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

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Supplementary Table 14. 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]	2010	Germany	Health insurance	50 years, or until age 100	Cost-utility	Markov model	Type 2 diabetes	Assess the most cost-effective time to start an ACEI (or an ARB if coughing as a side effect occurs) in patients with newly diagnosed type 2 diabetes
Airoldi et al.[2]	2008	UK	Primary Care Trusts	5 years	Cost-effectiveness	Markov chain	Type 1 diabetes	Outline framework that estimates health benefits and costs of different interventions in their populations; shows how modes produce estimates in a way that is transparent to commissioners
Bagust et al.[3]	2001	UK and USA	NR	NR	NR	Markov chain	Type 2 diabetes	Develop long-term economic model of health care for type 2 diabetes
Beckwith et al.[4]	2012	USA and Australia	NR	20-year follow-up	Cost-effectiveness	Markov model and Monte Carlo simulations	Type 1 diabetes	Perform a cost-effectiveness analysis comparing inlet transplantation with standard insulin therapy using Markov modelling and Monte Carlo simulations
Bertram et al.[5]	2010	Australia	Healthcare	Lifetime	Cost-effectiveness	Discrete-time micro-simulation model	Pre-diabetes	Evaluate the cost-effectiveness of a screening programme for pre-diabetes, which was followed up by treatment with pharmaceutical interventions or lifestyle interventions in order to prevent or slow the onset of diabetes in those at high risk
Boehringer Ingelheim Ltd (TA336[6])	2014	UK	NHS	Lifetime	6 months	Micro-simulation	Type 2 diabetes	Asses the cost-effectiveness of empagliflozin for treating patients with type 2 diabetes
Brown et al.[7]	2000	USA	NR	NR	1 year	Micro-simulation	Type 2 diabetes	Document the architecture, assumptions, and features of Release 3.0 of the user-friendly version of the global diabetes model (GDM)
Campbell et al.[8]	2007	USA	Health payer	8 years	Cost-effectiveness	Markov model	Type 2 diabetes	Determine the incremental cost-effectiveness ratios of ACEI initiation in normoalbuminuric, microalbuminuric and macroalbuminuric patients with newly diagnosed type 2 diabetes
Caro et al.[9]	2000	USA	Payer	95 years	Cost-consequence	Adapted Eastman model (1997)	Type 2 diabetes	Assess the economic efficiency of adding troglitazone to sulfonylurea therapy to improve glycemic control
Chen et al.[10]	2001	Taiwan	NR	NR	Cost-effectiveness and cost-utility	Markov Monte Carlo simulation model	Type 2 diabetes	Develop disease natural history of type 2 diabetes; quantify efficacy of early detection of type 2 diabetes in slowing or reducing the progression of major complications; evaluate the effect of inter-screening interval and age at start of screening; compare the cost effectiveness of organized screening; assess cost-effectiveness of type 2 diabetes screening by age-specific groups
Chen et al.[11]	2008	USA	NR	Death or age 100 years	Cost-effectiveness	Discrete-event simulation model	Type 2 diabetes	Project the long-term impacts on life expectancy and occurrence over 5, 10, and 40 years of microvascular and macrovascular complications of diabetes when using different haemoglobin A1c (HbA1c) thresholds for intensifying treatment of type 2 diabetes
Clark et al.[12]	2000	Canada	Government	21-year follow-up	Cost-utility	Decision analysis tree	Type I diabetes with macroproteinuria	Perform a cost-utility analysis from the government's perspective to see whether the province or territory should pay for ACEIs for type I diabetic nephropathy
Clarke et al.[13]	2004	UK	NR	NR	NR	Simulation model	Type 2 diabetes	Develop a simulation model for type 2 diabetes that can be used to

