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1. Title of paper

Full title: A systematic review of economic models across the entire schizophrenia pathway

Running title: Review of economic models for schizophrenia

2. Journal Name: PharmacoEconomics

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Supplementary material

This supplementary material contains three sections. Section 1 reports the search strategy and results, Section 2 reports evidence table and Section 3 reports quality assessment results.

Section 1: Electronic search strategies

1.1 MEDLINE search strategy

Database used:

- Ovid MEDLINE(R) 1946 to March Week 4 2018,
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 02, 2018

	Search terms	Results
1	exp "schizophrenia spectrum and other psychotic disorders"/	136760
2	exp psychotic disorders/ or exp perceptual disorders/ or delusions/ or hallucinations/ or speech disorders/ or catatonia/ or paranoid disorders/	90516
3	(at risk mental state or clinical high risk or ultra high risk or psychos?s risk syndrome\$ or attenuated psychos?s syndrome).mp.	1533
4	((at risk or high risk or prodrom\$ or earl\$ or subclinic\$ or preclinic\$ or subthreshold or onset or transition\$ or convert\$) adj2 (psychos?s or psychotic or schizo\$)).mp.	7117
5	(schizo\$ or psychotic\$ or psychosis or psychoses or ((thinking or thought) adj2 (disorder\$ or disturbance\$ or problem\$)) or delusion\$ or catatoni\$ or hallucinat\$ or hebephreni\$ or oligophreni\$ or paranoi\$).mp.	224440
6	((chronic\$ or long term or persistent or serious\$ or sever\$) adj2 (mental\$ or psychiatric or psycho\$) adj2 (ill\$ or disorder\$ or disease\$ or problem\$ or disturb\$ or disable\$)).mp.	15378
7	1 or 2 or 3 or 4 or 5 or 6	259790
8	exp Cost-Benefit Analysis/	72027
9	(cost\$ adj2 (effect\$ or benefit\$ or utility or utilities or outcome\$ or consequence\$)).mp.	166166

	Search terms	Results
10	(cost\$ adj minimi\$).mp.	1229
11	8 or 9 or 10	166732
12	exp Decision Theory/ or exp Decision Making, Computer-Assisted/ or Decision Support Systems, Management/ or exp Decision Making/ or Decision Support Systems, Clinical/ or Decision Trees/ or Decision Making, Organizational/ or exp Decision Support Techniques/	388496
13	Computer Simulation/ or Patient Simulation/ or models, theoretical/ or exp models, organizational/ or exp models, statistical/ or exp models, economic/ or monte carlo method/ or Markov Chains/	657020
14	(decision adj (tree\$ or analysis or analyses or analytic\$ or support)).mp.	46519
15	((disease or mathematical or optimization or optimisation or decision\$ or economic\$ or pharmacoeconomic or simulation or cohort or Markov or Markov chain or state transition or patient level or individual level or individual sampling or event history or agent based) adj model\$).mp.	362442
16	((discrete event or discrete individual or agent based or hybrid or inverse or monte carlo or real time) adj simulation).mp.	9837
17	(system dynamics or DES).mp.	349782
18	12 or 13 or 14 or 15 or 16 or 17	1676906
19	7 and 11 and 18	290
20	(letter or news or editorial or historical article).pt.	1935389
21	19 not 20	286
22	exp animals/ not humans/	4435919
23	21 not 22	276
24	limit 23 to english language	247

1.2 EMBASE search strategy

Database used: EMBASE Classic & EMBASE (1947 to 2018 week 14)

	Search terms	Results
1	exp schizophrenia/	179615
2	exp psychosis/ or exp thinking disorder/ or exp delusion/ or exp hallucination/ or exp speech disorder/ or catatonia/ or hebephrenia/ or oligophrenia/ or paranoia/	749574
3	(at risk mental state or clinical high risk or ultra high risk or psychos?s risk syndrome\$ or attenuated psychos?s syndrome).mp.	3261
4	((at risk or high risk or prodrom\$ or earl\$ or subclinic\$ or preclinic\$ or subthreshold or onset or transition\$ or convert\$) adj2 (psychos?s or psychotic or schizo\$)).mp.	12366
5	(schizo\$ or psychotic\$ or psychosis or psychoses or ((thinking or thought) adj2 (disorder\$ or disturbance\$ or problem\$)) or delusion\$ or catatoni\$ or hallucinat\$ or hebephreni\$ or oligophreni\$ or paranoi\$).mp.	350393
6	((chronic\$ or long term or persistent or serious\$ or sever\$) adj2 (mental\$ or psychiatric or psycho\$) adj2 (ill\$ or disorder\$ or disease\$ or problem\$ or disturb\$ or disable\$)).mp.	21514
7	1 or 2 or 3 or 4 or 5 or 6	824647
8	*economic evaluation/ or exp "cost benefit analysis"/ or exp "cost effectiveness analysis"/ or exp "cost minimization analysis"/ or exp "cost utility analysis"/	206729
9	(cost\$ adj2 (effect\$ or benefit\$ or utility or utilities or outcome\$ or consequence\$)).mp.	293914
10	(cost\$ adj minimi\$).mp.	3978
11	8 or 9 or 10	297220

	Search terms	Results
12	exp decision support system/ or decision making/ or "decision tree"/ or clinical decision making/ or decision theory/ or medical decision making/	334710
13	exp simulation/ or computer model/ or individual based population model/ or population model/ or exp mathematical model/ or stochastic model/ or exp disease model/ or hidden Markov model/ or statistical model/	669682
14	(decision adj (tree\$ or analysis or analyses or analytic\$ or support)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	47638
15	((disease or mathematical or optimization or optimisation or decision\$ or economic\$ or pharmacoeconomic or simulation or cohort or Markov or Markov chain or state transition or patient level or individual level or individual sampling or event history or agent based) adj model\$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	277684
16	((discrete event or discrete individual or agent based or hybrid or inverse or monte carlo or real time) adj simulation).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	12330
17	(system dynamics or DES).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	491078
18	12 or 13 or 14 or 15 or 16 or 17	1538100
19	7 and 11 and 18	1154
20	(letter or editorial or note).pt.	2279668
21	19 not 20	1053
22	animal/	1838994

	Search terms	Results
23	exp animal experiment/	2204175
24	nonhuman/	5393773
25	(rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.	6050564
26	22 or 23 or 24 or 25	8800912
27	exp human/	19609898
28	human experiment/	402383
29	27 or 28	19611482
30	26 not (26 and 29)	6648319
31	21 not 30	1020
32	limit 31 to english language	964

1.3 PsycINFO search strategy

Database used: PsycINFO (1806 to March Week 4 2018)

	Search terms	Results
1	exp Schizophrenia/	84386
2	exp psychosis/ or exp thought disturbances/ or exp delusions/ or exp hallucinations/ or exp speech disorders/ or exp catatonia/ or exp paranoia/	138246
3	(at risk mental state or clinical high risk or ultra high risk or psychos?s risk syndrome\$ or attenuated psychos?s syndrome).mp.	1579
4	((at risk or high risk or prodrom\$ or earl\$ or subclinic\$ or preclinic\$ or subthreshold or onset or transition\$ or convert\$) adj2 (psychos?s or psychotic or schizo\$)).mp.	8313
5	(schizo\$ or psychotic\$ or psychosis or psychoses or ((thinking or thought) adj2 (disorder\$ or disturbance\$ or problem\$)) or delusion\$ or catatoni\$ or hallucinat\$ or hebephreni\$ or oligophreni\$ or paranoi\$).mp.	195990
6	((chronic\$ or long term or persistent or serious\$ or sever\$) adj2 (mental\$ or psychiatric or psycho\$) adj2 (ill\$ or disorder\$ or disease\$ or problem\$ or disturb\$ or disable\$)).mp.	20652
7	1 or 2 or 3 or 4 or 5 or 6	232113
8	(cost\$ adj2 (effect\$ or benefit\$ or utility or utilities or outcome\$ or consequence\$)).mp.	22966
9	(cost\$ adj minimi\$).mp.	137
10	8 or 9	23069
11	exp Decision Support Systems/ or exp Decision Making/ or exp Decision Theory/ or exp Management Decision Making/	97733
12	exp simulation/ or models/	111446
13	(decision adj (tree\$ or analysis or analyses or analytic\$ or support)).mp.	7011

	Search terms	Results
14	((disease or mathematical or optimization or optimisation or decision\$ or economic\$ or pharmacoeconomic or simulation or cohort or Markov or Markov chain or state transition or patient level or individual level or individual sampling or event history or agent based) adj model\$).mp.	22754
15	((discrete event or discrete individual or agent based or hybrid or inverse or monte carlo or real time) adj simulation).mp.	1493
16	(system dynamics or DES).mp.	31679
17	11 or 12 or 13 or 14 or 15 or 16	242172
18	7 and 10 and 17	144
19	(editorial or letter or dissertation or abstract).dt.	521331
20	18 not 19	140
21	(animal or animals or rat or rats or mouse or mice or hamster or hamsters or dog or dogs or cat or cats or bovine or sheep or ovine or pig or pigs).ab,ti,id,de.	331981
22	20 not 21	132
23	limit 22 to english language	121

1.4 NHS Economic Evaluation Database (NHSEED) and the Health Technology Assessment Database

(HTA) search strategy

Database used: NHSEED and HTA accessed via Cochrane library interface

(<http://onlinelibrary.wiley.com/cochranelibrary/search>) on 23/June/2015

	Search terms	Results
1	MeSH DESCRIPTOR Schizophrenia Spectrum and Other Psychotic Disorders EXPLODE ALL TREES IN NHSEED,HTA	286
2	MeSH DESCRIPTOR Perceptual Disorders EXPLODE ALL TREES IN NHSEED,HTA	7
3	MeSH DESCRIPTOR Delusions EXPLODE ALL TREES IN NHSEED,HTA	1
4	MeSH DESCRIPTOR Hallucinations EXPLODE ALL TREES IN NHSEED,HTA	5
5	MeSH DESCRIPTOR Speech Disorders EXPLODE ALL TREES IN NHSEED,HTA	23
6	MeSH DESCRIPTOR Catatonia EXPLODE ALL TREES IN NHSEED,HTA	3
7	MeSH DESCRIPTOR Paranoid Disorders EXPLODE ALL TREES IN NHSEED,HTA	0
8	(at risk mental state or clinical high risk or ultra high risk or psychos*s risk syndrome* or attenuated psychos*s syndrome) IN NHSEED, HTA	1
9	((at risk or high risk or prodrom* or earl* or subclinic* or preclinic* or subthreshold or onset or transition* or convert*) adj2 (psychos*s or psychotic or schizo*)) IN NHSEED, HTA	14
10	((schizo* or psychotic* or psychosis or psychoses or ((thinking or thought) adj2 (disorder* or disturbance* or problem*)) or delusion* or catatoni* or hallucinat* or hebephreni* or oligophreni* or paranoi*)) IN NHSEED, HTA	432

Search terms	Results
11 (((chronic* or long term or persistent or serious* or sever*) adj2 (mental* or psychiatric or psycho*) adj2 (ill* or disorder* or disease* or problem* or disturb* or disable*))) IN NHSEED, HTA	95
12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	510
13 MeSH DESCRIPTOR Decision Support Techniques EXPLODE ALL TREES IN NHSEED,HTA	1314
14 MeSH DESCRIPTOR Decision Making EXPLODE ALL TREES IN NHSEED,HTA	266
15 MeSH DESCRIPTOR Decision Making, Computer-Assisted EXPLODE ALL TREES IN NHSEED,HTA	338
16 MeSH DESCRIPTOR Decision Making, Organizational EXPLODE ALL TREES IN NHSEED,HTA	13
17 MeSH DESCRIPTOR Decision Support Systems, Clinical EXPLODE ALL TREES IN NHSEED,HTA	50
18 MeSH DESCRIPTOR Decision Support Systems, Management EXPLODE ALL TREES IN NHSEED,HTA	1
19 MeSH DESCRIPTOR Decision Theory EXPLODE ALL TREES IN NHSEED,HTA	857
20 MeSH DESCRIPTOR Computer Simulation IN NHSEED,HTA	468
21 MeSH DESCRIPTOR Patient Simulation IN NHSEED,HTA	13
22 MeSH DESCRIPTOR Models, Economic EXPLODE ALL TREES IN NHSEED,HTA	1990
23 MeSH DESCRIPTOR Models, Theoretical EXPLODE ALL TREES IN NHSEED,HTA	3159
24 MeSH DESCRIPTOR Markov Chains EXPLODE ALL TREES IN NHSEED,HTA	2018

