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Appendix

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Are adverse effects incorporated in economic models? An initial review of current practice

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Appendix 5

Data extraction of HTA technology assessment reports

Abubakar 2006[73]		
Objective	To determine the diagnostic accuracy of tests for the rapid diagnosis of bacterial food poisoning in clinical and public health practice and to estimate the cost-effectiveness of these assays in a hypothetical population to inform policy on the use of these tests	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Infection	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity, specificity
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Adi 2007[37]		
Objective	To assess the clinical and cost-effectiveness of naltrexone in helping formerly opioid-dependent people from relapsing to illicit drug use. The review also addressed the effectiveness of treatment packages aimed at increasing compliance with naltrexone treatment	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Any serious adverse effects reported in the included trials were considered
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. In addition to the RCTs, adverse effects data were sought from systematic reviews of analytical observational studies looking at adverse effects
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (1 year)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Retention in treatment and relapse into drug misuse
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Note relapse to drug misuse (opioid-positive or -negative urine test) was used in combination with data on numbers injecting/not injecting to get an estimate of the level and nature of drug misuse
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. The clinical review found no significant difference between naltrexone and placebo for any serious adverse event
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Avenell 2004[38]		
Objective	In the systematic review, long-term effects of obesity treatments on body weight, risk factors for disease, and disease were investigated. The economic model estimated the effect of a lifestyle treatment (diet and exercise) on the onset of diabetes in overweight people. It was compared to no intervention	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals, surgery, psychological and behavioural, physical
	Prevention of disease and conditions, and promotion of well-being	Primary prevention interventions to modify behaviours or promote well-being, nutrition and chemoprevention
Health category	Other – obesity	
Research type	Primary research/secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The authors stated that adverse events were a criterion for considering studies for the review
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (6 years; this was the length of follow-up available in the literature)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Rate of onset of diabetes
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Data from a single trial conducted in Finland of diet and exercise
Are AEs included as a parameter in the model(s)?		No. Adverse effects may have been included in QALYs but that is not clearly stated
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. Economic model was of diet and exercise to prevent diabetes. There were no adverse effects of diet and exercise in the clinical review. Adverse effects of other interventions not relevant to model
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No

Bamford 2007[39]		
Objective	To assess the clinical and cost-effectiveness of HealOzone for the management of pit and fissure caries and root caries	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Ear	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The adverse effects of school-based hearing screening was one of the research questions
Were there separate inclusion criteria in relation to obtaining AE data?		No. The inclusion criteria for study design to be eligible for the review were broad: any systematic review or any design of study
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Short term as stated by the authors (1 year, with sensitivity analyses at 6 and 11 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No. The authors state that no adverse events data were reported in any of the included studies
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Black 2007[40]		
Objective	To assess the clinical and cost-effectiveness of inhaled insulin in patients with type 1 or type 2 diabetes as a replacement for or supplement to injectable forms of insulin	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Metabolic and endocrine	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, narrow focus. Hypoglycaemic episodes, lung effects and weight gain. Other adverse effects were included if reported	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	Unclear. Details of the model were not reported. It was a model that has been presented and validated and is considered to be a reputable model in diabetes (the EAGLE model)	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Not applicable	
What is the time horizon of the model(s)?	Number of years (20 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Glycosylated haemoglobin (HbA1c); however, as the clinical review found no difference between treatments for this outcome it was not actually included in the model	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
Are AEs included as a parameter in the model(s)?	Yes. As two formulations of insulin were being compared it was only adverse effects on lung function that might have differed between the treatments. However, as the clinical review found there to be no difference, lung function was not actually modelled	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes	
What sources were used to obtain the AE data?	The accompanying systematic review. As no effect on lung function found it was not actually included in the model	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	No	
If the model used utilities, were these based on judgement?	Not applicable	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Not applicable	
If the model used utilities, were preferences derived from patients on treatment?	Not applicable	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Brazzelli 2006[41]		
Objective	To assess the clinical and cost-effectiveness of HealOzone for the management of pit and fissure caries and root caries	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Oral or gastrointestinal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse effects specified as an outcome for the review but no details given
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable. None of the RCTs included in the review reported adverse events data
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Two similar models: one for non-cavitated pit and fissure caries, and one for non-cavitated root caries
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (5 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. The rate of reversal (cure) of caries
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. The authors do comment that none of the included studies reported adverse events
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Bridle 2004[42]		
Objective	To evaluate the clinical and cost-effectiveness of quetiapine, olanzapine and valproate semisodium in the treatment of mania associated with bipolar disorder	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Adverse events such as gastrointestinal disturbance, weight gain and extrapyramidal effects were of interest. Gastrointestinal disturbances, dry mouth, somnolence, dizziness, postural hypotension, asthenia, tremor, weight gain, extrapyramidal side effects, akathisia were reported	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	Yes	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	Decision tree	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Not applicable	
What is the time horizon of the model(s)?	Short term as stated by the authors (3 weeks)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Response rate (at least 50% improvement in baseline mania symptoms)	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	Yes. The costs of adverse events were not formally considered in the model because of the lack of suitable cost data. The exclusion of the adverse events identified in the clinical review was considered to have little impact on the results of the model given the very short time horizon considered in the model	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	No	
If the model used utilities, were these based on judgement?	Not applicable	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Not applicable	
If the model used utilities, were preferences derived from patients on treatment?	Not applicable	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Brown 2006[43]		
Objective	To assess the clinical and cost-effectiveness of five strategies for the prevention of non-steroidal anti-inflammatory drug (NSAID)-induced gastrointestinal (GI) toxicity: Cox-1 NSAIDs plus histamine 2 receptor antagonists; Cox-1 NSAIDs plus proton pump inhibitors; Cox-1 NSAIDs plus misoprostol; 4a Cox-2 coxib NSAIDs; and 4a Cox-2 preferential NSAIDs	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Oral or gastrointestinal	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Serious GI complications: symptomatic ulcers; endoscopic ulcers; GI symptoms; anaemia; occult bleeding; mortality. Also serious cardiovascular and renal illness
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. GI toxicity was the main focus of the review and therefore the inclusion criteria for the review were specifically for the identification of studies relevant to this outcome
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Short term as stated by the authors. Actual duration unclear: 'treatment effect not extended beyond the length of the trials'
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. From the meta-analysis in the systematic review where results were available
Are AEs included as a parameter in the model(s)?		Yes. GI adverse events: freedom from GI adverse events; GI discomfort; uncomplicated (symptomatic or endoscopic) confirmed ulcer; serious complication of ulcer
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. GI adverse events: freedom from GI adverse events; GI discomfort; uncomplicated (symptomatic or endoscopic) confirmed ulcer; serious complication of ulcer
What sources were used to obtain the AE data?		Both systematic review and other sources. Results from systematic review used for probability of no GI adverse event; GI discomfort; uncomplicated (symptomatic or endoscopic) ulcer and serious GI complication. Meta-analysis results could not be used for probabilities of events occurring as a result of these outcomes and these were obtained from individual trials/studies
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Bryant 2004[44]		
Objective	To examine the clinical and cost-effectiveness of the Sugarbaker procedure for the treatment of pseudomyxoma peritonei based on a systematic literature review and modelling of costs	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals, surgery
Health category	Cancer, oral or gastrointestinal	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Any complications, as secondary outcomes, were eligible. Those most commonly mentioned were anastomatic leaks, fistula formation, wound infection, small bowel perforations/obstructions and pancreatitis
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (5 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		No
How was/were the parameter value(s) used derived?		Unclear
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. Only cost of procedure included in the model: efficacy and other outcomes not included
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Buxton 2006[45]		
Objective	To assess the clinical and cost-effectiveness of implantable cardioverter defibrillators (ICDs) compared with conventional therapy for patients at risk of sudden cardiac death (SCD) due to arrhythmias	
Research activity area	Evaluation of treatments and therapeutic interventions	Medical devices
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Adverse events were summarised from the original review. Health-related quality of life (HRQoL) was one of the three main outcomes of interest	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Number of years (20 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Relative survival and admission rates between ICD and patients receiving amiodarone (comparator of interest); HRQoL	
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies. The survival and admission rates parameter was derived from a single trial (CIDS) included in the systematic review. The authors of that trial provided the investigators with patient-specific resource use data from that trial. The base case assumed that HRQoL was the same for intervention and comparator. Sensitivity analysis used estimate based on CIDS study	
Are AEs included as a parameter in the model(s)?	Yes. Hospital admission for drug side effects from the comparator amiodarone. Hospital admissions for ICD maintenance and replacement were also included in the model although these were not explicitly defined as adverse events. Adverse events were also included in HRQoL	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. The clinical effectiveness review focuses mainly on HRQoL	
What sources were used to obtain the AE data?	Other sources, e.g. ad hoc selection or systematic searches. The data used seem to be additional data (not reported as part of clinical effectiveness) obtained from the authors of one of the studies included in the systematic review	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	Yes	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	No	

Castelnuovo 2005[46]		
Objective	To estimate the effectiveness and cost-effectiveness of dual-chamber pacemakers vs single-chamber atrial or single-chamber ventricular pacemakers in the treatment of bradycardia due to sick sinus syndrome (SSS) or atrioventricular block (AVB)	
Research activity area	Evaluation of treatments and therapeutic interventions	Medical devices
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, narrow focus. Adverse events of implantation (perioperative mortality and non-fatal complications), pacemaker syndrome	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	Yes. A meta-analysis of pacemaker syndrome was undertaken	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. There are two separate models according to the underlying cause of bradycardia: a model for patients with AVB and one for patients with SSS	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Number of years (5 and 10 years); 10 years was considered a clinically realistic lifetime of the technologies given that the average age at entry to the model is 75 years	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Mortality, stroke, atrial fibrillation, heart failure, exercise capacity, functional status, quality of life, adverse events, pacemaker syndrome, and other outcomes were considered in the model (e.g. exercise capacity was not considered)	
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies. Annual rates for progression to stroke and heart failure were taken from the review. However, most parameter values were taken from single studies included in the review. Utility values for stroke were taken from a study not included in the review	
Are AEs included as a parameter in the model(s)?	Yes. Perioperative and subsequent complications, and pacemaker syndrome were considered in the model (costs as well as incidence rate)	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. All types of AE that were broadly specified in the outcomes eligible for inclusion	
What sources were used to obtain the AE data?	Other sources, e.g. ad hoc selection or systematic searches. Data were taken from studies also included in the systematic review	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	Yes	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	No	

