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HEALTH ECONOMICS RESEARCH UNIT
Briefing paper Feb 2011
Promoting Excellence in Health Economics

ECONOMIC EVALUATION OF AN EARLY REFERRAL STRATEGY FOR PEOPLE WITH CHRONIC KIDNEY DISEASE

Introduction

Chronic kidney disease is a long-term chronic condition defined by the gradual loss of kidney function over time. It is categorised according to the rate at which blood is filtered through the glomeruli of the kidneys and/or evidence of kidney damage (Table 1).[1] The glomerular filtration rate (GFR) can be estimated by a simple blood test, while evidence of kidney damage, such as protienurea, can be identified from analysis of the urine.

The inclusion of CKD management in the Quality Outcomes Framework (QOF) has encouraged GPs to identify people in the early stages of the disease. Many of these people would previously have gone undiagnosed, as CKD is often asymptomatic in its early stages. However, even in its early stages, CKD appears to be associated with an increased risk of cardiovascular disease, and a significant proportion of people with CKD are at risk of progressing to end-stage renal disease (ESRD). It has been hypothesised that early referral to specialist nephrology care might provide patients with access to an array of investigations and preventative treatments capable of reducing the risk of these adverse outcomes. The aim of this study was to model the potential cost-effectiveness of such an approach based on available evidence.[2]

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HERU is supported by the Chief Scientist Office (CSO) of the Scottish Government Health Directorates (SGHD) and the University of Aberdeen. The views expressed here are not necessarily those of the CSO
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Table 1: CKD stages according to Scottish Intercollegiate Guidelines Network[1]

CKD Stages	Definition	GFR (mL/min/1·73 m²)
Stage 1	Kidney damage with normal or raised GFR	**90 or more**
Stage 2	Kidney damage with mildly impaired GFR	60 to 89
Stage 3a	Moderately impaired GFR	**45 to 59**
Stage 3b	Moderately impaired GFR	**30 to 44**
Stage 4	Severely impaired GFR	15 to 29
Stage 5	End-stage renal disease	Less than 15

Notes: GFR, glomerular filtration rate

Methods

A Markov model was constructed to track disease progression for a cohort of patients identified in primary care as having CKD (Figure 1). The model allowed the cohort to be tracked according to estimated GFR (eGFR) and the presence of other complications known to influence CKD progression: micro-albuminuerea (MA), proteinurea (Prot), and co-morbid cardiovascular disease (CVD). Within each cycle of the model, individuals could progress to more severe CKD stages, experience fatal and non-fatal cardiovascular events, or die from other causes. The model was populated with transition probabilities derived from a systematic review of natural history studies,[2] in conjunction with cardiovascular (CV) event rates obtained from a validated risk prediction model.[3] Health service costs and health related quality of life weights associated with the modelled states and events were incorporated, allowing cumulative costs and quality adjusted life years (QALYs) to be tracked over a prolonged period of time.

The modelled intervention was based on a proposed shared care strategy.[4] Following an initial referral to specialist care, it was assumed that a proportion of patients would continue to be managed by specialists in secondary care, while others would be managed in primary care under the guidance of a specialist. It was further assumed that the involvement of specialists would bring about an increase in the proportion of patients receiving appropriate treatments for underlying CV risk factors and impaired renal function.[4,5] The overall effect of the shared care strategy was incorporated as a relative reduction in the risk of CKD progression and CV events. This risk reduction was obtained from an adjusted cohort analysis comparing progression of CKD in patients under specialist care with progression in those managed in primary care alone.[6]

All the individual cost elements of the referral strategy were estimated and incorporated in the model. Cost-effectiveness of implementing the strategy for patients at different stages of disease was then assessed compared with the historical practice of referral upon transit to end stage renal disease.

