Appendix 4. Assessment of methodological quality of economic studies based on the QHES instrument

Bridle et al., 2004					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Systematic review and network meta-analysis
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		X	Time horizon 3 weeks
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Hospitalization costs common across all arms; costs of side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Only short-term (3-week) outcomes considered; side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		Appropriate structure for the short time horizon chosen
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**75**		

Calvert et al., 2006					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Indirect comparisons using RCTs with different study designs & populations
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	X		Sub-analyses for people with most recent episode manic vs depressive conducted
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Deterministic analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		X	Data abstraction regarding utility values unclear
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		X	18 months; discounting not required
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published data, clinical guidelines and a physician survey; costs of treating side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**53**		

Caresano et al., 2014					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Efficacy based on post-hoc analysis of 2 RCTs and further assumptions
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1		X	Post-hoc analysis of RCTs
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Time horizon 9 weeks + 5 years; annual discount rate 3.5%
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published literature and expert opinion
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		Primary measure was the QALY. Utility data were based on a combination of published data, with decrements due to side effects also considered.
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		Changes on YMRS and MADRS
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**87**		

Chisholm et al., 2005					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not reported
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Literature review of RCTs and other longitudinal studies – not reported if it was done in a systematic way; narrative synthesis and further assumptions
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Deterministic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6		X	Comparisons versus no treatment only
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Lifetime duration
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Details on the estimation of resource use and unit costs not provided; costs of side effects not considered; only intervention costs considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**59**		

Chisholm et al., 2012					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not reported
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Review of RCTs & other longitudinal studies – unclear if it was done in a systematic way; narrative synthesis and further assumptions
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Limited probabilistic sensitivity analysis; only point estimates presented
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Lifetime duration
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Details on estimation not provided; costs of side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8		X	
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**57**		

Ekman et al., 2012					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7		X	Focus of study not explicitly stated
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Selection of perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Double-blind, placebo-controlled RCTs for quetiapine, published meta-analyses and indirect comparisons; some sources unclear. RCTs in indirect comparisons not similar regarding BD phase and outcomes
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		5 years, 3.5% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	National guidelines based on expert opinion, published data and assumptions
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	(X)		Yes for study on acute depression only
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**73/67**		(acute depression / maintenance)

Fajutrao et al., 2009					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	X		
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Pooled data from 2 RCTs
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Deterministic and probabilistic analysis, but results of probabilistic analysis presented in an unclear way
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		X	Data abstraction regarding utility values unclear
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		2 years, 3.5% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published data, clinical guidelines and a physician survey; costs of treating side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**72**		

Klok et al., 2007					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Efficacy assumed to be the same across treatment options based on observation of RCT data
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Limited deterministic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6		X	Not all options and outcomes were considered when estimating ICERs
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		X	
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Time horizon 100 days; discounting not needed
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7		X	Measure of response not defined
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8		X	
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**38**		

McKendrick et al., 2007					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	X		
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Based on RCT but modelled using further assumptions
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Deterministic analysis only
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		1 year, discounting not required
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published chart review and other published sources; side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**69**		

Namjoshi et al., 2002					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	RCT over 3 weeks; before-after study over 12 months
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Student's t-tests were used
6.	Was incremental analysis performed between alternatives for resources and costs?	6	NA		Cost consequence analysis
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Comparative outcomes assessed only over 3 weeks; before-after outcomes and costs assessed over 12 months; no discounting needed
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Costs assessed for 49 weeks open-label treatment compared with 12-month pre-randomisation costs
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	NA		Cost consequence analysis based on RCT
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS	**59**			

Rajagopalan et al., 2015					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Indirect comparisons of 2 pivotal trials, using placebo as common comparator. In the quetiapine study, 19.5% of patients had bipolar II disorder, which may affect the comparability of the study populations.
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		X	Time horizon 3 months
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Costs of side effects and laboratory testing not considered; cost year not reported
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Only short-term (6 to 8-week) outcomes considered; side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**75**		

Revicki et al., 2003					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	RCT, N=120; analysis based on n=52
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Student's t-tests were used
6.	Was incremental analysis performed between alternatives for resources and costs?	6	NA		Cost-consequence analysis
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Time horizon 12 weeks; no discounting needed
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	RCT data based on n=52
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	NA		Cost consequence analysis based on RCT
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8		X	
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**49**		

Revicki et al., 2005					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Maintenance phase of a pragmatic trial; study sample size had limited power to detect moderate differences in costs
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		X	Student's t-tests were used
6.	Was incremental analysis performed between alternatives for resources and costs?	6	NA		Cost-consequence analysis
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Time horizon 12 months after discharge; discounting not needed
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	X		
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	NA		Cost consequence analysis based on RCT
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		X	
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**68**		

Sawyer et al., 2014					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Efficacy based on post-hoc analysis of 2 RCTs and further assumptions
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1		X	Post-hoc analysis of RCTs
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Time horizon 9 weeks + 5 years; annual discount rate 3.5%
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published literature and expert opinion
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		Primary measure was the QALY. Utility data were based on a combination of published data, with decrements due to side effects also considered.
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		Changes on YMRS and MADRS
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**87**		

Soares-Weiser et al., 2007					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Selection of perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Systematic review and NMA of RCTs with different study designs & populations. Differential data for people with a most recent manic vs. depressive episode based on very limited evidence
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	X		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		Lifetime, 3.5% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	National guidelines based on expert opinion, published data and further assumptions; costs of treating side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**74**		

Uttley et al., 2013; refers to NICE TA 292					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	X		
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		NMA of pivotal published and unpublished RCTs (4 studies)
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5	X		
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		3 years, 3.5% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Expert opinion
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6	X		
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**92**		

Woodward et al., 2009					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		X	Perspective not justified
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8	X		Pooled data from 2 RCTs
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic and probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		X	Data abstraction regarding utility values unclear
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		2 years, 3% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published data, clinical guidelines and a physician survey; costs of treating side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8	X		
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**77**		

Woodward et al., 2010					
No	**Questions**	**Points**	**Yes**	**No**	**Comments**
1.	Was the study objective presented in a clear, specific, and measurable manner?	7	X		
2.	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4	X		
3.	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		X	Pooled data from 2 double-blind RCTs of Que (not Que XR) linked via indirect comparisons with other RCTs with different designs & populations, identified via a non-systematic review
4.	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	NA		
5.	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	X		Deterministic & probabilistic sensitivity analysis
6.	Was incremental analysis performed between alternatives for resources and costs?	6	X		
7.	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		X	Data abstraction regarding utility values unclear
8.	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7	X		2 years, 3% annual discount rate
9.	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		X	Published data, clinical guidelines and a physician survey; costs of treating side effects not considered
10.	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term, long-term, and negative outcomes?	6		X	Side effects not considered
11.	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7	X		
12.	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	X		
13.	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	X		
14.	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	X		
15.	Were the conclusions/recommendations of the study justified and based on the study results?	8		X	
16.	Was there a statement disclosing the source of funding for the study?	3	X		
	TOTAL POINTS		**65**		