as this would be unfeasible. We will approach the National Information Governance Board for Health and Social Care (NIGB). We will seek GP consent for the interviews.

CKM resources and costs

We will utilise the rich data from stage 1 and data from the survey to identify the range of inputs into CKM and varying clinical pathways in different units. These will include primary care and specialist palliative care inputs. We aim to identify the range of resources used, which would be predominately staff time but would also include other resources, e.g. EPO use.

In the 9 stage 1 units we will explore collection of more detailed data including the time spent on CKM related tasks by staff which might include a sample of practitioners completing diaries. In these 9 units we will combine data on resources with appropriate local and national unit cost data to estimate indicative costs of the different patterns of CKM care. The costing work in this study will inform any future study as it would identify the main drivers of cost, as well as the best way of collecting these data whilst imposing the minimum burden on practitioners and the best way of deciding on the optimum method of determining cost effectiveness in future studies, i.e. whether by economic evaluation alongside a trial (whether randomised or not) or by an economic model.

Contribution to collective research effort and research utilisation

Major outputs from the qualitative study and national survey will be of value in their own right for commissioners and providers of renal services. The findings will be written up and submitted for publication in general (e.g. BMJ), nephrology (e.g. Nephrology Dialysis Transplantation, Journal of Renal Nursing), palliative care (e.g. Palliative Medicine, BMC Palliative Care) and quality of life journals (e.g. Quality of Life Research). They will also be submitted for oral presentation at relevant conferences (e.g. Renal Association, European Renal Association, American Society of Nephrology, British Renal Society, European Association of Palliative Care, ISQoL). A report summarising the findings will be sent to all participating renal units, to the Renal Association and to the Renal Advisory Group at the Department of Health. Our patient group led by Fiona Loud will advise on appropriate dissemination of our findings to patients.

Plan of investigation and timetable

We will develop the ethics application, identify the sample and approach the stage 1 units in the pre-study period. There will be an initial 4 month preparation phase (0-4mths) for lit review/interview topic guide/confirm sites; 9 month qualitative data collection and iterative analysis (5-13mths); then 5 month questionnaire development, survey, data entry and analysis (14-18mths) and final write-up (19-21 mths). The GP study will be conducted between 6-12 mths.

Approval by Ethics Committees

We will apply for multi-site ethical approval to cover the nine centres in stage 1 and the survey. The GP study will require patient identifiable data and approach by nephrologists to the relevant GP. We will write to each GP to explain this component of the study and inviting them to participate in the short structured telephone interview with the local nephrologist. We will apply to the National Information Governance Board (NIGB) for the linkage and GP study.

Project management

The study will be co-coordinated on a day to day basis from the University of Southampton. PR will act as lead PI and will be responsible for the overall conduct and delivery of the study, and supervise specifically the survey and quantitative elements. Co-investigators will provide

expertise as follows. GL will jointly supervise the research fellow and meet regularly throughout the qualitative phase of the project, up to weekly as needed. DL will provide methodological input on questionnaire development, quality of life, and outcomes in elderly dialysis patients and HR, KF and FM will provide content advice, by phone, email or face to face meetings. Methodological input and support for the researcher on health economics will be provided by DT; JK and JP will advise on decision making and statistical issues respectively.

All applicants will be members of an Advisory Group Steering Group which will meet three times during the project: before and after stage 1, and to consider the main results and draft report (at approximately months 3, 12, 19 of the project). Project updates will be circulated for comment in the interim. In each of the nine centres (4 covered by applicants HR, KF, FC, FM) we will work with the clinical director or a nephrologist or senior nurse nominated by them to liaise about setting up and hosting the interviews, and with their renal IT manager for data aspects.

Service users/public involvement

We will form an email discussion group of 3-4 patients led by Fiona Loud. The patient members will comment on the draft of the topic guide for the interviews, on the findings of the qualitative research and on the draft unit survey questionnaire.

They will also contribute to the final study report and give advice on dissemination of results to patients.

Expertise and justification of support required

Professor Paul Roderick (co-PI) is an experienced clinical epidemiologist with longstanding interest in evaluation of RRT and experience of multicentre evaluation in kidney disease (e.g. he was PI for an HTA funded evaluation on renal satellite units in 24 centres)(38). He will oversee the whole study at the main centre at the University of Southampton.

Dr Hugh Rayner (co-PI) is a nephrologist at Heart of England Renal Unit, ex-Medical Director of Heart of England NHS FT, Clinical Director of Birmingham East and North PCT and UK Country Investigator, Dialysis Outcomes and Practice Patterns Study (DOPPS) from 1996 onwards. He will chair the Steering Group, provide content advice throughout and oversee all fieldwork in the Heart of England Renal Unit in E Birmingham.

2 full time research fellows: these are key posts; we will need an experienced researchers with skills in both qualitative and quantitative methods, one for the duration and the other for 12 months to undertake the patient interviews.

