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PRACTICE

GUIDELINES

Renal replacement therapy: summary of NICE guidance

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What you need to know

- Start exploring the options of dialysis, transplantation, or conservative management with patients at least a year before they are likely to need it
- Recommend patients start dialysis at an estimated glomerular filtration rate (eGFR) of 5-7 mL/min/1.73 m^2 or sooner if symptoms of their chronic kidney disease are affecting their daily life
- Haemodiafiltration is a form of haemodialysis with additional convection and is more effective than standard haemodialysis with a similar patient experience
- Transplantation has better outcomes than any form of dialysis, with pre-emptive transplantation being more effective than transplantation after dialysis
- Patients should not be excluded from receiving a kidney transplant based on body mass index alone

Approximately 8000 people a year start renal replacement therapy in the UK.[1] Box 1 describes the options available for people approaching the need for renal replacement therapy. Around 60 000 people are currently living with a kidney transplant or are receiving dialysis. Transplant is the most common form of renal replacement therapy (approximately 54% of prevalent renal replacement therapy patients), followed by haemodialysis (40%), and then peritoneal dialysis (6%).[1] The number of new transplants was around 3000 in 2016; this has gradually increased more recently. Some people will receive a kidney from a living donor, but those who have to join the waiting list for a kidney donation can expect to wait for 2.5-3 years.[2] Among those receiving dialysis, most people opt for haemodialysis or haemodiafiltration done at hospital or in a satellite centre rather than at home.

Box 1: Renal replacement therapy explained

Renal replacement therapy comprises either transplantation or dialysis. Some people decide not to receive renal replacement therapy but choose conservative management, which comprises full supportive management (including advance care planning and control of symptoms and complications).

Transplantation

- Can be from living or deceased donors
- Can be done pre-emptively (before the point at which dialysis would be needed)

Dialysis

- Dialysis is conventionally divided into haemodialysis (where the blood is filtered outside of the body using a dialysis machine) and peritoneal dialysis (where the person's abdominal lining is used to filter the blood)

Haemodiafiltration *v* haemodialysis

- Haemodiafiltration is a form of haemodialysis with additional convection, resulting in greater removal of larger waste metabolites
- The evidence reviewed in this guideline suggests that haemodiafiltration conveys a survival benefit over haemodialysis. The evidence of benefit (though limited) is based on a meta-analysis of nine randomised controlled trials including over 3000 participants
- For patients, the practical difference between haemodiafiltration and haemodialysis is minimal. Some machines can provide either treatment, although haemodiafiltration may be less readily available at home
- Not all machines or centres are capable of providing haemodiafiltration, but this proportion seems to be growing

Continuous ambulatory peritoneal dialysis (CAPD) *v* automated peritoneal dialysis (APD)

- CAPD and APD both involve infusing dialysis fluid into the abdomen and using the peritoneum as a membrane. When the dialysate has absorbed waste metabolites, it is drained and replaced by fresh dialysis fluid. The drainage and replacement is called an exchange
- CAPD typically involves around four sessions per day, each of about 45 minutes, APD typically involves a machine undertaking several exchanges overnight, with a total duration of treatment of about 9 hours
- There was no strong evidence in this guideline to suggest either option of peritoneal dialysis was superior
- The choice between CAPD and APD is primarily driven by patient preference based on how the practicalities of each option affect quality of life

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The National Institute for Health and Care Excellence (NICE) recently published a guideline on renal replacement therapy and conservative management for people with chronic kidney disease.[3] The guideline updates previous guidance on peritoneal dialysis and home haemodialysis and now includes recommendations on transplantation and conservative management. The guideline covers initiation, preparation, choice of modalities, switching or stopping modalities, recognising symptoms, information for patients, and coordinating care. Guidance in this area is particularly important because of the variety of options available for people considering renal replacement therapy and because of the high cost of these interventions. The guideline does not cover renal replacement therapy for acute kidney injury. The population of people requiring renal replacement therapy is a small proportion of the total number living with chronic kidney disease, but represents a substantial proportion of the healthcare spend.

Many decisions around the care for people undergoing renal replacement therapy or conservative management will be made in specialist settings. However, non-specialists will play a significant role in the overall treatment pathway (for example, in aiding recognition and management of symptoms, ensuring the assessment process begins at an appropriate time and coordinating care). It is important that non-specialists are aware of the latest guidance in this area so that they can aid in the engagement of patients with appropriate specialist services. This article summarises some of the most recent recommendations from the NICE renal replacement therapy guideline,[3] focusing on recommendations relevant for non-specialists such as how soon to begin preparation for renal replacement therapy, supporting people to make choices about modality of renal replacement therapy, when to start dialysis, and the role of body mass index (BMI) in transplantation.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

The level of evidence supporting the recommendations in this guideline varied. Most of the recommendations were based on a combination of non-randomised studies and committee consensus, due to the ethical and practical challenges of randomising participants to significantly different treatment options (such as transplant *v* haemodialysis). However, some recommendations were based on randomised controlled trials, such as those comparing haemodiafiltration with haemodialysis and the ideal time point at which to start renal replacement therapy.