	Search terms	Results
25	MeSH DESCRIPTOR Monte Carlo Method EXPLODE ALL TREES IN NHSEED,HTA	414
26	(((decision adj (tree* or analysis or analyses or analytic* or support))) IN NHSEED, HTA	3608
27	(((disease or mathematical or optimization or optimisation or decision* or economic* or pharmacoeconomic or simulation or cohort or Markov or Markov chain or state transition or patient level or individual level or individual sampling or event history or agent based) adj model*)) IN NHSEED, HTA	5705
28	(((discrete event or discrete individual or agent based or hybrid or inverse or monte carlo or real time) adj simulation)) IN NHSEED, HTA	856
29	((system dynamics or DES)) IN NHSEED, HTA	625
30	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	8891
31	#12 AND #30	130
32	(English:lp) IN NHSEED, HTA	21864
33	#31 AND #32	91

Section 2: Evidence table

2.1 Evidence table for studies assessing different antipsychotics versus each other, placebo or nothing

Table 1: Evidence table for studies assessing different antipsychotics versus each other, placebo or nothing

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
Aigbogun <i>et al.</i> [1]	US	CUA	Third-party payer	1-year	Decision tree	Patients with stable schizophrenia	<ul style="list-style-type: none"> Oral brexpiprazole Oral cariprazine Oral lurasidone 	US dollar \$30,000 per QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Brexpiprazole > cariprazine > lurasidone</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Brexpiprazole: Dominant Cariprazine: Dominated lurasidone: Dominated <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> Brexpiprazole: 1.00 Cariprazine: 0.00 lurasidone: 0.00 	Yes, Otsuka America Pharmaceutical and Lundbeck	No
Ascher-Svanum <i>et al.</i> [2]	US	CUA	Third-party payer	1-year	Micro-simulation	Stable adult patients treated for schizophrenia	<ul style="list-style-type: none"> Olanzapine SOT (standard oral tablets) Olanzapine ODT (orally disintegrating antipsychotic tablets) Risperidone SOT Risperidone ODT Aripiprazole SOT Aripiprazole ODT 	US dollar \$50,000 per QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Olanzapine ODT > Olanzapine SOT > Risperidone SOT > Risperidone ODT > Aripiprazole ODT > Aripiprazole SOT</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Olanzapine ODT: Base case Olanzapine SOT: \$19,643 per QALY Risperidone SOT: \$39,966 Risperidone ODT: Dominated Aripiprazole ODT: Dominated Aripiprazole SOT: Dominated <p><u>Probability of being cost-effective:</u> Cannot be calculated based on reported data.</p>	Yes, Eli Lilly	No
Beard <i>et al.</i> [3]	Germany	CUA	Healthcare system	1-year	Markov model	Atypical naive patients with a history of relapsing schizophrenia, without other concurrent psychotic diagnoses, currently suffering from an acute episode of schizophrenia, haven't received SGA before	<p>Different sequences of atypicals:</p> <ul style="list-style-type: none"> Oral olanzapine followed by oral risperidone Oral risperidone followed by oral olanzapine 	Not reported	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Oral olanzapine followed by oral risperidone > Oral risperidone followed by oral olanzapine</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Oral olanzapine followed by oral risperidone (dominant) Oral risperidone followed by oral olanzapine (dominated) <p><u>Probability of being cost-effective:</u> Not reported</p>	Yes, Eli Lilly	No
Bernardo <i>et al.</i> [4]	Spain	CEA	Healthcare system	1-year	Not reported	Spanish adult patients with stable chronic schizophrenia	<ul style="list-style-type: none"> Oral ziprasidone Placebo 	€2,830 per relapse	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Oral ziprasidone > Placebo</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Placebo: Base case Ziprasidone: €186 per relapse avoided <p><u>Probability of being cost-effective:</u> Not reported</p>	Yes, Pfizer	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
Bounthavong <i>et al.</i> [5]	US	CEA	Healthcare system	16 weeks	Decision tree	Acute patients with a diagnosis of schizophrenia or schizoaffective disorders, over 18 years of age	<ul style="list-style-type: none"> Oral olanzapine Oral risperidone Oral haloperidol 	Not reported	<u>Cost-effectiveness rankings as reported by the authors:</u> Oral risperidone>Oral olanzapine>Oral haloperidol <u>ICER:</u> <ul style="list-style-type: none"> Olanzapine: Dominated Risperidone: Dominant Haloperidol: Dominated <u>Probability of being cost-effective:</u> Not reported	No	No
Chue <i>et al.</i> [6]	Canada	CEA	Healthcare system	5-year	Discrete event simulation (DES)	High-risk, non-compliant patients with schizophrenia. Only fully recovered patients, who suffered multiple episodes (two or more relapses) with no or minor impairment between episodes, and partly recovered patients, who suffered (increasing) impairment with each of several episodes and did not return to normal between multiple episodes were included.	<ul style="list-style-type: none"> Haloperidol LAI Risperidone LAI Oral risperidone 	Not reported	<u>Cost-effectiveness rankings as reported by the authors:</u> Risperidone LAI>Haloperidol LAI <u>ICER:</u> <ul style="list-style-type: none"> Haloperidol LAI: Dominated Risperidone LAI: Dominant Oral risperidone: Dominated <u>Probability of being cost-effective:</u> Not reported	Yes, Janssen	No
Citrome <i>et al.</i> [7]	US	CEA	Healthcare system	1-year	Decision tree	Stable patients with schizophrenia in the US	<ul style="list-style-type: none"> Aripiprazole LAI Paliperidone LAI 	Not reported	<u>Cost-effectiveness rankings as reported by the authors:</u> Aripiprazole LAI>Paliperidone LAI <u>ICER:</u> <ul style="list-style-type: none"> Aripiprazole LAI: US\$13,280/relapse averted Paliperidone LAI: base case <u>Probability of being cost-effective:</u> Not reported	Yes, Lundbeck	No
Damen <i>et al.</i> [8]	Sweden	CUA	Third-party payer	5-year	DES	Patients who experience a relapse of schizophrenia	Atypicals with different compliance level	Swedish kronor 900,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> High compliance rate result in cost savings and QALY gains <u>ICER:</u> <ul style="list-style-type: none"> Atypicals with higher compliance rate: Dominant Atypicals with low compliance rate: Dominated <u>Probability of being cost-effective:</u> Not reported	Yes, Janssen	No
Davies <i>et al.</i> [9]	UK	CUA	Healthcare system	10-year	Markov	Stable patients with schizophrenia	12 alternative treatment sequences each containing two of four oral atypical antipsychotics (aripiprazole (ARI), olanzapine (OLZ), quetiapine (QTP) and risperidone (RSP)), followed by clozapine	UK pounds £30,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> ARI-RSP>RSP-ARI>RSP-OLZ>OLZ-RSP>QTP-RSP>ARI-OLZ>RSP-QTP>OLZ-ARI>ARI-QTP>QTP-ARI>QTP-OLZ>OLZ-QTP <u>ICER:</u> <ul style="list-style-type: none"> ARI-RSP: £9,440 per QALY 	Yes, Bristol-Myers Squibb	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> RSP-ARI: Dominated ARI-QTP: Dominated QTP-RSP: Dominated QTP-ARI: Dominated ARI-OLZ: Dominated RSP-QTP: Dominated RSP-OLZ: Base case OLZ-ARI: Dominated OLZ-RSP: Dominated QTP-OLZ: Dominated OLZ-QTP: Dominated <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> ARI-RSP: 0.45 RSP-OLZ: 0.20 RSP-ARI: 0.18 <u>ARI-OLZ: 0.09</u> <u>OLZ-RSP:0.08</u> 		
De Graeve <i>et al.</i> [10]	Belgium	CEA	Healthcare system	2-year	Decision tree	Young schizophrenic patients who had been treated for 1 year and whose disease had not been diagnosed for longer than 5 years	<ul style="list-style-type: none"> Risperidone LAI Oral olanzapine Haloperidol LAI 	Not reported	<p><u>Cost-effectiveness rankings as reported by the authors:</u></p> <p>Risperidone LAI>Oral olanzapine>Haloperidol LAI</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Risperidone LAI: Dominant Oral olanzapine: Dominated Haloperidol LAI: Dominated <p><u>Probability of being cost-effective:</u></p> <p>Not reported</p>	Yes, Janssen	No
Dilla <i>et al.</i> [11]	Spain	CUA	Healthcare system	5-year	DES	Schizophrenia patients who had earlier responded to oral medication and have a history of relapse due to adherence problems	<ul style="list-style-type: none"> Olanzapine LAI Risperidone LAI 	Euros €30,000/QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u></p> <p>Olanzapine LAI>Risperidone LAI</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Olanzapine LAI: Dominant Risperidone LAI: Dominated <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> Olanzapine LAI: 0.72 Risperidone: 0.28 	Yes, Eli Lilly	No
Druais <i>et al.</i> [12]	France	CUA	Third-party payer	5-year	Markov model	Adult patients with schizophrenia in France stabilised after a schizophrenic episode	<ul style="list-style-type: none"> Paliperidone LAI Risperidone LAI Aripiprazole LAI Olanzapine LAI Haloperidol LAI Oral olanzapine 	Euros €30,000/QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u></p> <p>Paliperidone LAI>Risperidone LAI>Aripiprazole LAI>Oral olanzapine>Haloperidol LAI>Olanzapine LAI</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Paliperidone LAI: €2,411 per QALY Risperidone LAI: €4,770,018 Aripiprazole LAI: Dominated Olanzapine LAI: Dominated Haloperidol LAI: Dominated Oral olanzapine: base case <p><u>Probability of being cost-effective (based on a threshold of €8,000 per QALY):</u></p> <ul style="list-style-type: none"> Paliperidone LAI: 0.51 Risperidone LAI:0.23 	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Aripiprazole LAI: 0.13 Olanzapine LAI: 0.04 Haloperidol LAI: 0.06 Oral olanzapine: 0.03 		
Einarson <i>et al.</i> [13]	Netherlands	CUA	Third-party payer	1-year	Decision tree	Stable patients with chronic schizophrenia	<ul style="list-style-type: none"> Paliperidone 3-monthly injection (PP3M) Paliperidone palmitate 1-monthly injection (PP1M) Haloperidol decanoate therapy (HAL-LAT) Risperidone microspheres therapy (RIS-LAT) Oral olanzapine (OLZ) 	Euros €10,000-80,000 per QALY	<p>Cost-effectiveness rankings as reported by the authors: PP3M > PP1M > RIS-LAT > HAL-LAT > OLZ</p> <p>ICER:</p> <ul style="list-style-type: none"> PP3M: Dominant PP1M: Dominated RIS-LAT: Dominated HAL-LAT: Dominated OLZ: Dominated <p>Probability of being cost-effective: The probability for PP3M to be dominant is 0.846.</p>	Yes, Janssen	No
Einarson <i>et al.</i> [14]	Portugal	CUA	Healthcare system	1-year	Decision tree	Patients with chronic, 'revolving door' schizophrenia patients	<ul style="list-style-type: none"> Paliperidone LAI Haloperidol LAI Risperidone LAI Oral olanzapine 	Euros €30,000/QALY	<p>Cost-effectiveness rankings as reported by the authors: Paliperidone LAI > Oral olanzapine > Haloperidol LAI > Risperidone LAI</p> <p>ICER:</p> <ul style="list-style-type: none"> Paliperidone LAI: €14,247 per QALY Haloperidol LAI: Dominated Risperidone LAI: Dominated Oral olanzapine: Base case <p>Probability of being cost-effective: The probability for paliperidone LAI to be more cost-effective than oral olanzapine is over 0.99</p>	Yes, Janssen	No
Einarson <i>et al.</i> [15]	Finland	CUA	Healthcare system	1-year	Decision tree	Patients with chronic, relapsing SCZ in Finland who had difficulty with adherence to oral AP and therefore require LAI	<ul style="list-style-type: none"> Aripiprazole LAI Paliperidone LAI Olanzapine LAI Risperidone-LAI 	Euros €24,800 QALY	<p>Cost-effectiveness rankings as reported by the authors: Paliperidone LAI > Aripiprazole LAI > Risperidone LAI > Olanzapine LAI</p> <p>ICER:</p> <ul style="list-style-type: none"> Aripiprazole LAI: Dominated Paliperidone LAI: Dominant Olanzapine LAI: Dominated Risperidone-LAI: Dominated <p>Probability of being cost-effective: The probability for paliperidone LAI to be more cost-effective than was cost-effective than aripiprazole LAI, risperidone-LAI and olanzapine LAI is 77.2%, 86.1%, and 96.3%.</p>	Yes, Janssen	No
Einarson <i>et al.</i> [16]	Sweden	CUA	Societal	1-year	Decision tree	Persons in Sweden having chronic schizophrenia with recurring relapses	<ul style="list-style-type: none"> Paliperidone (PP) long acting injectable (LAI)– 	Not reported	<p>Cost-effectiveness rankings as reported by the authors:</p>	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
							<ul style="list-style-type: none"> olanzapine (OLZ)-LAI • OLZ-LAI –PP-LAI • Risperidone (RIS)-LAI – Haloperidol (HAL)-LAI • HAL-LAI –oral-OLZ • Oral OLZ –HAL-LAI 		PP-LAI – OLZ-LAI is most cost-effective than all other strategies <u>ICER:</u> PP-LAI – OLZ-LAI dominates all other strategies <u>Probability of being cost-effective:</u> Pairwise PSA showed that the probability for PP-LAI – OLZ-LAI to dominate other strategies is over 0.50.		
Einarson <i>et al.</i> [17]	Finland		Third-party payer	1-year	Decision tree	Persons had stable chronic schizophrenia and were receiving LAIs because of frequent problems adhering to their drug regimens.	<ul style="list-style-type: none"> • Paliperidone (PP) LAI • Olanzapine (OLZ) LAI • Risperidone (RIS) LAI 	Euros €23,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> PP-LAI>OLZ-LAI>RIS-LAI-OLZ-LAI>OLZ-LAI-PP-LAI <u>ICER:</u> <ul style="list-style-type: none"> • PP-LAI-OLZ-LAI: Dominant • RIS-LAI-OLZ-LAI: Dominated • OLZ-LAI-PP-LAI: Dominated <u>Probability of being cost-effective:</u> Pairwise PSA showed that the probability for PP-LAI-OLZ-LAI to dominate other strategies is over 0.77.	Yes, Janssen	No
Einarson <i>et al.</i> [18]	Norway	CUA	Healthcare system	1-year	Decision tree	Persons with chronic schizophrenia who had a history of multiple relapses and hospitalisations (i.e. at least twice in the past). At baseline, they were outpatients with stable disease receiving average doses of medication and had no other chronic or acute diseases.	<ul style="list-style-type: none"> • Paliperidone LAI • Olanzapine LAI 	Norwegian kroner 180,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> Paliperidone LAI > olanzapine LAI <u>ICER:</u> <ul style="list-style-type: none"> • Paliperidone LAI: Dominant • Olanzapine LAI: Dominated <u>Probability of being cost-effective:</u> The probability for Paliperidone LAI to dominate Olanzapine LAI is 0.545.	Yes, Janssen	No
Einarson <i>et al.</i> [19]	Czech Republic	CUA	Healthcare system	1-year	Decision tree	Persons had stable chronic schizophrenia and were receiving LAIs because of frequent problems adhering to their drug regimens.	<ul style="list-style-type: none"> • Paliperidone LAI • Olanzapine LAI • Risperidone LAI 	Euros €30,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> Paliperidone LAI > risperidone LAI > olanzapine LAI <u>ICER:</u> <ul style="list-style-type: none"> • Paliperidone LAI: Dominant • Olanzapine LAI: Dominated • Risperidone LAI: Dominated <u>Probability of being cost-effective:</u> Pairwise PSA showed that the probability for Paliperidone LAI to dominate other strategies is over 0.90.	Yes, Janssen	No
