ECONOMIC MODELLING OF CHRONIC KIDNEY DISEASE: A SYSTEMATIC LITERATURE REVIEW TO INFORM CONCEPTUAL MODEL DESIGN

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Supplementary Table 11. Summary of unique models: Model setting

Study	Year	Country	Perspective	Time horizon	Type of analysis	Model type	Disease setting	Research question
Adarkwah et al.[1]	2011	Germany	German statutory health insurance	57 years	Cost-effectiveness	Markov model	Advanced renal disease	Cost–effectiveness of ACEI therapy in nondiabetic proteinuric patients with advanced renal disease
Adarkwah et al.[2]	2013	Netherlands	Healthcare payer	Lifetime	Cost-utility	Markov model	Advanced renal disease	Cost–effectiveness of ACEI therapy in nondiabetic proteinuric patients with advanced renal disease
Beby et al.[3]	2016	Netherlands	Payer	5 years	Cost-effectiveness	Markov model	ESRD	Cost-effectiveness of high dose haemodialysis, both in-center and at home, in comparison to conventional in- centre haemodialysis
Clement et al.[4]	2010	Canada	Healthcare payer	Lifetime	Cost-utility	Markov model	Anaemic CKD	Cost-effectiveness of treating anaemic patients with CKD with ESAs to a low (9-10.9 g/dL), intermediate (11-12 g/dL), or high (>12 g/dL) haemoglobin level target compared with a strategy of managing anaemia without ESAs
Dany et al.[5]	2015	France	NR	NR	NR	Markov model	ESRD	Build a multi-state model with either incidence or repeated prevalence data in order to estimate the transition rates between different states of RRT
de Vries et al.[6]	2016	Netherlands	Societal	NR	Cost-utility	State-transition model	CKD 4	Cost-effectiveness of delaying ESRD in 7 European countries: the Netherlands, United Kingdom, Germany, Italy, Spain, Finland and Hungary
de Wit et al.[7]	1998	Netherlands	Societal	NR	Cost-effectiveness and cost-consequence	Markov model	ESRD	The influence of substitutive policies on the overall cost-effectiveness of the ESRD treatment program
Gonzalez-Perez et al.[8]	2005	UK	NR	5 and 10 years	Cost-effectiveness	Markov model	Dialysis	Assess the costs and benefits of the three different modalities: home haemodialysis, satellite haemodialysis, hospital haemodialysis
Hiremath et al.[9]	2011	USA	NR	Lifetime	NR	Markov model and decision model	CKD 4	Determine the optimal vascular access referral strategy (refer all stage 4 chronic kidney disease patients for an arteriovenous fistula versus wait until the patient starts dialysis) for stage 4 (GFR <30 ml/min/1.73 m^2) CKD patients using a decision analytic framework
Howard et al.[10]	2009	Australia	Healthcare payer	NR	Cost-effectiveness	Markov model	ESKD	Assess the costs and health outcomes of proposed changes in service provision for increasing kidney transplantation and improving the rate of home-based dialysis
Kiberd[11]	1997	Canada	Patient	NR	NR	Markov model	Renal vascular disease	Determine how effective invasive therapy for renal vascular disease to prevent renal failure should be from the perspective of the patient to warrant implementation
Kirby et al.[12]	2001	UK	NR	NR	Cost-effectiveness	Markov model	Dialysis	Determine which method of dialysis, continuous ambulatory peritoneal dialysis or haemodialysis, a patient should have as the initial method of RRT
Lee et al.[13]	2006	USA	NR	NR	Cost-effectiveness	Simulation model	ESRD	Developed a simulation model of individuals progressing towards ESRD and requiring dialysis to analyse dialysis