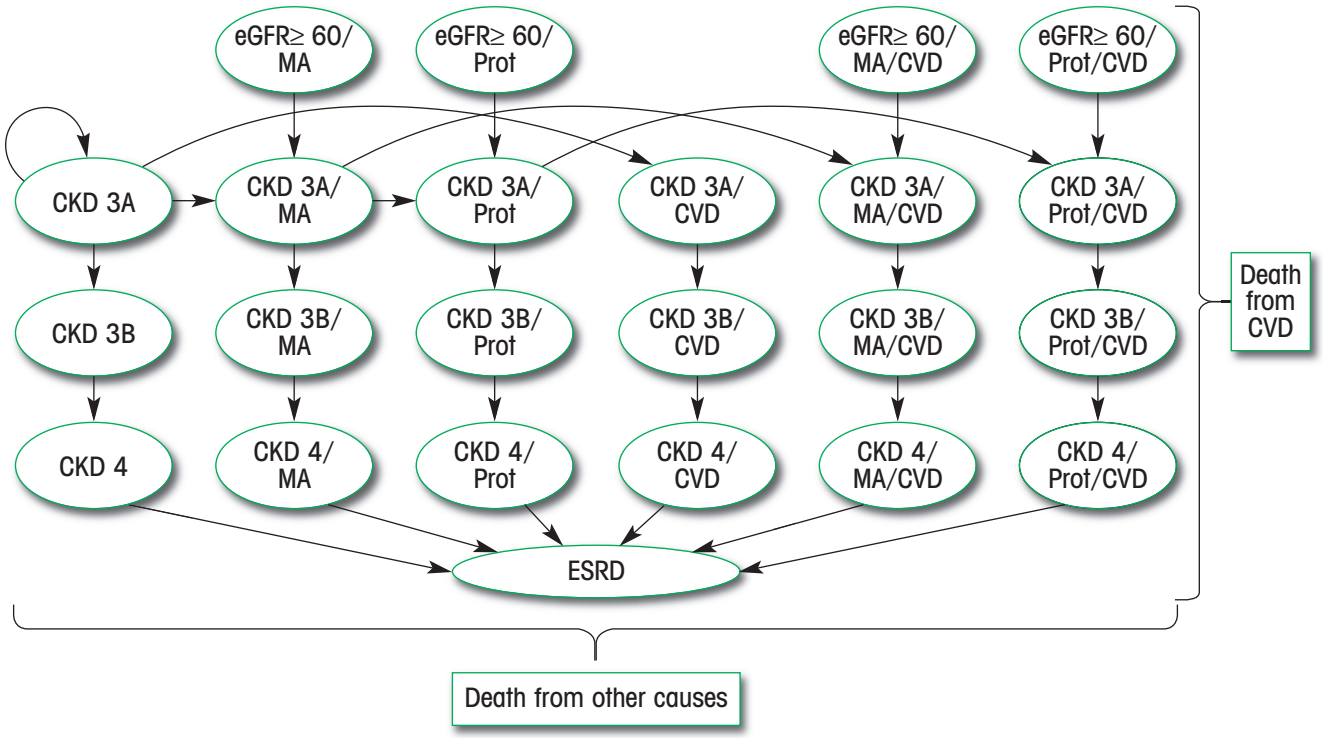
Results

Under baseline parameter estimates and assumptions, all strategies generated more QALYs than referral upon transit to ESRD (Table 2). Referral for everyone at stage 4 cost an additional £5,923 per extra QALY gained over historical practice. Referral for everyone at stage 3B cost £4352 per QALY gained over historical practice, and £3858 per extra QALY compared with referral at stage 4. Referral for everyone at stage 3A or worse generated the most QALYs, costing £3,806 and £3,751 per additional QALY compared with historical practice and referral at stage 3B respectively. The QALY gains associated with early referral were attributable to survival improvements and a reduction in progression to more severe disease states.

Sensitivity Analysis

Given the uncertainty surrounding a number of parameter estimates used in the model, the values for these parameters were varied within feasible ranges, and the impact on results was observed. The results were most sensitive to the underlying risk of developing MA and proteinuria, the cost of care under nephrology referral, and the effect of referral on CKD progression (Table 3). When several parameters were simultaneously weighted against early nephrology referral, the ICER for referral at stage 3A CKD approached a value unlikely to be considered cost-effective in the UK (final row of Table 3).

Figure 1: Representation of the Markov model structure



Notes: as well as transiting down through the CKD stages, individuals could transit across the co-morbidity states and develop MA, proteinuria and cardiovascular disease (CVD). Individuals in all states could die from CVD or other causes in any cycle of the model. Not all of the possible transitions are marked on the diagram (Individuals with stage 3b and stage 4 CKD could also transit to MA, proteinuria and CVD states).

Table 2: Base case cost-effectiveness results (per individual with CKD)

Strategy [a]	Total cost	Incremental cost	Effectiveness (QALYs)	Incremental effectiveness	ICER (cost per additional QALY)
Historical practice	£11,796		5.579		
Refer at CKD 3a	£13,487	£1,691	5.992	0.413	£4,091
Refer at CKD 3b	£12,808	£1,012	5.811	0.232	£4,352
Refer at CKD 4	£12,129	£332	5.635	0.056	£5,923

Notes: All strategies compared incrementally to historical practice (referral upon transit to end stage renal disease); CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life years.

Table 3: Deterministic sensitivity analyses - referral for everyone with CKD 3a compared with historical practice (referral around time of transit to CKD 5)

Scenarios	Incremental cost	Incremental effectiveness (QALYs)	ICER (cost per additional QALY)
Refer at CKD 3a (base case)	£1,691	0.413	£4,091
Risks for MA and proteinuria development zero	£2,031	0.322	£6,314
Effect of referral on CKD progression and CVD events halved and constrained to last 5 years	£2,360	0.095	£24,908
Costs of care under nephrology referral doubled	£6,624	0.413	£16,027
Costs under early nephrology referral doubled, effect sizes halved, base risk for MA and proteinuria development halved	£6,856	0.200	£34,323

Notes: CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESRD, end stage renal disease, ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life years; MA, microalbuminuria.

Conclusions

As patients progress to more severe stages of disease, they experience higher costs associated with CKD management and experience a higher risk of CV events and death. This modelling study suggests that it may be worth intervening early in the disease process in order to slow progression, improve survival, and reduce future health service expenditure. The earlier in the disease process that referral occurs, the lower the cumulative incidence of ESRD, which is associated with very high annual costs (~£27,000 per patient per year) and high mortality. However, evidence relating to the progression of CKD in the early stages and the effectiveness of early specialist referral is very limited. When more conservative effect estimates and underlying progression rates were applied, the incremental cost per QALY for early referral rose to a level unlikely to be considered cost effective in the UK. This finding raises questions over the cost-effectiveness of the strategy.

The affordability and feasibility of early referral is also questionable. Budget impact calculations based on the model suggested that implementation of the shared care strategy, for everyone with stage 3A disease or worse, would cost the NHS in Scotland and England an additional ~1.02 billion over three years and require somewhere in the region of 1,300 additional nephrologists.

While this study shows there is scope to improve health outcomes and reduce costs to the NHS by improving the management of people with CKD, there is too much uncertainty surrounding key model parameters to reach a definitive conclusion on the cost-effectiveness of the shared care strategy examined here. Moreover, feasibility and affordability are likely to prove prohibitive. Prospective follow-up studies are required to ascertain whether improved health outcomes can be achieved for people with early stage CKD through improved management in a primary care setting.

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Acknowledgements

This project was funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme. It will be published in full in the Health Technology Assessment journal series; Vol.14(21):1-184. Visit the HTA programme website for more details http://www.hta.ac.uk/execsumm/summ1421.htm. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health.

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