								estimate the likely occurrence of major diabetes-related complications over a lifetime
Dall et al.[14]	2015	USA	Societal	10 years	NR	Markov model	Pre-type 2 diabetes	Illustrate the potential clinical and economic benefits of treating prediabetes with lifestyle intervention to prevent or delay onset of type 2 diabetes and sequelae
Dong et al.[15]	2004	USA	Single payer	Death or age 95 years	Cost-effectiveness	Semi-Markov model	Type 1 diabetes	Examine the cost effectiveness of treating adults aged over 20 years with an ACEI (captopril) immediately following diagnosis of type 1 diabetes versus treating them after the onset of microalbuminuria
Eastman et al.[16]	1997	USA	Single payer	Lifetime	Cost-effectiveness	Markov model	Type 2 diabetes	Develop a model of NIDDM for analysing prevention strategies for NIDDM
Eddy et al.[17]	2003	USA	NA	NR	NA	Object-oriented approach, differential equations, and a construct called "features	Type 1 and type 2 diabetes	Build a mathematical model of the anatomy, pathophysiology, tests, treatments, and outcomes pertaining to diabetes that could be applied to a wide variety of clinical and administrative problems and that could be validated
Garattini et al.[18]	1997	Italy	Italian NHS	10 years	Cost-effectiveness	Decision model	Type 1 diabetes	Evaluate the likely cost savings associated with using an ACEI in patients with IDDM and proteinuria
Golan et al.[19]	1999	USA	Societal	Lifetime	Cost-effectiveness	Markov model	Type 2 diabetes	Evaluate the cost-effectiveness of treating all patients with type 2 diabetes
Grima et al.[20]	2007	Canada	Public healthcare payer	36 years	Cost-effectiveness	State-transition model	Type 1 and type 2 diabetes	Assess the cost effectiveness of insulin glargine compared with NPH insulin in patients with type 1 or 2 diabetes who had inadequate glycaemic control
Hayashino et al.[21]	2010	Japan	Societal	Lifetime	NR	Markov model	Diabetes with CKD 3 or 4	Evaluate the cost-effectiveness of using AST-120 to treat patients with type 2 diabetes and advanced-stage CKD
Hayes et al.[22]	2013	UK and Australia	NR	NR	NA	Simulation model	Type 2 diabetes	Build a new version of the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS-OM1), a patient-level simulation tool for predicting lifetime health outcomes of people with type 2 diabetes mellitus
Hoerger et al.[23]	2004	USA	Health care system	Lifetime	Cost-effectiveness	Markov model	Type 2 diabetes	Estimate the incremental cost-effectiveness of type 2 diabetes screening strategies: screening targeted to people with hypertension and universal screening
Kiberd et al.[24]	1995	Canada	Third party and government	60 years	Cost-effective and cost-utility are used interchangeably in the report	Markov model	Type 1 diabetes	Examine the conditions necessary to make screening for microalbuminuria in patients with insulin dependent diabetes mellitus cost effective
McEwan et al.[25]	2016	UK	NR	80 years	NR	Simulation model	Type 1 diabetes	Quantify the individual and combined contribution of changes in hypoglycaemia frequency, weight and HbA1c to predicted QALYs within a type 1 diabetes population
McEwan et al.[26]	2006	UK	NR	20 years or 60 years	Cost-effectiveness and cost-utility	Simulation model	Type 2 diabetes	Determine the mean costs and outcomes associated with modifiable risk factors in patients with type 2 diabetes and to determine equivalent changes to these risk factors in terms of financial costs and health outcomes
McEwan et al.[27]	2007	UK	NHS	40 years	Cost-utility	Discrete event simulation model	Type 1 diabetes	Evaluate relative cost-effectiveness of insulin glargine versus NPH insulin for the treatment of type 2 diabetes
McQueen et al.[28]	2011	USA	Societal	33 years	Cost-effectiveness	Markov model	Type 1 diabetes	Determine the cost-effectiveness of Continuous Glucose Monitoring (CGM) technology with intensive insulin therapy compared to self-monitoring of blood glucose (SMBG) in adults with type 1 diabetes