Einarson <i>et al.</i> [20]	Greece	CUA	Healthcare system	1-year	Decision tree	Patients having chronic schizophrenia with multiple relapses, frequent hospitalizations, and problems with adherence to	<ul style="list-style-type: none"> • Paliperidone LAI • Risperidone LAI 	Not reported	<u>Cost-effectiveness rankings as reported by the authors:</u> Paliperidone LAI > risperidone LAI <u>ICER:</u> <ul style="list-style-type: none"> • Paliperidone LAI: Dominant 	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
						prescribed medications. At initiation of the analysis, all patients were stable and treated as outpatients with maintenance doses of their LAIs, no other chronic or acute diseases			<ul style="list-style-type: none"> Risperidone LAI: <u>Dominated</u> <u>Probability of being cost-effective:</u> Paliperidone LAI: 0.746 Risperidone LAI: 0.254 		
Furiak <i>et al.</i> [21]	US	CUA	Third-party payer	1-year	Micro-simulation	Outpatients with schizophrenia who have been non-adherent or partially adherent with oral antipsychotics	<ul style="list-style-type: none"> Olanzapine LAI risperidone LAI paliperidone LAI haloperidol LAI oral olanzapine 	US dollars \$50,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> Olanzapine LAI> oral olanzapine>Risperidone LAI>Paliperidone LAI>Haloperidol LAI <u>ICER</u> <ul style="list-style-type: none"> Olanzapine LAI: \$26,824 per QALY risperidone LAI: Dominated paliperidone LAI: Dominated haloperidol LAI: Dominated oral olanzapine: base case <u>PSA results</u> Pairwise PSA showed that the probability for Olanzapine LAI to be more cost-effective than the other strategies is over 0.92.	Yes, Eli Lilly	No
Furiak <i>et al.</i> [22]	US	CUA	Third-party payer	1-year	Micro-simulation	Community-dwelling adult patients with schizophrenia who had a history of schizophrenia	<ul style="list-style-type: none"> Oral olanzapine Oral risperidone Oral quetiapine Oral ZSD Oral ARI 	US dollars \$50,000 – 100,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> Oral olanzapine>Oral risperidone>Oral ZIP>Oral ARI>Oral quetiapine <u>ICER</u> <ul style="list-style-type: none"> Oral olanzapine: Dominant Oral risperidone: Dominated Oral quetiapine: Dominated Oral ZSD: Dominated Oral ARI: Dominated <u>PSA results</u> The probability for oral olanzapine LAI to be cost-effective than the other strategies is over 0.73.	Yes, Eli Lilly	No
Garcia-Ruiz <i>et al.</i> [23]	Spain	CUA	Third-party payer	1-year	Decision tree	Stable patients with schizophrenia	<ul style="list-style-type: none"> Oral amisulpride Oral aripiprazole Oral olanzapine Oral paliperidone extended release Oral risperidone Oral haloperidol 	Euros €30,000 per QALY	<u>Cost-effectiveness rankings as reported by the authors:</u> Oral paliperidone extended release > Oral risperidone > Oral olanzapine> Oral haloperidol > Oral Amisulpride > Oral Aripiprazole <u>ICER</u> <ul style="list-style-type: none"> Oral amisulpride: Dominated Oral aripiprazole: Dominated Oral olanzapine: Dominated Oral paliperidone extended release: Dominant 	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Oral risperidone: Dominated Oral haloperidol: Dominated <p><u>PSA results</u> Not reported</p>		
Geitona <i>et al.</i> [24]	Greece	CEA	Healthcare system	1-year	Decision tree	Patients who suffer from schizophrenia with acute exacerbation	<ul style="list-style-type: none"> Oral paliperidone extended release Oral risperidone Oral olanzapine Oral quetiapine Oral ARI Oral ZSD 	Not reported	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Oral paliperidone extended release > Oral olanzapine > Oral risperidone > Oral haloperidol > Oral quetiapine, oral amisulpride and oral ziprasidone</p> <p><u>ICER</u> Oral paliperidone extended release dominates all other strategies.</p> <p><u>PSA results</u> Not reported</p>	Yes, Janssen	No
Graham <i>et al.</i> [25]	US	CUA	Third-party payer	1-year	Decision tree	Acute schizophrenia patients	<ul style="list-style-type: none"> Oral olanzapine Oral ziprasidone 	US dollars \$50,000 per QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Oral olanzapine followed by oral risperidone > Oral olanzapine followed by oral ziprasidone > Oral ziprasidone followed by oral risperidone > oral ziprasidone followed by oral olanzapine</p> <p><u>ICER</u> Oral olanzapine followed by oral risperidone dominates all other strategies.</p> <p><u>PSA results</u> Pairwise PSA showed that the probability for olanzapine pathway (i.e. using olanzapine as the first-line antipsychotic) to be cost-effective is over 0.55.</p>	Yes, Eli Lilly	No
Heeg <i>et al.</i> [26]	Portugal	CEA	Healthcare system and social care	5-year	DES	Patients with schizophrenia who experience multiple episodes of acute psychopathology, excluding the first episode, and continuously psychotic patients.	<ul style="list-style-type: none"> Haloperidol LAI Risperidone LAI Oral risperidone 	Not reported	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Risperidone LAI is more cost-effective than the other strategies</p> <p><u>ICER</u> Risperidone LAI dominates other strategies</p> <p><u>PSA results</u> Not reported</p>	Yes, Janssen	No
Heeg <i>et al.</i> [27]	UK	CUA	Healthcare system and social care	5-year	DES	Patients suffering an episode for which the care of a psychiatrist is sought. It is assumed the patient is presenting early on in the course of the illness, but it is not the first episode of psychosis (as distinct from first episode of schizophrenia). Patients may not be treatment naïve	<ul style="list-style-type: none"> Oral typicals Oral atypicals 	UK pounds £20,000-30,000 per QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u> Oral atypicals > Oral typicals</p> <p><u>ICER</u> Oral atypicals dominates oral typicals</p> <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> Oral typicals (0.982) Oral atypicals (0.018) 	Yes, Janssen	No
Hensen <i>et al.</i> [28]	Sweden	CUA	Healthcare system	5-year	DES	High-risk non-compliant schizophrenia population, and the general	<ul style="list-style-type: none"> High risk non-compliant population: risperidone LAI vs haloperidol LAI 	Euros €43,300 per QALY	<p><u>Cost-effectiveness rankings as reported by the authors:</u></p> <ul style="list-style-type: none"> High-risk non-compliant schizophrenia 	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
						schizophrenia population	<ul style="list-style-type: none"> General schizophrenia population: risperidone LAI vs oral olanzapine 		<p>population: risperidone LAI>haloperidol LAI.</p> <ul style="list-style-type: none"> General schizophrenia population: risperidone LAI>oral olanzapine <p><u>ICER</u></p> <ul style="list-style-type: none"> High-risk non-compliant schizophrenia population: risperidone LAI dominates haloperidol LAI. General schizophrenia population: risperidone LAI dominates oral olanzapine <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> High-risk non-compliant schizophrenia population: risperidone LAI (1.00), haloperidol LAI (0.00) General schizophrenia population: risperidone LAI (0.78), oral olanzapine (0.22) 		
Jukic <i>et al.</i> [29]	Croatia	CUA	Third-party payer	1-year	Decision tree	Persons with stable chronic schizophrenia but who had a history of relapses and hospitalizations	<ul style="list-style-type: none"> Paliperidone LAI Risperidone LAI olanzapine LAI 	Not reported	<p><u>Cost-effectiveness ranking reported by the authors:</u></p> <p>Paliperidone LAI>risperidone LAI>olanzapine LAI</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Paliperidone LAI: Dominant Risperidone LAI: Dominated olanzapine LAI: Dominated <p><u>Probability of being cost-effective</u></p> <p>Pairwise PSA showed that the probability for Paliperidone LAI to be more cost-effective than other strategies is over 0.77</p>	Yes, Janssen	No
Kasteng <i>et al.</i> [30]	Sweden	CUA	Societal	Lifetime	Markov model	Patients with schizophrenia, with a mean age of 38 years at baseline	<ul style="list-style-type: none"> Oral aripiprazole Oral olanzapine 	Swedish kronor 500,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u></p> <p>Oral aripiprazole>Oral olanzapine</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Oral aripiprazole: Dominant Oral olanzapine: Dominated <p><u>Probability of being cost-effective</u></p> <ul style="list-style-type: none"> Oral aripiprazole: 0.77 Oral olanzapine: 0.23 	Yes, Bristol-Myers Squibb	No
Kim <i>et al.</i> [31]	South Korea	CUA	Healthcare system	5-year	Markov model	Patients with treatment-resistant schizophrenia requiring hospitalization	<ul style="list-style-type: none"> Oral sertindole Oral risperidone Oral olanzapine Oral quetiapine 	Not reported	<p><u>Cost-effectiveness ranking reported by the authors:</u></p> <p>Oral risperidone>Oral quetiapine>Oral sertindole>Oral olanzapine</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Oral sertindole: base case Oral risperidone: Korean won 710 million per QALY 	Yes, Lundbeck	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Oral olanzapine: Dominant Oral quetiapine: Korean won 1,600 million per QALY Probability of being cost-effective Not reported		
Kim <i>et al.</i> [32]	Norway	CEA	Third-party payer	1-year	Decision tree	Schizophrenia patients with acute episode	<ul style="list-style-type: none"> Oral olanzapine Oral risperidone 	Not reported	Cost-effectiveness ranking reported by the authors: Oral olanzapine>Oral risperidone ICER: <ul style="list-style-type: none"> Oral olanzapine: Dominant Oral risperidone: Dominated Probability of being cost-effective <ul style="list-style-type: none"> Oral olanzapine: 0.671 Oral risperidone: 0.329 	Not reported	No
Lachaine <i>et al.</i> [33]	Canada	CUA	Societal	5-year	Markov model	Moderate-to-severe SCZ and onset at age 40 years	<ul style="list-style-type: none"> Oral asenapine Oral olanzapine 	Canadian dollars \$50,000 per QALY	Cost-effectiveness ranking reported by the authors: Oral asenapine>Oral olanzapine ICER: <ul style="list-style-type: none"> Oral asenapine: Dominant Oral olanzapine: Dominated Probability of being cost-effective: <ul style="list-style-type: none"> Oral asenapine: 1.00 Oral olanzapine: 0.00 	Yes, Lundbeck	No
Laux <i>et al.</i> [34]	Germany	CUA	Third-party payer	5-year	DES	Schizophrenia patients with multiple relapses who experience total or partial recovery between episodes. Subgroup analyses considered patients with a relatively high risk of non-compliance to oral atypical agents and those with more severe disease.	<ul style="list-style-type: none"> Risperidone LAI Haloperidol LAI Oral olanzapine 	Not reported	Cost-effectiveness ranking reported by the authors: Risperidone LAI>Haloperidol LAI >Oral olanzapine ICER: <ul style="list-style-type: none"> Risperidone LAI: Dominant Haloperidol LAI: Dominated Oral olanzapine: Dominated Probability of being cost-effective: Not reported	Yes, Janssen	No
Lin <i>et al.</i> [35]	Singapore	CUA	Healthcare system	Lifetime	Markov model	Patients with remitted schizophrenia in Singapore	<ul style="list-style-type: none"> Oral amisulpride Oral aripiprazole Oral chlorpromazine Oral haloperidol Oral olanzapine Oral paliperidone Oral quetiapine Oral risperidone Oral sulphiride Oral trifluoperazine Oral ziprasidone 	Singapore dollars, \$70,000 per QALY	Cost-effectiveness ranking reported by the authors: Oral olanzapine>Oral risperidone>Oral trifluoperazine>Oral sulphiride>Oral haloperidol>Oral amisulpride>Oral quetiapine>Oral chlorpromazine>Oral paliperidone>Oral ziprasidone>Oral aripiprazole ICER: Olanzapine dominates all other strategies. Probability of being cost-effective: <ul style="list-style-type: none"> Oral olanzapine: 0.75 Oral sulphiride: 0.20 Oral risperidone: 0.03 	Not reported	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Other interventions: 0.00 		
Lindner <i>et al.</i> [36]	Brazil	CUA	Healthcare system	5-year	Markov model	Patients with chronic schizophrenia in need of continuous outpatient treatment	<ul style="list-style-type: none"> Oral haloperidol Oral risperidone Oral olanzapine 	Not reported	<p>Cost-effectiveness ranking reported by the authors: Oral risperidone>Oral haloperidol>Oral olanzapine</p> <p>ICER:</p> <ul style="list-style-type: none"> Oral haloperidol: base case Oral risperidone: \$39,890 per QALY Oral olanzapine: \$1,329,394 per QALY <p>Probability of being cost-effective: Not reported</p>	Not reported	No
Lindstrom <i>et al.</i> [37]	Sweden	CUA	Third-party payer or societal	5-year	Markov model	Schizophrenia patients experiencing intolerance to their antipsychotic treatment during an episode of psychopathology requiring psychiatric services	<ul style="list-style-type: none"> Oral sertindole Oral olanzapine Oral risperidone Oral aripiprazole Oral haloperidol 	Swedish kroner: 344,000 per QALY	<p>Cost-effectiveness ranking reported by the authors: Oral sertindole>Oral risperidone>Oral olanzapine>Oral haloperidol>Oral Aripiprazole</p> <p>ICER: Oral sertindole dominates all other strategies.</p> <p>Probability of being cost-effective: Oral sertindole: 0.86</p>	Yes, Lundbeck	No
Lubinga <i>et al.</i> [38]	Uganda	CUA	Societal	Lifetime	Markov model	A hypothetical cohort of 25-years-old schizophrenia patients in the residual state on their first antipsychotics	<ul style="list-style-type: none"> Oral chlorpromazine Oral haloperidol Oral olanzapine Oral risperidone Oral Quetiapine 	US dollar \$547 per QALY	<p>Cost-effectiveness ranking reported by the authors: Oral risperidone>Oral haloperidol>Oral olanzapine>Oral Chlorpromazine>Oral Quetiapine</p> <p>ICER:</p> <ul style="list-style-type: none"> Oral chlorpromazine: \$3,933 per QALY Oral haloperidol: \$2,667 per QALY Oral olanzapine: Dominated Oral risperidone: Base case Oral Quetiapine: Dominated <p>Probability of being cost-effective: Oral risperidone: 0.85</p>	Not reported	No
