

## **Appendix A. Acknowledgments**

*Clinical and Policy Advisory team (CaPA):* <redacted>

*Technical Expert Panel (TEP):* <redacted>

*Stakeholder meeting attendees (stakeholders):* <redacted>

This manuscript reflects solely the opinions of the authors and does not reflect the opinions of AHRQ, the Department of Health and Human Services, meeting participants, or the institutions with which they are affiliated.

## Appendix B. Systematic review search strategy

Summary	Search strings
Recreated Philips et al. 2004 search{ Philips, 2004 198 /id}:	
"Recommendation-related" terms	1 (checklist? or check list? or standards or standardi?ation or peer review\$ or rules or critiquing or criteria or good or bad or correct\$ or bias or fundamentals or recommend\$ or best or strength\$ or weakness\$ or quality or qualities or validity or guideline? or validation or checkpoint?).ti.
	2 (properly or critically appraise or problems or limitations or rating scale? or framework\$ or protocol? or audit or principles or methodology\$).ti.
	3 (validate or validation or evaluating or properties or guidance or integrity or evaluation or pros or cons).ti.
	4 or/1-3
"Modeling-related" terms	5 (decision adj (tree or triage or data or analytic or analysis)).ti.
	6 exp models, economic/ or exp models, econometric/
	7 (exp decision support techniques/ or exp data interpretation, statistical/ or exp decision theory/ or exp models, statistical/ or exp likelihood functions/ or exp linear models/ or exp logistic models/ or exp proportional hazards models/) and exp costs/ and cost analysis/
	8 ((economic? or pharmaco-economic? or decision? or cost? or costing?) and model\$).ti.
	9 (markov or crystal ball).ti.
	10 exp markov chain/
	11 or/4-9
Critical appraisal of models	12 ((markov model\$ or economic model\$ or mathematical model\$ or cost\$ model\$ or pharmaco-economic model\$ or decision model\$) adj2 (checklist? or check list? or standards or standardi?ation or peer review\$ or rules or critiquing or criteria or good or bad or correct\$ or bias or fundamentals or recommend\$ or best or strength\$ or weakness\$ or quality or qualities or validity or guideline? or validation or checkpoint?)).ab.
	13 ((markov model\$ or economic model\$ or mathematical model\$ or cost\$ model\$ or pharmaco-economic model\$ or decision model\$) adj2 (properly or critically appraise or problems or limitations or rating scale\$ or good practice\$ or framework\$ or protocol\$ or audit or principles or methodology\$)).ab.
	14 ((markov model\$ or economic model\$ or mathematical model\$ or cost\$ model\$ or pharmaco-economic model\$ or decision model\$) adj2 (validate or validation or evaluating or properties or guidance or integrity or avoiding bias or evaluation or pros or cons)).ab.
	15 ((decision tree or decision triage or decision data or decision analytic\$ or decision analysis or crystal ball) adj2 (checklist? or check list? or standard\$ or peer review\$ or rules or critiquing or criteria or good or bad or correct\$ or bias or fundamentals or recommend\$ or best or strength\$ or weakness\$ or quality or qualities or validity or guideline? or validation or checkpoint?)).ab.
	16 ((decision tree or decision triage or decision data or decision analytic\$ or decision analysis or crystal ball) adj2 (properly or critically appraise or problems or limitations or rating scale\$ or framework\$ or protocol\$ or audit or principles or methodology\$)).ab.
17 ((decision tree or decision triage or decision data or decision analytic\$ or decision analysis or crystal ball) adj2 (validate or validation or evaluating or properties or guidance or integrity or evaluation or pros or cons)).ab.	

Summary	Search strings
	18 ((economic evaluation? or economic analysis or economic stud\$ or economic submission?) and guideline\$.ti.
	19 or/12-18
Total Philips search	20 or/4, 11, 19
Additional terms added for this systematic review, restricted to targeted journals:	
Targeted journals	21 Value in health.jn.
	22 (Health technology assessment or "Health Technology Assessment (Winchester, England)").jn.
	23 Pharmacoeconomics.jn.
	24 Journal of Medical Economics.jn.
	25 Annals of Internal Medicine.jn.
	26 Medical Decision Making.jn.
	27 BMC Health Services Research.jn.
	28 Clinical Therapeutics.jn.
	29 European Journal of Health Economics.jn.
	30 (The Journal of the American Medical Association or jama).jn.
	31 (British Medical Journal or BMJ).jn.
	32 Current Medical Research & Opinion.jn.
	33 Health Economics.jn.
	34 Journal of Health Economics.jn.
	35 Medical care.jn.
	36 International Journal of Technology Assessment in Health Care.jn.
	37 BMC Medical Research Methodology.jn.
	38 Journal of Clinical Epidemiology.jn.
	39 Journal of general internal medicine.jn.
	40 American journal of managed care.jn.
	41 Journal of managed care pharmacy.jn.
	42 The European journal of health economics.jn.
	43 Journal of evaluation in clinical practice.jn.
	44 The Journal of the american board of family practice.jn.
	45 Statistics in medicine.jn.
	46 Archives of Internal Medicine.jn.
	47 Clinical Therapeutics.jn.
	48 Current Medical Research & Opinion.jn.
	49 The New England Journal of Medicine.jn.
	50 Lancet.jn.
	51 PLOS medicine.jn.
	52 Annual review of genomics.jn.
	53 Human genetics.jn.
	54 Population health metrics.jn.
	55 Radiology.jn.
	56 Journal of the national cancer institute.jn.
	57 Health care management science.jn.
	58 (Canadian medical association journal or cmaj).jn.
	59 or/21-58
Recommendation-related terms, restricted to journals	60 (consensus or standard\$ or framework\$ or principle\$ or committee\$).mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx]
	61 59 and 60

Summary	Search strings
	62 (cost\$ and (effectiv\$ or utility or benefit) and (analy\$ or model\$)).mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx]
	63 exp cost-benefit/
	64 (decision and (analy\$ or model\$ or analy\$)).mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx]
	65 exp decision support techniques/
	66 ((model and (microsimulation or dynamic or discrete event or simulation or state transition or agent based or infectious disease transmission or transmission or seir)) or computer simulation).mp. [mp=ti, ab, ot, nm, hw, kf, ps, rs, ui, tx]
Modeling-related terms, restricted to journals	67 or/62-66
	68 59 and 67
Additional terms, total	69 61 or 68
Total (combined Philips search and additional terms)	70 20 or 69
Restriction by publication date	71 limit 70 to yr = 1990 -Current