Mueller et al.[29]	2006	Germany, UK, Belgium, USA	NR	NR	NR	Discrete event Monte-Carlo simulation application. A Markov process (with memory)	Type 1 and type 2 diabetes	Develop and validate the EAGLE model to provide a flexible and comprehensive tool for the simulation of the long-term effects of diabetes treatment and related costs in type 1 and type 2 diabetes
Nagy et al.[30]	2016	Hungary	Policymaker	Lifetime	Cost-effectiveness	Markov model	Type 2 diabetic and non-diabetic populations	Develop a long-term economic model for type 2 diabetes to describe the entire spectrum of the disease over a wide range of healthcare programmes
Palmer et al.[31]	2000	Switzerland	Swiss Health insurance payer	Lifetime	Cost-effectiveness	Markov model	Type 1 diabetes	Determine the health outcomes and economic consequences of different combinations of diabetes interventions in newly diagnosed patients with type I (insulin-dependent) diabetes in Switzerland
Palmer et al.[32]	2004a	Switzerland and USA	Adaptable	Between 1 and 90 years	NR	Markov model	Type 1 and type 2 diabetes	Develop an internet-based, interactive computer model to determine the long-term health outcomes and economic consequences of implementing different treatment policies or interventions in type 1 and type 2 diabetes mellitus
Palmer et al.[33]	2004b	Switzerland, Belgium France, USA, Netherlands, Denmark	Third party payer	NR	Cost-effectiveness	Markov model	Type 2 diabetes (hypertensive patients with renal disease)	Determine the most cost-effective time point for initiation of irbesartan treatment in hypertensive patients with type 2 diabetes and renal disease
Palmer et al.[34]	2006	France	Third party health	25 years	Cost-consequence	Markov model	Type 2 diabetes (hypertensive patients	Assess the health economic impact of nephropathy screening in hypertensive patients with type 2 diabetes followed by optimal antihypertensive/nephroprotective therapy in those who have nephropathy
Rodby et al.[35]	2003	Switzerland, USA, France, Belgium	Healthcare	3, 10 and 25 years	Cost-effectiveness	Markov Model	Type 2 diabetes (hypertensive patients with nephropathy)	Estimate the cost-effectiveness of ibersartan compared with placebo or amlodipine in the treatment of patients with type 2 diabetes, hypertension and overt nephropathy
Rodby et al.[36]	1996	USA	Payer	31 years for patients with IDDM 12 years for patients with NIDDM	Cost-benefit and cost-effectiveness	Markov-type decision analysis model	Type 1 and 2 diabetes	Determine the cost-benefit and cost-effectiveness of captopril as a therapy in patients with IDDM as well as the potential savings for all patients with diabetes and nephropathy
Sakthong et al.[37]	2001	Thailand	NR	25 years	Cost-effectiveness	Markov model	Type 2 diabetes	Assess the cost-effectiveness of prescribing ACEI to delay progression of diabetic nephropathy in normotensive patients with type 2 diabetes and microalbuminuria
Shearer et al.[38]	2004	UK	Societal and patient	10 years	Cost-effectiveness	Markov model	Type 1 diabetes	Determine the cost-effectiveness of a structured treatment and teaching programme combining dietary freedom with insulin adjustment for type 1 diabetes
Smith et al.[39]	2004	USA	Third party payer	8 years	Cost-effectiveness	Markov model	Type 2 diabetes	Estimate 8-year health and economic outcomes of the angiotensin II receptor blocker valsartan versus the calcium channel blocker amlodipine in therapy of patients with type 2 diabetes and microalbuminuria based on clinical endpoints from a 6-month randomized controlled clinical trial
Srisubat et al.[40]	2014	Thailand	Socioeconomic	Lifetime	Cost-effectiveness	Markov model	Type 2 diabetes	Assess the cost-effectiveness of annual microalbuminuria screening in type 2 diabetic patients
Steen Carlsson et al.[41]	2014	Sweden	Societal	40 years	Cost-effectiveness	Markov model	Type 2 diabetes	Evaluate long-run cost-effectiveness in a Swedish setting for liraglutide compared with sulphonylureas (glimepiride) or sitagliptin, all as add-on to metformin for patients with type 2 diabetes insufficiently controlled with metformin in monotherapy
CDC Diabetes Cost-effectiveness	2002	USA	Health care system	NR	Cost-effectiveness	Markov model	Type 2 diabetes	Estimate the incremental cost-effectiveness of intensive glycemic control (relative to conventional control), intensified hypertension