What's new in this guidance

- Consider starting dialysis when indicated by the impact of symptoms of uraemia on daily living, or biochemical measures or uncontrollable fluid overload, or at an estimated glomerular filtration rate (eGFR) of around 5-7 mL/min/1.73 m^2 if there are no symptoms
- Do not exclude people from receiving a kidney transplant based on body mass index alone
- For people who choose haemodialysis or haemodiafiltration, consider haemodiafiltration if it is done in a treatment centre (hospital or satellite unit)

Indications for starting renal replacement therapy

The new recommendations broadly reflect current practice for starting renal replacement therapy, although there may be some variability. In the past, dialysis may have been started at a higher estimated glomerular filtration rate (eGFR), around 10 mL/min/1.73 m^2. The only available evidence from clinical trials suggests there is no benefit from starting at this higher eGFR.[4] People approaching the need for dialysis were randomised to start at an eGFR of 10-14 mL/min/1.73 m^2 or at 5-7 mL/min/1.73 m^2. Long term follow-up showed no difference in quality of life or mortality between these two groups.[4] However, in this trial most of the people assigned to start at a low eGFR (that is, later) ended up starting sooner than planned due to symptoms of uraemia (such as fatigue, nausea, and vomiting).

The Guideline Committee agreed that there was no need to aim to start renal replacement therapy at a higher eGFR but to be guided by the symptoms arising from kidney disease. However, not all people have symptoms even at a low eGFR, so it was important to identify a minimum eGFR target to prevent people from delaying initiation of therapy to the extent that they could become acutely unwell.

- Consider starting dialysis when indicated by the impact of symptoms of uraemia on daily living, or biochemical measures, or uncontrollable fluid overload, or at an eGFR of around 5-7 mL/min/1.73 m^2 if there are no symptoms. [*Based on low quality evidence from a randomised controlled trial, cost effectiveness evidence and the experience and opinion of the Guideline Committee (GC)*]
- Ensure the decision to start dialysis is made jointly by the person (or, where appropriate, their family members or carers) and their healthcare team. [*Based on the experience and opinion of the GC*]
- Before starting dialysis in response to symptoms, be aware that some symptoms may be caused by non-renal conditions. [*Based on the experience and opinion of the GC*]

Preparing for renal replacement therapy or conservative management

The Guideline Committee also considered those people who start renal replacement therapy in an unplanned way. Unplanned starts generally result in worse clinical outcomes (missed opportunities for pre-emptive transplantation and higher morbidity and mortality rates).[5,6] People who start unplanned renal replacement therapy include those who were previously known to renal services but were inadequately prepared because of patient or service factors; those with previously undiagnosed chronic kidney disease; and those with acute kidney injury which fails to resolve. The committee recommended that assessment for renal replacement therapy or conservative management be started at least one year before dialysis or transplant is likely to be needed. The committee hope this will increase opportunities for supporting patient choice and reduce the frequency of unplanned starts.

- Start assessment for renal replacement therapy or conservative management at least one year before therapy is likely to be needed, including for those with a failing transplant. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]

Choosing modalities of renal replacement therapy or conservative management

When choosing between modalities of renal replacement therapy there was no strong evidence that any one option was better than any other (for example, comparing haemodialysis with peritoneal dialysis or comparing haemodialysis more than 3 times a week versus 3 times a week). There were two exceptions:

- Transplantation has better outcomes than any form of dialysis, with pre-emptive transplantation being more effective than transplantation after dialysis
- Haemodiafiltration performed in a treatment centre is more effective than in haemodialysis in a treatment centre.

New economic analysis also found that haemodiafiltration was likely to be cost effective for the NHS, with additional health benefits for patients justifying any additional costs.

Based on this evidence, it is recommended that patient choice be the key driver for most decisions about renal replacement therapy. The full guideline includes recommendations on how to conduct these patient-centred discussions and the information people may require to make decisions. Decision making aids are available (such as the Kidney Research UK Dialysis Decision Aid booklet), but the committee did not find sufficient evidence to make recommendations on their use.[7]

There was no evidence identified in the guideline about the optimum approach to conservative management. This is likely to vary depending on individual circumstances but will have considerable overlap with end of life care.