Chen 2006[47]		
Objective	To review the clinical effectiveness and cost-effectiveness of adalimumab, etanercept and infliximab, agents that inhibit tumour necrosis factor-alpha (TNF-alpha), when used in the treatment of rheumatoid arthritis (RA) in adults	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Serious adverse events, serious infections and malignancy
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. Postmarketing surveillance, major observational studies and registries were used
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models. The Birmingham Rheumatoid Arthritis Model (BRAM) – a discrete event simulation model
If a state transition model was used, was a cohort- or patient-level simulation employed?		Patient level
What is the time horizon of the model(s)?		Lifetime – patients are followed through to death
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Note that the authors state this but it is not clear how the data were used
Are AEs included as a parameter in the model(s)?		Yes. AEs may be incorporated in Health Assessment Questionnaire (HAQ) (and hence QALY) scores, which also appears to incorporate toxicity. Early withdrawals due to toxicity included in the model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. AEs leading to withdrawals, but time to withdrawal was not in review
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		Yes

Clar 2005[48]		
Objective	To investigate the clinical and cost-effectiveness of autologous chondrocyte implantation (ACI) for cartilage defects in knee joints	
Research activity area	Evaluation of treatments and therapeutic interventions	Surgery
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Not specifically identified as of interest in the methods but surgical complications reported by included studies are summarised	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. Short-, medium- and long-term cost-effectiveness was modelled	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Long term as stated by the authors (the long-term model was 50 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Quality of life in short-term model and treatment success in medium- and long-term models	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review. Medium-term success rate was based on case series reported in the clinical effectiveness review	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis. Short-term quality of life was based on expert opinion and treatment success data for the long-term model appears to be based on assumptions	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	Yes. Complication rates were assumed to be the same between the alternative treatments and assumed to net out as there were no firm data available on the extent of variation in the complications rate between interventions	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	Yes	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	No	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Clark 2004[28]		
Objective	To assess the clinical benefits and harms of using anakinra in adults with rheumatoid arthritis and to evaluate its cost-effectiveness	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. All adverse events reported in studies included as outcomes
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. In evaluating adverse effects, data from postmarketing surveillance studies and tertiary sources [Summary of Product Characteristics (SPC), USA prescribing information] were used in addition to RCTs
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable (no AEs were included in the clinical effectiveness review)
What sources were used to obtain the AE data?		Both systematic review and other sources
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Clegg 2005[49]		
Objective	To assess the clinical and cost-effectiveness of left ventricular assist devices (LVADs) for people with end-stage heart failure when used as a bridge to heart transplantation (BTT), as a bridge to myocardial recovery or as long-term chronic support (LTCS)	
Research activity area	Evaluation of treatments and therapeutic interventions	Medical devices
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. No specific adverse events of interest identified as part of inclusion criteria. Adverse events resulting in mortality, infections, thromboembolic events or bleeding and mechanical failure were reported in the clinical effectiveness review
Were there separate inclusion criteria in relation to obtaining AE data?		No. Wide range of study designs already included for efficacy outcomes
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. One for LVADs as BTT and one of LVAD as LTCS for patients with end-stage heart failure
What type(s) of economic model(s) was/were used?		Decision tree (for BTT model)
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models (for LTCS model)
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort (for LTCS model)
What is the time horizon of the model(s)?		Number of years (5 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Survival
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Survival data were obtained from a single study for each model because of limitations in the data available from the other studies in the clinical effectiveness review
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable (no AEs were included in the clinical effectiveness review)
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. AEs of heart transplantation from other publications; those for LVADs from hospital programme data
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were preferences derived from patients on treatment?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Collins 2007[50]		
Objective	The review aimed to determine the diagnostic accuracy of duplex ultrasound (DUS), magnetic resonance angiography (MRA) and computed tomography angiography (CTA), alone or in combination, for the assessment of lower limb peripheral artery disease (PAD). It also aimed to evaluate the impact of these technologies on management of PAD, the attitudes of patients to these assessment methods and the adverse effects of these technologies and to assess their cost-effectiveness. The economic model compared DUS, MRA and CTA with contrast angiography/arteriography (CA)	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events relating to the index test or to currently used contrast agents
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. For adverse effects data, studies of any design (other than case reports) in patients with symptoms suggestive of PAD were included, whereas for diagnostic accuracy only cohort or case–control studies were eligible
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Short-term model on the period of diagnosis and formulation of the treatment plan. Long-term model considered diagnosis and formulation of the treatment plan and also follow-up of patients including community care
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (1 year)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Test accuracy
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Costs of complications due to CA from a published economic evaluation and utilities based on clinical judgement and published data
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Collins 2007[51]		
Objective	To evaluate the clinical and cost-effectiveness of docetaxel in combination with prednisone/prednisolone compared with other chemotherapy regimens, best supportive care or placebo for the treatment of metastatic hormone-refractory prostate cancer. The economic model compared docetaxel plus prednisone/prednisolone, mitoxantrone plus prednisone/prednisolone, and prednisone/prednisolone	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. All adverse effects extracted. The most commonly occurring were presented together with details of grade 3 or grade 4 events
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (15 years, which was considered a lifetime horizon for the condition of interest)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Overall survival
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Hazard ratios from indirect comparison for survival using methods and data from clinical review
Are AEs included as a parameter in the model(s)?		Yes. A utility decrement based on the probability of experiencing a grade 3/4 (major) adverse event was applied as a sensitivity analysis
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Probability of a major (grade 3/4) adverse event
What sources were used to obtain the AE data?		Unclear. The probability of experiencing a grade 3/4 adverse effect was estimated using a meta-analysis of grade 3/4 adverse effect data using a hierarchical Bayesian model. It is not clear from the report that the adverse events data are derived form the systematic review; however, no other source is cited for them
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Connock 2006[52]		
Objective	To determine the clinical and cost-effectiveness of enzyme replacement therapy (ERT) in the treatment of symptomatic Gaucher's disease	
Research activity area	Evaluation of treatments and therapeutic interventions	Cellular and gene therapies
Health category	Congenital disorders	
Research type	HTA assessment report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Not explicitly specified in methods section but reported in results	
Were there separate inclusion criteria in relation to obtaining AE data?	No. The inclusion criteria were already very broad to obtain a wide range of information on the intervention and disease	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Lifetime. Life expectancy set at 65 years	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Disease progression	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review. Disease progression for untreated patients was based on the systematic review of the natural history of the disease (because of an absence of controlled data)	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis. The assumption was made that ERT is a complete cure for Gaucher's type I. The authors state that this was one of several substantial assumptions that had to be made in the model because of the weak evidence base. The clinical effectiveness review reported that on average most of the outcomes approached normality in the majority of patients after 1 year although uncertainty remains about the prevention of skeletal complications. The economic model made an assumption about skeletal complications based on clinical opinion	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Expert opinion	
Is the absence of AE data explained?	Yes. The absence of adverse events in the model is not explicitly explained but the authors comment that most studies did not report adverse events or reported that no serious events occurred	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	Yes	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Connock 2006[53]		
Objective	What is the clinical effectiveness, tolerability and cost-effectiveness of newer antiepileptic drugs (as monotherapy or as add-on therapy) compared with current standard drug treatment for epilepsy in children	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Neurological	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Aim of review included 'tolerability'. Outcomes specified were 'all outcomes which study protocols stated would be measured'	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Patient level	
What is the time horizon of the model(s)?	Number of years. As the model is of childhood epilepsy patients can only enter if they are aged 3 years or more and patients have to exit the model at age 18 years, therefore the longest time that an individual patient can be in the model is 15 years and the shortest time is a few days	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Proportion of patients withdrawing early because of side effects or lack of efficacy; proportion of patients achieving complete remission	
How was/were the parameter value(s) used derived?	Unclear. Data for model appear to have been derived from studies in the clinical effectiveness review but it is unclear exactly how	
Are AEs included as a parameter in the model(s)?	Yes. The model used four defined outcomes of drug treatment: intolerable side effects leading to early discontinuation; failure of efficacy leading to early discontinuation; partial efficacy with tolerable side effects; complete remission with tolerable side effects	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. Withdrawal because of unacceptable side effects	
What sources were used to obtain the AE data?	Both systematic review and other sources. Data for some drugs taken from trials in the effectiveness review. For the older drugs estimates were made based on an assumption of an increase in toxicity and slight decrease in efficacy compared with previous drug in preferred order of treatment use	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	Yes	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes	
If the model used utilities, were preferences derived from patients on treatment?	No	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	Yes	