Group[42]								control, and reduction in serum cholesterol level for patients with type 2 diabetes
DCCT group[43]	1996	USA	Health care system	Lifetime	Cost-effectiveness	Simulation model	Type 1 diabetes	Examine the cost-effectiveness of alternative management of IDDM
Thokala et al.[44]	2014	UK	Health service	Lifetime	Cost-effectiveness	Markov Model	Type 1 diabetes	Build a flexible and comprehensive long-term type 1 diabetes mellitus model incorporating the most up-to-date methodologies to allow a number of cost-effectiveness evaluations
Van Os et al.[45]	2000	Netherlands	Health care	Lifetime (50 years for type 1 diabetes, 30-years for type 2 diabetes)	Cost-effectiveness	Semi-Markov model	Type 1 and 2 diabetes	Examine the cost-effectiveness of guideline recommendations for prevention of nephropathy in diabetes mellitus type 1 and 2
Willis et al.[46]	2013	Sweden, Finland USA	NR	NR	Validation of model	Micro-simulation model	Type 2 diabetes	Present results of a formal validation exercise of the ECHO-T2DM model
Wu et al.[47]	2017	China	Chinese healthcare	Lifetime	Cost-effectiveness	Decision tree and Markov model	Type 2 diabetes	Assess the cost-effectiveness of preventing diabetic kidney disease in patients with newly diagnosed type 2 diabetes from the Chinese healthcare perspective
Zhou et al.[48]	2005	USA	Health system	10years	Cost-effectiveness and cost-utility	Semi-Markov model	Type 2 diabetes	Develop and validate a comprehensive computer simulation model to assess the impact of screening, prevention, and treatment strategies on type 2 diabetes and its complications, comorbidities, quality of life, and cost

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blockers; CGM: continuous glucose monitoring; CKD: chronic kidney disease; CVD; cardiovascular disease; DCCT: Diabetes control and complications trial; IDDM: insulin dependent diabetes mellitus; NA: not applicable; NHS: National Health System; NPH: Neutral Protamine Hagedorn; NIDDM: Non-insulin-dependent diabetes mellitus; NR: not reported; SMBG: self-monitoring of blood glucose; QALY: quality-adjusted life year.

Supplementary Table 15. 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]	Normoalbuminuria, microalbuminuria, macroalbuminuria, ESRD (treated with dialysis or renal transplantation), death	Transition rates	NA	3%
Airoldi et al.[2]*	Normoalbuminuria, microalbuminuria, microalbuminuria, ESRD	Transition rates	NR	3.5%
Bagust et al.[3]*	No nephropathy, microalbuminuria, gross proteinuria, ESRD	Transition probabilities	Framingham risk score	NR
Beckwith et al.[4]*	ESRD	NR	Probability of CHD, derived from Nathan (2005)	3%
Bertram et al.[5]	Diabetes, diabetic renal disease, dead	Transition probabilities	Transition probabilities dependent on age and gender	3%
Boehringer Ingelheim Ltd (TA336[6])	Renal failure	Risk equation	Risk equation, used UKPDS equations	3.5%
Brown et al.[7]*	No nephropathy, microalbuminuria, gross proteinuria, ESRD	Incidence rates	Probability of MI< stroke, CHF, derived from Framingham risk score	NR
Campbell et al.[8]	Rosen (2005)	Transition probabilities	Probability of CVD event, derived from Parving (2001), USRDS, Yuyun (2004)	3%
Caro et al.[9]	Adapted Eastman model (1997)	NR	NR	3%
Chen et al.[10]	No nephropathy, microalbuminuria, proteinuria, ESRD	Transition parameters	Incidence of CV, derived from Framingham risk score	3%
Chen et al.[11]	Diabetes-related events: renal failure	Risk equations	NR	NR
Clark et al.[12]	Diabetes with macroproteinuria, ESRD treatment, short dialysis short transplant, death	Rate of decline for creatinine clearance	NR	5%
Clarke et al.[13]	NR in detail; seven diabetes-related complications (includes renal)	Equation 7 using a combination of Gompertz and logistic regression equations (Table 2)	Used Weibull equations	NR
Dall et al.[14]	Renal failure	Transition probabilities Renal failure: Age and sex specific incidence rates	Probability of MI, stroke, IHD, LVH, CHF, derived from UKPDS Outcomes model, Framingham heart study and Framingham offspring study amongst others	3%
Dong et al.[15]	Normoalbuminuria, microalbuminuria, macroalbuminuria, ESRD	Transition probabilities	Risk of CAD, derived from Krolewski (1987)	3%
Eastman et al.[16]*	No nephropathy, Microalbuminuria, proteinuria, ESRD	Hazard rate (per year)	Probability of CVD, derived from USRDS	3%