- Offer a choice of renal replacement therapy or conservative management to people who are likely to need renal replacement therapy. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- Ensure that decisions about renal replacement therapy modalities or conservative management are made jointly with the person (or with their family members or carers for children or adults lacking capacity) and healthcare team, taking into account:
  - Predicted quality of life
  - Predicted life expectancy
  - Person's preferences
  - Other factors such as co-existing conditions.

  [*Based on qualitative evidence and the experience and opinion of the GC*]
- Offer people (and their family members or carers, as appropriate) regular opportunities to:
  - Review the decision regarding renal replacement therapy modalities or conservative management
  - Discuss any concerns or changes in their preferences.

  [*Based on qualitative evidence and the experience and opinion of the GC*]

Transplantation

- Discuss the individual factors that affect the risks and benefits of transplantation with all people who are likely to need renal replacement therapy, and their family members or carers (as appropriate). [*Based on qualitative evidence and the experience and opinion of the GC*]
- Include living donor transplantation in the full informed discussion of options for renal replacement therapy. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- Offer a pre-emptive living donor transplant (when there is a suitable living donor) or pre-emptive listing for deceased donor transplantation to people considered eligible after a full assessment. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- Do not exclude people from receiving a kidney transplant based on BMI alone. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]

Choice of dialysis modality

- Offer a choice of dialysis modalities at home or in centre, ensuring that the decision is informed by clinical considerations and patient preferences (see above). [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- Offer all people who choose peritoneal dialysis a choice of continuous ambulatory peritoneal dialysis or automated peritoneal dialysis if this is medically appropriate. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- Consider peritoneal dialysis as the first choice for children aged ≤2 years old. [*Based on very low quality evidence from non-randomised studies and the experience and opinion of the GC*]
- For people who choose haemodialysis or haemodiafiltration:
  - Consider haemodiafiltration rather than haemodialysis if performed in a treatment centre (hospital or satellite unit)
  - Consider either haemodiafiltration or haemodialysis at home, taking into account the suitability of the space and facilities.

  [*Based on very low quality evidence from randomised controlled trials, cost effectiveness analysis, and the experience and opinion of the GC*]

Implementation

The main implementation issue arising from this guideline is the recommendation to use haemodiafiltration over haemodialysis when a person opts for dialysis done at hospital or in a satellite centre (as opposed to at home). Not all haemodialysis machines are capable of delivering haemodiafiltration, and the availability of haemodiafiltration-capable machines varies between centres. Data from an email survey of the British Association of Renal Technologists found that 68% of machines were haemodiafiltration-capable among respondents (nine treatment centres, 972 machines), ranging from 30% to 100% by centre. This is only a limited selection of renal units, and so may not be representative for the whole country. Some committee members thought that the number would be lower overall. There may be additional costs for machines where haemodiafiltration-capable machines are not currently used. However, most centres seem to have some haemodiafiltration-capable machines, and the committee agreed that it is likely that these will be able to accommodate any initial increased demand for haemodiafiltration in-centre and that

provision can be expanded as demand increases within the usual replacement cycles.

Guidelines into practice

- Are you aware of the criteria for starting dialysis in patients with chronic kidney disease, and how would you explain this to patients?
- Do you ensure all people with chronic kidney disease have begun assessment and preparation at least 12 months before they are likely to require renal replacement therapy or conservative management?
- What will you do differently as a result of reading this article?

How patients were involved in the creation of this article

The Guideline Committee included lay members who contributed to the formulation of all of the recommendations in the guideline, including those summarised here.

Further information on the guidance

Methods

This guidance was developed by the National Guideline Centre (NGC) in accordance with NICE guideline development methods (see www.nice.org.uk/process/pmg20/chapter/introduction-and-overview). A Guideline Committee (GC) was established by the NGC, incorporating healthcare professionals and lay members. The GC identified relevant questions and collected and appraised clinical and cost effectiveness evidence. The quality of the evidence was rated based on GRADE methodology. The GC made recommendations based on what evidence was available, supplemented with their experience and opinion. The scope and draft of the guideline went through public consultation in which stakeholder organisations were invited to comment on both the scope and the draft. The GC took all comments into consideration in the final version of the guideline.

Different versions of this guideline have been produced: a full version, a short version, and an online pathway. These are available from the NICE website (www.nice.org.uk/guidance/ng107).

Future research

The GC identified areas in which evidence was low quality or absent and made recommendations for further research. Below are the research recommendations most relevant to the focus of this summary:

- What is the most clinical and cost effective strategy for the timing of pre-emptive transplant?
- What is the clinical and cost effectiveness of initial haemodialysis or haemodiafiltration versus initial peritoneal dialysis for people who start dialysis in an unplanned way?
- What is the most clinical and cost effective frequency of review of people on peritoneal dialysis, haemodialysis or haemodiafiltration, or conservative management?

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