Magnus <i>et al.</i> [39]	Australia	CUA	Healthcare system	Lifetime	Markov model	Established schizophrenia, defined by ICD-10 codes and includes paranoid, hebephrenic, catatonic, undifferentiated, schizoaffective, delusional disorder and other non-organic nonaffective psychotic disorders. Patient subgroups: <ul style="list-style-type: none"> Patients experiencing adverse events of typicals Treatment-resistant schizophrenia 	<ul style="list-style-type: none"> Oral typical Oral risperidone Oral olanzapine Oral clozapine 	Australian dollars \$50,000/DALY	<p>Cost-effectiveness ranking reported by the authors:</p> <ul style="list-style-type: none"> All schizophrenia patients: Oral typical (low dose)>Oral risperidone>Oral typical>Oral olanzapine>Oral olanzapine Patients experiencing adverse events of typicals: Oral risperidone>Oral olanzapine>Oral Typical Treatment-resistant schizophrenia: Oral CLZ>Oral typical <p>ICER for all schizophrenia patients: Oral typical: Dominated</p>	Not reported	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Oral typical (low dose): Base case Oral risperidone: \$81,818 per averted DALY Oral olanzapine: \$300,000 per averted DALY <p><u>ICER for patients experiencing adverse events of typicals:</u></p> <ul style="list-style-type: none"> Oral typical: Base case Oral risperidone: \$20,000 per averted DALY Oral olanzapine: \$600,000 per averted DALY <p><u>ICER for patients with treatment-resistant schizophrenia:</u></p> <ul style="list-style-type: none"> Oral typical: Base case Oral clozapine: ranging from \$23,000 - \$42,000 per DALY averted <p><u>Probability of being cost-effective:</u> Cannot be calculated based on the data reported.</p>		
McIntyre <i>et al.</i> [40]	Canada	CUA	Healthcare system	5-year	Markov model	Adult patients (≥18 years) with recurrent or chronic schizophrenia including partially remitted outpatients as well as inpatients experiencing exacerbation of illness	<ul style="list-style-type: none"> Oral ziprasidone Oral olanzapine Oral quetiapine Oral risperidone 	Canada dollars \$50 000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Oral risperidone>Oral ziprasidone>Oral quetiapine>Oral olanzapine</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Oral ziprasidone: \$218,060 per QALY Oral olanzapine: Dominated Oral quetiapine: Dominated Oral risperidone: base case <p><u>Probability of being cost-effective:</u> Cannot be calculated based on the data reported.</p>	Yes, Pfizer	No
Mehnert <i>et al.</i> [41]	Sweden	CUA	Healthcare system	5-year	Markov model	Schizophrenia patients had previously experienced at least two relapses and had received prior oral treatment from which they are able to change to a new treatment	<ul style="list-style-type: none"> Paliperidone LAI Risperidone LAI Oral olanzapine 	Swedish Krona 300,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Paliperidone LAI>risperidone LAI>olanzapine LAI</p> <p><u>ICER:</u></p> <ul style="list-style-type: none"> Paliperidone LAI: Dominant Risperidone LAI: Dominated Oral olanzapine: Dominated <p><u>Probability of being cost-effective:</u></p> <ul style="list-style-type: none"> Paliperidone LAI vs Risperidone LAI: 0.86 for Paliperidone LAI Risperidone LAI vs oral olanzapine: 0.93 for Paliperidone LAI 	Yes, Janssen	No
Mould-Quevedo <i>et al.</i> [42]	Mexico	CEA	Healthcare system	1-year	Markov model	Patients with chronic schizophrenia in hospital	<ul style="list-style-type: none"> Oral ziprasidone Oral olanzapine Oral risperidone Oral haloperidol 	Not reported	<p><u>Cost-effectiveness ranking reported by the authors:</u> Oral ziprasidone>Oral risperidone and oral</p>	Yes, Pfizer	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
							<ul style="list-style-type: none"> • Oral clozapine 		CLZ>Oral olanzapine>Oral haloperidol <u>ICER:</u> Oral ziprasidone dominated all other strategies. <u>Probability of being cost-effective:</u> 0.60 for oral ziprasidone.		
NCCMH <i>et al.</i> [43]	UK	CUA	Healthcare system and social care	Lifetime	Markov model	25-year old schizophrenia patients in remission	<ul style="list-style-type: none"> • Oral olanzapine • Oral amisulpride • Oral zotepine • Oral aripiprazole • Oral paliperidone • Oral risperidone • Oral haloperidol 	UK pounds £20,000 - 30,000 per QALY	<u>Cost-effectiveness ranking reported by the authors:</u> Oral zotepine>Oral paliperidone>Oral olanzapine>Oral haloperidol>Oral Aripiprazole>Oral risperidone>Oral Amisulpride <u>ICER:</u> Oral Zotepine dominated all other strategies. <u>Probability of being cost-effective (WTP=£20,000 per QALY):</u> <ul style="list-style-type: none"> • Oral olanzapine: 0.1060 • Oral amisulpride: 0.1349 • Oral zotepine: 0.3046 • Oral aripiprazole: 0.1171 • Oral paliperidone: 0.1485 • Oral risperidone: 0.1331 • Oral haloperidol: 0.0558 	Not reported	No
Németh <i>et al.</i> [44]	Hungary	CUA	Third-party payer	2-year	Markov model	Patients with negative symptoms of schizophrenia	<ul style="list-style-type: none"> • Oral cariprazine • Oral risperidone 	Euros €34,764 per QALY	<u>Cost-effectiveness ranking</u> cariprazine > risperidone <u>ICER</u> <ul style="list-style-type: none"> • cariprazine: €28,897 per QALY; • risperidone: base case. <u>Probability of being cost-effective</u> <ul style="list-style-type: none"> • Cariprazine: over 0.7; • Risperidone: <0.3 	Yes, Gedeon Richter	No
Nuhoho <i>et al.</i> [45]	United Arab Emirates	CUA	Third-party payer	1-year	Decision tree	Schizophrenia patients in the United Arab Emirates on any oral antipsychotic	<ul style="list-style-type: none"> • Paliperidone LAI • Oral antipsychotics 	US dollars \$38,000 per QALY	<u>Cost-effectiveness ranking reported by the authors:</u> Paliperidone LAI>Oral antipsychotics <u>ICER</u> Paliperidone LAI dominates oral antipsychotics <u>Probability of being cost-effective</u> <ul style="list-style-type: none"> • Paliperidone LAI: 0.99998 • Oral antipsychotics: 0.00002 	Yes, Janssen	No
Obradovic <i>et al.</i> [46]	Slovenia	CEA	Healthcare system	1-year	Decision tree	Outpatients with chronic schizophrenia	<ul style="list-style-type: none"> • Oral amisulpride • Oral aripiprazole • Oral haloperidol • Oral olanzapine • Oral risperidone • Oral quetiapine • Oral ziprasidone • haloperidol LAI • Risperidone LAI 	Not reported	<u>Cost-effectiveness ranking reported by the authors:</u> Oral olanzapine and oral risperidone are likely to be cost-effective <u>ICER</u> <ul style="list-style-type: none"> • Oral amisulpride: Dominated • Oral aripiprazole: Extendedly dominated • Oral haloperidol: base case 	Not reported	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> Oral olanzapine: € 3,952 per remission Oral risperidone: Extendedly dominated Oral quetiapine: Dominated Oral ziprasidone: Dominated Haloperidol LAI: € 102 per remission Risperidone LAI: Dominated <p><u>Probability of being cost-effective</u> Not reported</p>		
Park <i>et al.</i> [47]	US	CUA	Healthcare system	10-year	Markov model	40-year-old patients with schizophrenia	Different sequences of oral atypicals: olanzapine (OLZ), risperidone (RSP), quetiapine (QTP) and ziprasidone (ZSD)	US dollars \$50,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Oral ziprasidone followed by oral risperidone> Oral risperidone followed by oral ziprasidone> Oral ziprasidone followed by oral quetiapine> other strategies</p> <p><u>ICER</u> Dominated strategies: QTP-RSP, RSP-QTP, QTP-ZSD, OLZ-RSP, RSP-OLZ, OLZ-ZSD, ZSD-OLZ, OLZ-QTP and QTP-OLZ.</p> <p><u>Undominated strategies:</u></p> <ul style="list-style-type: none"> RSP-ZSD: Base case ZSD-RSP: \$5,197 per QALY ZSD-QTP: 542,451 per QALY <p><u>Probability of being cost-effective</u></p> <ul style="list-style-type: none"> RSP-ZSD: 0.12 ZSD-RSP: 0.43 ZSD-QTP: 0.45 	Not reported	No
Pribylova <i>et al.</i> [48]	Czech Republic	CUA	Third-party payer	24-week	Micro-simulation	Adult patients with a Structured Clinical Interview for DSM-IV Disorders (SCID)-confirmed DSM-IV diagnosis of schizoaffective disorder and experiencing an acute exacerbation	<ul style="list-style-type: none"> Oral paliperidone extended release Placebo 	Euros €39,720 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Oral paliperidone extended release>Placebo</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> Oral paliperidone extended release: €28,935/QALY Placebo: Base case <p><u>Probability of being cost-effective</u></p> <ul style="list-style-type: none"> Oral paliperidone extended release: 0.995 Placebo: 0.005 	Yes, Janssen	No
Rajagopalan <i>et al.</i> [49]	UK	CUA	Healthcare system	10-year	Markov model	Acute adults with schizophrenia	<ul style="list-style-type: none"> Oral lurasidone Oral aripiprazole 	UK pounds £20,000-30,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Oral lurasidone>Oral aripiprazole</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> Oral lurasidone: Dominant Oral aripiprazole: Dominated <p><u>Probability of being cost-effective</u></p> <ul style="list-style-type: none"> Oral lurasidone: 0.75 Oral aripiprazole: 0.25 	Yes, Sunovion Pharmaceuticals	No
Tempest <i>et al.</i> [50]	UK	CUA	Healthcare system and social care	10-year	Markov model	Chronic, stable schizophrenia patients in the UK initiating	<ul style="list-style-type: none"> Aripiprazole LAI Risperidone LAI 	UK pounds £20,000-30,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors:</u> Aripiprazole LAI>risperidone</p>	Yes, Lundbeck	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
						maintenance treatment with LAI antipsychotics	<ul style="list-style-type: none"> Paliperidone LAI Olanzapine LAI 		LAI>Paliperidone LAI>olanzapine LAI <u>ICER</u> <ul style="list-style-type: none"> Aripiprazole LAI: £3,686 per QALY Risperidone LAI: base case Paliperidone LAI: Dominated Olanzapine LAI: Dominated <u>Probability of being cost-effective</u> <ul style="list-style-type: none"> Aripiprazole LAI: 0.51 Risperidone LAI: 0.48 Paliperidone LAI: 0.01 Olanzapine LAI: 0.00 		
Thavornwatt anayong <i>et al.</i> [51]	Thailand	CUA	Society	Lifetime	Markov model	Patients 15 years or older with stable schizophrenia who had no diabetes or hyperprolactinemia	<ul style="list-style-type: none"> Oral aripiprazole Oral risperidone 	Baht 160,000 per QALY	<u>Cost-effectiveness ranking</u> Aripiprazole> Risperidone <u>ICER</u> <ul style="list-style-type: none"> Aripiprazole: dominant Risperidone: dominated <u>Probability of being most cost-effective</u> <ul style="list-style-type: none"> Aripiprazole: 0.975 Risperidone: 0.025 	Not reported	No
Treur <i>et al.</i> [52]	Spain	CUA	Third-party payer	5-year	DES	Schizophrenia patients who just experienced a relapse which necessitates the involvement of a psychiatrist. not necessarily treatment-naive	<ul style="list-style-type: none"> Paliperidone extended release Oral olanzapine Oral aripiprazole 	Euros €20,000 and €30,000 per QALY	<u>Cost-effectiveness ranking reported by the authors:</u> Paliperidone extended release> Oral aripiprazole>Oral olanzapine <u>ICER</u> <ul style="list-style-type: none"> Paliperidone extended release: Dominant Oral olanzapine: Dominated Oral aripiprazole: Dominated <u>Probability of being most cost-effective</u> (WTP=€20,000 per QALY) <ul style="list-style-type: none"> Paliperidone extended release vs oral olanzapine: 0.799 for paliperidone extended release Paliperidone extended release vs oral aripiprazole: 0.732 	Yes, Janssen	No
Treur <i>et al.</i> [53]	Germany	CUA	Healthcare system	5-year	DES	Schizophrenia patients currently on branded risperidone	<ul style="list-style-type: none"> Branded oral risperidone Generic oral risperidone 	Euros €40,000 per QALY	<u>Cost-effectiveness ranking reported by the authors:</u> Branded oral risperidone>Generic oral risperidone <u>ICER for branded risperidone compared to generic risperidone, based on different probabilities of non-compliance after switching from branded risperidone to generic risperidone:</u> <ul style="list-style-type: none"> 2.5%: €189,250 per QALY 5.0%: €49,000 per QALY Over 7.5%: Dominant <u>Probability of being most cost-effective</u> (assuming 7% probability of non-compliance after switching)	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									from branded risperidone to generic risperidone) <ul style="list-style-type: none"> • Branded oral risperidone: 0.85 • Generic oral risperidone: 0.25 		
Yang <i>et al.</i> [54]	China	CEA	Healthcare system	2-year	Decision tree	Stable schizophrenic patients who met the DSM criteria for schizophrenia or schizoaffective disorder, between 20 to 45 years old, treated for at least 1 year, and whose disease had not been diagnosed for longer than 5 years and it has the best therapeutic potential	<ul style="list-style-type: none"> • Risperidone LAI • Oral olanzapine • Oral quetiapine 	Not reported	<u>Cost-effectiveness ranking reported by the authors:</u> Risperidone LAI>Oral olanzapine <u>ICER</u> <ul style="list-style-type: none"> • Risperidone LAI: RMB 163,063 per successfully treated patient • Oral olanzapine: Dominated • Oral quetiapine: base case <u>Probability of being most cost-effective</u> Not reported	Yes, Janssen	No
Yang <i>et al.</i> [55]	Taiwan	CEA	Healthcare system	2-year	Decision tree	A group of stable schizophrenia patients whose scores on the BSRS were <40 (BPRS <40, each item ranged from 1 to 7). These patients also met the following criteria: (i) under 35 years of age; (ii) illness duration no longer than 5 years; and (iii) under treatment for at least 1 year.	<ul style="list-style-type: none"> • Risperidone LAI • haloperidol LAI • oral olanzapine 	Not reported	<u>Cost-effectiveness ranking reported by the authors:</u> Risperidone LAI>haloperidol LAI and oral olanzapine <u>ICER (assuming all patients receiving psychiatric intervention during follow up)</u> <ul style="list-style-type: none"> • Risperidone LAI: \$NT 253,709 per responded patient • haloperidol LAI: Base case • oral olanzapine: dominated <u>ICER (assuming patients only using psychiatric intervention when needed during follow up)</u> <ul style="list-style-type: none"> • Risperidone LAI: \$NT 88,300 per responded patient • haloperidol LAI: Base case • oral olanzapine: \$NT 592,454 per responded patient <u>Probability of being most cost-effective</u> Not reported	Yes, Janssen	No
Zeidler <i>et al.</i> [56]	Germany	CUA	Third party payer	5-year	Markov model	Patients with schizophrenia in Germany	<ul style="list-style-type: none"> • paliperidone LAI • olanzapine LAI • Risperidone LAI • Zuclopenthixol LAI • Oral olanzapine • Oral risperidone • Oral quetiapine • Oral haloperidol 	Euros €30,000 per QALY	<u>Cost-effectiveness ranking reported by the authors:</u> Oral atypical>Oral risperidone>Oral olanzapine> Paliperidone LAI>Oral haloperidol>Oral quetiapine>Zuclopenthixol LAI>Risperidone LAI > olanzapine LAI <u>ICER</u> <ul style="list-style-type: none"> • paliperidone LAI: €67,447 per QALY • olanzapine LAI: Dominated • Risperidone LAI: Dominated • Zuclopenthixol LAI: Dominated 	Yes, Janssen	No