Connock 2007[54]		
Objective	The evaluation of the clinical and cost-effectiveness of methadone and buprenorphine in the treatment of opioid-dependent adults in comparison with other non-methadone- or non-buprenorphine-based therapies. The review aimed to investigate the impact of these interventions across a range of subgroups including drug use (injector vs non-injector), comorbidity (e.g. HIV vs non-HIV), sociodemographics (e.g. male vs female) and treatment setting	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Only major adverse effects investigated, e.g. drug interactions, liver disease, cardiac abnormalities, exacerbation of comorbidities
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes. Pooled data on some adverse events were reported from included systematic reviews
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (1 year)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Retention in therapy, continued opioid use
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Connock 2006[55]		
Objective	To determine the clinical and cost-effectiveness of intravenous enzyme replacement therapy (ERT) for the prevention of long-term damage and symptoms in symptomatic Fabry's disease and mucopolysaccharidosis type I (MPS1)	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Congenital disorders	
Research type	HTA assessment report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Not explicitly specified in the methods although outcomes reported by the included papers are reported in the review
Were there separate inclusion criteria in relation to obtaining AE data?		No. The inclusion criteria were already very broad
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Unclear. Appears to be a state transition model but not clear
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Disease-specific mortality and risk of developing specific disease-related symptoms (although these were obtained from the systematic review of the natural history of Fabry's disease because of the limited data available from the clinical effectiveness review)
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Data for the untreated cohort were obtained from single studies from the review of the natural history of Fabry's disease
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. For the cohort treated with ERT, the assumption was made that treated patients regain full health and have no disease-specific mortality
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Dalziel 2004[56]		
Objective	Evaluation of the effectiveness of imatinib as first-line treatment for chronic myeloid leukaemia (CML) compared with interferon-alpha, hydroxyurea and bone marrow transplantation, and the cost-effectiveness of imatinib compared with interferon-alpha and hydroxyurea	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. It was stated that 'adverse effects' were included
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No. The authors stated that there was a lack of suitable randomised evidence (this referred to all outcomes, not adverse effects alone)
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Three alternative treatment pathways were considered
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort. Cohorts of 1000 CML patients
What is the time horizon of the model(s)?		Number of years (20 years; 'realistic period in which the majority of CML patients' lives could be hypothetically captured')
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. All types of outcomes appear to have been considered (progression, mortality and cytogenetic response), except haematological response
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Only one study by a manufacturer directly measured relevant utility values. Values from this study were used to inform the model. Transition probabilities were calculated 'from rates reported in studies using the drug in question'. It is unclear if these are studies included in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. The authors acknowledge that adverse effects not included but point out that the intervention of interest was found to be cost-effective and the inclusion of AEs in the model would only make it more so
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Davies 2006[31]		
Objective	To compare patient outcomes, resource use and costs to the NHS and NHS Blood Transfusion Authority associated with cell salvage and alternative methods of minimising perioperative allogeneic blood transfusion	
Research activity area	Evaluation of treatments and therapeutic interventions	Surgery
Health category	Blood	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The authors conducted an update of two Cochrane reviews and a review of systematic reviews. In both reviews adverse transfusion reactions were included as secondary outcomes
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Other. The time horizon used for the primary analysis was 1 month. Other time horizons were tested (1, 10, 30 years) in secondary analyses. However, based on a review of economic studies, the evidence about long-term outcomes was generally considered limited and uncertain. The time horizon of 1 year was chosen to reflect the extent of short-term adverse events
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Likelihood of needing allogeneic blood transfusion compared with alternative strategies; likelihood of adverse events
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. 'Adverse events' in general were included
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes
What sources were used to obtain the AE data?		The accompanying systematic review. The results of the meta-analysis comprised only some of the model input for adverse effects
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Dretzke 2004[18]		
Objective	To determine the role of autoantibody tests for autoimmune disease (specifically coeliac disease and thyroid disease) in children with newly diagnosed type I diabetes mellitus	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Metabolic and endocrine	
Research type	HTA assessment report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Test sensitivity and specificity
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. A disutility for biopsy was used. It was estimated as the anxiety preceding and the unpleasantness of a general anaesthetic and possible mild discomfort following biopsy (e.g. sore throat, vomiting). Serious adverse events considered too rare to consider
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable (no AEs were included in the clinical effectiveness review)
What sources were used to obtain the AE data?		Other sources: assumptions
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Dundar 2007[57]		
Objective	To assess the comparative clinical effectiveness and cost-effectiveness of pemetrexed disodium combination with cisplatin for the treatment of unresectable malignant pleural mesothelioma (MPM) in chemotherapy-naive patients	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. For pemetrexed, adverse events include nausea, vomiting, fatigue and leucopenia. Other toxicities considered include skin rash, mucositis, nausea and liver function abnormalities. Cisplatin is associated with nausea and vomiting
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Unclear. Based on individual patient data (IPD)
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Unclear
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Survival
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. There was only a single trial included in the review
Are AEs included as a parameter in the model(s)?		Yes. Adverse event-related hospitalisations
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Unclear. The clinical review reviewed serious toxicities (grade 3/4), whereas the model incorporated hospitalisations due to adverse events. It is unclear if these are the same
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. NHS reference costs for hospital treatment
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Fayter 2007[58]		
Objective	The aim of the review was to clarify the role of growth monitoring in primary school children, including obesity, and to examine the clinical and cost-effectiveness of possible strategies of monitoring. The clinical evaluation included studies of the clinical effectiveness of routine monitoring, the diagnostic performance of growth monitoring programmes, the human resource requirements of growth monitoring programmes and the attitudes to growth monitoring programmes	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Metabolic and endocrine	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. There were two models, one for obesity and one for stature
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. For the stature model, probability of short stature conditions was used. For the obesity model – unclear
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No. Some suggestion in final discussion that there are as yet no data
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Garrison 2007[59]		
Objective	To assess the clinical effectiveness and cost-effectiveness of bone morphogenetic protein (BMP) for the treatment of spinal fusions and the healing of fractures compared with the current standards of care	
Research activity area	Evaluation of treatments and therapeutic interventions	Cellular and gene therapies
Health category	Musculoskeletal	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Any adverse events reported were considered
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Two economic models are assessed and modified and form the basis of the updated models. These were for the economic evaluation of BMP for acute open tibial fracture (OTF) and the use of BMP for spinal fusion
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Short term as stated by the authors (2 years for the BMP-SF model)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Time to fracture healing, secondary interventions for spinal fusion model only; quality of life
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Outcomes used from single studies
Are AEs included as a parameter in the model(s)?		No. AEs may have been included in the QALYs but that is not clearly stated
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Garside 2007[60]		
Objective	To assess the clinical and cost-effectiveness of cinacalet for the treatment of secondary hyperparathyroidism (SHPT) or people on dialysis because of end-stage renal disease (ESRD)	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Metabolic and endocrine, renal and urogenital	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Adverse events were as reported in the included studies: deaths, serious adverse events, withdrawals due to adverse events, all adverse events and some specific ones (nausea and vomiting, hypocalcaemia, seizures)	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort. Cohort of 1000 people aged 55 years with SHPT modelled until death	
What is the time horizon of the model(s)?	Lifetime	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Control of parathyroid hormone levels; deaths, cardiovascular events and fractures. Note: although these are reported as 'adverse effects' they are in fact a measure of the failure of efficacy of the drug rather than true adverse effects	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis	
Are AEs included as a parameter in the model(s)?	Yes	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. Adverse events resulting in withdrawal were incorporated into the model	
What sources were used to obtain the AE data?	The accompanying systematic review and NHS reference sources for costs	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes	
If the model used utilities, were preferences derived from patients on treatment?	No	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	Yes	

Garside 2006[19]		
Objective	To assess the impact of endoscopic surveillance in preventing morbidity and mortality from adenocarcinoma in patients with Barrett's oesophagus	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Cancer	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (20 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Proportion of cancer diagnosed at initial endoscopy; progression and regression rates
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable (no adverse effect in clinical review)
What sources were used to obtain the AE data?		Both systematic review and other sources: review and assumptions
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Garside 2005[61]		
Objective	To investigate the clinical and cost-effectiveness of pimecrolimus for mild to moderate atopic eczema and tacrolimus for moderate to severe atopic eczema compared with current standard treatment in adults and children	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Skin	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Adverse outcomes are not specifically identified as an outcome of interest in the methods (inclusion criteria for outcomes not specified) but they are reported in the results	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	Yes, for some outcomes for which data were available (skin infections and skin burning for tacrolimus; viral skin infections, bacterial skin infections and skin burning for pimecrolimus)	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. Eight separate models for different treatment options in different cohorts of patients	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Number of years (1 year for adult cohorts and 14 years for child cohorts)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Two disease control outcomes were used for the different models: Investigator's Global Assessment and Physicians Global Evaluation (at least 90% improvement)	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review. For pimecrolimus in mild to moderate eczema, low-potency topical steroids in mild to moderate eczema and emollient only use pooled estimates from the systematic review were used	
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies. When pooled data were not available, single RCTs from the systematic review were used for effectiveness data. This was the case with 14 parameters	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis. When pooled data or good-quality RCTs were not available UK observational studies were used and, finally, if none of the above was available clinical opinion was sought. This was the case for seven parameters	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	No	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	Yes	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Garside 2004[62]		
Objective	To evaluate the clinical effectiveness and cost-effectiveness of microwave endometrial ablation and thermal balloon endometrial ablation for heavy menstrual bleeding (HMB), compared with the existing first-generation endometrial ablation techniques of transcervical resection and rollerball ablation and hysterectomy	
Research activity area	Evaluation of treatments and therapeutic interventions	Surgery
Health category	Reproductive health and childbirth	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Outcomes were not specified but adverse events (perioperative and postoperative) were reviewed. Adverse events reported were uterine infection, perforation, visceral burn, bleeding, haematometra, laceration, intra-abdominal injury, cyclical pain
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. In addition to the RCTs and controlled clinical trials used for efficacy, large observational studies were used as a source of adverse event data
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort. Five hypothetical cohorts of 1000 women with HMB who are treated by thermal balloon endometrial ablation, microwave endometrial ablation, transcervical resection, rollerball endometrial ablation or hysterectomy
What is the time horizon of the model(s)?		Number of years (10 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Complications, repeat ablation, hysterectomy and treatment failure
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Intraoperative and postoperative adverse effects were considered in the model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. All types of AE broadly specified were eligible for inclusion
What sources were used to obtain the AE data?		Both systematic review and other sources. Data were taken from studies included in the systematic review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Goodacre 2006[21]		
Objective	To estimate the diagnostic accuracy of non-invasive tests for proximal deep vein thrombosis (DVT) and isolated calf DVT in patients with clinically suspected DVT or at high risk of DVT and identify factors associated with variation in diagnostic performance. It also aimed to identify practical diagnostic algorithms for DVT and to estimate the diagnostic accuracy, clinical effectiveness and cost-effectiveness of each	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity of diagnostic tests. However, model focused on algorithms whereas the review is of individual diagnostic tests
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. Accuracy of algorithms was evaluated by estimating the mean parameter in each algorithm. It is unclear where the data for each parameter are derived from
Are AEs included as a parameter in the model(s)?		Yes. Adverse effects associated with venography were included in the model. These were the risk of fatal reaction to intravenous contrast medium and the 1% risk of inducing DVT. The probability of adverse events due to anticoagulant therapy was included in the model. These events comprised fatal bleeds, non-fatal intracranial haemorrhages and non-fatal major bleeds. However, these are adverse effects of treatments, not of the diagnostic testing strategy
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No. Adverse effects of venography were included in the model but venography was not one of the diagnostic tests reviewed, it being the 'gold standard'
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Data taken from reports on adverse effects of venography. These were not included in the clinical review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Green 2005[63]		
Objective	To assess the clinical and cost-effectiveness of drotrecogin alfa (activated) for the treatment of adults with severe sepsis in a UK context	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Infection	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The general side effect profile was of interest
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. Only RCTs were included to establish clinical effectiveness. To establish drug safety, all studies conducted in relevant participants were included. The results of a previously published safety review are also reported
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. The primary outcome 28-day all-cause mortality was used
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Two RCTs were included in the clinical effectiveness review although the main evidence on effectiveness came from one of these, which was a substantially larger trial than the other. The parameter value for the model was used from the single large pivotal trial
Are AEs included as a parameter in the model(s)?		Yes. Risk of serious bleeding event
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Serious bleeding event was included as the pivotal trial reported a clinically significant difference in events between groups. The review of adverse events also identified serious bleeding events and intracranial haemorrhage associated with drotrecogin
What sources were used to obtain the AE data?		The accompanying systematic review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Greenhalgh 2005[22]		
Objective	To establish the clinical and cost-effectiveness of electroconvulsive therapy (ECT) for depressive illness, schizophrenia, catatonia and mania	
Research activity area	Evaluation of treatments and therapeutic interventions	Psychological and behavioural
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. The stated primary indicators of safety were adverse events including memory loss and all-cause and cause-specific mortality (including suicide)
Were there separate inclusion criteria in relation to obtaining AE data?		No. Although there were not separate review inclusion criteria the included systematic review from which adverse event data were obtained included non-randomised studies
Were the AE data synthesised in a meta-analysis?		Unclear. Mainly systematic reviews included. It was unclear whether these conducted a quantitative synthesis of adverse event data
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. One for depressive illness and one for schizophrenia
What type(s) of economic model(s) was/were used?		Decision tree. The schizophrenia model was based on an earlier decision tree model and the depressive illness model was a newly developed model
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Short term as stated by the authors (both models used a 1-year time horizon)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. For both models, treatment success rate (defined as at least a 50% decrease on the Hamilton Rating Scale for Depression) and failure to complete treatment
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. For the depressive illness model single studies were used for each parameter. It is not totally clear but it may have been taken from one of the systematic reviews included in the review. The schizophrenia model was a development of an earlier model and this model used a single study from a meta-analysis they conducted as it was the only study reporting outcomes in a treatment-resistant population
Are AEs included as a parameter in the model(s)?		Yes. They were not included in the main models but were considered in sensitivity analyses. For the schizophrenia model an estimate of adverse events for clozapine and ECT are used as parameters in a threshold analysis. For the depressive illness model they used utility values that explicitly included side effects of drug treatments. The probability of treatment failure is linked to both lack of efficacy and adverse events
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Unclear from where values for clozapine adverse effects for schizophrenia model were derived. Utilities for depression model derived from a published study