								strategies and scenarios
Levy et al.[14]	2014	USA	NR	20 years	NR	Markov model	Transplant	Project long-term graft- and survival-related outcomes occurring among renal transplant recipients based on short-term outcomes including acute rejection and estimated GFR observed in randomised trials
Littlewood et al.[15]	2007	Germany	Healthcare payer	3 years	Cost-effectiveness	Markov model	ESRD	To understand the longer-term effects and costs of moxonidine, a decision analytic model was developed, and a cost-effectiveness analysis performed
Liu et al.[16]	2015	UK	Payer	Lifetime	Cost-effectiveness	Markov model	Dialysis	Investigate the cost-effectiveness of high-dose haemodialysis versus conventional in-center haemodialysis
Manns et al.[17]	2007	Canada	Healthcare payer	Lifetime	**four strategies:** 1. primary model 2. cost minimization model 3. mortality over time model 4. mortality by age model	Markov model	ESRD	Economic analysis which compared the use of sevelamer with calcium carbonate in a simulated cohort of North American dialysis patients with hyperphosphataemia
NICE TA48[18]	2002	UK	NHS	Five or ten year follow up	Cost-effectiveness	Markov model	Dialysis	Cost effectiveness of home haemodialysis, hospital haemodialysis and satellite haemodialysis
Naci et al.[19]	2012	USA	Third party payer	NR	Cost-effectiveness	Markov model	ESRD	Determine whether Medicare's decision to cover routine administration of ESAs to treat anaemia of ESRD has been a cost-effective policy relative to standard of care at the time
Nguyen et al.[20]	2016	Singapore	Third party payer	30 years	Cost-utility	Markov model	Pre-dialysis CKD with hyperphosphatemia	Estimate the lifetime costs and QALYs gained for treatment with sevelamer versus calcium carbonate
Nuijten et al.[21]	2015	Italy, Netherlands and USA	Italian payer	9 years	Cost-effectiveness	Markov model	CKD 5	Determine the cost effectiveness of two innovative therapies, paricalcitol versus cinacalcet + calcitriol (oral) in patients with CKD stage 5
Pike et al.[22]	2017	Norway	Societal	5 years	Cost-effectiveness	Markov model	ESRD	Effectiveness and cost-effectiveness of haemodialysis performed at different locations (hospital, satellite, and home) and peritoneal dialysis
Rosselli et al.[23]	2015	Colombia	Colombian healthcare system	5 years	Cost-effectiveness	Markov Model	ESRD	Estimate the costs and effectiveness measured in QALY of kidney transplantation compared with dialysis in adults suffering from ESRD
Ruggenenti et al.[24]	2001	Italy	Payer	Lifetime	Cost-effectiveness	NR: two models	Chronic proteinuric nephropathies	Predict the long-term cost and efficacy of the angiotensin-converting enzyme, ramipril, in patients with nondiabetic chronic nephropathies
Sennfalt et al.[25]	2002	Sweden	Societal	5 years	Cost-utility and cost-effectiveness	Decision model	CKD	Compare both health-related quality of life and costs for haemodialysis and peritoneal dialysis in patients with kidney failure
Shechter et al.[26]	2014	Canada	Patient	Lifetime	Comparative effectiveness analysis	Decision analysis	CKD	Use a data-driven decision-analytic model to provide an objective approach to timing arteriovenous fistula referral in patients with CKD
Takahashi et al.[27]	2008	USA and Japan	Japanese reimbursement	3 years	Cost-effectiveness	Markov model	CKD	Evaluate the cost-effectiveness of AST-120, an oral adsorbent that attenuates the progression of chronic kidney disease

Teerawattananon et al.[28]	2007	Thailand	Societal	Lifetime	Cost-effectiveness and cost-utility	Markov model	ESRD	Examine the value for money of including peritoneal dialysis or haemodialysis
Thaweethamcharoen et al.[29]	2014	Thailand	Societal	Lifetime	Cost-utility	Markov model	ESRD with anaemia, on haemodialysis	Compare the cost utility of using erythropoietin to maintain different haemoglobin target levels in haemodialysis patients
Thompson et al.[30]	2013	UK	NHS	Lifetime	Cost-effectiveness	Markov model	CKD 3-4, and not on dialysis with hyperphosphatemia	Cost effectiveness of sevelamer vs calcium carbonate in patients with CKD and not on dialysis (CKD-ND)
Vegter et al.[31]	2011	Netherlands and USA	NHS	Lifetime	Cost-effectiveness	A decision analytical structure was linked to a time-dependent Markov model	Second-line treatment in patients receiving dialysis	Cost-effectiveness of the noncalcium-based phosphate binder lanthanum carbonate as second-line treatment of hyperphosphatemia after therapy failure with calcium-based binders
Villa et al.[32]	2012	Spain	Public administration	Lifetime temporal horizon of 45 years	Cost-effectiveness	Markov model	Renal disease	Cost-effectiveness analysis of timely dialysis referral after renal transplant failure
Yang et al.[33]	2016	Singapore	Societal	10 years	Cost-utility	Markov Model	ESRD	Cost-effectiveness of haemodialysis, continuous ambulatory peritoneal dialysis and automated peritoneal dialysis for patients with ESRD

ACEI: angiotensin converting enzyme inhibitor; CKD: chronic kidney disease; ESA: erythropoiesis-stimulating agents; ESRD: end-stage renal disease; ESKD: end-stage kidney disease; GFR: glomerular filtration rate; NHS: National Health System; NR: not reported; QALY: quality-adjusted life year; RRT: renal replacement therapy.