## Appendix C. Health Technology Assessment Organizations

Health Technology Assessment (HTA) Organization	Website
AAZ (Agency for Quality and Accreditation in Health Care, Croatia)	<a href="http://www.aaz.hr/">http://www.aaz.hr/</a>
AETMIS (Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé)	<a href="http://www.aetmis.gouv.qc.ca/site/accueil.phtml">http://www.aetmis.gouv.qc.ca/site/accueil.phtml</a>
AETS ICS III (Agencia de Evaluación de Tecnologías Sanitarias)	<a href="http://www.isciii.es/hdocs/en/investigacion/Agencia_quees.jsp">http://www.isciii.es/hdocs/en/investigacion/Agencia_quees.jsp</a>
AETSA (Andalusian Agency for Health Technology Assessment)	<a href="http://www.juntadeandalucia.es/salud/servicios/aetsa/">http://www.juntadeandalucia.es/salud/servicios/aetsa/</a>
Age.Na:s (Agenzia Nazionale per I Servizi Sanitari Regionali)	<a href="http://www.agenas.it/">http://www.agenas.it/</a>
Agency for Health Technology Assessment in Poland (AHTApol/Poland)	<a href="http://www.aotm.gov.pl/index.php?id=397">http://www.aotm.gov.pl/index.php?id=397</a>
AHRQ (US Agency for Healthcare Research and Quality)	<a href="http://www.ahrq.gov/clinic/cpgsix.htm">http://www.ahrq.gov/clinic/cpgsix.htm</a>
AHTA (Adelaide Health Technology Assessment)	<a href="http://www.adelaide.edu.au/ahta/">http://www.adelaide.edu.au/ahta/</a>
AIFA (Agenzia Italiana Del Farmaco)	<a href="http://www.agenziafarmaco.it/en">http://www.agenziafarmaco.it/en</a>
ARESS (Agenzia Regionale per i Servizi Sanitari)	<a href="http://www.ress.piemonte.it/Links.aspx">http://www.ress.piemonte.it/Links.aspx</a>
ARSENÁL (Veneto's Research Centre for e-Health Innovation)	<a href="http://www.consortioarsenal.it/en/web/guest/home">http://www.consortioarsenal.it/en/web/guest/home</a>
ASERNIP-S (Australian Safety and Efficacy Register of New Interventional Procedures –Surgical)	<a href="http://www.surgeons.org/racs/research-and-audit/asernip-s/asernip-s-publications">http://www.surgeons.org/racs/research-and-audit/asernip-s/asernip-s-publications</a>
ASSR (Regione Emilia Romagna, Agenzia Sanitaria e Sociale Regione Emilia Romagna)	<a href="http://asr.regione.emilia-romagna.it/">http://asr.regione.emilia-romagna.it/</a>
AVALIA-T (Galician Agency for Health Technology Assessment)	<a href="http://www.sergas.es/MostrarContidos_Portais.aspx?IdPaxina=60538">http://www.sergas.es/MostrarContidos_Portais.aspx?IdPaxina=60538</a>
BAG (Bundesamt für Gesundheit) / FOPH (Federal Office of Public Health)	<a href="http://www.bag.admin.ch/index.html?lang=de">http://www.bag.admin.ch/index.html?lang=de</a>
BCBS (Blue Cross BlueShield Association)	<a href="http://www.bcbs.com/">http://www.bcbs.com/</a>
Belgian Federal Health Care Knowledge Centre (KCE/Belgium)	<a href="https://kce.fgov.be/">https://kce.fgov.be/</a>
BS-CA (Blue Shield of California Foundation)	<a href="http://www.blueshieldcafoundation.org/">http://www.blueshieldcafoundation.org/</a>
CAHIAQ (Catalan Agency for Health Information, Assessment and Quality) (formerly CAHTA)	<a href="http://www.gencat.cat/salut/depsan/units/aatrm/html/en/dir394/index.html">http://www.gencat.cat/salut/depsan/units/aatrm/html/en/dir394/index.html</a>
Canadian Agency for Drugs and Technologies in Health (CADTH/Canada)	<a href="http://www.cadth.ca/en">http://www.cadth.ca/en</a>
CAST (Centre for Applied Health Services Research and Technology Assessment, University of Southern Denmark)	<a href="http://www.sdu.dk/Om_SDU/Institutter_centre/CAST?sc_lang=en">http://www.sdu.dk/Om_SDU/Institutter_centre/CAST?sc_lang=en</a>
CDE (Center for Drug Evaluation)	<a href="http://www.cde.org.tw/English/Pages/e-default.aspx">http://www.cde.org.tw/English/Pages/e-default.aspx</a>
CEDIT (Comité d'Évaluation et de Diffusion des Innovations Technologiques)	<a href="http://cedit.aphp.fr/-Pays-.html?rubrique&amp;lang=en&amp;dir=ltr">http://cedit.aphp.fr/-Pays-.html?rubrique&amp;lang=en&amp;dir=ltr</a>
CEM (Cellule d'expertise médicale)	<a href="http://www.ms.public.lu/fr/actualites/2011/04/02-offre-d-emploi/index.html">http://www.ms.public.lu/fr/actualites/2011/04/02-offre-d-emploi/index.html</a>
CENETEC (Centro Nacional de Excelencia Tecnológica en Salud)	<a href="http://www.cenetec.salud.gob.mx/">http://www.cenetec.salud.gob.mx/</a>
CMeRC - HTA Unit	Not available

<b>Health Technology Assessment (HTA) Organization</b>	<b>Website</b>
CMTP (Center for Medical Technology Policy)	<a href="http://www.cmtpNet.org/">http://www.cmtpNet.org/</a>
CNHTA (Committee for New Health Technology Assessment)	<a href="http://www.cha.ac.kr/">http://www.cha.ac.kr/</a>
CRD (Centre for Reviews and Dissemination)	<a href="http://www.york.ac.uk/inst/crd/">http://www.york.ac.uk/inst/crd/</a>
CVZ (College voor Zorgverzekeringen, Dutch health care insurance board)	<a href="http://www.cvz.nl/en/home">http://www.cvz.nl/en/home</a>
DAHTA@DIMDI (Deutsche Agentur für Health Technology Assessment - Bewertung gesundheitsrelevanter Verfahren – Deutsches Institut für medizinische Dokumentation und Information)	<a href="http://www.dimdi.de/static/de/index.html">http://www.dimdi.de/static/de/index.html</a>
Danish Centre for Health Technology Assessment (DACEHTA/Denmark)	<a href="http://www.sst.dk/English/DACEHTA.aspx">http://www.sst.dk/English/DACEHTA.aspx</a>
DECIT-CGATS - Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Departamento de Ciência e Tecnologia	<a href="http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=25516">http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=25516</a>
DSI (Danish Institute for Health Services Research)	<a href="http://dsi.dk/english/">http://dsi.dk/english/</a>
EMKI (Institute for Healthcare Quality Improvement and Hospital Engineering)	<a href="http://www.emki.hu/site/index.php">http://www.emki.hu/site/index.php</a>
ESKI (National Institute for Strategic Health Research)	<a href="http://www.eski.hu/index_en.php">http://www.eski.hu/index_en.php</a>
ETESA (Department of Quality and Patient Safety of the Ministry Health of Chile)	<a href="http://www.redsalud.gov.cl/portal/url/page/minsalcl/g_home/home.html">http://www.redsalud.gov.cl/portal/url/page/minsalcl/g_home/home.html</a>
FEGAS (School of Health Administration)	<a href="http://www.sergas.es/MostrarContidos_Portais.aspx?IdPaxina=50200">http://www.sergas.es/MostrarContidos_Portais.aspx?IdPaxina=50200</a>
FIMEA (Finnish Medicines Agency)	<a href="http://www.fimea.fi/frontpage">http://www.fimea.fi/frontpage</a>
FinOHTA (Finnish Office for Health Technology Assessment)	<a href="http://finohta.stakes.fi/EN/index.htm">http://finohta.stakes.fi/EN/index.htm</a>
G-BA (Gemeinsamer Bundesausschuss)	<a href="http://www.g-ba.de/">http://www.g-ba.de/</a>
GÖG/BIQG (Gesundheit Österreich GmbH)	<a href="http://www.goeg.at/">http://www.goeg.at/</a>
GR (Gezondheidsraad)	<a href="http://www.gezondheidsraad.nl/">http://www.gezondheidsraad.nl/</a>
GYEMSZI (National Institute for Quality- and Organizational Development in Healthcare and Medicines)	<a href="http://www.ogyi.hu/gyemszi/">http://www.ogyi.hu/gyemszi/</a>
HA (Hospital authority Hong Kong)	<a href="http://www.ha.org.hk/visitor/ha_index.asp">http://www.ha.org.hk/visitor/ha_index.asp</a>
HAS (Haute Autorité de Santé)	<a href="http://www.has-sante.fr/portail/jcms/c_5443/english?cid=c_5443">http://www.has-sante.fr/portail/jcms/c_5443/english?cid=c_5443</a>
Health Information and Quality Authority (HIQA/ Ireland)	<a href="http://www.hiqa.ie/">http://www.hiqa.ie/</a>
HIS (Health Care Improvement Scotland)	<a href="http://www.healthcareimprovementscotland.org/home.aspx">http://www.healthcareimprovementscotland.org/home.aspx</a>
HITAP (Health Intervention and Technology Assessment Program)	<a href="http://www.hitap.net/en/splash">http://www.hitap.net/en/splash</a>
HSAC (Health Services Assessment Collaboration)	<a href="http://www.healthsac.net/">http://www.healthsac.net/</a>
HTA-HSR/DHTA (HTA & Health Services Research)	<a href="http://www.centerforfolkesundhed.dk/om+centret/in+english">http://www.centerforfolkesundhed.dk/om+centret/in+english</a>
HVB, Hauptverband der Österreichischen Sozialversicherungsträger	<a href="http://www.sozialversicherung.at/portal27/portal/esvportal/start/startWindow?action=2&amp;p_menuid=2&amp;p_t_abid=1">http://www.sozialversicherung.at/portal27/portal/esvportal/start/startWindow?action=2&amp;p_menuid=2&amp;p_t_abid=1</a>