continued

Is the absence of AE data explained?	Not applicable
Did the model use a clinical AE parameter?	Yes
Did the model use utilities?	Yes
If the model used utilities, were these based on judgement?	No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No
If the model used utilities, were preferences derived from patients on treatment?	Yes
Did the model incorporate the cost/resources of AEs?	Yes
Did the model incorporate withdrawals?	Yes

Hartwell 2005[29]		
Objective	To review the clinical and cost-effectiveness of immediate angioplasty compared with thrombolysis for acute myocardial infarction	
Research activity area	Evaluation of treatments and therapeutic interventions	Surgery
Health category	Cardiovascular	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events of interest included mortality, reinfarction, stroke, ischaemia, coronary artery bypass graft (CABG) and bleeding, although it was not explicit which were regarded as indicators of efficacy and which may have been complications, or adverse effects, of treatment
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (6 months)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. All types of outcomes were considered in the model
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Morbidity factors (reinfarction, stroke, ischaemia, CABG, bleeding) were considered in the model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. All types of AE considered would appear to have been incorporated in the model
What sources were used to obtain the AE data?		The accompanying systematic review. The differentiation between what was an efficacy outcome and what could be considered an adverse effect was blurred
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Hill 2004[64]		
Objective	To investigate the effectiveness and cost-effectiveness of the use of coronary artery stents in patients with coronary heart disease and specifically to compare stent vs percutaneous transluminal coronary angioplasty; stent vs coronary artery bypass grafting; and drug-eluting stents (DES) vs non-DES	
Research activity area	Evaluation of treatments and therapeutic interventions	Medical devices
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Adverse events were encompassed in the event rate, which was reported as a composite measure of major adverse cardiac or cardiac and cerebral adverse events by most of the primary studies. The definition varied between studies but could include mortality, acute myocardial infarction or revascularisation. These outcomes were also included as individual outcomes when available
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Other. The model was based on a hierarchical life table structure
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (5 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Mortality, acute myocardial infarction, repeat revascularisations
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. The authors state that the trials in the clinical effectiveness meta-analysis addressed the question, 'What has happened to date?', whereas the economic model needed to project forward. The bulk of the trial evidence was of short duration, therefore survival curves were estimated from the best data available
Are AEs included as a parameter in the model(s)?		Yes. The overall outcomes of interest encompassed clinical effectiveness and adverse events
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. In addition to the outcomes that encompassed clinical effectiveness/adverse effects, additional adverse events following a revascularisation procedure were also incorporated into the model: severe episodes of bleeding and frequency of acute renal failure
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Hind 2007[65]		
Objective	To establish the clinical and cost-effectiveness of the aromatase inhibitors (AIs) anastrozole, letrozole and exemestane compared with tamoxifen in the adjuvant treatment of early oestrogen receptor-positive breast cancer in postmenopausal women	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. A broad range of side effects were considered. The adverse events of interest are those associated with AIs or tamoxifen (bone health, cardiovascular events, hypercholesterolaemia, endometrial cancer and vaginal bleeding)
Were there separate inclusion criteria in relation to obtaining AE data?		No. Only phase III RCTs included for all outcomes
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Unclear
What is the time horizon of the model(s)?		Number of years (35 years post surgery)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Disease-free survival, quality of life and adverse events
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Fractures, vaginal bleeding and discharge, endometrial cancer, hypercholesterolaemia, cardiovascular events, venous thromboembolic events, ischaemic cerebrovascular events
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Fractures, vaginal bleeding and discharge, endometrial cancer, hypercholesterolaemia, cardiovascular events, venous thromboembolic events, ischaemic cerebrovascular events
What sources were used to obtain the AE data?		The accompanying systematic review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		Yes

Jones 2004[66]		
Objective	Clinical and cost-effectiveness of two alternative antiplatelet agents, clopidogrel and modified-release (MR)-dipyridamole, relative to prophylactic doses of aspirin for the secondary prevention of occlusive vascular events	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Bleeding complications and other adverse events
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. Postmarketing surveillance studies with a clearly defined protocol and denominator were eligible for inclusion but none were found. Only RCTs were included to assess effectiveness
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Non-fatal myocardial infarction, non-fatal stroke, vascular and non-vascular death
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Fatal and non-fatal bleed
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Bleeding is a key adverse event of interest in the clinical effectiveness review
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Data from another meta-analysis were used
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Kaltenthaler 2006[67]		
Objective	The aim of the review was to evaluate the clinical and cost-effectiveness of computerised cognitive behavioural therapy (CCBT) delivered alone or as part of a package of care compared with treatments for depression and anxiety including phobias	
Research activity area	Evaluation of treatments and therapeutic interventions	Psychological and behavioural
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Unclear. Adverse effects not specifically mentioned; however, with this type of indication and intervention it may be difficult to distinguish between lack of efficacy and worsening of the condition (adverse effect)
Were there separate inclusion criteria in relation to obtaining AE data?		No. Non-RCTs were to be included only in the absence of RCT data for efficacy
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. There were two models: one of depression and one of panic and phobias
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Patient level; for some transitions but not all
What is the time horizon of the model(s)?		Number of years (1.5 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Depression model: between-group treatment effect for depression score (Beck Depression Index); panic/phobia model: global phobia item from the FQ (Fear Questionnaire)
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Each parameter taken from single studies included in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No. Adverse effects not specifically mentioned. However, with this type of indication and intervention it may be difficult to distinguish between lack of efficacy and worsening of the condition (adverse effect)
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Kaltenthaler 2004[68]		
Objective	To compare the clinical and cost-effectiveness of magnetic resonance cholangiopancreatography (MRCP) with diagnostic endoscopic retrograde cholangiopancreatography (ERCP). The cost-effectiveness model was specifically concerned with the relative cost-effectiveness of the two procedures in patients for whom undergoing either was an option	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Oral or gastrointestinal	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Any adverse effects
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No. The authors note that the majority of the included studies did not report on adverse effects making it difficult to determine the extent to which they occur
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (1 year)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Probability of death and overall complications following ERCP (cost of complications with ERCP also included although not follow-up and treatment of complications). MRCP is regarded as free of complication risks
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. ERCP death and complications
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Estimates for death after diagnostic ERCP and overall complications obtained from a paper not included in the clinical effectiveness review. None of the included studies in the clinical effectiveness review reported mortality associated with ERCP; six reported adverse effects associated with ERCP
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Kanis 2007[69]			
Objective	The review aimed to evaluate the clinical effectiveness and cost-effectiveness of pharmacological agents in the prevention of osteoporotic fractures in patients on long-term glucocorticoid therapy. The pharmacological agents considered were biphosphonates; vitamin D with and without calcium; derivatives of vitamin D (including calcidiol and calcitriol); calcitonin; pharmacological doses of calcium; oestrogens (opposed and unopposed); oestrogen-like molecules; anabolic steroids; fluoride salts; thiazide diuretics; selective oestrogen (estrogen) receptor modulators (SERMs); testosterone; parathyroid hormone		
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals	
Health category	Musculoskeletal		
Research type	Secondary research		
Adverse effects in the clinical effectiveness review			
Do the specified outcomes include AEs?			Yes, broad focus
Were there separate inclusion criteria in relation to obtaining AE data?			No
Were the AE data synthesised in a meta-analysis?			No
Adverse effects in the economic model			
Is more than one economic model presented or does an economic model consist of two or more parts?			No
What type(s) of economic model(s) was/were used?			State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?			Patient level
What is the time horizon of the model(s)?			Number of years (10 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?			Yes. Relative risk of fracture of spine, hip, forearm and humerus for risedronate and bisphosphonates, these being the only two treatments considered in the economic model
How was/were the parameter value(s) used derived?			Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?			No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?			Not applicable
What sources were used to obtain the AE data?			Not applicable
Is the absence of AE data explained?			Yes. The authors state that the prevalence of adverse effects with bisphosphonates is not well documented and impact on quality of life expressed in utilities is unknown. Also the impact of adverse effects on compliance is unknown. Thus, although acknowledging that adverse effects could impact on cost effectiveness, they are not included in the analysis
Did the model use a clinical AE parameter?			No
Did the model use utilities?			Yes
If the model used utilities, were these based on judgement?			Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?			No
If the model used utilities, were preferences derived from patients on treatment?			No
Did the model incorporate the cost/resources of AEs?			No
Did the model incorporate withdrawals?			No

