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**Timely listing for kidney transplantation:  
A summary of the literature**

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## Reader Page

Title	Timely listing for kidney transplantation: A summary of the literature.
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Description/purpose	This review examines the evidence for strategies that improve and the barriers that impede the timely listing of patients with chronic kidney disease for transplantation. The purpose of this work is to support units working on the timely listing project and provide a resource for NHS Kidney Care.

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## **Timely listing for kidney transplantation: A summary of the literature**

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# 1 Introduction

## 1.1 Background

Patients with severe and progressive chronic kidney disease may be managed conservatively or receive renal replacement therapy in the form of dialysis or kidney transplantation. Early transplantation is transplantation within the first 6-12 months after initialization of dialysis [1], whereas pre-emptive transplantation refers to the receipt of a kidney transplant before dialysis is required.

There is a consensus that kidney transplantation is the best treatment in suitable patients and that pre-emptive transplantation and early transplantation of suitable patients improves clinical outcomes [2][3].

When last analysed, significant variation in listing time, that is the duration of time between being listed for kidney transplantation and requiring dialysis, and access to kidney transplantation existed between UK renal units that cannot be explained by case mix [4][5].

In the UK, guidelines recommend that all patients with stage 5 chronic kidney disease (eGFR < 15 ml/min/1.73m<sup>2</sup>) be assessed and placed on a waiting list for kidney transplantation if judged to be within six months of their anticipated dialysis start date [2]. Assessment should start earlier when the eGFR is approximately 20ml/min where live donor transplantation is being considered[6].

NHS Kidney Care is currently supporting several projects which aim to improve timely listing for kidney transplantation.

## 1.2 Aim

This review examines the evidence for strategies that have been shown to influence the timely listing of patients with chronic kidney disease for transplantation to provide a summary for local project leads to see what lessons have been learnt by other investigators.

## 1.3 Objectives

1. To identify evidence relevant to the timely listing of patients for kidney transplantation
2. To create a summary of evidence identified to act as a reference tool for project leads involved in the Timely Listing for Kidney Transplantation project hosted by NHS Kidney Care

## 1.4 Review Question

The focus of the review will be the following issues:

- Summary of current UK guideline advice
- Explore the variation in listing that is influenced by: race, sex, socio-economic, educational status, and geographic disparity
- Evidence based strategies to improve the timely listing of chronic kidney disease patients for transplantation.

## 2 Method

### 2.1 Search Strategy

Combinations of the key terms “Kidney Transplantation”, “Chronic kidney disease”, “listing“, “planning“, and “pre-emptive“ were searched for using pubmed and google scholar. For papers identified of interest cited papers and papers citing the paper were also reviewed.

Pubmed search was "Kidney Transplantation" [Mesh] AND "Kidney Failure, Chronic"[Mesh] AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Practice Guideline[ptyp] OR Randomized Controlled Trial[ptyp] OR Review[ptyp] OR Classical Article[ptyp] OR Clinical Trial, Phase I[ptyp] OR Clinical Trial, Phase II[ptyp] OR Clinical Trial, Phase III[ptyp] OR Clinical Trial, Phase IV[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Evaluation Studies[ptyp] OR Journal Article[ptyp] OR Multicenter Study[ptyp]) AND (English[lang] OR French[lang]))

8110 results

Filter list listing OR list OR planning OR pre-emptive OR preemptive

361 results

Results of the authors search were combined with the librarian’s search and reviewed and excluded or included as shown.

## 3 Results

### 3.1 Papers identified

26 papers were identified as being useful to the review. Of these, four were published guidelines, two were review papers, nine were retrospective cohort studies, 10 were perspective or opinion papers, and one was a prospective cohort study.

#### 3.1.1 Exclusion criteria

Papers were excluded if their title and abstract did not relate directly to the review questions stated above. Excluded papers included those which focused on kidney allocation, statistical models, psychology and sociology, paediatric patients, cancer patients, and medical insurance.

### 3.2 Findings of the review

#### 3.2.1 What Renal Association and British Transplant Society guidelines already say should happen

The Renal Association Clinical Practice Guideline on the assessment of potential kidney transplant recipients makes a number of clear evidence based recommendations which include [2]:

- Kidney transplantation should be the renal replacement therapy of choice where patients are fit enough for major surgery and chronic immunosuppression because it offers significant survival benefit
- Living donor transplantation is preferred because it facilitates planning and offers the best chance of rehabilitation
- Patients with progressive deterioration in renal function suitable for transplantation should be placed on the national transplant list within six months of their anticipated dialysis start date
- All transplant units should have written criteria for acceptance on to the waiting list. Limitation of access to transplantation by age, gender, social and ethnic background is unacceptable and must be prevented by a standardized assessment mechanism.