<b>Health Technology Assessment (HTA) Organization</b>	<b>Website</b>
ICER (Institute for Clinical and Economic Review)	<a href="http://www.icer-review.org/">http://www.icer-review.org/</a>
ICTAHC (Israel Center for Technology Assessment in Health Care)	<a href="http://www.health.gov.il/subjects/">http://www.health.gov.il/subjects/</a>
IECS (Institute for Clinical Effectiveness and Health Policy)	<a href="http://www.iecs.org.ar/">http://www.iecs.org.ar/</a>
IER (Institute for Economic Research)	<a href="http://www.ier.si/index.php">http://www.ier.si/index.php</a>
IHE (Institute of Health Economics)	<a href="http://www.ihe.ca/">http://www.ihe.ca/</a>
INESSS - Institut national d'excellence en santé et en services	<a href="http://www.inesss.qc.ca/index.php?id=50&amp;L=1">http://www.inesss.qc.ca/index.php?id=50&amp;L=1</a>
Institute for Quality and Efficiency in Health Care (IQWiG/Germany)	<a href="https://www.iqwig.de/en/home.2724.html">https://www.iqwig.de/en/home.2724.html</a>
IPP (Institut für Public Health und Pflegeforschung, Universität Bremen)	<a href="http://www.ipp.uni-bremen.de/index.php">http://www.ipp.uni-bremen.de/index.php</a>
IRF (Institute for Rational Pharmacotherapy)	<a href="http://www.irf.dk/en/home.htm">http://www.irf.dk/en/home.htm</a>
JAZMP (Agency for Medicinal Products and Medical Devices)	<a href="http://www.jazmp.si/index.php?id=105">http://www.jazmp.si/index.php?id=105</a>
Kaiser Permanente	<a href="https://www.kaiserpermanente.org/">https://www.kaiserpermanente.org/</a>
KDTD (Turkish Evidence-Based Medicine Association)	<a href="http://www.kanitadayalitip.org/index_eng.html">http://www.kanitadayalitip.org/index_eng.html</a>
Kela (The Social Insurance Institution of Finland)	<a href="http://www.kela.fi/in/internet/english.nsf">http://www.kela.fi/in/internet/english.nsf</a>
Laziosanità (Agenzia di Sanità Pubblica, Regione Lazio)	<a href="http://www.regione.lazio.it/web2/contents/sanita.php">http://www.regione.lazio.it/web2/contents/sanita.php</a>
LBI (Ludwig Boltzmann Institute for Health Technology Assessment)	<a href="http://hta.lbg.ac.at/page/homepage">http://hta.lbg.ac.at/page/homepage</a>
MaHTAS (Health Technology Assessment Section, Ministry of Health Malaysia)	<a href="http://www.moh.gov.my/health_assesments">http://www.moh.gov.my/health_assesments</a>
MAS (Medical Advisory Secretariat, within the Ontario Ministry of Health and Long-Term Care Health Strategies Division)	<a href="http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html">http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html</a>
Medical Services Advisory Committee (MASC/Australia)	<a href="http://www.msac.gov.au/">http://www.msac.gov.au/</a>
MHRA (Medicines and Healthcare Products Regulatory Agency)	<a href="http://www.mhra.gov.uk/index.htm/">http://www.mhra.gov.uk/index.htm/</a>
MOH Indonesia (Ministry of Health – Republic of Indonesia)	<a href="http://www.depkes.go.id/en/">http://www.depkes.go.id/en/</a>
MOH RS (Ministry of Health – Serbia)	<a href="http://www.zdravlje.gov.rs/index.php?">http://www.zdravlje.gov.rs/index.php?</a>
MOH Singapore (Ministry of Health – Singapore)	<a href="http://www.moh.gov.sg/content/moh_web/home.html">http://www.moh.gov.sg/content/moh_web/home.html</a>
MOH Spain (Ministry of Health – Spain)	<a href="http://www.msc.es/">http://www.msc.es/</a>
MOH-CZ (Ministry of Health - Czech Republic)	<a href="http://www.mzcr.cz/En/">http://www.mzcr.cz/En/</a>
MTAA (Medical Technologies Association of Australia)	<a href="http://www.mtaa.org.au/pages/index.asp">http://www.mtaa.org.au/pages/index.asp</a>
MTU-SFOPH (Medical Technology Unit - Swiss Federal Office of Public Health)	<a href="http://www.bag.admin.ch/">http://www.bag.admin.ch/</a>
National Authority of Medicines and Health Products (INFARMED/Portugal)	<a href="http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH">http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH</a>
National Institute for Clinical Excellence (NICE/UK)	<a href="http://www.nice.org.uk/">http://www.nice.org.uk/</a>
NBoH (National Board of Health)	<a href="http://www.sst.dk/">http://www.sst.dk/</a>

<b>Health Technology Assessment (HTA) Organization</b>	<b>Website</b>
NCPE (National Centre for Pharmacoeconomics, St. James's Hospital)	<a href="http://www.stjames.ie/Departments/DepartmentsA-Z/N/NationalCentreforPharmacoeconomics/DepartmentOverview/">http://www.stjames.ie/Departments/DepartmentsA-Z/N/NationalCentreforPharmacoeconomics/DepartmentOverview/</a>
NCPHP (National Centre of Public Health Protection)	<a href="http://ncphp.government.bg/">http://ncphp.government.bg/</a>
NECA - National Evidence-based healthcare Collaboration Agency	<a href="http://www.neca.re.kr/eng/">http://www.neca.re.kr/eng/</a>
NETSCC, HTA - NIHR (Coordinating Centre for Health Technology Assessment)	<a href="http://www.hta.ac.uk/">http://www.hta.ac.uk/</a>
Newcastle University	<a href="http://www.ncl.ac.uk/">http://www.ncl.ac.uk/</a>
NHG (National Healthcare Group)	<a href="http://www.nhg.com.sg/">http://www.nhg.com.sg/</a>
NHMRC	<a href="http://www.nhmrc.gov.au/">http://www.nhmrc.gov.au/</a>
NHS QIS (Quality Improvement Scotland)	<a href="http://www.nhshealthquality.org/nhsqis/CCC_FirstPage.jsp">http://www.nhshealthquality.org/nhsqis/CCC_FirstPage.jsp</a>
NHSC (National Horizon Scanning Centre)	<a href="http://www.haps.bham.ac.uk/publichealth/horizon/">http://www.haps.bham.ac.uk/publichealth/horizon/</a>
NIPH-RS (National Institute of Public Health of the Republic of Slovenia)	<a href="http://www.ivz.si/">http://www.ivz.si/</a>
NLM (National Library of Medicine)	<a href="http://www.nlm.nih.gov/">http://www.nlm.nih.gov/</a>
NOKC (Norwegian Knowledge Centre for the Health Services)	<a href="http://www.kunnskapscenteret.no/Home?language=english">http://www.kunnskapscenteret.no/Home?language=english</a>
NSPH (National School of Public Health)	<a href="http://www.nsph.gr/default.aspx?page=home">http://www.nsph.gr/default.aspx?page=home</a>
OSTEBA (Basque Office for Health Technology Assessment)	<a href="http://www.osanet.euskadi.net/r85-ostebe/es/contenidos/informacion/ostebe/es_ostebe/ostebe.html">http://www.osanet.euskadi.net/r85-ostebe/es/contenidos/informacion/ostebe/es_ostebe/ostebe.html</a>
PATH (Programs for Assessment of Technology in Health Research Institute)	<a href="http://www.path-hta.ca/Home.aspx">http://www.path-hta.ca/Home.aspx</a>
PenTAG (Peninsula Technology Assessment Group)	Not available
Pharmaceutical Benefits Advisor Committee (PBAC, Australia)	<a href="http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-outcomes-info">http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-outcomes-info</a>
Pharmaceutical Management Agency of New Zealand (PHARMAC/New Zealand)	<a href="http://www.pharmac.govt.nz/">http://www.pharmac.govt.nz/</a>
QPACT (Queensland Policy and Advisory Committee for New Technology)	<a href="http://www.health.qld.gov.au/newtech/html/QPACT.asp">http://www.health.qld.gov.au/newtech/html/QPACT.asp</a>
Regione Veneto (Regione Veneto, Direzione Piani e Programmi Socio Sanitari)	<a href="http://www.regione.veneto.it/channels">http://www.regione.veneto.it/channels</a>
Reglom-DGSAN (Regione Lombardia Direzione Generale Sanita)	<a href="http://www.sanita.regione.lombardia.it/cs/Satellite?c=Page&amp;childpagename=DG_Sanita/DGHomeLayout&amp;cid=1213277054618&amp;pagenam=DG_SANWrapper">http://www.sanita.regione.lombardia.it/cs/Satellite?c=Page&amp;childpagename=DG_Sanita/DGHomeLayout&amp;cid=1213277054618&amp;pagenam=DG_SANWrapper</a>
RIZIV (Rijksinstituut voor ziekte- en invaliditeitsverzekering)	<a href="http://www.riziv.fgov.be/presentation/nl/index.htm">http://www.riziv.fgov.be/presentation/nl/index.htm</a>
santésuisse (Branchenverband der schweizerischen Krankenversicherer)	<a href="http://www.santesuisse.ch/de/dyn_output.html?content.vname=portal">http://www.santesuisse.ch/de/dyn_output.html?content.vname=portal</a>
SBU (Swedish Council on Technology Assessment in Health Care)	<a href="http://www.sbu.se/en/">http://www.sbu.se/en/</a>
SchARR (Technology Assessment Group, University of Sheffield)	<a href="http://www.shef.ac.uk/scharr/sections/heds/collaborations/tag">http://www.shef.ac.uk/scharr/sections/heds/collaborations/tag</a>
SIDC (State Institute for Drug Control)	<a href="http://www.sukl.sk/en/about-us">http://www.sukl.sk/en/about-us</a>
SingHealth (Singapore Health Service)	<a href="http://www.singhealth.com.sg/Pages/Home.aspx">http://www.singhealth.com.sg/Pages/Home.aspx</a>