Karnon 2004[70]	
Objective	Assessment of the clinical and cost-effectiveness of liquid-based cytology; comparison with conventional smear
Research activity area	Detection, screening and diagnosis Evaluation of markers and technologies
Health category	Cancer
Research type	NICE TAR
Adverse effects in the clinical effectiveness review	
Do the specified outcomes include AEs?	No
Were there separate inclusion criteria in relation to obtaining AE data?	No
Were the AE data synthesised in a meta-analysis?	Not applicable
Adverse effects in the economic model	
Is more than one economic model presented or does an economic model consist of two or more parts?	No
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort
What is the time horizon of the model(s)?	Other. First screen age 24 years to last screen age 64 years
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Unclear
How was/were the parameter value(s) used derived?	Unclear
Are AEs included as a parameter in the model(s)?	No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable
What sources were used to obtain the AE data?	Not applicable
Is the absence of AE data explained?	No
Did the model use a clinical AE parameter?	No
Did the model use utilities?	Yes
If the model used utilities, were these based on judgement?	No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes
If the model used utilities, were preferences derived from patients on treatment?	No
Did the model incorporate the cost/resources of AEs?	No
Did the model incorporate withdrawals?	No

King 2006[27]		
Objective	To assess the clinical and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Adverse events of interest were loss of appetite, insomnia, stomach ache and weight loss
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. In addition to the RCTs for efficacy, systematic reviews were used to obtain information on adverse events
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Number of years (1 year with some longer-term modelling)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		No. The clinical effectiveness review used outcomes based on various scores and scales, whereas the economic model used response to treatment
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Response to treatment was defined in various ways depending upon which scores were available. Not all trials in the clinical effectiveness review provided data that could be translated into response to treatment
Are AEs included as a parameter in the model(s)?		Yes. Withdrawal from treatment with a specific drug because of intolerable adverse events was included in the model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No. Clinical review did not specify adverse events leading to withdrawal as an outcome of interest
What sources were used to obtain the AE data?		The accompanying systematic review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		Yes

Knight 2004[71]		
Objective	To determine the clinical and cost-effectiveness of rituximab in conjunction with the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy regime as first-line therapy for diffuse large B-cell lymphoma (DLBCL)	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Defined as any adverse change from baseline condition, including intercurrent illness, occurring during the course of the trial, whether or not considered related to the treatment
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No. Only one trial
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort. One < 60 years and one > 60 years
What is the time horizon of the model(s)?		Number of years (15 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Complete responder rate (defined as complete and unconfirmed complete responders) and disease-free survival
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. The authors state that in costing R-CHOP vs CHOP they attempted to include elements for which the costs differ significantly between the two treatments. Trial results indicated that there was no statistically significant difference in adverse events between the two groups, therefore adverse event costs were not included in the model
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Loveman 2006[72]		
Objective	The research aimed to assess the clinical and cost-effectiveness of donepezil, rivastigmine and galantamine for mild to moderate Alzheimer's disease, and memantine for moderately severe to severe Alzheimer's disease	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Mental health	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Adverse events as reported in the included trials were included in the review	
Were there separate inclusion criteria in relation to obtaining AE data?	No. RCTs only for all outcomes	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. The company models developed for each of the four drugs reviewed were used, as well as a single simple disease progression model used to compare the four treatments	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort. Patients with mild to moderately severe Alzheimer's disease	
What is the time horizon of the model(s)?	Number of years. The model used to compare all three drugs for moderate to severe disease used a 5-year time horizon. The manufacturers' models had time horizons of 5 years (donepezil), 5 years (rivastimine), 10 years (galantamine) and 2 years (memantine for moderately severe to severe disease)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Three of the manufacturer's models use the mini-mental state examination (MMSE), which is also reported in the clinical effectiveness sections. One manufacturer's model and the review team's model used a risk equation for full-time care that incorporates other outcome measures. The review team's model also used Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) scores	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review. For the review team's model for dopezil, rivastigmine and galantamine, the ADAS-cog scores were derived from the systematic review	
Are AEs included as a parameter in the model(s)?	No. However it does seem that utilities are likely to have incorporated quality of life and possibly adverse effects	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	No. The authors acknowledge that patient withdrawals were not incorporated into the model. Authors may feel AEs included under HRQoL	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Main 2006[30]		
Objective	To examine the clinical effectiveness and cost-effectiveness of intravenous formulations of topotecan monotherapy, pegylated liposomal doxorubicin hydrochloride (PLDH) monotherapy and paclitaxel used alone or in combination with a platinum-based compound for the second-line or subsequent treatment of advanced ovarian cancer	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Serious adverse events (grades 3 and 4), haematological toxicity and non-haematological toxicity	
Were there separate inclusion criteria in relation to obtaining AE data?	No	
Were the AE data synthesised in a meta-analysis?	Yes	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. Analysis 1 is restricted to a comparison of the three trials that included both platinum-sensitive and -resistant/-refractory patients. Analysis 2 broadens the model to include the full range of relevant comparators by relaxing the requirement for direct hazard ratios and by incorporating those licensed comparators that were not formally included in the systematic review	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Unclear	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Progression-free survival and overall survival	
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies. Data from only those trials that reported hazard ratios were used in the model	
Are AEs included as a parameter in the model(s)?	Yes	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. Probability of a grade 3/4 adverse event	
What sources were used to obtain the AE data?	The accompanying systematic review. The data were derived from the systematic review but the method of meta-analysis was different for the model: probability of experiencing grade 3 or 4 adverse events using a Bayesian meta-analysis	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	Yes	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes	
If the model used utilities, were preferences derived from patients on treatment?	No	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	No	

Main 2004[73]		
Objective	To assess the clinical effectiveness and cost-effectiveness of clopidogrel used in combination with standard therapy, including aspirin, compared with standard therapy alone for the treatment of non-ST-segment elevation acute coronary syndromes (ACS)	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Bleeding complications (major and minor) and haematological parameters. Other adverse events included nausea, vomiting, diarrhoea, gastric and duodenal ulceration, headache, dizziness, vertigo, paraesthesia, rash, pruritis, hepatic and biliary disorders, neutropenia and thrombocytopenia
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Two models: short term (12 months) and long term (lifetime)
What type(s) of economic model(s) was/were used?		Decision tree (short-term model)
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models (long-term model)
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (40 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. All-cause mortality; non-fatal myocardial infarction, non-fatal stroke
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Major bleeds
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Major bleeds
What sources were used to obtain the AE data?		The accompanying systematic review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Martin 2006[74]		
Objective	To identify and synthesise studies of diagnostic processes for urinary incontinence and to construct an economic model to examine the cost-effectiveness of simple, commonly used primary care tests	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Renal and urogenital	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Other. The focus was on the cost-effectiveness of commonly used primary care tests only in terms of diagnosing urinary conditions. QALY gains not considered
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity of each of the diagnostic methods
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. The model includes only primary care tests whereas the systematic review also includes more invasive tests used in secondary care. However, the data on the primary care tests are taken directly from the pooled sensitivity and specificity for each of the primary care tests
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

McCormack 2005[75]		
Objective	To determine whether laparoscopic methods are more effective and cost-effective than open-mesh methods of inguinal hernia repair, and whether laparoscopic transabdominal preperitoneal (TAPP) repair is more effective and cost-effective than laparoscopic totally extraperitoneal (TEP) repair	
Research activity area	Evaluation of treatments and therapeutic interventions	Surgery
Health category	Oral or gastrointestinal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Haematoma, seroma, wound/superficial infection, mesh/deep infection, port-site hernia, vascular injury, visceral injury, persisting numbness
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes. Vascular and visceral injury, persisting numbness, persisting pain
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years [two time horizons: 5 years (reliable data from RCTs available) and 25 years]
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Risk of serious complications
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Meta-analysis taken from the systematic review was used and supplemented by other data, which were mostly epidemiological
Are AEs included as a parameter in the model(s)?		Yes. Utilities for numbness and long-term pain; serious complications (discrete choice experiment)
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Data from another trial were used
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

McLeod 2007[76]		
Objective	To assess the comparative clinical effectiveness and cost-effectiveness of adalimumab, etanercept and infliximab for the treatment of ankylosing spondylitis (AS). The following comparisons are made: adalimumab and conventional management vs conventional management; etanercept and conventional management vs conventional management; infliximab and conventional management vs conventional management; and between adalimumab, etanercept and infliximab	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Any adverse effects of treatment
Were there separate inclusion criteria in relation to obtaining AE data?		No. AE data on adalimumab derived from full manufacturers' submissions rather than published reports of RCTs
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Short-term and long-term models
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort (1000 males aged 40 years)
What is the time horizon of the model(s)?		Number of years (short-term model was 1 year and long-term model 2–20 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Bath Ankylosing Spondylitis Disease Index (BASDI) and Bath Ankylosing Spondylitis Functional Index (BASFI)
How was/were the parameter value(s) used derived?		Unclear. Actual data were converted to response rates
Are AEs included as a parameter in the model(s)?		Yes. All types of AE, plus tuberculosis (TB) incidence and costs
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. All types of AE
What sources were used to obtain the AE data?		Unclear. Most data including costs were taken from a manufacturer's submission
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		Yes

Mowatt 2004[77]		
Objective	To assess the effectiveness and cost-effectiveness of single photon emission computed tomography myocardial perfusion scintigraphy (SPECT MPS) for the diagnosis and management of angina and myocardial infarction	
Research activity area	Detection, screening and diagnosis	Discovery and preclinical testing of markers and technologies
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. AEs not clearly specified as review outcomes. Review reported AEs as reported in the included studies
Were there separate inclusion criteria in relation to obtaining AE data?		No. Broad range of studies eligible: prospective and retrospective primary studies
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Decision tree for diagnosis and Markov model for management
What type(s) of economic model(s) was/were used?		Decision tree
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (25 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		No
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. Parameter values for utilities were taken from the literature and the Cost-Effectiveness Analysis (CEA) Registry
Are AEs included as a parameter in the model(s)?		Yes. Mortality risk associated with the diagnostic test included in the decision tree model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No. In the clinical review the adverse effects of the test reported were those associated with the exercise electrocardiogram, e.g angina, or those associated with dipyridamole or dobutamine-atropine. These were not included in the model
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Parameter values taken from earlier economic evaluation. However, the original source of the data is unclear
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Murray 2006[78]	
Objective	To determine the clinical effectiveness and cost-effectiveness of laparoscopically assisted and hand-assisted laparoscopic surgery in comparison with open surgery for the treatment of colorectal cancer
Research activity area	Evaluation of treatments and therapeutic interventions — Surgery
Health category	Cancer
Research type	NICE TAR
Adverse effects in the clinical effectiveness review	
Do the specified outcomes include AEs?	Yes, narrow focus. The authors specify several surgical complications of interest
Were there separate inclusion criteria in relation to obtaining AE data?	No
Were the AE data synthesised in a meta-analysis?	No
Adverse effects in the economic model	
Is more than one economic model presented or does an economic model consist of two or more parts?	No
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort
What is the time horizon of the model(s)?	Long term as stated by the authors (25 years; rationale: the majority of the patients will have died within this period)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?	Yes. Risk of hernia was included as it was identified as a potentially important long-term complication; complications requiring non-operative management were not explicitly included based on the rationale that these would be captured through longer operating times and length of stay; anastomotic leakage was included as it was assumed that this would require emergency reoperation
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes. Risk of hernia and anastomotic leakage
What sources were used to obtain the AE data?	Both systematic review and other sources
Is the absence of AE data explained?	Not applicable
Did the model use a clinical AE parameter?	Yes
Did the model use utilities?	Yes
If the model used utilities, were these based on judgement?	No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes
If the model used utilities, were preferences derived from patients on treatment?	No
Did the model incorporate the cost/resources of AEs?	Yes
Did the model incorporate withdrawals?	No