Supplementary Table 12. Summary of unique models: health states, disease progression, CV events and discount rates

Study	Health states related to kidney disease	Approach used to model CKD progression	Approach used to model CV events	Discounting
Adarkwah et al.[1]	Advanced renal disease, ESRD, death	Transition probabilities	NR	3%
Adarkwah et al.[2]	Advanced renal disease, ESRD, death	Transition probabilities	NR	Costs: 4% Benefits: 1.5%
Beby et al.[3]	Conventional ICHD, conventional HD at home, high dose ICHD, high dose HD at home, PD, kidney transplantation	Transition probabilities	NR	Costs: 4% Benefits: 1.5%
Clement et al.[4]	Alive, not on dialysis (NDD), dialysis, transplanted, continue dialysis	Age-specific risk of initiating dialysis therapy	NR	5%
Dany et al.[5]	HD, PD, transplantation, death	Transition rates	NR	NR
de Vries et al.[6]	CKD4 conventional treatment, CKD prolongation due to new intervention under investigation, ESRD dialysis, ESRD transplantation, death	Annual incidence of CKD, transplantation and transplantation probability (Table 1)	NR	3%
de Wit et al.[7]	36 different states (combination of six treatment modalities: CHD, LCHD, HHD, CAPD, CCPD, transplant, three age groups and two treatment stages	Transition probabilities	NR	5%
Gonzalez-Perez et al.[8]	Home HD, Satellite HD, hospital HD, CAPD, transplant, death	Transition probabilities	NR	1.5%
Hiremath et al.[9]	CKD 4, CKD 4 with AVF, Dialysis with CVC, dialysis with AVF, death	Transition probabilities	Probability of HF, derived from expert opinion	NR
Howard et al.[10]	New ESKD patients requiring RRT, pre-emptive transplant, dialysis (hospital HD, home HD, satellite HD, PD), transplant, dead graft failure, continued graft function, continued dialysis, regraft, continued graft function, death ESKD causes, death other causes	Transition probabilities	NR	5%
Kiberd[11]	No screen, screen, non-operable, dialysis, survive, death	Annual progression	NR	NR
Kirby et al.[12]	HD, CAPD, complication, death	Transition probabilities	NR	6%
Lee et al.[13]	eGFR deterioration, transplant arrival, graft failure, hospitalisation, death	eGFR deterioration rate	NR	3%
Levy et al.[14]	Phase 1: Functioning graft: 2, 3a, 3b, 4 NODM, AR, graft loss, death Phase 2 (Markov model): functioning graft, failed graft (return to dialysis) functioning regraft, death	Annual probabilities of experiencing graft failure or death (Weibull models)	NR	NR
Littlewood et al.[15]	Non-ESRD state (NESRD), ESRD, death	Mean decline in GFR and transition probability	NR	Costs: 4% Life-years: 1.5%
Liu et al.[16]	Conventional ICHD, high dose HD (in-centre or home), transplant, PD	Transition probabilities	NR	3.5%
Manns et al.[17]	Dialysis, transplanted, continue dialysis, death	Transition probabilities	NR	5%
NICE TA48[18]	Hospital HD, satellite HD, home HD, CAPD, transplantation, death	Transition probabilities	NR	Costs: 6% QoL values: 1.5%
Naci et al.[19]	Dialysis without transplant, dialysis after failed transplant, transplant, dead	Transition probabilities	NR	NR