<b>Health Technology Assessment (HTA) Organization</b>	<b>Website</b>
SLOVATHA (Slovak Agency for Health Technology Assessment)	
SNHTA (Swiss Network for HTA)	<a href="http://www.snhta.ch/">http://www.snhta.ch/</a>
SNSPMS (National School of Public Health, Management and Professional Development)	<a href="http://www.snspms.ro/">http://www.snspms.ro/</a>
SPC on Standardization and HTA	Not available
SSD/MSOC (Ministry for Social Policy, Strategy and Sustainability Division)	Not available
Sundhed.dk (Centre for Public Health, Central Denmark Region, department HTA & Health Services Research)	<a href="http://www.cfk.rm.dk/om+os/in+english/health+technology+assessment+and+health+services+research">http://www.cfk.rm.dk/om+os/in+english/health+technology+assessment+and+health+services+research</a>
TLV (Dental and Pharmaceutical Benefits Agency)	<a href="http://www.tlv.se/in-english-old/in-english/">http://www.tlv.se/in-english-old/in-english/</a>
UCEETS - The National Coordination Unit of Health Technology Assessment and Implementation	<a href="http://www.msal.gov.ar/pngcam/">http://www.msal.gov.ar/pngcam/</a>
UETS (Unidad de Evaluación de Tecnologías Sanitarias)	<a href="http://www.madrid.org/cs/Satellite?cid=1142494649964&amp;language=es&amp;pagename=PortalSalud/Page/PTSA_pintarContenidoFinal&amp;vest=1142494649964">http://www.madrid.org/cs/Satellite?cid=1142494649964&amp;language=es&amp;pagename=PortalSalud/Page/PTSA_pintarContenidoFinal&amp;vest=1142494649964</a>
UFI-SALUD (Unidad de Financiamiento Internacional de Salud)	<a href="http://www.ufisalud.gov.ar/">http://www.ufisalud.gov.ar/</a>
UMIT (Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik)	<a href="http://www.umat.at/page.cfm?vpath=index">http://www.umat.at/page.cfm?vpath=index</a>
University Hospital A. Gemelli	<a href="http://www.rm.unicatt.it/">http://www.rm.unicatt.it/</a>
UTA (University of Tartu , Department of Public Health)	<a href="http://www.ut.ee/en">http://www.ut.ee/en</a>
UVT (HTA Unit in A. Gemelli Teaching Hospital)	<a href="http://www.policlinicogemelli.it/area/?s=206">http://www.policlinicogemelli.it/area/?s=206</a>
VASPVT (State Health Care Accreditation Agency under the Ministry of Health of the Republic of Lithuania)	<a href="http://www.vaspvt.gov.lt/index.php?2719160486">http://www.vaspvt.gov.lt/index.php?2719160486</a>
VATAP (VA Technology Assessment Program)	Not available
VEC (Centre of Health Economics)	<a href="http://www.vec.gov.lv/english/default.html">http://www.vec.gov.lv/english/default.html</a>
ZonMw (The Medical and Health Research Council of The Netherlands)	<a href="http://www.zonmw.nl/">http://www.zonmw.nl/</a>

## Appendix D. HTA organization data extraction

Question	Agency for Health Technology Assessment in Poland (AHTApol/Poland)
Integration of modeling	The situations in which modeling is recommended include: <ul style="list-style-type: none"> <li>- the need to evaluate the results in real practice when only the results of experimental tests are available and the results obtained in one country can be transposed into another one,</li> <li>- indirect comparative synthesis if relevant direct trials are missing,</li> <li>- providing estimates if direct measurements are missing,</li> <li>- preliminary assessment and scheduling of trials,</li> <li>- early stage of development of a new technology if comprehensive trials are missing.</li> <li>- the need to extrapolate the results beyond the time horizon of the clinical trials included in the clinical analysis,</li> <li>- the need to transpose the experimental effectiveness measured (i.e. indirect results expressed on a disease-specific scale) to final utility results (e.g. life years gained, gained QALY),</li> </ul>
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	If modeling is necessary, the model structure should be presented. Assumptions of the model should be clear, well justified and tested in a sensitivity analysis. If data in the model are extrapolated over time horizon of the primary trials, the following scenarios should be analyzed: optimistic, pessimistic and neutral. The analytical task consists in taking into account Polish data concerning the use of resources and costs.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	The situations in which modeling is recommended include: <ul style="list-style-type: none"> <li>- the need to transpose the experimental effectiveness measured (i.e. indirect results expressed on a disease-specific scale) to final utility results (e.g. life years gained, gained QALY),</li> </ul>
Inclusion of costs	The analytical task consists in taking into account Polish data concerning the use of resources and costs.
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Canadian Agency for Drugs and Technologies in Health (CADTH/Canada)</b>
Integration of modeling	nd
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	Economic evaluations of health care technologies typically involve building and then using models to synthesize evidence and assumptions from multiple sources to estimate the long-term incremental costs and outcomes of new therapies. Because the outputs (results) depend on the model structure, the data, and the assumptions used, the model should be as transparent as possible. As a result, decision makers should be critical when reviewing the results of a model-based evaluation.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	Economic evaluations of health care technologies typically involve building and then using models to synthesize evidence and assumptions from multiple sources to estimate the long-term incremental costs and outcomes of new therapies.
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Danish Centre for Health Technology Assessment (DACEHTA/Denmark)</b>
Integration of modeling	<p>Modeling is used frequently in connection with HTA since it is here attempted to take existing literature as the basis. There is often evidence for the effect of a technology in the form of clinical data, survival data and/or data concerning health-related quality of life, and one will then, where appropriate, content oneself with collecting cost data and comparing these with the effects in a model ...</p> <p>In some cases, modeling will need to be used in the economic analysis – whether completely or only partially. There are a number of reasons for this (Buxton et al.)</p>
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	<p>Extrapolation of short-term clinical data for the purpose of predicting these data in the longer term, e.g. survival probabilities, or linkage of intermediate endpoints to final endpoints, can lead to modeling in the economic analysis. The performance of the clinical study in a controlled and randomised design which ensures a high degree of internal validity often conversely means that the study has a low degree of external validity. Here, it can be necessary to model the economic analysis in order to be able to generalise about daily practice or between regions in the country. As mentioned previously, it may also happen to be placebo that the new technology is compared with in the clinical study. Here, it may be necessary to use models in the economic analysis to investigate the cost-effectiveness of the new technology in relation to daily practice. Lastly, there may be insufficient economic and clinical data, particularly early in the development/life cycle of a health technology. The economic analysis can, in such a situation, be modeled entirely on the basis of the best available evidence and the expectations that one may have.</p> <p>Regardless of whether modeling is necessary, or the economic analysis can be based directly on the clinical study, it may be a good idea, purely in order to gain a comprehensive view, to draw up a decision tree for the possible patient streams as referred to above.</p>
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	There is often evidence for the effect of a technology in the form of clinical data, survival data and/or data concerning health-related quality of life, and one will then, where appropriate, content oneself with collecting cost data and comparing these with the effects in a model ...
Inclusion of costs	As mentioned previously, it may also happen to be placebo that the new technology is compared with in the clinical study. Here, it may be necessary to use models in the economic analysis to investigate the cost-effectiveness of the new technology in relation to daily practice.
Budget analysis done	nd
Impact on project budget	nd

