Early referral strategies for management of people with markers of renal disease: a systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis


CRD summary
This review concluded that there was some evidence to support the role of early referral for chronic kidney disease, with benefits in blood pressure control and renal progression. The evidence showed the need for good quality randomised controlled trials (RCTs) to assess methods of care delivery and timing of interventions. These conclusions appear likely to be reliable.

Authors' objectives
To assess the clinical and cost-effectiveness of early referral strategies for management of people with markers of renal disease. The characteristics of an effective early referral strategy were explored, as were with the barriers to early referral. The natural progression of patients with chronic kidney disease was also explored, but this lay outside the scope of this abstract.

Searching
Eleven databases including MEDLINE, EMBASE, The Cochrane Library and CINAHL were searched from dates between 1950 and 1988 up to February 2009. NHS EED was searched for the evaluation of cost-effectiveness. Abstracts of two relevant conferences were searched for 2006 and 2007. The search strategy was reported. References of included studies were checked for additional studies. Only studies published in English since 1990 were eligible for inclusion.

Study selection
Studies of any design that compared a strategy for early referral to specialist nephrology care of people with markers for renal disease (in either primary or secondary care) with a relevant comparator were eligible for inclusion. Definitions of what was considered an eligible early referral varied by study design; these definitions were reported. Comparators which were included were usual care, later referral (less than 12 months prior to renal replacement therapy in retrospective studies) or primary care. Included outcomes were: renal function; onset of renal replacement therapy; quality of life; all-cause mortality; cardiovascular mortality; hospitalisation; emergency dialysis; and survival on dialysis.

All included studies had mostly male participants (range 51% to 100%) and all contained substantial numbers of patients with diabetes; in one study only patients with diabetes were enrolled. Most studies did not report information on the stage of chronic kidney disease at diagnosis or first referral. Most studies were conducted in the USA or Europe and all studies recruited patients during the 1990s (where reported).

Two reviewers independently assessed the papers for inclusion in the review at both title and abstract stage; disagreements were resolved by discussion and consultation with a third reviewer if necessary.

Assessment of study quality
Studies were assessed for validity by two independent reviewers with the published checklists of the Centre for Reviews and Dissemination and checklists adapted from ones developed by NICE.

Data extraction
Data were extracted on study characteristics, including demographics, and outcome measures.

Two independent reviewers extracted the data using standardised forms. Discrepancies were resolved through discussion and consultation with a third reviewer if necessary.

Methods of synthesis
The studies were combined in a narrative synthesis structured by outcome and population characteristics.
Results of the review
Seven studies were included in the review (114,073 participants); all of these were cohort studies, five of which had retrospective designs and two of which were prospective (1,670 participants). Only the prospective studies included predialysis participants. Sample sizes varied from 117 to 109,321. Follow-up ranged from six months to five years. Study quality was limited, with substantial differences in baseline characteristics in all but one study. No studies had adequate descriptions of the intervention and only the two prospective studies reported definitions of chronic kidney disease (but not the criteria for specialist referral).

The five retrospective studies showed a reduction in mortality with early referral which was sustained up to five years after initiation of renal replacement therapy. Of the two prospective studies, one (in patients screened for diabetic nephropathy) reported a reduction in decline in renal function compared to a group with no access to nephrology services before they required dialysis. A second study found a reduction in a composite outcome of death or disease progression in veterans given nephrology follow-up after two creatinine levels of at least 140mg/dL compared to those followed up in primary care. This effect was greatest in those with stage 3 or more severe disease (stage 3 hazard ratio 0.8, 95% confidence interval 0.61 to 0.90; stage 4 hazard ratio 0.75, 95% confidence interval 0.45 to 0.89). Patients who received specialist care generally had lower blood pressure and received more aggressive anti-hypertensive therapy; quality of life was not reported.

The review also included a chapter that explored different models of care for people with chronic kidney disease.

Cost information
All early referral strategies produced more quality-adjusted life years (QALYs) than referral at transit to stage 5 of chronic kidney disease. Referral at stage 3a generated the most QALYs and had an incremental cost-effectiveness ratio (ICER) of £3,806 per QALY compared to referral at stage 4 disease. However, referral of all patients with stage 3 or higher disease would have required specialist nephrology capacity which was unavailable and was unlikely to be affordable or feasible.

Authors' conclusions
There was some evidence to support the role of early referral for chronic kidney disease; benefits in blood pressure control and renal progression were identified. The evidence showed the need for good quality RCTs to assess the methods of care delivery and the timing of intervention.

CRD commentary
The review question was clear and was supported by appropriate inclusion criteria. The search was comprehensive, but the decision to limit the review to studies published in English may have led to the introduction of publication and/or language bias. The authors reported using methods designed to reduce reviewer bias and error at all stages of the review process and carrying out an appropriate validity assessment of the included studies. The narrative synthesis presented was appropriate and the authors' conclusions reflect the results of the review and appear likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that the review supported the adoption of approaches that seek to develop shared care between primary and secondary care rather than focusing on early specialist referral.

Research: The authors identified some priorities for further research; cohort studies of the natural history of chronic kidney disease through stages 1 to 3, a review of the clinical and cost-effectiveness of the principal pharmacological interventions in these early stage patients and RCTs of models of care in patients with chronic kidney disease. As a priority, an RCT should be undertaken to compare shared care with standard specialist nephrology and primary care. Trials should include prospective economic evaluations.

Funding
National Institute for Health Research through the Health Technology Assessment Programme.

Bibliographic details

PubMedID
20441712

DOI
10.3310/hta14210

Original Paper URL
http://www.hta.ac.uk/execsumm/summ1421.htm

Other URL
Link to record on HTA database: http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=32008100356& UserID=0

Link to record on NHS EED: http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=2201000951& UserID=0

Indexing Status
Subject indexing assigned by NLM

MeSH
Biomarkers /metabolism; Cardiovascular Diseases /epidemiology /etiology /prevention & control; Cost-Benefit Analysis; Creatinine /metabolism; Disease Progression; Early Diagnosis; Evidence-Based Practice; Great Britain /epidemiology; Humans; Kidney Function Tests; Markov Chains; Models, Econometric; Models, Organizational; Nephrology /organization & administration; Outcome Assessment (Health Care); Referral and Consultation /organization & administration; Renal Insufficiency, Chronic /complications /diagnosis /epidemiology /metabolism /therapy; Research Design

AccessionNumber
12010003513

Date bibliographic record published
28/07/2010

Date abstract record published
11/08/2012

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.