Eddy et al.[17]	Nephropathy submodel	Equations	NR	NR
Garattini et al.[18]	No ESRD, ESRD, death	Event probabilities	NR	5%
Golan et al.[19]	Normoalbuminuria, microalbuminuria, gross proteinuria, ESRD	Transition rates	NR	3%
Grima et al.[20]	ESRD is a complication in the model	Complication rates	Probability of MI, stroke and HF, derived from UKPDS	5%
Hayashino et al.[21]	CKD, ESRD, death	CCr yearly decline rate and yearly rate of progression to ESRD	NR	3%
Hayes et al.[22]*	Event history: renal	Risk equations (renal failure: equation 13)	Annual event rate for MI, stroke and CHF, calculated from total number of events/total patient-years	NA
Hoerger et al.[23]*	Normal, low/high microalbuminuria, clinical nephropathy, ESRD, ESRD death	Transition probabilities	Probability of stroke to death	3%
Kiberd et al.[24]	Strategy A: IDDM, hypertension, microalbuminuria, macroalbuminuria, ESRD Strategy B: IDDM, microalbuminuria, macroalbuminuria, ESRD	Transition probabilities	Probability of hypertension	5%
McEwan et al.[25]	No nephropathy, micro-albuminuria, macro-albuminuria with or without impaired GFR and ESRD. Upon progression to ESRD patients can receive transplant, experience graft failure and return to dialysis or die either whilst receiving dialysis or from the functioning graft health state	Transition probabilities	Probability of MI, derived from Swedish National Diabetes registry	3.5%
McEwan et al.[26]	No nephropathy, microalbuminuria, gross proteinuria, ESRD	Eastman model (1997)	Probability of CHD, derived from UKPDS	Costs: 6% and benefits: 1.5%
McEwan et al.[27]*	Nephropathy	Transition probabilities	Derived probabilities from Framingham risk score	3.5%
McQueen et al.[28]*	Nephropathy, nephropathy and CHD, neuropathy and nephropathy, ESRD	Transition probabilities	NR	3%
Mueller et al.[29]*	Microalbuminuria, macro-albuminuria, ESRD	Risk equations	Probabilities of MI, stroke, angina and HF calculated for non-fatal and fatal events	NR
Nagy et al.[30]	No nephropathy, undetected microalbuminuria, detected microalbuminuria, undetected gross proteinuria, detected gross proteinuria, dialysis, with renal transplant and death	Transition probabilities	Transition probabilities	3.78%
Palmer et al.[31]*	No renal disease, microalbuminuria, macro-albuminuria, ESRD, kidney transplantation, haemodialysis, peritoneal dialysis, graft failure, ESRD-specific mortality, non-specific mortality	Transition probabilities	NR	3%
Palmer et al.[32]*	No renal complications, microalbuminuria, gross proteinuria, ESRD (either haemodialysis, peritoneal dialysis or kidney transplant) and death following ESRD	Transition probabilities	NR	NR