Question	Health Information and Quality Authority (HIQA/Ireland)
Integration of modeling	The use of modeling is typically required as part of an economic evaluation to make clinical and cost-effectiveness estimates relevant to the time frame under review.
Modeling alongside SR	In the reference case, evidence on outcomes should be obtained by means of a systematic review with all data sources clearly described.(15) Evidence generated from this phase is necessary to inform decision making, but may also be used to populate economic decision-analytic models. These models can be used to project the potential health and economic consequences of using different technologies over an adequate time frame.
Timing of modeling	<p>Economic evaluations may be run alongside a clinical trial, where the patient outcomes and associated costs generated in the trial are used to populate the economic model, rather than data from multiple trials or gathered in a systematic review. In such cases there are a number of risks of bias (e.g., protocol-driven costs, lack of longer-term follow-up data, inappropriate outcomes) that can impact on the results. Adequate steps must be taken to show that the data are appropriate and generalisable to the relevant population in Ireland (e.g., it may be reasonable to make the trial data available for independent assessment).</p> <p>Models will frequently require numerous additional parameters which may be directly or indirectly related to the effectiveness of a technology (e.g., uptake rate, disease severity). The values for these sorts of parameters will often be informed by local data on disease prevalence, service utilisation and expert opinion. As they are not typically derived from systematic review, care must be taken to adequately address potential bias in the parameter estimates and to take into account the uncertainty or lack of precision in the estimates. As such, a sensitivity analysis should also include these parameters. Where expert opinion is used, it should be elicited in a manner which minimises bias and the process should be documented in sufficient detail.</p>
Use of pre-existing vs. established models	nd
Model recommendations	<p>modeling (See section 2.12)</p> <p>There is no one optimal modeling technique, rather the choice of model should depend on the research question to be addressed.</p> <p>Models used to synthesise and extrapolate available evidence should be developed in accordance with good modeling practice guidelines. The model should be clearly described, with the assumptions and inputs documented and justified. The methods for the quality assurance of the model should be detailed and the model validation results documented. The model and its key inputs should be subjected to comprehensive sensitivity analysis.</p> <p>Uncertainty (Section 2.15) The effects of model uncertainty (i.e., structure, methods and assumptions) and parameter uncertainty on the outcome of the economic evaluation must be systematically evaluated using sensitivity analysis and scenario analyses for the range of plausible scenarios. The range of values provided for each parameter must be clearly stated and justified. Justification for the omission of any model input from the sensitivity analysis should be included. For the reference case, a one-way sensitivity analysis should be conducted to identify the key model inputs/assumptions contributing most to uncertainty. Multivariate analysis should be used for key model inputs. Probabilistic sensitivity analysis (PSA), in the form of a Monte Carlo simulation, should be used to assess parameter uncertainty. The expected value of perfect information (EVPI) should also be evaluated.</p>

The use of extrapolation modeling is typically required when adopting a lifetime horizon as long-term primary data on the safety and effectiveness of a new technology will only be available after the product has been in routine clinical use for some time. When extrapolating data beyond the duration of the clinical trials, inherent assumptions regarding future treatment effects and disease progression should be clearly outlined and tested as part of the sensitivity analysis (see also Section 2.15).

Models will frequently require numerous additional parameters which may be directly or indirectly related to the effectiveness of a technology (e.g., uptake rate, disease severity). The values for these sorts of parameters will often be informed by local data on disease prevalence, service utilisation and expert opinion. As they are not typically derived from systematic review, care must be taken to adequately address potential bias in the parameter estimates and to take into account the uncertainty or lack of precision in the estimates. As such, a sensitivity analysis should also include these parameters. Where expert opinion is used, it should be elicited in a manner which minimises bias and the process should be documented in sufficient detail.

Currently, there are no agreed Irish cost models available. As a result, the generation of valid Irish cost data is challenging and time consuming. Until a valid Irish cost model is established, there is a need for flexibility regarding cost valuation. To maximise reproducibility and transferability, all assumptions and cost estimates must be clearly reported and subjected to one-way and probabilistic sensitivity analysis (see also Section 2.15). In particular, where costs are applied from other countries, the assumptions necessary to transfer this data must be explicitly reported, with all costs converted to their Irish equivalent in euro using Purchasing Power Parity indices.<sup>(21)</sup> An example of how to transfer costs is included in Appendix 2.

The evidence supporting the biological or clinical plausibility of the subgroup effect should be fully documented, including details of statistical analyses. Since the goal of the health system is to maximise the potential for health gain from its finite resources, a stratified analysis that allows cost-effectiveness to be modeled separately for each subgroup, may contribute important information to the final advice.

Probabilistic sensitivity analysis (PSA) is the preferred approach for exploring uncertainty arising from parameter imprecision (e.g. uncertainty around the true mean values of cost and efficacy inputs) in decision-analytic modeling. With this approach, probability distributions are applied using specified plausible ranges for the key parameters rather than the use of varied point estimates for each parameter.

IPD from a single or small number of trials may also be used as a basis for developing a micro-simulation model. Patient characteristics are used to populate the model and simulate the impact of introducing a treatment in terms of endpoints and costs. Such an exercise should not be considered as either evidence synthesis or meta-analysis, but rather a form of subgroup analysis. The use of IPD for micro-simulation is beyond the scope of these Guidelines.

How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	The preferred evaluation type for the reference case is a cost-utility analysis (CUA) with the outcomes expressed in terms of quality-adjusted life-years (QALYs).

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Valuing Outcomes (See section 2.11) For the reference case, health effects should be valued in QALYs.