The optimal time for pre-emptive kidney transplantation has not yet been defined. In the US a recent national cohort study of 19,147 first time pre-emptive kidney transplant recipients (of whom 59% received a live donor transplant) identified a trend towards earlier pre-emptive transplantation, from 9.2 ml/min/1.73m<sup>2</sup> in 1995 to 13.8 ml/min/ 1.73m<sup>2</sup> in 2009 (P0.001). The authors noted there was no association between earlier transplantation and patient or graft survival, suggesting that earlier pre-emptive transplantation may subject donors and recipients to premature operative risk and waste the native kidney function of recipients [30]. However other large registry data, for example from the collaborative transplant study [7] strongly suggest that prompt transplantation offers a significant survival advantage whether from a cadaveric or live donor source (Figure 1).

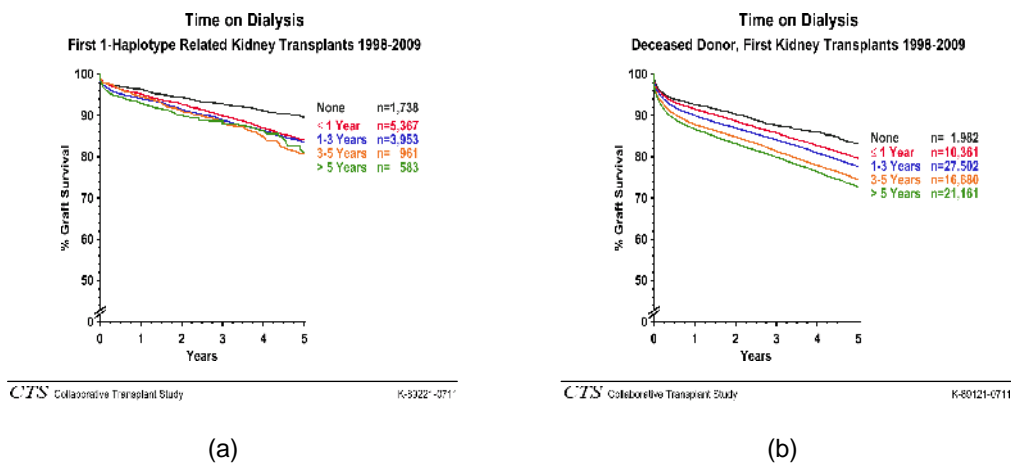


Figure 1: Transplantation offers a significant survival advantage whether from a cadaveric (a) or live (b) donor

### 3.2.2 Time to listing varies by race, sex, socioeconomic class, educational background and geography

In the UK disparities in listing for kidney transplantation exist. Two large cohort studies have found statistically significant inter-centre variability in access associated with social deprivation, age, sex, location, ethnicity, and primary renal diagnosis which cannot be explained by differences in case mix [5][4].

Similar clinically unexplained variation in listing has been found in a number of countries internationally including the USA [8].

It has been hypothesized that a patient's chance of both needing, and of securing, a living donor depends on their social network. Patients nested within a "risky" network might impart disadvantage by decreasing the patient's number of eligible donors [9]. The authors quote Clark et al. [10] who examined whether social support networks facilitate completion of pre-transplantation evaluations and reduce corresponding racial disparities. Clark et al found that compared to patients

with low levels of instrumental support (the number of friends or family to help with daily activities), those with higher levels were more likely to have complete evaluations.

Psychosocial factors such as depression have also been associated with a lower rate of timely listing and transplantation. One cross sectional study [11] of haemodialysis patients in the USA (N = 2033) and seven European countries (N = 4350) assessed self-reported depressive symptoms by the Center for Epidemiologic Studies-Depression scale, 10-item version (CES-D) and health-related quality of life (HR-QoL) by the Kidney Disease Quality of Life Short Form 12 scale Physical Component Score (PCS). At study entry, 27% (USA) to 53% (UK) of patients were wait-listed in participating countries. Variables associated with lower odds of being on the waiting list included worse HR-QoL, more severe depressive symptoms, older age, fewer years of education, lower serum albumin, lower hemoglobin, shorter time on dialysis and presence of multiple comorbid conditions .

Variation in work up criteria for patients being considered for listing may also contribute to inter-centre differences. One study [12] published in 2008 analysed responses to an online survey of transplantation assessment practice from 20 out of the 23 UK transplant centres. Eight out of the 20 centers did not give cytomegalovirus (CMV)-negative patients the option to receive kidneys from a CMV-positive donor. There was considerable variation in the investigation of cardiovascular disease and exclusion criteria based on cardiovascular status of the patients.

### **3.2.3 Evidence based strategies to improve the timely listing of chronic kidney disease patients for transplantation**

It is obvious that late referral to specialist services from other health care providers or patients first presenting when they already have severe kidney failure precludes timely listing [13][14]. In 2009, 19% of UK patients requiring renal replacement therapy were late presenters (defined as first being seen by a nephrologist less than 90 days before requiring renal replacement). In 2004 this figure was approximately 27% [15].

The Chronic Care Model [16] has been at least partially adopted for chronic kidney disease [17]. The model posits, among other things, that closer integration of primary and secondary care services is likely to improve the quality of chronic kidney disease care and reduce costs by, for example, using decision support in primary care to assist in the identification and appropriate management and referral of patients with chronic kidney disease.