Palmer et al.[33]	Microalbuminuria, early overt nephropathy, advanced overt nephropathy, DSC, ESRD treated with dialysis, ESRD treated with renal transplant, and death	Transition probabilities	NR	3%
Palmer et al.[34]	Not screened: no nephropathy, microalbuminuria, early overt nephropathy, advanced overt nephropathy, doubling serum creatinine, dialysis, kidney transplant, death. Screened: no nephropathy irbesartan treated, microalbuminuria irbesartan treated, early overt nephropathy irbesartan treated, advanced overt nephropathy irbesartan treated, doubling serum creatinine irbesartan treated, dialysis, kidney transplant, death No nephropathy not irbesartan treated, microalbuminuria, early overt nephropathy, advanced overt nephropathy, doubling serum creatinine, dialysis, kidney transplant, death	Transition probabilities	NR	3%
Rodby et al.[35]	Survive, doubling of serum creatinine, ESRD + dialysis, ESRD + transplant, death	Transition probabilities	Modelled as transitions and were temporary	3%
Rodby et al.[36]	Diabetic nephropathy, routine care, complication comorbidity ESRD, death, dialysis, transplant	Transition rates	Relative risk of CV events	5%
Sakthong et al.[37]	Microalbuminuria, macroalbuminuria, ESRD, death	Transition rates	NR	8%
Shearer et al.[38]	Normoalbuminuria, microalbuminuria, overt diabetic nephropathy, ESRD, death	HbA1C levels	NR	Costs: 6% and benefits: 1.5%
Smith et al.[39]*	Normal albumin levels, microalbuminuria, nephropathy, ESRD, death	Transition rates	Probability of CV derived from MARVAL study	3%
Srisubat et al.[40]	Normalbuminuria, microalbuminuria, macroalbuminuria elevated serum creatine, ESRD, death	Transition rates	NR	3%
Steen Carlsson et al.[41]	None, microalbuminuria, macroalbuminuria, ESRD	Risk equations	Calculated from the characteristics of the cohort and risk equations	3%
CDC Diabetes Cost-effectiveness Group[42]	Normal, low micro/high micro, clinical nephropathy, ESRD, death	Transition probabilities	NR	3%
DCCT group[43]	Normoalbuminuria, microalbuminuria, albuminuria, ESRD	Annual probabilities	NR	3%
Thokala et al.[44]	No nephropathy, microalbuminuria, macroalbuminuria, ESRD, death	Transition rates	Probability of MI, stroke, angina and revascularisation derived from DCCT/EDIC	3.5%
Van Os et al.[45]	Diabetes type 1 or 2, microalbuminuria, macroalbuminuria, ESRD, death	Transition rates	NR	3%
Willis et al.[46]*	No nephropathy, microalbuminuria, gross proteinuria, ESRD	NR	NR	NR
Wu et al.[47]*	Markov model module: diabetes normal, microalbuminuria, macroalbuminuria, ESRD, death	Transition rates	NR	3%

Zhou et al.[48]*	Normal, microalbuminuria, proteinuria, ESRD with dialysis, ESRD with transplant, death due to ESRD	Transition rates	NR	0%

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blockers; CAD: coronary artery disease; CHD: congestive heart disease; CHF: coronary heart failure; CVD; cardiovascular disease; DCCT: Diabetes control and complications trial; GFR: glomerular filtration rate; IDDM: insulin dependent diabetes mellitus; IHD: ischaemic heart disease; LVH: Left ventricular hypertrophy; MI: myocardial infarction; NIDDM: Non-insulin-dependent diabetes mellitus; NR: not reported.