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Inclusion of costs	<p>The use of modeling is typically required as part of an economic evaluation to make clinical and cost-effectiveness estimates relevant to the time frame under review.</p> <p>Currently, there are no agreed Irish cost models available. As a result, the generation of valid Irish cost data is challenging and time consuming. Until a valid Irish cost model is established, there is a need for flexibility regarding cost valuation. To maximise reproducibility and transferability, all assumptions and cost estimates must be clearly reported and subjected to one-way and probabilistic sensitivity analysis (see also Section 2.15). In particular, where costs are applied from other countries, the assumptions necessary to transfer this data must be explicitly reported, with all costs converted to their Irish equivalent in euro using Purchasing Power Parity indices.(21) An example of how to transfer costs is included in Appendix 2.</p> <p>The evidence supporting the biological or clinical plausibility of the subgroup effect should be fully documented, including details of statistical analyses. Since the goal of the health system is to maximise the potential for health gain from its finite resources, a stratified analysis that allows cost-effectiveness to be modeled separately for each subgroup, may contribute important information to the final advice.</p>
Budget analysis done	Entire report recently released on Budget Impact Analysis: <a href="http://www.higa.ie/system/files/Budget-Impact-Analysis-Guidelines-2014.pdf">http://www.higa.ie/system/files/Budget-Impact-Analysis-Guidelines-2014.pdf</a>
Impact on project budget	nd

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<b>Question</b>	<b>National Authority of Medicines and Health Products (INFARMED/Portugal)</b>
Integration of modeling	nd
Modeling alongside SR	nd
Timing of modeling	An important problem that pharmaco-economic studies have to face is that only efficacy data are available when a new product is launched. Any studies carried out at this stage will inevitably have to extrapolate the effectiveness of the treatment on the basis of its estimated efficacy in the clinical trials. modeling is normally used to do this.
Use of pre-existing vs. established models	nd
Model recommendations	If no data on effectiveness are available from clinical trials...efficacy data obtained in appropriate clinical trials can be used after being corrected by modeling.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Institute for Quality and Efficiency in Health Care (IQWiG/Germany)</b>
Integration of modeling	Economic data are not regularly collected in clinical trials. If this is done, however, these data alone are often not sufficient for a full and substantiated depiction of the costs of a health technology. Clinical trials seldom provide information on the long-term economic consequences associated with the introduction of a new technology. In addition, they do not always adequately and comprehensively reflect all cost aspects relevant to the German health care setting. Moreover, protocol-induced resource consumption in clinical trials may bias cost estimation. For these reasons, the modeling of the economic effects of a health technology is an essential component in health economic evaluation.
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	nd
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	Economic data are not regularly collected in clinical trials. If this is done, however, these data alone are often not sufficient for a full and substantiated depiction of the costs of a health technology. Clinical trials seldom provide information on the long-term economic consequences associated with the introduction of a new technology. In addition, they do not always adequately and comprehensively reflect all cost aspects relevant to the German health care setting. Moreover, protocol-induced resource consumption in clinical trials may bias cost estimation. For these reasons, the modeling of the economic effects of a health technology is an essential component in health economic evaluation.
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Belgian Federal Health Care Knowledge Centre (KCE/Belgium)</b>
Integration of modeling	Modeling should be applied if the available data are insufficient to allow a full assessment of the cost-effectiveness or cost-utility of a product.
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	nd
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	Modeling should be applied if the available data are insufficient to allow a full assessment of the cost-effectiveness or cost-utility of a product.
Inclusion of costs	Modeling should be applied if the available data are insufficient to allow a full assessment of the cost-effectiveness or cost-utility of a product.
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>MAS (Medical Advisory Secretariat, within the Ontario Ministry of Health and Long-Term Care Health Strategies Division/Canada)</b>
Integration of modeling	nd
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	The time horizon chosen for an economic evaluation is important and can dramatically affect the size of the incremental cost-effectiveness ratio. However, the data on which efficacy is based usually is derived from randomized trials or non-experimental studies that follow patients for a relatively short period of time. modeling techniques must be used to project lifetime costs and effects if such a time frame is appropriate. Unfortunately, however, the data on which to project lifetime costs and clinical effects must almost certainly be much more speculative than those with a short time frame. Submissions should clearly state the time horizon chosen. The analysis should delineate the time horizon on which estimates can be based from currently available high quality empirical data (e.g., randomized trials that follow patients for months to a few years) or from modeled data based on extrapolations.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	The time horizon chosen for an economic evaluation is important and can dramatically affect the size of the incremental cost-effectiveness ratio. However, the data on which efficacy is based usually is derived from randomized trials or non-experimental studies that follow patients for a relatively short period of time. modeling techniques must be used to project lifetime costs and effects if such a time frame is appropriate. Unfortunately, however, the data on which to project lifetime costs and clinical effects must almost certainly be much more speculative than those with a short time frame. Submissions should clearly state the time horizon chosen. The analysis should delineate the time horizon on which estimates can be based from currently available high quality empirical data (e.g., randomized trials that follow patients for months to a few years) or from modeled data based on extrapolations.
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Medical Services Advisory Committee (MASAC/Australia)</b>
Integration of modeling	nd
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	<p>The aim of the economic evaluation is to use the clinical studies ... to determine the economic cost of substituting the proposed service for the main comparator in the setting for the requested listing (the base-case economic evaluation). MASAC requires a full and transparent description of the variables used in the economic evaluation. Generally, two steps are involved:</p> <ol style="list-style-type: none"> <li>1. a study-based economic evaluation (effectively, a cost-consequences analysis), which is based on the study variables (eg population, setting, time horizon)</li> <li>2. a modeled economic evaluation, in which study-based variables are modified using modeling techniques ('translated') to take account of differences between the study variables and the target variables for the proposed service.</li> </ol>
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	The aim of the economic evaluation is to use the clinical studies ... to determine the economic cost of substituting the proposed service for the main comparator in the setting for the requested listing (the base-case economic evaluation).
Budget analysis done	nd
Impact on project budget	nd

Question	National Institute for Clinical Excellence (NICE/UK)
Integration of modeling	<p>Modeling provides an important framework for synthesising available evidence and generating estimates of clinical and cost effectiveness in a format relevant to the Appraisal Committee’s decision-making process. Models are required for most technology appraisals. Situations when modeling is likely to be required include those where:</p> <ul style="list-style-type: none"> <li>-all the relevant evidence is not contained in a single trial</li> <li>-patients participating in trials do not match the typical patients likely to use the technology within the NHS</li> <li>-intermediate outcomes measures are used rather than effect on HRQL and survival</li> <li>-relevant comparators have not been used or trials do not include evidence on relevant subgroups</li> <li>-the long-term costs and benefits of the technologies extend beyond trial follow-up</li> </ul> <p>In the multiple technology assessment (MTA) process, the Assessment Group prepares the assessment report, which is an independent synthesis of the evidence from published information and the submissions from manufacturers and sponsors about the clinical and cost effectiveness of the technology/technologies. The report provides a systematic review of the literature and a review of manufacturer and sponsor economic models submitted to the Institute. It usually includes a new assessment of cost effectiveness based on an economic model.</p>
Modeling alongside SR	<p>In the multiple technology assessment (MTA) process, the Assessment Group prepares the assessment report, which is an independent synthesis of the evidence from published information and the submissions from manufacturers and sponsors about the clinical and cost effectiveness of the technology/technologies. The report provides a systematic review of the literature and a review of manufacturer and sponsor economic models submitted to the Institute. It usually includes a new assessment of cost effectiveness based on an economic model.</p>
Timing of modeling	nd
Use of pre-existing vs. established models	<p>The report provides a systematic review of the literature and a review of manufacturer and sponsor economic models submitted to the Institute. It usually includes a new assessment of cost effectiveness based on an economic model.</p>
Model recommendations	<p>Economic models should also:</p> <ul style="list-style-type: none"> <li>be replicable</li> <li>have face validity (that is, be plausible)</li> <li>be open to external scrutiny.</li> </ul> <p>The models used to synthesise available evidence to generate estimates of clinical and cost effectiveness for the Institute’s needs should follow accepted guidelines...Providing an all-embracing definition of what constitutes a high-quality model is not possible, but some guidelines are available....(see page 42).</p> <p>It is essential that clinical and cost effectiveness is considered over an appropriate time horizon to reflect UK practice and patients, and to compare treatment options that represent routine care and/or current best practice for the relevant patient groups. Therefore, it will be necessary to construct an analytical framework within which to synthesise the available evidence so that estimates of clinical and cost effectiveness can be made that are relevant to the clinical decision-making context. This framework will usually require the development of a model using aggregated or individual patient data to estimate parameters.</p> <p>It is essential that clinical and cost effectiveness is considered over an appropriate time horizon to reflect UK practice and patients, and to compare treatment options that</p>

represent routine care and/or current best practice for the relevant patient groups. Therefore, it will be necessary to construct an analytical framework within which to synthesise the available evidence so that estimates of clinical and cost effectiveness can be made that are relevant to the clinical decision-making context. This framework will usually require the development of a model using aggregated or individual patient data to estimate parameters.