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness results	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
									<ul style="list-style-type: none"> • Oral olanzapine: Extendedly dominated • Oral risperidone: Dominated • Oral quetiapine: Extendedly dominated • Oral haloperidol: Dominated <p><u>Probability of being most cost-effective</u></p> <ul style="list-style-type: none"> • paliperidone LAI vs risperidone LAI: 0.925 for paliperidone LAI • paliperidone LAI vs olanzapine LAI: 0.944 for paliperidone LAI • paliperidone LAI vs zuclopenthixol LAI: 0.904 for paliperidone LAI 		
Zhao <i>et al.</i> [57]	China	CUA	Third party payer	1-year	Microsimulation	Patients with stable schizophrenia	<ul style="list-style-type: none"> • olanzapine-ODT (orally disintegrating tablet) • olanzapine-SOT (standard oral tablet) • aripiprazole-SOT 	USD dollars \$25,772.67	<p><u>Cost-effectiveness ranking as reported by the authors</u></p> <p>Olanzapine-ODT > olanzapine-SOT > aripiprazole-SOT</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> • olanzapine-ODT: \$16,798 per QALY • olanzapine-SOT: base case • aripiprazole-SOT: dominated <p><u>Probability of being most cost-effective</u></p> <ul style="list-style-type: none"> • olanzapine-ODT: 0.844 • olanzapine-SOT: 0.156 • aripiprazole-SOT: 0.00 	Yes, Eli Lilly	No