Supplementary Table 16. 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	Discount rate, the absolute risk for progression from micro- to macro-albuminuria without ACE inhibition as well as the relative risk for progression from normo- to microalbuminuria with ACEI therapy	NR
Airoldi et al.[2]	Conducted, details NR	NR	Compared the prevalence of complications resulting from the initial condition with data from the literature
Bagust et al.[3]	Conducted, details NR	Monetary value of health benefits	NR
Beckwith et al.[4]	Conducted, details NR	NR	NR
Bertram et al.[5]	Conducted, details NR	NR	NR
Boehringer Ingelheim Ltd (TA336[6])	Probabilistic sensitivity analysis	Results are robust to a number of sensitivity analysis and that the key drivers are the clinical effectiveness and adverse events rather than any of the assumptions	Expert meetings with a UK clinical diabetologists were conducted by Boehringer Ingelheim. IMS model used to validate the analysis by conducting a series of cost effectiveness analyses using where possible the same input parameters. Internal verification of the model was conducted throughout the model implementation process
Brown et al.[7]	NR	NR	NR
Campbell et al.[8]	One-way and two-way	Drug costs	NR
Caro et al.[9]	Conducted, details NR	NR	NR
Chen et al.[10]	NR	NR	NR
Chen et al.[11]	NR	NR	NR

Clark et al.[12]	One-way and two-way	Compliance, effect of benefit and the cost of drug therapy	Evidence for construct validity was based on correlation with the Spitzer Quality of Life Index and a provider visual analogue scale
Clarke et al.[13]	NR	NR	Tested the consistency of the forecast cumulative incidence of different complications and death to the cumulative incidence calculated using non-parametric (life-table) methods
Dall et al.[14]	One-way and deterministic	Predicting annual changes in HbA1c as a person ages and as other risk factors change	Followed guidelines published by the International Society for Pharmacoeconomics and Outcomes Research and Society for Medical Decision Making
Dong et al.[15]	Conducted, details NR	How effective ACEIs are in delaying the onset of microalbuminuria	NR
Eastman et al.[16]	NR	Age at onset of clinical diabetes, ethnicity of the cohort	NR
Eddy et al.[17]	NR	NR	Validated against clinical trials
Garattini et al.[18]	Conducted, details NR	NR	NR
Golan et al.[19]	Conducted, details NR	Age at diagnosis of diabetes, cost of ACEIs, relative risk for progression to microalbuminuria, and quality-of-life adjustment for ACEIs	NR
Grima et al.[20]	One-way	Baseline HbA1c, the efficacy of insulin gargine and diabetes costs	Model was validated in terms of its ability to accurately estimate the 5- year incidence of diabetes-related complications reported in the HOPE study
Hayashino et al.[21]	One-way	Effectiveness of AST-120	NR
Hayes et al.[22]	One-way and deterministic	Classic risk factors (SBP, HbA1c and lipids) in predicting life expectancy importance of many of the novel risk factors, in particular eGFR, micro- or macro-albuminuria, heart rate and white blood cell count	Internal validation of the simulation model by testing its performance in replicating the incidence of complications and mortality over 25 years of follow-up. Compared simulated cumulative failure of each of the major outcomes of the model with the observed (Kaplan–Meier) cumulative failure of events under the assumption adopted in many clinical studies that death as well as date of last contact are censoring events
Hoerger et al.[23]	One-way and probabilistic	Effects of intensive hypertension control	NR
Kiberd et al.[24]	Conducted	NR	NR
McEwan et al.[25]	NR	NR	Regression analysis indicated that endpoint predictions and costs had non- significant intercept terms (p = 0.009 and p = 0.652 respectively) indicating no systematic over or under-prediction
McEwan et al.[26]	One-way	NR	Face validation of the model was conducted to ensure correct logical functioning. The output was validated by comparing how well the model reconstructed data from the UKPDS, Eastman and Cardiff model
McEwan et al.[27]	Extensive one-way	Price of glargine, the utility decrement associated with hypoglycaemia, and the cohorts' mean weight. The ICER was also sensitive to the	Model epidemiological outputs were tested versus published data