In a review article it was highlighted that important impediments to pre-emptive transplantation include provider and patient education, insurance coverage (in the USA) and patient reluctance to



ask for living donation. Patients' self-reported barriers to discussing pre-emptive kidney transplantation include the belief that dialysis must precede transplant, that transplant is the last resort treatment and discomfort in asking family members and friends for a living-donor transplant [3][18].

#### **3.2.4 The role of chronic kidney disease clinics**

One single-centre retrospective cohort study [19] found mean transplant clinic referral times were significantly different between patients followed at a dedicated chronic kidney disease clinic and patients who were not. The mean time for referral before dialysis commenced was 234 (SD, 392) days for chronic kidney disease clinic patients versus 161 (SD, 525) days before referral for non-chronic kidney disease clinic patients ( $P = 0.01$ ).

Another single-centre retrospective chart review study [20] investigated the adherence to National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-K/DOQITM) [21] guidelines of nephrologists in training and working in a renal-hypertension clinic, compared with an experienced renal nurse practitioner working in a dedicated chronic kidney disease clinic. The study found that a nurse practitioner, working to protocol, would be more likely to adhere to guidelines than multiple nephrology trainees rotating through a nephrology clinic. Importantly, while the guidelines considered in this study do explicitly include timely listing, the study did not measure this outcome. The study found that at the initiation of dialysis, patients followed in the CKD clinic had higher haemoglobin ( $11.6 \pm 1.5$  vs  $10.8 \pm 1.7$  g/dl,  $P = 0.0239$ ) and serum albumin ( $3.4 \pm 0.5$  vs  $3.0 \pm 0.7$  g/dl,  $P = 0.0020$ ) concentrations. More of the CKD clinic patients had a functioning permanent vascular access ( $P < 0.0001$ ), and the number of all-cause hospitalizations in the 12 months after initiation of dialysis was significantly lower in the CKD clinic group ( $P = 0.0024$ ), but no significant differences were noted in all-cause mortality.

A small number of studies have found that the multidisciplinary management of patients with advanced chronic kidney disease in a dedicated chronic kidney disease clinic improves patient survival and markers of quality care such as correction of anaemia. However, none have specifically investigated the effect of a chronic kidney disease clinic on timely listing [22] [18] [23] [24]. One single-centre retrospective cohort study found the mean time to referral to a transplant clinic (to start transplant work up) was 73 days shorter for patients followed at a chronic kidney disease clinic compared to patients who were not [19].

#### **3.2.5 Increasing living donation**

In Scandinavia early referral to the pre-dialysis clinic occurs where live transplantation is promoted with tips and strategies to overcome patient discomfort in asking other people to

donate. This is coupled with educational materials and close support from a transplant coordinator [25]. In the USA early awareness of living donor transplantation has also been seen to be associated with an overall increased likelihood of undergoing pre-emptive transplantation [3].

Investigation of how the USA achieved higher rates of pre-emptive transplantation than the UK in 2005 found that there was a widespread view in the USA that living donor transplantation was the best treatment option for all patients with deteriorating kidney function who are approaching renal replacement therapy. Education materials were also clear and effective, with a combination of locally recorded videos, DVDs, and written information being provided for donor and recipient [26]. Many authors have promoted clear communication of factual information about the advantages and disadvantages of different renal replacement modalities as a way to increase rates of living donation [26] [27] [28] [24] [1].

A review of the means to increase pre-emptive transplantation rates emphasized the role of education and the importance of transplant candidates understanding and supporting living donation. In particular the review highlights the use of stories in conveying, to the patient and the wider population, an understanding of the short and long term outcomes for patient and donor, the care available to living donors, and how to refer potential donors to accurate sources of information regarding the living donor transplantation [3].

## 4 Key Findings

- UK Guidelines recognise renal transplantation as the gold standard renal replacement therapy and recommend that patients with stage 5 chronic kidney disease (eGFR <15 ml/min/1.73m<sup>2</sup>) be assessed and placed on a waiting list for kidney transplantation if judged to be within six months of their anticipated dialysis start date [2]. Assessment should start earlier when the eGFR is approximately 20ml/min where live donor transplantation is being considered [6].
- There is significant unexplained variation in timely listing and transplantation rates which correlates with patient characteristics such as race, sex, socio-economic, educational status, and geographic location.
- There is some evidence that chronic kidney disease clinics improve the quality of chronic kidney disease care but no evidence that they improve timely listing specifically.
- There is evidence that early patient education and discussion of renal replacement therapy modalities can increase living donation rates and improve timely listing.

## 5 Limitations

No studies were identified that specifically looked at evidence-based strategies to improve timely listing. From the literature reviewed, timely listing is not a commonly used outcome measure in studies of chronic kidney disease despite it being present as a recommendation in national and international guidelines.

## 6 Conclusion

The equitable distribution of scarce medical interventions, such as kidney transplantation, poses a challenging ethical and technical problem [29] [4].

In the UK there has been widespread recognition in the kidney community of the benefit to patients of pre-emptive and early transplantation but transplant rates remain low [15]. The evidence reviewed in this summary supports the role of chronic kidney disease clinics and early education as means to improve the quality of predialysis care but no robust evidence exists to guide changes in service delivery that might improve the number of patients timely listed for transplantation. [22] [18] [23] [24].

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