Abbreviations

CEA: cost-effectiveness analysis; CUA: cost-utility analysis; DES: discrete-event simulation; QALY: quality-adjusted life year.

2.2 Evidence table for studies assessing psychosocial interventions

Table 2: Evidence table for studies assessing psychosocial interventions

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness rankings as reported by the authors	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
Anh <i>et al.</i> [58]	Vietnam	CUA	Healthcare system	Lifetime	Markov model	All schizophrenia patients in 2006 in Vietnam, age ≥15 y	<ul style="list-style-type: none"> Do nothing Typicals Risperidone Olanzapine Typicals (67%) +risperidone (33%) Typicals (67%) + olanzapine (33%) Typicals (67%) + clozapine (33%) Risperidone (67%)+olanzapine (33%) Risperidone (67%)+clozapine (33%) Typicals + family intervention Risperidone + family intervention 	International dollars \$2,388 per DALY averted	Cost-effectiveness ranking as reported by the authors Risperidone + family intervention>Typicals + family intervention>Typicals (67%) +risperidone (33%)>Risperidone>Olanzapine>Risperidone (67%)+olanzapine (33%)>Typicals (67%) + olanzapine (33%)>Typicals>Risperidone (67%)+clozapine (33%)>Typicals (67%) + clozapine (33%)>do nothing <u>ICER</u> <ul style="list-style-type: none"> Do nothing: Dominated Typicals: Dominated Risperidone: Dominated Olanzapine: Dominated Typicals (67%) +risperidone (33%): Dominated Typicals (67%) + olanzapine (33%): Dominated Typicals (67%) + clozapine (33%): Dominated Risperidone (67%)+olanzapine (33%): Dominated Risperidone (67%)+clozapine (33%): Dominated Typicals + family intervention: base case: Dominated Risperidone + family intervention: \$0.029 per DALY averted: Dominated Probability of being most cost-effective: Not reported	No	No
Chisholm <i>et al.</i> 2012 [59]	Sub-Saharan Africa and South East Asia countries	CUA	Healthcare system	Lifetime	Markov model	General schizophrenia patients in Sub-Saharan Africa and South East Asia	<ul style="list-style-type: none"> Older antipsychotic drug (Community model) Newer antipsychotic drug (Community model) Older antipsychotic + psychosocial treatment (Community model) Newer antipsychotic + psychosocial treatment (Community model) Older antipsychotic (hospital model) Newer antipsychotic (hospital model) Older antipsychotic + psychosocial treatment (hospital model) 	International dollars \$2,000 per DALY averted	Cost-effectiveness ranking as reported by the authors Older antipsychotic + psychosocial treatment> Newer antipsychotic + psychosocial treatment>antipsychotics alone <u>ICER</u> <ul style="list-style-type: none"> Older antipsychotic drug (Community model): Dominated Newer antipsychotic drug (Community model): Dominated Older antipsychotic + psychosocial treatment (Community model): \$2,748 per DALY averted Newer antipsychotic + psychosocial treatment (Community model): \$36,504 per DALY averted Older antipsychotic (hospital model): Dominated Newer antipsychotic (hospital model): Dominated Older antipsychotic + psychosocial treatment (hospital model): Dominated Newer antipsychotic + psychosocial treatment (hospital model): Dominated Probability of being most cost-effective: Not reported	No	No

							<ul style="list-style-type: none"> Newer antipsychotic + psychosocial treatment (hospital model) 		Cannot be derived based on reported data		
Chisholm et al. 2008 [60]	Chile, Nigeria and Sri Lanka	CUA	Healthcare system	Lifetime	Markov model	General population in Chile, Nigeria and Sri Lanka	<ul style="list-style-type: none"> Current situation Older (typical) antipsychotic drug Newer (atypical) antipsychotic drug Older antipsychotic drug + psychosocial treatment Newer antipsychotic drug + psychosocial treatment 	International dollars \$2,000 per DALY averted	<u>Cost-effectiveness ranking as reported by the authors</u> Older (typical) antipsychotic drug> Older (typical) antipsychotic drug> Newer (atypical) antipsychotic drug> Current situation>Newer antipsychotic drug + psychosocial treatment <u>ICER for WHO Subregion D, Africa</u> <ul style="list-style-type: none"> Current situation: Dominated Older (typical) antipsychotic drug: Base case Newer (atypical) antipsychotic drug: Dominated Older antipsychotic drug + psychosocial treatment: \$9 per DALY averted Newer antipsychotic drug + psychosocial treatment: \$200,882 per DALY averted <u>ICER for WHO Subregion B, Americas</u> <ul style="list-style-type: none"> Current situation: Dominated Older (typical) antipsychotic drug: Dominated Newer (atypical) antipsychotic drug: Dominated Older antipsychotic drug + psychosocial treatment: Base case Newer antipsychotic drug + psychosocial treatment: \$532,380 per DALY averted <u>ICER for WHO Subregion B, South-east Asia</u> <ul style="list-style-type: none"> Current situation: Dominated Older (typical) antipsychotic drug: Dominated Newer (atypical) antipsychotic drug: Dominated Older antipsychotic drug + psychosocial treatment: Base case Newer antipsychotic drug + psychosocial treatment: \$400,956 per DALY averted <u>Probability of being most cost-effective:</u> Cannot be derived based on reported data	No	No
Gutierrez-Recacha et al. [61]	Spain	CUA	Societal (but exclude productivity and patient and informal carer time)	Lifetime	Markov model	All schizophrenia patients in Spain	<ul style="list-style-type: none"> Antipsychotics alone Antipsychotic plus family intervention, social skills training and CBT 		<u>Cost-effectiveness ranking as reported by the authors</u> Antipsychotics plus family intervention, social skills training and CBT> antipsychotics alone <u>ICER</u> <ul style="list-style-type: none"> Antipsychotics alone: Dominated Antipsychotic plus family intervention, social skills training and CBT: Dominant <u>Probability of being most cost-effective:</u> Cannot be derived based on reported data	No	No
Phanthunane et al. [62]	Thailand	CUA	Healthcare system	Until patient age 80 or death	Markov model	All schizophrenia patients in Thailand in the year 2005	<ul style="list-style-type: none"> Antipsychotics alone Antipsychotic plus family intervention (10 sessions, followed by 2 booster 	110,000 baht per DALY averted	<u>Cost-effectiveness ranking as reported by the authors</u> Antipsychotics plus psychosocial intervention> antipsychotics alone <u>ICER</u> <ul style="list-style-type: none"> Antipsychotics alone: Base case 	No	No

sessions every
year)

- Antipsychotic plus family
intervention: 1,900 baht per
DALY
Probability of being most cost-
effective:
Not reported
-

Abbreviations

CUA: cost-utility analysis; DALY: disability-adjusted life year; QALY: quality-adjusted life year.

2.3 Evidence table for studies assessing other interventions

Table 3: Evidence table for studies assessing other interventions

Reference	Country	Type of economic evaluation	Perspective of cost	Time horizon	Modelling method	Target population	Intervention & Comparator	Threshold of willingness-to-pay for one additional unit of health benefit	Cost-effectiveness rankings as reported by the authors	Conflicts of interest?	Meet the pre-defined criteria of a WDM?
Greenhalgh <i>et al.</i> [63]	UK	CUA	Healthcare system and social care	1-year	Decision tree	Treatment-resistant schizophrenia	<ul style="list-style-type: none"> • Clozapine • Haloperidol • Electroconvulsive therapy (ECT) 	UK pounds £20,000-30,000 per QALY	<p><u>Cost-effectiveness ranking as reported by the authors</u> Clozapine>ECT>Haloperidol</p> <p><u>ICER for patients who respond to and who can tolerate clozapine</u></p> <ul style="list-style-type: none"> • Clozapine: Dominant • Haloperidol: Dominated • ECT: Dominated <p><u>ICER for patients who not respond to, or who cannot tolerate clozapine</u></p> <ul style="list-style-type: none"> • Haloperidol: Dominated • ECT: Domant <p><u>Probability of being most cost-effective:</u> Not reported</p>	No	No
Girardin <i>et al.</i> [64]	Switzerland	CUA	Healthcare system	3-year	Decision tree + Markov model	Men and women aged 18–54 years with schizophrenia who were receiving clozapine as third-line treatment	Four strategies for monitoring white blood cell count: national strategies used in the UK, USA, and European countries, and a hypothetical 8-week strategy	US dollars \$100,000 per QALY	<p><u>Cost-effectiveness ranking as reported by the authors</u> No monitoring>any monitoring strategies</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> • UK strategy: Dominated • USA strategy: Dominated • EU strategy: Dominated • A hypothetical 8-week strategy: \$970,000 per QALY • No monitoring: Base case <p><u>Probability of being most cost-effective</u> (WTP=\$100,000 per QALY):</p> <ul style="list-style-type: none"> • No monitoring: 1 • Other strategies: 0 	No	No
Girardin <i>et al.</i> [65]	US	CUA	Third-party payer	3-year	Semi-Markov model	Stable adult patients with treatment-resistant schizophrenia who were taking clozapine	<ul style="list-style-type: none"> • Current US absolute neutrophil count monitoring (ANCM) schemes; • Human leukocyte antigen (HLA) genotyping followed by clozapine, with ANCM only for patients who tested positive for one or both alleles (genotype-guided blood sampling); • HLA genotyping followed by clozapine for low-risk patients and alternative antipsychotics for patients who tested positive (clozapine substitution scheme). 	US dollars \$50,000 per QALY	<p><u>Cost-effectiveness ranking:</u> Genetically guided strategy>Current US strategy> clozapine substitution scheme</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> • Current US strategy: \$3.93 million per QALY; • Genetically guided strategy: base case; • clozapine substitution scheme: dominated. <p><u>Probability of being most cost-effective:</u></p> <ul style="list-style-type: none"> • Genetically guided strategy: 1 • Other strategies: 0 	Not reported	No
Jin <i>et al.</i> [66]	UK	CUA	Healthcare and social care	Lifetime	Markov model	Stable patients with schizophrenia who failed a first-line antipsychotic	<ul style="list-style-type: none"> • Treatment as usual (TAU); • Stratified medicine algorithm (SMA) with a stratifier with 60% sensitivity and specificity in 	UK pounds £20,000 per QALY	<p><u>Cost-effectiveness ranking reported by the authors</u> SMA>TAU.</p> <p><u>ICER</u></p> <ul style="list-style-type: none"> • SMA: dominant • TAU: dominated <p><u>Probability of being cost-effective</u></p>	Not reported	No