		duration of HbA1c treatment effect with the baseline ICER of £3189 for scenario 5 increasing to £7485, £14 755 and £47 445 with 10-, 5- and 2-year treatment effects duration, respectively	
McQueen et al.[28]	One-way and multivariate probabilistic	Utility of diabetes with no complications, the annual cost of CHD, and the probability of going from diabetes with no complications to the CHD disease state	NR
Mueller et al.[29]	Probabilistic	NR	Both the epidemiological and health economic modules of the EAGLE model were tested and debugged internal validation of EAGLE was performed
Nagy et al.[30]	NR	NR	NR
Palmer et al.[31]	One-way	Cost of renal failure, intensive therapy	NR
Palmer et al.[32]	Conducted, details NR	NR	Addressed in a separate publication (Palmer, 2004), which describes a total of 66 second-(internal) and third- (external) order validation analyses performed across a range of complications and outcomes simulated by the CORE Diabetes Model
Palmer et al.[33]	Second-order Monte Carlo simulation	NR	NR
Palmer et al.[34]	Conducted, details NR	Patient age	NR
Rodby et al.[35]	One-way	Transition probabilities from the survive, to death states and from ESRD dialysis to death for the irbesartan strategy	NR
Rodby et al.[36]	Conducted, details NR	NR	NR
Sakthong et al.[37]	Conducted, details NR	Cost of the drug, cost of ESRD treatment, effectiveness of the drug	NR
Shearer et al.[38]	One-way and multivariate	Discount percentage, first year HbA1c reduction, mortality rates, progression of neuropathy and nephropathy, cost of foot ulcers and dialysis, utility, structured treatment and teaching programme course cost, benefit from ketoacidosis	NR
Smith et al.[39]	NR	Costs and utility weights assigned to health states	NR
Srisubat et al.[40]	One-way and probabilistic	Positive predictive value of urine dipsticks, cost of urine dipsticks, discount rate, transition probability of microalbuminuria to macroalbuminuria, cost of dialysis, relative risk of ACEI for microalbuminuria to macro-albuminuria, increased travel cost and utility	NR
Steen Carlsson et al.[41]	Second order probabilistic	Number of hypoglycemic events when on insulin treatment, initiation of second line treatment at different HbA1c levels, BMI	The IHE Cohort Model of type 2 diabetes has been validated against published trial data and large population cohort data
CDC Diabetes Cost- effectiveness Group[42]	One-way	Case management costs, assumption that patients with hypertension progressed faster to nephropathy and retinopathy	NR
DCCT group[43]	Conducted, details NR	Changes in the incidence of microalbuminuria, the cost of therapy, and the discount rate	NR
Thokala et al.[44]	Probabilistic	NR	Internal validation of the model code (visual logic in Simul8) was

			conducted throughout model implementation. Patient characteristics and complication statuses were checked to ensure that they were changing as expected, and that patients were following expected routes. The costs and utility value outputs each year were checked against the patient status outputs for face validity. The aggregated outputs were also cross-checked against the sum of individual patient outputs. Internal validation was also conducted, whereby the risk model for each complication was validated against the data from which it was estimated
Van Os et al.[45]	NR	Health care costs of renal replacement therapy in elderly diabetes patients	Validation of the model was done using diabetes and dialysis prevalence data from national statistics
Willis et al.[46]	NR	NR	Followed the ISPOR-SMDM principles of good practice
Wu et al.[47]	Second-order Monte Carlo technique	Probability for developing macro albuminuria, diabetes diagnosis, daily cost of ACEI/ARB therapy	NR
Zhou et al.[48]	NR	NR	Model validated on the basis of its ability to predict outcomes when tested under hypothetical conditions in which the results should be obvious and by its ability to predict outcomes as defined by a long term epidemiologic study

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blockers; BMI: body mass index; CHD: coronary heart disease; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; ICER: incremental cost- effectiveness ratio; ISPOR: international society for pharmacoeconomics and outcomes research; NR: not reported; SBP: systolic blood pressure.

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