Nguyen et al.[20]	CKD with no dialysis, ESRD, all-cause mortality	Transition probabilities	NR	3.5%
Nuijten et al.[21]	Predialysis, PD, HD, transplant, death	Transition probabilities	Relative risk of CV event, derived from Cunningham (2005)	3%
Pike et al.[22]	HD (hospital, self-care, satellite, home), PD (CAPD, APD), transplantation, death	Probability	Occurrence rate of MI and angina derived from Norwegian Renal Registry	4%
Rosselli et al.[23]	Second line, healthy graft, dialysis, chronic rejection, acute rejection, PD, HD, death	Transition probabilities	NR	3%
Ruggenenti et al.[24]	Proteinuric chronic nephropathy, treatment (ramipril or placebo), conservative therapy, RRT, death	GFR rate of decline event-based-incidence of ESRD	NR	5%
Sennfalt et al.[25]	PD, HD, transplant, infection, death	Probability	NR	3%
Shechter et al.[26]	Figure 1: overview of Monte Carlo simulation model	Mean rate of eGFR decline	NR	NR
Takahashi et al.[27]	CKD, serum creatinine 5, serum creatinine 6, serum creatinine 7, serum creatine 8, dialysis, death	Transition probabilities (calculated slope of the reciprocal of serum creatinine = the rate of disease progression)	NR	3%
Teerawattananon et al.[28]	ESRD, initial mode of dialysis, switching to another mode of dialysis, death	Transition probabilities	NR	3.5%
Thaweethamcharoen et al.[29]	Alive with HD, alive with HD and cardiovascular disease	Transition probabilities	NR	3%
Thompson et al.[30]	Alive without dialysis, alive with dialysis, dead	Treatment-specific monthly probabilities for the initiation of dialysis	NR	3.5%
Vegter et al.[31]	Pre-dialysis patients, patients receiving dialysis, death	CKD progression rate	NR	3.5%
Villa et al.[32]	HD, PD, kidney transplantation, late referral haemodialysis, late referral peritoneal dialysis, death	Transition probabilities	NR	3%
Yang et al.[33]	Dialysis, kidney transplantation, death	Transition probabilities	NR	3%

AVF: arteriovenous fistula; CAPD: Continuous ambulatory peritoneal dialysis; CCPD: continuous cycling peritoneal dialysis; CVC: central venous catheter; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; ESKD: end-stage kidney disease; ESRD: end-stage renal disease; ECD: expanded criteria donor; HD: haemodialysis; HF: heart failure; HHD; home haemodialysis; ICHD: in-center haemodialysis; KT: kidney transplant; LCHD: limited care haemodialysis; LDKT: living donor kidney transplant; MI: myocardial infarction; NESRD: non ESRD; NODM: new-onset diabetes mellitus; NDD: non dialysis dependent; NA: not applicable; NR: not reported; PD: peritoneal dialysis; SCD: standard criteria donor.

**Studies included additional non-renal health states.*

Supplementary Table 13. Summary of unique models: Sensitivity analyses and drivers of cost-effectiveness

Study	Sensitivity analyses	Drivers of cost-effectiveness	Validation
Adarkwah et al.[1]	One-way	Effectiveness of ACEI treatment, the discount rate of costs and effects, and the cost of ESRD	NR
Adarkwah et al.[2]	One-way and multivariate (Monte Carlo)	Effectiveness of ACEI treatment, the costs of ESRD, and the discount rates of costs and effects	NR
Beby et al.[3]	One-way and probabilistic	Utilities associated with conventional home HD benefit and the reimbursement tariff for conventional HD and high dose HD at home, hospital reimbursement levels and the frequency of HD	Secondary validation of the model and its input parameters with healthcare payers as well as key opinion leaders
Clement et al.[4]	Monte Carlo and scenario	NR	NR
Dany et al.[5]	NR	NR	NR
de Vries et al.[6]	NR	NR	NR
de Wit et al.[7]	One-way and scenario	NR	NR
Gonzalez-Perez et al.[8]	Conducted, details NR	Cost-effectiveness of both home and satellite HD are considerably affected by changes in staff costs	NR
Hiremath et al.[9]	Probabilistic and two-way	NR	Model verification (debugging) was done by building up the model from simple to more complex, checking each step visually, examining the state probabilities from the cohort analysis, exploring certain extreme values and doing a sensitivity analysis on all variables. The model was calibrated by comparing simulated events (mortality for dialysis patients in the model) to observed ones (from the USRDS report)
Howard et al.[10]	Conducted, details NR	No drivers	NR
Kiberd[11]	NR	NR	NR
Kirby et al.[12]	Scenario	NR	NR