						identifying patients who respond to a 2 nd line non-clozapine antipsychotic			<ul style="list-style-type: none"> SMA: 0.82; TAU: 0.18. 		
NCCMH <i>et al.</i> [43]	UK	CUA	Healthcare system and social care	11.8 years	Decision tree + Markov model	Adults with psychosis and schizophrenia actively seeking employment	<ul style="list-style-type: none"> Supported employment programme Treatment as usual 	£20,000-30,000 per QALY	<p>Cost-effectiveness ranking reported by the authors</p> <p>Supported employment programme>treatment as usual</p> <p>ICER</p> <ul style="list-style-type: none"> Supported employment programme: £5,723 per QALY Treatment as usual: base case <p>Probability of being cost-effective</p> <ul style="list-style-type: none"> Supported employment programme: 0.66 Treatment as usual: 0.34 	No	No
Perez <i>et al.</i> [67]	UK	CEA	Healthcare system and social care	2-year	Decision tree	Young people at high risk of psychosis (HR) or with a first episode of psychosis (FEP)	<ul style="list-style-type: none"> Treatment as usual Low or high-intensity interventions for the identification and referral of people at clinical high risk of psychosis or people with first-episode psychosis 	Not reported	<p>Cost-effectiveness ranking reported by the authors</p> <p>High-intensity intervention> Low-intensity intervention> Treatment as usual</p> <p>ICER</p> <ul style="list-style-type: none"> High-intensity intervention: Dominant Low-intensity intervention: Dominated Treatment as usual: Dominated <p>Probability of being cost-effective (WTP= £0 for additional true positives identified per practice)</p> <ul style="list-style-type: none"> High-intensity intervention: 0.46 Low-intensity intervention: 0.13 Treatment as usual: 0.41 <p>Probability of being cost-effective (WTP= £10,000 for additional true positives identified per practice)</p> <ul style="list-style-type: none"> High-intensity intervention: 0.68 Low-intensity intervention: 0.14 Treatment as usual: 0.18 	No	No
Perlis <i>et al.</i> [68]	US	CUA	Societal	Lifetime	Decision tree + Markov model	30-year old schizophrenia patients in an acute psychotic episode	<ul style="list-style-type: none"> Clozapine as first line Clozapine as third line Test and treat those who test positive with clozapine as first line, those who test negative with clozapine as third line. The sensitivity and specificity of the test is 96% and 38%, respectively. 	Not reported	<p>Cost-effectiveness ranking reported by the authors</p> <p>No test>test strategy</p> <p>ICER</p> <ul style="list-style-type: none"> Test strategy versus Clozapine as first line strategy: Test strategy was dominated; Test strategy versus Clozapine as third line strategy: \$47,705 per QALY for test strategy <p>Probability of being cost-effective</p> <p>Not reported</p>	No	No
Rejon-Parrilla <i>et al.</i> [69]	UK	CUA	Healthcare system	2-year	Decision tree + Markov model	Patients with a first diagnose of schizophrenia aged 25, beginning treatment with risperidone	<ul style="list-style-type: none"> Strategy A: 'Traditional dosing' represented by standard care where the dose of risperidone is prescribed as usual with all patients 	UK pounds £20,000-30,000 per QALY	<p>Cost-effectiveness ranking reported by the authors</p> <p>Strategy B > Strategy A</p> <p>ICER</p> <ul style="list-style-type: none"> Strategy A: Base case Strategy B: £19,252 per QALY 	Yes	No

							receiving the same dose			<u>Probability of being cost-effective</u> Not reported		
							<ul style="list-style-type: none"> Strategy B: 'Patient stratification' where dosing is individualized for each patient based on the results of a pharmacogenetic test that predicts an individual patient's response to the drug. The accuracy of the test was assumed to be 100% 					
Smith <i>et al.</i> [70]	US	CUA	Third-party payer	1-year	Decision tree + Markov model	all schizophrenia patients in 2006 in Vietnam, age ≥15 y	Medicare drug plans with <ul style="list-style-type: none"> 1. Generic coverage 2. No gap coverage 	US dollar \$100,000 per QALY		<u>Cost-effectiveness ranking reported by the authors</u> Generic coverage > No gap coverage <u>ICER</u> <ul style="list-style-type: none"> Generic coverage: Dominant No gap coverage: Dominated <u>Probability of being cost-effective</u> <ul style="list-style-type: none"> Generic coverage: 0.62-0.81 No gap coverage: 0.38-0.19 	No	No
Wijnen <i>et al.</i> [71]	Netherlands	CUA	Healthcare system	10-year	Markov model	Individuals with ultra-high risk (UHR) of developing psychosis or with first episode psychosis (FEP).	<ul style="list-style-type: none"> Care as usual Care as usual + CBT 	Euros 10,000 – 100,000 per QALY		<u>Cost-effectiveness ranking reported by the authors</u> Care as usual + CBT > CBT <u>ICER</u> <ul style="list-style-type: none"> Care as usual (dominated) Care as usual + CBT (dominant) <u>Probability of being cost-effective (WTP=10,000 per QALY)</u> <ul style="list-style-type: none"> Care as usual: >0.75 Care as usual + CBT <0.25 	Not reported	No
Zala <i>et al.</i> [72]	UK	CEA	NHS	1-year	Decision tree	Psychosis or bipolar disorder	Improving Access to Psychological Therapies (IAPT) Programme vs no IAPT	Not reported		<u>Cost-effectiveness ranking reported by the authors</u> No definite conclusion can be drawn <u>ICER:</u> <ul style="list-style-type: none"> No IAPT: base case IAPT: £12.9 per WSAS point (work and social adjustment scale) <u>Probability of being cost-effective</u> PSA results suggested 72% probability of IAPT having higher costs compared to no IAPT.	No	No

Abbreviations

CEA: cost-effectiveness analysis; CUA: cost-utility analysis; DALY: disability-adjusted life year; QALY: quality-adjusted life year.

Section 3: Quality assessment

3.1 NICE checklist

Table 4: Performance of included studies assessed by Section 2 of the NICE checklist

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
<i>Aigbogun et al. [11]</i>	Yes	Partly	Yes	Partly	Partly	Yes	Yes	Partly	Yes	Yes	Yes	Very serious limitations
<i>Anh et al. [58]</i>	Partly	Yes	Partly	Partly	Yes	Partly	Partly	Yes	Yes	Partly	No	Very serious limitations
<i>Ascher-Svanum et al.[2]</i>	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Partly	Yes	Yes	Yes	Potentially serious limitations
<i>Beard et al.[3]</i>	Partly	Partly	Partly	No	Yes	Partly	No	Partly	Yes	Partly	Yes	Very serious limitations
<i>Bernardo et al.[4]</i>	Not clear	Partly	Not clear	Partly	Yes	Not clear	Partly	Yes	Yes	Partly	Yes	Very serious limitations
<i>Bounthavong et al.[5]</i>	Yes	No	Partly	Partly	Yes	Partly	Partly	Not clear	Yes	Partly	No	Very serious limitations
<i>Chisholm et al. 2012 [59]</i>	Partly	Yes	Partly	Yes	Yes	Partly	Partly	Partly	Yes	Partly	No	Very serious limitations
<i>Chisholm et al. 2008 [60]</i>	Partly	Yes	Partly	Yes	Yes	Partly	Not clear	Not clear	Yes	Partly	No	Very serious limitations
<i>Chue et al.[6]</i>	Yes	Partly	No	Not clear	Not clear	No	No	Yes	Yes	Partly	Yes	Very serious limitations
<i>Citrome et al.[7]</i>	Yes	Partly	Yes	Partly	No	Yes	Partly	Partly	Yes	Partly	Yes	Very serious limitations
<i>Damen et al.[8]</i>	Partly	Partly	No	Not clear	No	No	Not clear	Yes	Yes	Partly	Yes	Very serious limitations

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
Davies <i>et al.</i> [9]	Yes	Partly	Partly	Partly	Yes	Yes	No	Yes	Yes	Yes	Yes	Very serious limitations
De Graeve <i>et al.</i> [10]	Partly	Partly	Partly	No	No	Partly	Yes	Yes	Yes	Partly	Yes	Very serious limitations
Dilla <i>et al.</i> [11]	Yes	Partly	No	Partly	Yes	No	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Druais <i>et al.</i> [12]	Yes	Partly	Yes	Partly	No	Yes	Partly	Partly	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [13]	Yes	Partly	No	Partly	Partly	No	Not clear	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [14]	Yes	Partly	No	Partly	Partly	No	Not clear	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [15]	Yes	Partly	No	Partly	Partly	No	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [16]	Yes	Partly	No	Partly	Partly	No	Not clear	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [17]	Yes	Partly	No	Partly	No	No	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [18]	Yes	Partly	No	Partly	No	No	Not clear	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [19]	Yes	Partly	No	Partly	Yes	No	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Einarson <i>et al.</i> [20]	Yes	Partly	No	Partly	No	No	Not clear	Partly	Yes	Yes	Yes	Very serious limitations
Furiak <i>et al.</i> [21]	Yes	Partly	Yes	Yes	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Furiak <i>et al.</i> [22]	Yes	Partly	Yes	Yes	Partly	Yes	Partly	Partly	Yes	Yes	Yes	Very serious limitations
Garcia-Ruiz <i>et al.</i> [23]	Yes	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Partly	Yes	Very serious limitations

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
Geitona <i>et al.</i> [24]	Yes	Partly	Partly	Partly	Yes	Yes	No	Yes	Yes	Partly	Yes	Very serious limitations
Girardin <i>et al.</i> [65]	No	Partly	No	Not clear	Not clear	No	Partly	Partly	Yes	Yes	No	Very serious limitations
Girardin <i>et al.</i> [64]	Yes	Partly	Yes	Partly	No	Yes	Yes	Yes	Yes	Yes	No	Very serious limitations
Graham <i>et al.</i> [25]	Yes	Partly	Yes	Partly	Yes	No	Partly	Partly	Yes	Yes	Yes	Very serious limitations
Greenhalgh <i>et al.</i> [63]	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	No	Potentially serious limitations
Gutierrez-Recacha <i>et al.</i> [61]	Not clear	Yes	Partly	Yes	Yes	Partly	Not clear	Yes	Yes	Partly	No	Very serious limitations
Heeg <i>et al.</i> [26]	Yes	Partly	Yes	Partly	Yes	No	Not clear	Yes	Yes	Partly	Yes	Very serious limitations
Heeg <i>et al.</i> [27]	Yes	Partly	Yes	Partly	Yes	Yes	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Hensen <i>et al.</i> [28]	Yes	Partly	Yes	Not clear	Yes	No	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Jin <i>et al.</i> [66]	Yes	Yes	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	No	Potentially serious limitations
Jukic <i>et al.</i> [29]	Yes	Partly	No	Yes	No	No	Not clear	Yes	Yes	Yes	Yes	Very serious limitations
Kasteng <i>et al.</i> [30]	No	Yes	No	Partly	Yes	No	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Kim <i>et al.</i> [31]	No	Partly	No	Partly	Yes	No	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Kim <i>et al.</i> [32]	Yes	Partly	Partly	Partly	Yes	Partly	Partly	Yes	Yes	Yes	Yes	Very serious limitations