Trial data may not be sufficient to quantify baseline risk of some health outcomes or events for the population of interest. Quantifying the baseline risk of health outcomes and how the disease would naturally progress with the comparator intervention can be a useful step when estimating absolute health outcomes in the economic analysis. Relative treatment effects observed in randomised trials may then be applied to data on the baseline risk of health outcomes for the populations or subgroups of interest. The methods used to identify and critically appraise sources of data for these estimates should be stated and justified.

Table 5.1 Summary of the reference case.

How SR incorporated into the model	Synthesis of evidence on outcomes [always] based on a systematic review
Who conducts the model?	nd
Inclusion of quality of life	Multiple sections, as follows: 2.2.6, Table 5.1, 5.12, 5.2.11, 5.2.12, 5.4.1, 5.4.2,5.4.9,5.4.10,5.9.2,5.9.3,6.2.26
Inclusion of costs	It is essential that clinical and cost effectiveness is considered over an appropriate time horizon to reflect UK practice and patients, and to compare treatment options that represent routine care and/or current best practice for the relevant patient groups. Therefore, it will be necessary to construct an analytical framework within which to synthesise the available evidence so that estimates of clinical and cost effectiveness can be made that are relevant to the clinical decision-making context. This framework will usually require the development of a model using aggregated or individual patient data to estimate parameters. Further details of modeling methods are provided in section 5.7.
	<p>The models used to synthesise available evidence to generate estimates of clinical and cost effectiveness for the Institute’s needs should follow accepted guidelines...Providing an all-embracing definition of what constitutes a high-quality model is not possible, but some guidelines are available....(see page 42).</p> <p>If the use of the technology is conditional on the outcome of a diagnostic test, the accuracy of the test and associated costs should be incorporated into the assessments of clinical and cost effectiveness.</p>
Budget analysis done	Multiple sections as follows: 5.2.12, 5.5.9, 5.13.6, 5.13.8, 6.2.14
Impact on project budget	

<b>Question</b>	<b>Pharmaceutical Benefits Advisor Committee (PBAC/Australia)</b>
Integration of modeling	The primary purpose of submission section C is to guide the presentation of analyses conducted to translate the systematic overview of the results of direct randomised trial evidence to the listing requested, and thus to the framework of the economic evaluation (submission section D--NEED TO FURTHER EXTRACT SECTION). This is particularly important when one or more variables incorporated into the economic evaluation are derived from, but not directly based on, the clinical evaluation presented in submission section B....The need for premodeling studies arises because the study protocols for the trials used for the clinical evaluation might differ from the proposed clinical practice setting for the main indication
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	This is particularly important when one or more variables incorporated into the economic evaluation are derived from, but not directly based on, the clinical evaluation presented in submission section B. These variables may be derived using a number of analyses that modify the results of the clinical evaluation to help construct a modeled economic evaluation.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>Pharmaceutical Management Agency of New Zealand (PHARMAC/New Zealand)</b>
Integration of modeling	Decisions have to be made regardless of data availability. modeling in economic analysis is necessary in order to inform decision making at a particular point in time.
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	nd
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>AAZ (Agency for Quality and Accreditation in Health Care/Croatia)</b>
Integration of modeling	nd
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	<p>It is important to identify potential selection bias in the inputs to the model and for the model to quantify the decision uncertainty associated with a technology (that is, the probability that a different decision would be reached if the true cost effectiveness of each technology could be ascertained before making the decision).The models used to synthesize available evidence to generate estimates of clinical and cost-effectiveness for the Agency’s needs should follow accepted guidelines. Full documentation and justification of structural assumptions and data inputs should be provided. When there are alternative plausible assumptions and inputs, sensitivity analyses of their effects on model outputs should be undertaken.</p> <p>It is important to identify potential selection bias in the inputs to the model and for the model to quantify the decision uncertainty associated with a technology (that is, the probability that a different decision would be reached if the true cost effectiveness of each technology could be ascertained before making the decision).</p>
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	The models used to synthesize available evidence to generate estimates of clinical and cost-effectiveness for the Agency’s needs should follow accepted guidelines.
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>HITAP (Health Intervention and Technology Assessment Program/Thailand)</b>
Integration of modeling	Time frame for economic evaluation: A full report may include an evidence review, an economic model and a budget impact analysis. If the evidence reviews systematic, the time frame will be longer than if the review is non-systematic.
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	Provides table of required economic modeling protocol components
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	May include economic evaluation
Budget analysis done	May include budget analysis
Impact on project budget	nd

<b>Question</b>	<b>ICER (Institute for Clinical and Economic Review/US)</b>
Integration of modeling	ICER's appraisal process includes the development of a de novo decision-analytic model to accompany the systematic review.
Modeling alongside SR	ICER's appraisal process includes the development of a de novo decision-analytic model to accompany the systematic review.
Timing of modeling	nd
Use of pre-existing vs. established models	ICER's appraisal process includes the development of a de novo decision-analytic model to accompany the systematic review.
Model recommendations	These models are aligned closely with the parameters of the systematic review to ensure that model outputs are generalizable to the appropriate patient populations and treatment settings. Sensitivity analyses of companion decision-analytic models
How SR incorporated into the model	To produce parameter estimates for use in sensitivity analyses of companion decision-analytic models, as a means of exploring the potential for these estimates to affect how the value of multiple interventions compares.
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>LBI (Ludwig Boltzmann Institute for Health Technology Assessment/Austria)</b>
Integration of modeling	Follow good modeling practices when constructing the model used to conduct the evaluation. Analysts are encouraged to consult good modeling practice guidelines as required.
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	<p>Modeling considerations:</p> <ul style="list-style-type: none"> <li>- Follow good modeling practices when constructing the model used to conduct the evaluation. Analysts are encouraged to consult good modeling practice guidelines as required.</li> <li>- Describe the model, including its scope, structure, and assumptions. Provide justification for assumptions and choices.</li> <li>- Use a model structure that is appropriate for addressing the study question. Build the model in such a way to permit updating of results as more data become available.</li> <li>- Explain and justify any causal relationships and extrapolation techniques used in the model. Base the extrapolation of data on valid techniques that reflect reasonable scientific evidence, and test through sensitivity analysis.</li> <li>- Formally validate the model, and state how this was done.</li> </ul>
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>MHRA (Medicines and Healthcare Products Regulatory Agency/UK)</b>
Integration of modeling	Models, which are typically detailed and complex formulations of the consequences of drug treatments, are required to consider disease evolution and treatment outcomes
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	Models, which are typically detailed and complex formulations of the consequences of drug treatments, are required to consider disease evolution and treatment outcomes
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	nd
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>NLM (National Library of Medicine/US)</b>
Integration of modeling	Decision models are also used to set priorities for HTA (Sassi 2003).
Modeling alongside SR	nd
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	<p>The basic steps of decision analysis are:</p> <ol style="list-style-type: none"> <li>1. Develop a model (e.g., a decision tree) that depicts the set of important choices (or decisions) and potential outcomes of these choices. For treatment choices, the outcomes may be health outcomes (health states); for diagnostic choices, the outcomes may be test results (e.g., positive or negative).</li> <li>2. Assign estimates (based on available literature) of the probabilities (or magnitudes) of each potential outcome given its antecedent choices.</li> <li>3. Assign estimates of the value of each outcome to reflect its utility or desirability (e.g., using a HRQL measure or QALYs).</li> <li>4. Calculate the expected value of the outcomes associated with the particular choice(s) leading to those outcomes. This is typically done by multiplying the set of outcome probabilities by the value of each outcome.</li> <li>5. Identify the choice(s) associated with the greatest expected value. Based on the assumptions of the decision model, this is the most desirable choice, as it provides the highest expected value given the probability and value of its outcomes.</li> <li>6. Conduct a sensitivity analysis of the model to determine if plausible variations in the estimates of probabilities of outcomes or utilities change the relative desirability of the choices. (Sensitivity analysis is used because the estimates of key variables in the model may be based on limited data or simply expert conjecture.) The assumptions and estimates of variables used in models should be validated against actual data as it becomes available, and the models should be modified accordingly. Modeling should incorporate sensitivity analyses to quantify the conditional relationships between model inputs and outputs.</li> </ol> <p>The assumptions and estimates of variables used in models should be validated against actual data as it becomes available, and the models should be modified accordingly. Modeling should incorporate sensitivity analyses to quantify the conditional relationships between model inputs and outputs.</p>
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	<p>Assign estimates of the value of each outcome to reflect its utility or desirability (e.g., using a HRQL measure or QALYs).</p> <p>Conduct a sensitivity analysis of the model to determine if plausible variations in the estimates of probabilities of outcomes or utilities change the relative desirability of the choices.</p>
Inclusion of costs	<p>Models and their results are only aids to decision-making, not statements of scientific, clinical, or economic fact. The report of any modeling study should carefully explain and document the assumptions, data sources, techniques, and software. Modelers should make clear that the findings of a model are conditional upon these components. The use of decision modeling in cost-effectiveness analysis in particular has advanced in recent years,</p>