Nelson 2006[79]		
Objective	To review the evidence on the performance of diagnostic tests used to identify infection in diabetic foot ulcers (DFUs) and interventions to treat infected DFUs and also to use estimates derived from the systematic reviews to create a decision-analytic model to identify the most effective method of diagnosing and treating infection	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Skin	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Although adverse events were not specified as an outcome of interest in the methods, adverse event data were extracted
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Other. Sufficient reliable data on the populations of interest were not available to populate the model, therefore the model was not run
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Not applicable
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		No/not applicable – model was not run. The authors state that there was insufficient information from the systematic reviews or interviews with experts to populate the model with transition probabilities for the sensitivity and specificity of diagnosis of infection in DFUs or on the probabilities of healing, amputation or death in the treatment studies
How was/were the parameter value(s) used derived?		Unclear/not applicable
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable. Model not run because of lack of data
What sources were used to obtain the AE data?		Not applicable – model was not run
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Pandor 2004[80]		
Objective	To evaluate the clinical and cost-effectiveness of tandem mass spectrometry-based neonatal screening for inborn errors of metabolism	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Metabolic and endocrine	
Research type	HTA report	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Not explicitly stated as an outcome of interest but 'any outcome of treatment' was of interest and information on adverse events of the intervention was reported in the review
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Other. Bayesian probabilistic framework using Monte Carlo simulation
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Other: 1 year (cost-effectiveness of number of specimens per system per year was calculated)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity, specificity
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Pandor 2006[81]		
Objective	To assess the clinical and cost-effectiveness of oxaliplatin in combination with 5-fluorouracil/leucovorin, and capecitabine monotherapy, as adjuvant therapies in the treatment of patients with stage III colon cancer after complete surgical resection of the primary tumour, compared with adjuvant chemotherapy with an established fluorouracil-containing regimen	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse effects and toxicity were included as outcomes
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (50 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Overall survival, disease-free survival, adverse events (in terms of costs only), HRQoL
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Additional searches were undertaken for long-term overall and disease-free survival
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. Costs of adverse events were taken from a model submitted by industry. Quality of life data were taken from studies not included in the clinical effectiveness review
Are AEs included as a parameter in the model(s)?		Yes. Costs of grade 3+ adverse events (nausea, neutropenia, neuropathy, diarrhoea) were included
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Costs of adverse events were taken from a model submitted by industry
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		Yes

Robinson 2005[82]		
Objective	To assess the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in patients with non-ST elevation acute coronary syndrome	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Rates for adverse events; only major bleeding was extracted
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. There is a short- and a long-term model
What type(s) of economic model(s) was/were used?		Decision tree (short-term model)
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models (long-term model)
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Short term as stated by the authors (6 months)
What is the time horizon of the model(s)?		Lifetime. A period of 50 years is considered a lifetime horizon. A secondary analysis was reported over a 5-year time horizon
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Non-fatal myocardial infarction, death and revascularisation by coronary artery bypass graft or percutaneous coronary intervention
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review (for the short-term model)
How was/were the parameter value(s) used derived?		Independently/alternative synthesis (two cohort studies for the long-term model)
Are AEs included as a parameter in the model(s)?		Yes. Bleeding complications were included
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes. Bleeding complications
What sources were used to obtain the AE data?		The accompanying systematic review (for the short-term model)
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches (for the long-term model)
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Rodgers 2006[83]		
Objective	To determine the most effective diagnostic strategy for the investigation of microscopic and macroscopic haematuria in adults	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Renal and urogenital	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events were not included in the inclusion/exclusion criteria but it was stated that information on adverse events was extracted
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. Three models were presented: (1) haematuria detection, (2) imaging of the upper urinary tract, (3) investigation of the lower urinary tract
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Short term as stated by the authors (not specified further)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity estimates
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review for model 1: sources of sensitivity and specificity data were the systematic review except for those for routine microscopy for which estimates by clinician advisors were used
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies for models 2 and 3
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Ross 2004[84]		
Objective	(1) To investigate the clinical effectiveness of bisphosphonates in malignancy for the treatment of hypercalcaemia, prevention of skeletal morbidity and in the adjuvant setting; (2) to model the cost-effectiveness of bisphosphonates in the treatment of hypercalcaemia and prevention of skeletal morbidity	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Toxicity	
Were there separate inclusion criteria in relation to obtaining AE data?	No. Only RCTs eligible for inclusion	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	Yes. There was one model for treatment of hypercalcaemia and two for prevention of skeletal morbidity (one for breast cancer and one for multiple myeloma)	
What type(s) of economic model(s) was/were used?	Decision tree for hypercalcaemia model	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models, for skeletal morbidity models	
What is the time horizon of the model(s)?	Number of years (4 years for the skeletal morbidity models; appears to be 5 weeks for the hypercalcaemia model)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Hypercalcaemia model: response rate (number of patients achieving normocalcaemia) and time to first relapse, which were used to calculate cumulative duration of normocalcaemia. Prevention of skeletal morbidity models: mortality and skeletal-related events (SRE) (vertebral fracture, non-vertebral fracture, hypercalcaemia, radiotherapy, orthopaedic surgery)	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review for the prevention of skeletal morbidity model. Incidence rates were obtained for SREs for the no bisphosphonate arm as available in individual studies from the clinical effectiveness review; estimates were made based on the available data when rates for specific SREs were not available. For the bisphosphonate arm for each SRE the pooled risk was derived using the same methods and data as in the clinical effectiveness review; when a pooled risk was not available an estimate from a single included study was used	
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies for the skeletal morbidity model. Mortality was based on the largest studies that measured this outcome	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis for the hypercalcaemia model. Costs and effectiveness data were taken from four studies selected for their relevance to policy, the quality of the study design and their sample size. Three of these had been included in the clinical effectiveness review and one had been excluded from that review	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	

continued

Is the absence of AE data explained?	Yes. Hypercalcaemia model: the costs of treating side effects were not included because the frequency of side effects was negligible and there were no statistically significant differences in side effects between treatment arms in any of the four studies. Skeletal morbidity models: costs of treating side effects were not included because of the rarity of serious side effects
Did the model use a clinical AE parameter?	No
Did the model use utilities?	No
If the model used utilities, were these based on judgement?	Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Not applicable
If the model used utilities, were preferences derived from patients on treatment?	Not applicable
Did the model incorporate the cost/resources of AEs?	No
Did the model incorporate withdrawals?	No

Shepherd 2004[85]		
Objective	To assess the clinical effectiveness and cost-effectiveness of pegylated interferon combined with ribavirin in the treatment of chronic hepatitis C	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Infection	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Specific AE of interest not specified
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (30 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sustained virological response, which was the key outcome of interest in the clinical effectiveness review
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Shepherd 2007[24]		
Objective	To assess the clinical effectiveness and cost-effectiveness of pegylated interferon alfa and non-pegylated interferon alfa and ribavirin for the treatment of adults with histologically mild chronic hepatitis C infection	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Infection	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. 'Adverse effects of treatment' were included
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Virological response, quality of life
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Results for virological response from studies included in the clinical review were used
Are AEs included as a parameter in the model(s)?		Yes. Adverse effects of antiviral treatment on HRQoL were included; utilities were reduced during the year in which treatment occurred
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No. Specific adverse events were not included but an adjustment to health state utilities was made
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Shepherd 2006[86]		
Objective	To assess the clinical effectiveness and cost-effectiveness of adefovir dipivoxil (ADV) and pegylated interferon alfa-2a (PEG) for the treatment of chronic hepatitis B	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Infection	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Interested in broad adverse effects of treatment
Were there separate inclusion criteria in relation to obtaining AE data?		No. Only RCTs eligible for inclusion
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Seroconversion rates (for up to 1 year of treatment) and alanine aminotransferase (ALT) normalisation
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. For HBeAg-positive patients data were taken from three of the included trials for seroconversion rates (for PEG, interferon, lamivudine and ADV). Additional studies not included in the review of effectiveness seem to have been used to provide longer follow-up. Two trials reported data for HBeAg-negative patients and ALT normalisation rates were used from these
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Speight 2006[87]		
Objective	To determine the incremental costs and outcomes of alternative oral cancer screening programmes conducted in a primary care environment	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Cancer	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. A three-part model: a prognostic model of disease progression and survival of patients whose disease remains undetected; a prognostic model for patients whose disease is detected; a screening model reflecting the diagnostic performance of the alternative screening strategies included
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime (60 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity of screening programmes; detection of cancer/precancer in routine clinical practice (in the absence of a screening programme)
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Sensitivity and specificity were derived from the systematic review of test performance in screening for oral cancer and precancer
How was/were the parameter value(s) used derived?		Independently/alternative synthesis. The systematic review of effectiveness in screening for oral cancer and precancer did not identify data on the probability that cancer will be detected as part of routine clinical practice without a screening programme. Expert clinical opinion was therefore sought
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Stevenson 2007[88]		
Objective	To estimate the clinical and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fractures in postmenopausal women who are at different levels of absolute risk of fracture	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. Authors extracted into review all adverse effects reported in the RCTs	
Were there separate inclusion criteria in relation to obtaining AE data?	No. Only adverse effect data from RCTs in the clinical effectiveness section. However, in the methods it states that 'the use of relevant evidence from other sources was not excluded in relation to adverse events'. It is unclear how or whether such other data were used	
Were the AE data synthesised in a meta-analysis?	Yes	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Patient level	
What is the time horizon of the model(s)?	Number of years (10 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Relative risk of fracture [hip, spinal (vertebral) and all non-vertebral]	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review. Point estimate for one parameter taken from meta-analysis	
How was/were the parameter value(s) used derived?	Independently/alternative synthesis. When data could not be acquired from the review, relative risks from published systematic reviews were used	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	No	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Stevenson 2005[89]		
Objective	To assess the clinical effectiveness and cost-effectiveness of selective oestrogen receptor modulators, bisphosphonates and parathyroid hormone for the prevention and treatment of osteoporosis and the prevention of osteoporotic fractures in postmenopausal women	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Musculoskeletal	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. The authors state that associated effects were of interest; this appears to include adverse events	
Were there separate inclusion criteria in relation to obtaining AE data?	No. The authors stated that evidence from other sources had been used when relevant in discussing the various incidental effects, whether adverse or beneficial, associated with the various treatments for postmenopausal osteoporosis. However, there are no additional inclusion criteria or they are not explicitly stated	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort. A cohort of 100 women was followed but patients pass though the model one at a time	
What is the time horizon of the model(s)?	Number of years (10 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Vertebral and non-vertebral fractures, quality of life	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
Are AEs included as a parameter in the model(s)?	Yes. The risk of breast cancer and the risk of coronary heart disease (CHD) are both included in the model. They were included because oestrogen has been associated with them	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	No. In the clinical review gastrointestinal complications and thromboembolism are mentioned as adverse effects of one or more of the drugs considered in the model. These AEs are not included in the model	
What sources were used to obtain the AE data?	Other sources, e.g. ad hoc selection or systematic searches. Data on breast cancer risk taken from a previous model of breast cancer. The parameter value for the risk of CHD was an assumption. The same values were used for all treatments considered. Costs from other publication	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes	
If the model used utilities, were preferences derived from patients on treatment?	No	
Did the model incorporate the cost/resources of AEs?	Yes	
Did the model incorporate withdrawals?	No	

