



Title 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

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Reference Volume 14.21. ISSN 1366-5278. www.hta.ac.uk/project/1688.asp

Aim

To systematically review the evidence of the clinical and cost effectiveness of early referral strategies in managing people with markers of renal disease.

Conclusions and results

Despite the focus on the early identification and proactive management of chronic kidney disease (CKD) in the past few years, we have identified significant evidence gaps about how best to manage people with CKD. Some evidence suggests that care of people with CKD could improve, and because these people are at risk for both renal and cardiovascular outcomes, strategies to improve the management of people with CKD could potentially offer efficient use of care resources. Given the number of people having markers of kidney impairment, the need for further research to support change is urgent. In 36 relevant natural history studies, CKD was found to be a marker of increased risk of mortality, renal progression, and end-stage renal disease. Mortality was generally high and increased with stage of CKD. After adjustment for comorbidities, the relative risk of mortality among those with CKD identified in the general population increased with stage. Relative risk was higher in clinical populations. All 3 outcomes increased as the estimated glomerular filtration rate (eGFR) fell. Only 7 studies (no randomized controlled trials) were identified as relevant to assessing the clinical effectiveness of early referral strategies for CKD. In the 5 retrospective studies constructed from cohorts starting on renal replacement therapy (RRT), mortality was reduced in the early referral group (more than 12 months prior to RRT) even as late as 5 years after initiation of RRT. Only 2 studies included predialysis participants. One study, in people screened for diabetic nephropathy, reported a reduction in the decline of renal function associated with early referral to nephrology specialists (eGFR decline 3.4 ml/min/1.73 m²) when compared with a similar group that had no access to nephrology services until dialysis was required (eGFR decline 12.0 ml/min/1.73 m²). The second study, in a group of veterans with 2 creatinine levels

of at least 140 mg/dl, reported that a composite endpoint of death or progression was lower in the group receiving nephrology follow-up than in those receiving primary care follow-up alone. The greatest effect was observed in those with stage 3 disease, or worse, after adjusting for comorbidities, age, race, smoking, and proteinuria – stage 3: hazard ratio (HR) 0.8 (95% confidence interval [CI] 0.61 to 0.9) or stage 4: HR 0.75 (95% CI 0.45 to 0.89). In the base-case analysis, all early referral strategies produced more quality-adjusted life-years (QALYs) than referral upon transit to stage 5 CKD (eGFR 15 ml/min/1.73 m²). Referral for everyone with an eGFR below 60 ml/min/1.73 m² (stage 3a CKD) generated the most QALYs, and compared with referral for stage 4 CKD (eGFR < 30 ml/min/1.73 m²) had an incremental cost-effectiveness ratio of approximately 3806 pounds sterling (GBP) per QALY. Limitations: The Markov model relied on many assumptions due to a lack of data on the natural history of CKD in individuals without diabetes and a lack of evidence on the costs and effects of early referral. The findings were particularly sensitive to changes in eGFR decline rates and the relative effect of early referral on CKD progression and cardiovascular events; the latter parameter being derived from a single nonrandomized study.

Recommendations

See Executive Summary link www.hta.ac.uk/project/1688.asp.

Methods

See Executive Summary link www.hta.ac.uk/project/1688.asp.

Further research/reviews required

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