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	with development of checklists and standards for these applications (Gold 1996; Soto 2002; Weinstein 2003).
Budget analysis done	nd
Impact on project budget	nd

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Question	AHRQ (US Agency for Healthcare Research and Quality/US)
Integration of modeling	Implicitly not always: p 26 "Out of 193 evidence reports, 10 reports and 1 supplement to a technology assessment were identified through the search process."
Modeling alongside SR	nd
Timing of modeling	<p>p ES5 "The timing of a modeling project in connection with a systematic review is important. One approach would be to have the report from the modeling study coincide with that of the systematic review. However, the results from the systematic review typically will be required to conduct the final modeling analysis. Thus, the addition of a decision model could delay the overall project. Another concern is the ability to determine the opportunity or need for a model before the project has started or before the question refinement phase has been completed. The proposal process could be augmented to include a more collaborative question refinement prior to proposal submissions, which would involve a relatively quick review of the literature to determine if there were aspects of the disease and interventions that were suitable for modeling." p 14 "The first step in the process should be to engage the stakeholder in discussions about the goals of decision modeling and how it could potentially add value to the topic being addressed (though there may be timing issues discussed below). This will likely require that the stakeholder be educated on what a decision model is, how they have been used in practice, and what their value is in this context." p 42 "When to conduct a modeling project in connection with a systematic review is a concern. Ideally, one would complete the systematic review first and then develop/refine a decision model that is designed to optimize the use of the evidence results. For example, the final results from a systematic review could inform modeling decisions about ways to categorize a disease that maximizes the use of the evidence. Or the results may indicate several options for categorizing a disease that would allow the modelers to build in different structural assumptions that could be evaluated in sensitivity analyses. This ideal situation, however, is unlikely to happen in practice and the modeling work will likely need to be completed at the same time, or close to the same time, as the systematic review. This is not an insurmountable problem and it is reasonable to assume that, with adequate interactions between the systematic review team and the modeling team, the modeling work could be done concurrently with the systematic review, with interim model parameter estimates used prior to completion of the reviews. Figure 1 illustrates this framework." p 55 "The issues surrounding the timing of when a decision analysis is conducted alongside a review pose several challenges. Ideally, a decision analysis would not be done unless it was deemed to add substantial value to the questions being addressed by the systematic review. This may not become clear until after the systematic review has begun. However, it typically takes about the same time to develop and analyze a decision model as it does to conduct a systematic review, and the final decision analysis results should incorporate the results from the review. Thus the addition of a simulation model alongside a systematic review may add time to the overall project in some cases."</p>
Use of pre-existing vs. established models	<p>p 54 "[pre-existing or established models] may not fit the question precisely and it does not allow for input from the stakeholders" p 55 "[Don't use pre-existing models in] cases where the structure of existing models is not flexible enough to simulate the interventions of interest."</p>
Model recommendations	<p>Table 21. Assessing the quality of decision and simulation models p 75 "key issues to be addressed: the scientific and technical quality of the model, the interaction between the model and the decisionmaker(s) the model is intended to inform"</p>
How SR incorporated into the model	<p>p 6 "Decision models provide a way to synthesize multiple pieces of direct evidence in cases where only indirect evidence exists on the relationship between an intervention and the health outcomes of interest. Decision models can be used to structure the linkages between the intervention and the key health outcomes, where direct evidence can be used to inform each link. Thus, even though both systematic reviews and decision models are</p>

	used to combine data, we view systematic reviews as an interpolation of the evidence with a goal of enhancing our knowledge, and decision modeling as an extrapolation of the evidence with the goal of decisionmaking."
Who conducts the model?	p 43 "Because decision modeling requires a different skill set, it is not always feasible to have the modeling work done by systematic review research teams, such as EPCs. Modeling is a multidisciplinary field that requires several disciplinary experts in order to conduct a credible modeling analysis on a wide variety of topics on timelines typical of a systematic review. It is beneficial for those conducting the modeling to have frequent interactions with researchers conducting the systematic review to ensure that the model is developed in such a way to incorporate the synthesized data, and that all relevant data are collected and synthesized to inform the model structure. In the ideal circumstance, the systematic review team and the decision analysis team would reside in the same place in order to facilitate a close working relationship."
Inclusion of quality of life	p ES3 "Models can be used to: . . . (3) incorporate data from multiple sources (e.g., clinical and health-related quality-of-life endpoints), "
Inclusion of costs	p 1 "One type of decision analysis is a cost-effectiveness analysis, which incorporates both the benefits and the costs of competing alternatives and explicitly considers a limited budget. Our report is focused on modeling more broadly and not on economic evaluations that use modeling to project costs and health benefits. Our framework would, in general, allow for inclusion of costs as an outcome."
Budget analysis done	nd
Impact on project budget	p 37 "An essential issue is the resource intensiveness of models and modeling efforts. Most interviewees with experience with models in EPC reports responded that modeling efforts could easily consume 20–40 percent of the budget for a systematic review, and thus could not be accomplished without either inclusion in the budget at project inception, or an increased budget and timeline after the question refinement phase."

Question	CAST (Centre for Applied Health Services Research and Technology Assessment, University of Southern Denmark)
Integration of modeling	The state of the art of economic evaluations carried out as part of health technology assessments do not differ remarkably from that of economic evaluations in general. A notable exception is in the design, where the majority of the HTAs completed an economic evaluation retrospectively using secondary data in the form of a literature review or a meta-analysis. These data were often put together in a decision analytical model. This picture is not seen to this extent in economic evaluation in general, and is probably due to the nature of a health technology assessment as a synthesis of clinical and other evidence gathered from a systematic literature review.
Modeling alongside SR	The majority of the HTAs completed an economic evaluation retrospectively using secondary data in the form of a literature review or a meta-analysis. These data were often put together in a decision analytical model. This picture is not seen to this extent in economic evaluation in general, and is probably due to the nature of a health technology assessment as a synthesis of clinical and other evidence gathered from a systematic literature review.
Timing of modeling	The majority of the HTAs completed an economic evaluation retrospectively using secondary data in the form of a literature review or a meta-analysis. These data were often put together in a decision analytical model.
Use of pre-existing vs. established models	nd
Model recommendations	A model is an excellent way to combine this information; usually, a decision tree or a Markov model is applied in modeling studies.
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	Economic evaluations often seek to estimate lifetime costs and consequences
Budget analysis done	nd
Impact on project budget	nd

<b>Question</b>	<b>CDE (Center for Drug Evaluation/Taiwan)</b>
Integration of modeling	nd
Modeling alongside SR	HTA team members retrieve and summarize the key issues stated in the health technology assessment or appraisal reports from the world leading HTA agencies, follows with analyzing the possible product adoptability in Taiwan, eventually conduct systematic review of published literatures before recommendations sent to BNHI.
Timing of modeling	nd
Use of pre-existing vs. established models	nd
Model recommendations	nd
How SR incorporated into the model	nd
Who conducts the model?	nd
Inclusion of quality of life	nd
Inclusion of costs	Budget Impact analysis for all parties involved was constantly conducted.
Budget analysis done	nd
Impact on project budget	nd