Takeda 2007[90]		
Objective	To assess the clinical effectiveness and cost-effectiveness of gemcitabine, used in combination with paclitaxel, as a second-line treatment for people with metastatic breast cancer who have relapsed following treatment with anthracycline-based chemotherapy	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse effects of treatment were included as an outcome (in the included RCT, neutropenia, anaemia, thombocytopenia and febrile neutropenia were reported)
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Lifetime
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Survival, time to disease progression, HRQoL and adverse effects of treatment
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. The clinical effectiveness review identified only one RCT; additional sources were used
Are AEs included as a parameter in the model(s)?		Yes. The proportion discontinuing treatment because of adverse events was included. It was also stated that the aim was to identify adverse effects of treatment with an impact on quality of life, and to include these effects in estimates of health state utility while on treatment
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Yes
What sources were used to obtain the AE data?		The accompanying systematic review
What sources were used to obtain the AE data?		Unclear. The source was unclear regarding the inclusion of adverse events in utilities
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Tappenden 2007[91]		
Objective	To assess the clinical effectiveness and cost-effectiveness of bevacizumab and cetuximab in the treatment of individuals with metastatic colorectal cancer	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events (grade 3/4)/ toxicity were outcomes of interest
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. The first model estimates the cost-effectiveness of first-line bevacizumab in combination with irinotecan and 5-FU/FA compared with irinotecan and 5-FU/FA. The second model estimates the cost-effectiveness of first-line bevacizumab in combination with 5-FU/FA compared with 5-FU/FA alone
What type(s) of economic model(s) was/were used?		Other. The model presented was based on survival modelling methods
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Overall survival, HRQoL
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. The authors state that data on clinical effectiveness were derived directly from two of the three trials included in the systematic review
Are AEs included as a parameter in the model(s)?		Yes. Hospital admissions resulting from the incidence of adverse events and drug use to manage adverse events were included in terms of health-care resource use and costs
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. None of the sources used to obtain the data for costs of adverse events was included in the clinical effectiveness review
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Thomas 2006[92]		
Objective	To model the likely cost-effectiveness of cryotherapy and salicylic acid for the treatment of warts and to explore whether commissioning an RCT comparing the two interventions was likely to be worthwhile	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Skin	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The stated objectives of the study included assessing the risks and benefits of the treatment. The clinical effectiveness data for this HTA were based on a Cochrane review as no further studies were available since that review had been conducted. The Cochrane review provided cure probabilities, and information on adverse effects was obtained through a survey of patients who had used the treatments
Were there separate inclusion criteria in relation to obtaining AE data?		No. The data on adverse events were not obtained through a systematic review
Were the AE data synthesised in a meta-analysis?		No. Adverse effects data were from a survey
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (18 weeks)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Cure probability
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Not all of the RCTs from the systematic review could be used to calculate the weighted average as some used warts rather than patients as the unit of analysis and some reported only proportion cured and could therefore not be weighted
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Ward 2007[93]		
Objective	To evaluate the clinical effectiveness and cost-effectiveness of statins for the primary and secondary prevention of cardiovascular events in adults with, or at risk of, coronary heart disease	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
	Prevention of disease and conditions, and promotion of well-being	Nutrition and chemoprevention
Health category	Cardiovascular	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events (including cancer and trauma) were included as outcomes if they also reported relevant mortality, morbidity, cardiovascular events or quality of life outcomes
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort (1000 patients)
What is the time horizon of the model(s)?		Other. Patients process through the model until they either die or reach the age of 100 years
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Mortality (due to all causes, coronary heart disease, cardiovascular events), non-fatal stroke and HRQoL
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. The data were supplemented by postmarketing surveillance data
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Yes. A rationale was given as to why costs and disutilities of adverse events were not modelled. Costs: It was stated that the drug under investigation is known to be well tolerated and to have a good safety profile as was shown by the evidence of the trials included in this review and by postmarketing surveillance data. Therefore, associated costs of managing adverse events were expected to be small and were not modelled. Disutilities: A 12-month study designed to determine the effects of pravastatin on HRQoL in older adults found that the drug was well tolerated and did not adversely affect HRQoL. It was stated that the drug is prescribed for life and so there may be a disutility associated with this, but it was assumed that this is small in comparison to the benefits received

continued

Did the model use a clinical AE parameter?	No
Did the model use utilities?	Yes
If the model used utilities, were these based on judgement?	No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No
If the model used utilities, were preferences derived from patients on treatment?	Yes
Did the model incorporate the cost/resources of AEs?	No
Did the model incorporate withdrawals?	No

Wardlaw 2006[20]		
Objective	To determine whether less invasive imaging tests (ultrasound, magnetic resonance angiography, computed tomographic angiography and contrast-enhanced magnetic resonance angiography), alone or combined, could replace intra-arterial angiography, what effect this would have on strokes and deaths, endarterectomies performed and costs, and whether less invasive tests were cost-effective	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Cardiovascular	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (20 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity estimates
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes. Number of adverse clinical events occurring in each of the investigated strategies; costs of adverse events
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable (no AEs were included in the clinical effectiveness review)
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Costs of adverse events were taken from a cost investigation reported by the authors. Data on incidence of adverse events were taken from an epidemiological study
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Wardlaw 2004[94]		
Objective	To determine the cost-effectiveness of computed tomographic (CT) scanning after acute stroke; to assess the contribution of brain imaging to the diagnosis and management of stroke; to estimate costs, benefits and risks of different imaging strategies; to provide data to inform national and local policy on the use of brain imaging in stroke	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Cardiovascular	
Research type	Primary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Unclear
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity and specificity of CT scans (and additional epidemiological data)
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review. Sensitivity and specificity of CT scans were used (epidemiological data were taken from a review of the accuracy of the clinical diagnosis of stroke)
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Warren 2004[95]		
Objective	To evaluate the clinical and cost-effectiveness of insulin glargine (basal-bolus indication)	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Metabolic and endocrine	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse outcomes not explicitly stated as being of interest in the methods. Adverse events reported in the primary studies were summarised in the results. Most common AE was injection site pain
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. One model for type 1 diabetes patients and one for type 2 patients
What type(s) of economic model(s) was/were used?		Unclear. The model was based partly on an industry-submitted model that could not be reported as all details were submitted to NICE in confidence
If a state transition model was used, was a cohort- or patient-level simulation employed?		Unclear
What is the time horizon of the model(s)?		Unclear
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Glycosylated haemoglobin (HbA1c) and hypoglycaemic events
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Type 1 diabetes model: a quantitative synthesis was not performed in the clinical effectiveness review. Effectiveness data for the two models were taken from individual studies included in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No. Most of the AEs reported in the clinical effectiveness review related to injection site pain
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Whiting 2006[96]		
Objective	To evaluate the clinical effectiveness and cost-effectiveness of tests for the diagnosis and investigation of urinary tract infections in children under 5 years of age	
Research activity area	Detection, screening and diagnosis	Evaluation of markers and technologies
Health category	Renal and urogenital	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Information and adverse events related to the tests performed were extracted
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		Yes. There is a short- and a long-term model
What type(s) of economic model(s) was/were used?		Decision tree. A decision tree was used in the short-term model
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Unclear
What is the time horizon of the model(s)?		Unclear
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Sensitivity, specificity of included tests
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		No
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Wilby 2005[97]		
Objective	To examine the clinical effectiveness, tolerability and cost-effectiveness of gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate and vigabatrin for epilepsy in adults	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Neurological	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Withdrawal from therapy because of one or more adverse events; incidence, prevalence and severity of adverse events at different time points
Were there separate inclusion criteria in relation to obtaining AE data?		Yes. Non-randomised, experimental studies and observational studies were included in an assessment of serious, rare and long-term adverse events
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Unclear; 10,000 samples
What is the time horizon of the model(s)?		Number of years (15 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Withdrawals, change in seizure frequency
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. Clinical trials that met certain criteria were included: dose of drug employed was within a specific range, drug was licensed, the studies used a parallel group design, the required trial outcomes were reported
Are AEs included as a parameter in the model(s)?		No, although it was stated that AEs would have an impact on withdrawals from therapy
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable (because no AE data considered or source not specified)
Is the absence of AE data explained?		Yes. Costs of adverse events were considered small
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		Yes
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Willis 2005[98]		
Objective	To assess the immediate effects, the wider consequences and costs, and the overall cost-effectiveness and cost–utility of introducing automated image analysis to a cervical screening programme	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Cancer	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		No
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Not applicable
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Long term as stated by the authors (screening programme entered at age 20 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Detected cancer
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
How was/were the parameter value(s) used derived?		Unclear
Are AEs included as a parameter in the model(s)?		No
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		Not applicable
What sources were used to obtain the AE data?		Not applicable
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		No
Did the model incorporate withdrawals?		No