Dr Fliss Murtagh is a Clinical Senior Lecturer in palliative care and researcher with a major interest in evaluation of alternatives to dialysis. She will provide content advice in this area, especially specialist palliative care aspects throughout the study (e.g. reviewing the topic guide, interpreting interview data and questionnaire development). She will co-ordinate fieldwork at King's Renal Unit.

Professor Ken Farrington is a nephrologist at the Lister Hospital Renal Unit and co -author of End of Life Care in Advanced Kidney Disease: a Framework for Implementation. With Dr Roger Greenwood they have pioneered CKM and observational research into CKM. He will provide content advice and lead fieldwork in Lister Renal Unit.

Dr Fergus Caskey is a nephrologist at Southmead Hospital Renal Unit, Bristol. He has a major interest in health services research on renal services and PROMS, and will lead fieldwork in the Bristol Renal Unit.

Dr Gerry Leydon is an NIHR postdoctoral fellow with substantial qualitative expertise and interests in palliative care. She will oversee all aspects of the qualitative phase.

Mr David Turner is a health economist with experience of economic evaluation of trials and economic modelling. He will oversee collection of data on resource use and costing analysis and write up.

Dr Jonathan Klein has expertise in decision making within organisations and will advise on the topic guide, and questionnaire design and the final write-up.

Professor Donna Lamping will provide methodological expertise on questionnaire development, quality of life, and patient-reported outcomes (PROs) in elderly dialysis patients. She is an internationally recognised expert in these areas, with a 30-year track record in PROs in renal disease, a former President of the Int'l Society for Quality of Life Research and published (with PR) the largest study of outcomes in elderly people on dialysis in the UK (39).

Fiona Loud is chair of the Kidney Alliance, an umbrella body representing the interests of patients, charities, industry and professional groups. The aim of the Kidney Alliance is to bring together the patients' voice and professionals committed to renal medicine. Its goal is 'to promote prevention and early identification of kidney disease, and high quality treatment for all patients at risk from or identified with kidney failure on an equal and uniform basis throughout the UK. Its membership includes the British Kidney Patient Association. She will oversee patient involvement.

No funding is requested for following who will all be members of the Advisory Group and available for ad hoc advice throughout the study:

Professor Janet Peacock: medical statistician with substantial expertise in observational study analysis

Dr Roger Greenwood: Nephrologist, UK Country Investigator, Dialysis Outcomes and Practice Patterns Study (DOPPS) from 1996 onwards.

Dr Richard Fluck: Nephrologist, UK Country Investigator, Dialysis Outcomes and Practice Patterns Study (DOPPS) from 2007 onwards. President-elect British Renal Society.

Dr Charlie Tomson: Nephrologist, recent Chairman of UK Renal Registry, President-elect Renal Association.

Dr Donal O'Donoghue: Nephrologist, National Clinical Director for Kidney Care, Department of Health.

Professor Julia Addington–Hall: international reputation for research into palliative care non renal and renal, and in survey research.

Natasha McIntyre: Renal nurse consultant, active research into CKD and RRT

Ian Wilkinson: GP, Renal NSF Clinical Champion.

Other costs

- A laptop for the research fellows, digital recorders, and costs of transcribing the 100+ interviews.
- Travel to 3 Steering groups is requested for all applicants
- Travel to the 9 renal units and overnight stay and subsistence is requested for the research fellows, two visits to each unit.
- Stationary-printing of the questionnaire, letters
- Postage of questionnaires to renal units
- Phone conference calls
- Dissemination of findings at one UK conference (e.g. Renal Association), one international (e.g. American Society of Nephrology)
- Funding for IT managers in the 9 Trusts
- Funding for 3 patient representatives including F Loud, 7 days over study at £150 per day

Planned or active related research grants

Dr Fliss Murtagh has a NIHR SDO grant on "Understanding place of death for patients with non malignant conditions". This focuses on six non malignant conditions, including end-stage renal disease, and resonates strongly with the proposed work. In conjunction with this NIHR SDO grant, she has also successfully gained an SDO Management Fellowship which is supporting implementation of the work on place of death for those with non malignant conditions into practice. Professor Ken Farrington with Maria da Silva Gane has just led a BRS funded prospective study comparing quality of life in patients with advanced kidney disease treated by CKM and those on dialysis which was carried out in a single centre at the Lister Hospital. Dr Gerry Leydon is collaborating with Prof Julia Addington-Hall on an NIHR SDO funded on out of hours care in palliative care and is co-PI on an South Central RfPB grant on Mindfulness Meditation and Breast cancer.

Professor Paul Roderick and Dr Gerry Leydon are co-applicants on an NIHR programme grant ATTOM which is investigating the kidney transplantation pathway. It is led by Prof Andrew Bradley and we are waiting it hear the final outcome shortly.

No applicant has had an NIHR programme contract which has been terminated, extended in time or in terms of funding.

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