Lee et al.[13]	One-way	Cost and event rate estimates	1. Compared simulated outcomes to historical data published by the USRDS. This part of the analysis ensured that the various outcomes generated by the model were realistic in absolute terms. 2. Performed sensitivity analysis based on the 3 hypothetical policies: Early Initiation, Late Initiation, and No Dialysis. We examined how the relative rankings of their cost-effectiveness ratios (calculated based on simulated sample of 1 million patients) were affected by perturbations in hazard rates (±20%), costs (±20%), quality-of-life scores (±20%), discount rate (±50%), and dose response model parameters for both hospitalization and mortality (±20%)
Levy et al.[14]	Probabilistic	NR	Model verification included testing for internal consistency using extensive debugging and testing extreme conditions and calibration against the source data (i.e. USRDS)
Littlewood et al.[15]	Probabilistic and scenario	NR	NR
Liu et al.[16]	One-way, probabilistic and scenario	A higher number of HD sessions per week or a higher tariff for those sessions is associated with a lower net benefit. HD survival parameters were also important drivers of model results	Model was validated at a clinical advisory board and with a UK-based nephrology key opinion leader who had been involved in both inpatient and outpatient NHS renal services and in NICE appraisals of HD and PD. Although the 2013-2014 PbR dialysis tariff was used for the analysis, the tariff represents the national average costs of providing dialysis care in England. In addition, consistent conclusions were drawn using PbR dialysis tariffs since 2011-2012, when a tariff for home HD was introduced
Manns et al.[17]	One-way and scenario	Impact of quality of life (but using baseline mortality rates from our Canadian cohort), the use of sevelamer, compared with calcium-based phosphate binders, resulted in a cost per life year gain of CAN $102,600	Tested for logical inconsistencies in our decision model by evaluating them under hypothetical conditions. Determined that the models had face validity and confirmed that the mathematical calculations were accurate and consistent with the specifications of the model. We also confirmed that our model had predictive validity by comparing model outputs (a function of both input variables and model structure) with observed data from the DCOR study (data not shown). This comprehensive validation increases confidence in each of these models
NICE TA48[18]	Conducted, details NR	Principle variables involved were the cost of dialysis machines and the length of the training period for home haemodialysis	NR
Naci et al.[19]	Probabilistic and scenario	All-cause mortality estimate: when relative risk of all-cause mortality was assumed to be higher for the transfusion cohort, the ESA cohort accrued higher QALYs and lower costs than the transfusion cohort between 1995 and 2004. Similarly, the model was sensitive to the hospitalization estimate used in the model	Validity of this approach was evaluated by comparing the predicted number of clinical outcomes obtained from the model to the total numbers experienced by the US ESRD patient population. Validity of this approach was evaluated by comparing the predicted cost estimate obtained from the model to the total Medicare inpatient and outpatient expenditures for USRDS patient population
Nguyen et al.[20]	Deterministic and probabilistic	Prices of sevelamer and dialysis	NR
Nuijten et al.[21]	One-way and scenario	Annual probability of clinical events for paricalcitol, which corresponds with hospitalization	NR
Pike et al.[22]	Probabilistic and scenario	NR	NR
Rosselli et al.[23]	One-way, multivariate and a Monte Carlo simulation	Monthly cost of immunosuppression and monthly cost of dialysis	NR
Ruggenenti et al.[24]	Conducted, details NR	NR	NR

Sennfalt et al.[25]	Conducted, details NR	NR	NR
Shechter et al.[26]	One-way, two-way and probabilistic	NR	Compared survival curves of simulated patients who enter the clinic in CKD 3 and 4 with the Kaplan-Meier survival curves of our kidney clinic cohort who entered in the same stages
Takahashi et al.[27]	One-way	NR	NR
Teerawattananon et al.[28]	Probabilistic	NR	NR
Thaweethamcharoen et al.[29]	Probabilistic performed by using Monte-Carlo simulation	NR	NR
Thompson et al.[30]	One-way and probabilistic	Time horizon, mean daily dose of sevelamer, alternative assumptions regarding the impact of sevelamer on initiation of dialysis, and cost of dialysis	NR
Vegter et al.[31]	Probabilistic and scenario	Rate of CKD progression in predialysis patients, unrelated future dialysis costs	External validity of our model is supported by observational data of 335 Canadian CKD predialysis patients (median survival of 6.4 years) (Devins, 2005) and more than 3000 Scottish incident dialysis patients (median survival of 3.2 years) (Sawhney, 2009)
Villa et al.[32]	One-way and probabilistic (Monte Carlo simulation)	HD and late referral HD prevalence costs, and HD utilities	NR
Yang et al.[33]	One-way, probabilistic and high-risk group analysis	Utility of HD	NR

ACEI: angiotensin-converting-enzyme inhibitor; ESA: erythropoiesis-stimulating agent; ESRD: end-stage renal disease; HD: haemodialysis; NA: not applicable; NICE: National Institute for Health and Care Excellence; NR: not reported; PD: peritoneal dialysis; QALY: quality-adjusted life year; USRDS; United States renal data system.

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