Wilson 2005[99]		
Objective	To assess the clinical and cost-effectiveness of imatinib in the treatment of unresectable and/or metastatic KIT-positive, gastrointestinal stromal tumours (GIST) compared with current standard treatments	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. Adverse events are not explicitly identified in the methods section as being of interest although they are reported in detail in the report. All adverse events appeared to be of interest
Were there separate inclusion criteria in relation to obtaining AE data?		No. The study design inclusion criteria were already broad
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Cohort
What is the time horizon of the model(s)?		Number of years (10 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Survival
How was/were the parameter value(s) used derived?		Synthesis conducted on a subset of studies. A survival curve for imatinib-treated patients was developed based on data from a single trial in the review. The authors state that this trial provided the most complete survival data available. Survival for control patients was based on a systematic review of prognostic studies as comparative studies were not available. Data were used from what the authors viewed was the most relevant study
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Data for costs of AEs taken from manufacturer's submission. Utilities and withdrawals do not explicitly capture AEs
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		Yes
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		No
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		Yes

Wilson 2007[100]		
Objective	To evaluate the effectiveness and cost-effectiveness of epoetin alfa, epoetin beta and darbepoetin alfa (epo) in anaemia associated with cancer, especially that attributable to cancer treatment	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Cancer	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, narrow focus. Hypertension, rash/ irritation, pruritis, mortality, thrombotic events, seizure, haemorrhage/thrombocytopenia, fatigue and pure red cell aplasia. A note was made of other adverse events
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		No
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?		Patient level
What is the time horizon of the model(s)?		Number of years (3 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Risk of red blood cell transfusion, survival, quality of life
How was/were the parameter value(s) used derived?		Directly from the synthesis of studies in the review
Are AEs included as a parameter in the model(s)?		Yes, although costs of serious adverse events were considered in the model
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No. Model uses probabilities and costs of serious adverse events
What sources were used to obtain the AE data?		Other sources, e.g. ad hoc selection or systematic searches. Models from manufacturers' submissions
Is the absence of AE data explained?		Not applicable. The authors comment that further research is required to reduce uncertainty regarding adverse events
Did the model use a clinical AE parameter?		Yes
Did the model use utilities?		Yes
If the model used utilities, were these based on judgement?		No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Yes
If the model used utilities, were preferences derived from patients on treatment?		No
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Woolacott 2006[26]		
Objective	To evaluate the clinical effectiveness, safety, tolerability and cost-effectiveness of etanercept and infliximab for the treatment of active and progressive psoriatic arthritis (PsA) in patients who have an inadequate response to standard treatment including disease-modifying antirheumatic drug therapy	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Inflammatory and immune system	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. All adverse event data considered	
Were there separate inclusion criteria in relation to obtaining AE data?	Yes. Studies of adults receiving treatment for additional conditions other than PsA were eligible. Observational and experimental studies (of more than 100 participants and of at least 24 weeks' duration) were also included. For the review of efficacy only RCTs of PsA patients were included. In addition, data were summarised from standard sources and other systematic reviews	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	Decision tree	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Not applicable	
What is the time horizon of the model(s)?	Lifetime. Four alternative time horizons were modelled: 1, 5, 10 and 40 years	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Response probability as measured by the Psoriatic Arthritis Response Criteria (PsARC) and change in the Health Assessment Questionnaire (HAQ)	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
Are AEs included as a parameter in the model(s)?	Yes. Authors state that AEs are captured by withdrawals, which are included in the model	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	No	
What sources were used to obtain the AE data?	Source of withdrawal rate data was a trial in the systematic review. The same data used for both interventions considered	
Is the absence of AE data explained?	Not applicable	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	Yes	

Woolacott 2006[23]		
Objective	To evaluate the clinical effectiveness, safety, tolerability and cost-effectiveness of etanercept and efalizumab for the treatment of moderate to severe chronic plaque psoriasis	
Research activity area	Evaluation of treatments and therapeutic interventions	Pharmaceuticals
Health category	Skin	
Research type	NICE TAR	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?	Yes, broad focus. All adverse event data were of interest	
Were there separate inclusion criteria in relation to obtaining AE data?	Yes. For the evaluation of efficacy RCTs with at least 20 participants were eligible for inclusion. To assess safety long-term experimental and observational studies of at least 24 weeks' duration with a minimum of 100 participants were also included. Data were also reported from standard reference sources and previous reviews on the adverse effects of etanercept	
Were the AE data synthesised in a meta-analysis?	No	
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?	No	
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models	
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort	
What is the time horizon of the model(s)?	Number of years (10 years)	
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Psoriasis Area and Severity Index (PASI) 50, 75 and 90 scores (PASI 75 was the primary outcome of interest in the clinical effectiveness review)	
How was/were the parameter value(s) used derived?	Directly from the synthesis of studies in the review	
Are AEs included as a parameter in the model(s)?	No	
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Not applicable	
What sources were used to obtain the AE data?	Not applicable	
Is the absence of AE data explained?	Yes. There is some discussion as to why the costs of adverse events were not included in the model. The report states that the cost implications of serious adverse events are unclear because of the uncertainty around the incidence of such events. Regarding common adverse events, the assumption was made that common adverse events generally resolve when therapy is discontinued, and discontinuation was explicitly considered in the model	
Did the model use a clinical AE parameter?	No	
Did the model use utilities?	Yes	
If the model used utilities, were these based on judgement?	No	
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	No	
If the model used utilities, were preferences derived from patients on treatment?	Yes	
Did the model incorporate the cost/resources of AEs?	No	
Did the model incorporate withdrawals?	No	

Wu 2006[101]		
Objective	To assess the risk of clinical complications associated with thrombophilia in three high-risk patient groups (women using oral oestrogen, women during pregnancy and people undergoing major orthopaedic surgery); to assess the effectiveness of prophylactic treatments in women during pregnancy and inpatients undergoing orthopaedic surgery; and to evaluate the cost-effectiveness of universal and selective history-based screening in the three high-risk groups	
Research activity area	Detection, screening and diagnosis	Population screening
Health category	Blood	
Research type	Secondary research	
Adverse effects in the clinical effectiveness review		
Do the specified outcomes include AEs?		Yes, broad focus. The adverse drug events were included in the review of clinical effectiveness of prophylaxis for thrombophilia. Those specified were haemorrhage, serious wound complications, thrombocytopenia and osteoporotic fractures
Were there separate inclusion criteria in relation to obtaining AE data?		No
Were the AE data synthesised in a meta-analysis?		Yes. Only for minor bleeding events, which were reported by two studies
Adverse effects in the economic model		
Is more than one economic model presented or does an economic model consist of two or more parts?		No
What type(s) of economic model(s) was/were used?		Decision tree
If a state transition model was used, was a cohort- or patient-level simulation employed?		Not applicable
What is the time horizon of the model(s)?		Unclear
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?		Yes. Clinical complications prevented is used in the model. This appears to be based on risk of venous thromboembolism and adverse pregnancy outcomes, which were the outcomes of interest in the risk review
How was/were the parameter value(s) used derived?		Unclear. The authors state that estimates of the probability of clinical events were obtained from the medical literature and the systematic review; however, it is not possible from the information reported to clearly link the data in the model and the precise source
Are AEs included as a parameter in the model(s)?		Yes
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?		No
What sources were used to obtain the AE data?		Expert opinion – used the Delphi process to identify clinical adverse parameters (it was not reported what these were) and then costs for these were included in the model
Is the absence of AE data explained?		Not applicable
Did the model use a clinical AE parameter?		No
Did the model use utilities?		No
If the model used utilities, were these based on judgement?		Not applicable
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?		Not applicable
If the model used utilities, were preferences derived from patients on treatment?		Not applicable
Did the model incorporate the cost/resources of AEs?		Yes
Did the model incorporate withdrawals?		No

Yao 2006[25]	
Objective	To assess the clinical and cost-effectiveness of basiliximab, daclizumab, tacrolimus, mycophenolate mofetil (MMF), mycophenolate sodium (MPS) and sirolimus as possible immunosuppressive therapies for renal transplantation in children
Research activity area	Evaluation of treatments and therapeutic interventions Pharmaceuticals
Health category	Renal and urogenital
Research type	NICE TAR
Adverse effects in the clinical effectiveness review	
Do the specified outcomes include AEs?	Yes, narrow focus. Specific adverse effects: cytomegalovirus (CMV) infection, post-transplant diabetes mellitus (PTDM), hyperlipidaemia, post-transplant lymphoproliferative disease (PTLD), withdrawal because of adverse effects and drug switching because of adverse effects
Were there separate inclusion criteria in relation to obtaining AE data?	No. RCTs in children were sought. When these were not available RCTs in adults and non-randomised comparative studies were used
Were the AE data synthesised in a meta-analysis?	No
Adverse effects in the economic model	
Is more than one economic model presented or does an economic model consist of two or more parts?	No
What type(s) of economic model(s) was/were used?	State transition model, incl. Markov models
If a state transition model was used, was a cohort- or patient-level simulation employed?	Cohort
What is the time horizon of the model(s)?	Number of years (10 years)
Has one or more of the outcomes considered in the clinical effectiveness review been used to inform the model(s)?	Yes. Biopsy-proven acute rejection (BPAR) and creatinine levels at 12 months' follow-up; this is a surrogate outcome
How was/were the parameter value(s) used derived?	Synthesis conducted on a subset of studies based on review of observational studies linking surrogate outcomes (BPAR and creatinine) to graft survival
Are AEs included as a parameter in the model(s)?	Yes. Adverse effects included as a generic outcome. This was incorporated into the QALYs
Do(es) the model(s) consider any of the AEs included in the clinical effectiveness review?	Yes
What sources were used to obtain the AE data?	Both systematic review and other sources. In the basic adult model a lack of relevant data from the studies included in the systematic review meant that adverse effects were included in the model by assuming that a fixed percentage of patients were affected and these were input as penalties in terms of loss of quality of life and cost. Default values were set at 10% of patients: quality of life loss = –0.1 QALYs and cost loss = –£200. In the paediatric model withdrawal because of AEs was used. From the clinical review it could be seen that there was only a difference between TAS and CAS and therefore this was the only comparison in the model that incorporated adverse effects. Data were taken from the systematic review
Is the absence of AE data explained?	Not applicable
Did the model use a clinical AE parameter?	No
Did the model use utilities?	Yes

continued

If the model used utilities, were these based on judgement?	No
If the model used utilities, were these obtained from a secondary source or derived using clinicians'/public preferences?	Yes
If the model used utilities, were preferences derived from patients on treatment?	No
Did the model incorporate the cost/resources of AEs?	No
Did the model incorporate withdrawals?	Yes

Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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