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
Lachaine <i>et al.</i> [33]	Partly	Partly	Partly	Partly	Yes	No	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Laux <i>et al.</i> [34]	Yes	Partly	Partly	Partly	Yes	No	Partly	Partly	Yes	Partly	Yes	Very serious limitations
Lin <i>et al.</i> [35]	Yes	Yes	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Yes	No	Minor limitations
Lindner <i>et al.</i> [36]	Partly	Partly	No	Partly	Yes	No	Yes	Yes	Yes	Partly	No	Very serious limitations
Lindstrom <i>et al.</i> [37]	Yes	Partly	Yes	Partly	Partly	Yes	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Lubinga <i>et al.</i> [38]	Yes	Yes	Yes	Partly	Partly	Yes	Partly	Partly	Yes	Yes	No	Very serious limitations
Magnus <i>et al.</i> [39]	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Very serious limitations
McIntyre <i>et al.</i> [40]	No	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Very serious limitations
Mehnert <i>et al.</i> [41]	Yes	Partly	Yes	Partly	Yes	Yes	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Mould-Quevedo <i>et al.</i> [42]	Yes	Partly	Yes	No	No	Not clear	No	Yes	Yes	Partly	Yes	Very serious limitations
NCCMH <i>et al.</i> [43] (<i>assessing antipsychotic</i>)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Minor limitations
NCCMH <i>et al.</i> [43] (<i>assessing employment interention</i>)	Yes	Partly	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	No	Potentially serious limitations
Németh <i>et al.</i> [44]	Partly	Partly	Partly	Partly	Yes	Partly	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Nuhoho <i>et al.</i> [45]	Partly	Partly	No	Partly	No	No	No	Yes	Yes	Yes	Yes	Very serious limitations

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
Obradovic <i>et al.</i> [46]	Partly	Partly	Partly	No	No	Partly	No	Yes	Yes	Partly	No	Very serious limitations
Park <i>et al.</i> [47]	Yes	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Yes	No	Potentially serious limitations
Perez <i>et al.</i> [67]	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	No	Potentially serious limitations
Perlis <i>et al.</i> [68]	Yes	Yes	Partly	Yes	Partly	Partly	Partly	Yes	Yes	Partly	No	Very serious limitations
Phanthunane <i>et al.</i> [73]	Partly	Yes	Partly	Yes	Yes	Partly	Yes	Yes	Yes	Partly	No	Very serious limitations
Pribylova <i>et al.</i> [48]	No	No	No	Partly	Yes	No	No	Partly	Yes	Yes	Yes	Very serious limitations
Rajagopalan <i>et al.</i> [49]	Not clear	Partly	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Very serious limitations
Rejon-Parrilla <i>et al.</i> [69]	Yes	Partly	Yes	Partly	Partly	Yes	Partly	No	Yes	Yes	Yes	Very serious limitations
Smith <i>et al.</i> [70]	Partly	Partly	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	No	Very serious limitations
Tempest <i>et al.</i> [50]	Yes	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Potentially serious limitations
Thavornwattayanong <i>et al.</i> [51]	Yes	Yes	Yes	Partly	Partly	Yes	Partly	Yes	Yes	Yes	No	Potentially serious limitations
Treur <i>et al.</i> [52]	Yes	Partly	Yes	Partly	Yes	Yes	No	Yes	Yes	Yes	Yes	Very serious limitations
Treur <i>et al.</i> [53]	Not clear	Partly	Yes	Not clear	No	Not clear	Not clear	Not reported	Yes	Partly	Yes	Very serious limitations

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8	Question 9	Question 10	Question 11	Overall assessment
Wijnen <i>et al.</i> [71]	Yes	Partly	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Partly	No	Minor limitations
Yang <i>et al.</i> [54]	Partly	Partly	Partly	No	No	Partly	No	Yes	Yes	Partly	Yes	Very serious limitations
Yang <i>et al.</i> [55]	Partly	Partly	Partly	Partly	Yes	Partly	No	Partly	Yes	Partly	Yes	Very serious limitations
Zala <i>et al.</i> [72]	Partly	Partly	Partly	Yes	Partly	Yes	Yes	Partly	Yes	Yes	No	Very serious limitations
Zhao <i>et al.</i> [57]	Yes	Partly	Yes	Partly	Partly	Yes	No	Yes	Yes	Yes	Yes	Very serious limitations
Zeidler <i>et al.</i> [56]	Yes	Partly	Yes	Partly	Partly	Partly	Partly	Partly	Yes	Yes	Yes	Very serious limitations

3.2 Cooper hierarchy

Table 5: Performance of included studies assessed by the Cooper hierarchy

Reference	A. Clinical effect size data	B. Adverse events		C. Baseline clinical data	D. Resource use data		E. Cost data		F. Utility data
		Min	Max		Min	Max	Min	Max	
Aigbogun <i>et al.</i> [1]	2	3	2	4	5	2	5	2	3
Anh <i>et al.</i> [58]	2+	6	2+	4	6	2	2	2	3
Ascher-Svanum <i>et al.</i> [2]	2	6	2	2	3	2	2	2	3
Beard <i>et al.</i> [3]	1	4	2	5	6	6	4	2	3
Bernardo <i>et al.</i> [4]	1	1	1	4	6	2	2	2	N/A
Bounthavong <i>et al.</i> [5]	1+	2	2	4	6	2	Not clear	2	N/A
Chisholm <i>et al.</i> 2012 [59]	2+	N/A	N/A	2	6	2	4	2	3
Chisholm <i>et al.</i> 2008 [60]	2+	N/A	N/A	2	6	2	Not reported	Not reported	6
Chue <i>et al.</i> [6]	Not reported	Not reported	Not reported	Not reported	6	2	2	2	3
Citrome <i>et al.</i> [7]	2	2	2	2	6	2	3	2	N/A
Damen <i>et al.</i> [8]	6	Not reported	Not reported	Not reported	Not reported	Not reported	2	2	3
Davies <i>et al.</i> [9]	2	4	2	4	6	2	2	2	3
De Graeve <i>et al.</i> [10]	4	4	4	4	6	2	2	2	N/A
Dilla <i>et al.</i> [11]	2+	2	1	3	6	2	2	2	3
Druais <i>et al.</i> [12]	4	6	2	4	6	2	3	2	3
Einarson <i>et al.</i> [13]	3	N/A	N/A	4	Not clear	2	2	2	3
Einarson <i>et al.</i> [14]	3	N/A	N/A	4	Not clear	2	2	2	3
Einarson <i>et al.</i> [15]	3	N/A	N/A	4	6	2	2	2	3
Einarson <i>et al.</i> [16]	2	N/A	N/A	4	Not reported	Not reported	2	2	3

Reference	A. Clinical effect size data	B. Adverse events		C. Baseline clinical data	D. Resource use data		E. Cost data		F. Utility data
		Min	Max		Min	Max	Min	Max	
Einarson <i>et al.</i> [17]	5	N/A	N/A	4	Not reported	Not reported	2	2	3
Einarson <i>et al.</i> [18]	5	N/A	N/A	4	Not reported	Not reported	2	2	3
Einarson <i>et al.</i> [19]	2	N/A	N/A	4	6	2	2	2	3
Einarson <i>et al.</i> [20]	5	N/A	N/A	4	Not reported	Not reported	4	2	3
Furiak <i>et al.</i> [21]	2	2	2	2	3	2	2	2	3
Furiak <i>et al.</i> [22]	2	4	2	2	4	2	3	2	3
Garcia-Ruiz <i>et al.</i> [23]	1+	1+	1+	4	6	2	2	2	3
Geitona <i>et al.</i> [24]	2+	6	2	4	6	6	2	2	N/A
Girardin <i>et al.</i> [65]	Not reported	Not reported	Not reported	Not reported	4	2	6	2	3
Girardin <i>et al.</i> [64]	6	4	4	4	2	2	2	2	3
Graham <i>et al.</i> [25]	1+	6	2	4	3	3	3	2	3
Greenhalgh <i>et al.</i> [63]	4	4	4	4	Not reported	Not reported	2	2	1
Gutierrez-Recacha <i>et al.</i> [61]	2+	2+	2+	2	Not reported	Not reported	2	2	3
Heeg <i>et al.</i> [26]	1+	2	1+	4	6	Not reported	2	2	N/A
Heeg <i>et al.</i> [27]	2+	2+	2+	5	6	2	2	2	3
Hensen <i>et al.</i> [28]	1+	Not clear	2	Not reported	6	1	2	2	3
Jin <i>et al.</i> [66]	4	4	1+	3	6	2	6	2	3
Jukic <i>et al.</i> [29]	4	N/A	N/A	2	Not reported	Not reported	2	2	3
Kasteng <i>et al.</i> [30]	1+	4	1+	4	6	2	2	2	3
Kim <i>et al.</i> [31]	1+	1+	1+	4	6	2	2	2	Not reported
Kim <i>et al.</i> [32]	1	1	1	4	6	2	2	2	N/A
Lachaine <i>et al.</i> [33]	1+	6	1	4	6	1	2	2	3
Laux <i>et al.</i> [34]	1+	2	2	4	6	2	6	2	3
Lin <i>et al.</i> [35]	1+	1+	1+	4	6	2	2	2	3
Lindner <i>et al.</i> [36]	1+	N/A	N/A	4	2	2	2	2	3
Lindstrom <i>et al.</i> [37]	2	2	2	4	6	1	2	2	4

Reference	A. Clinical effect size data	B. Adverse events		C. Baseline clinical data	D. Resource use data		E. Cost data		F. Utility data
		Min	Max		Min	Max	Min	Max	
Lubinga <i>et al.</i> [38]	2	2	1+	4	6	1	5	2	3
Magnus <i>et al.</i> [39]	1+	4	4	2	2	2	2	2	3
McIntyre <i>et al.</i> [40]	1	4	4	4	2	1	2	2	3
Mehnert <i>et al.</i> [41]	1+	4	1+	4	4	4	2	2	3
Mould-Quevedo <i>et al.</i> [42]	6	6	4	Not clear	6	6	2	2	N/A
NCCMH <i>et al.</i> [43] <i>(assessing antipsychotics)</i>	1+	1+	1+	4	6	2	2	2	3
NCCMH <i>et al.</i> [43] <i>(assessing employment interventions)</i>	1+	N/A	N/A	4	6	2	2	2	3
Németh <i>et al.</i> [44]	2	2	2	4	6	4	6	2	3
Nuhoho <i>et al.</i> [45]	6	6	6	4	6	6	2	2	3
Obradovic <i>et al.</i> [46]	5	6	3	3	6	4	2	2	N/A
Park <i>et al.</i> [47]	1	4	2	4	3	2	2	2	3
Perez <i>et al.</i> [67]	1	1	1	1	2	1	6	1	N/A
Perlis <i>et al.</i> [68]	4	4	4	4	3	2	3	2	3
Phanthunane <i>et al.</i> [73]	2+	6	2+	2	2	2	2	2	3
Pribylova <i>et al.</i> [48]	1	N/A	N/A	4	6	2	6	2	3
Rajagopalan <i>et al.</i> [49]	3	6	1	4	6	2	2	2	3
Rejon-Parrilla <i>et al.</i> [69]	6	4	1	4	2	2	4	2	3
Smith <i>et al.</i> [70]	4	4	4	1	2	2	1	1	3
Tempest <i>et al.</i> [50]	1+	1+	1+	4	6	2	2	2	3

Reference	A. Clinical effect size data	B. Adverse events		C. Baseline clinical data	D. Resource use data		E. Cost data		F. Utility data
		Min	Max		Min	Max	Min	Max	
Thavornwattayanong <i>et al.</i> [51]	1+	1+	1	4	3	2	2	2	3
Treur <i>et al.</i> [52]	1+	2	2	4	6	6	2	2	3
Treur <i>et al.</i> [53]	6	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	3
Wijnen <i>et al.</i> [71]	2	Not reported	Not reported	3	6	1	6	2	1
Yang <i>et al.</i> [54]	6	6	6	6	6	6	2	2	N/A
Yang <i>et al.</i> [55]	1	6	6	4	6	6	4	1	N/A
Zala <i>et al.</i> [72]	4	Not reported	Not reported	1	1	1	6	1	N/A
Zhao <i>et al.</i> [57]	4	4	1+	2	6	6	2	2	Not reported
Zeidler <i>et al.</i> [56]	2	4	1+	4	6	2	6	2	3

Section 4: List of excluded studies with reasons for exclusion

Table 6: List of excluded studies with reasons for exclusion

Study	Primary reason for exclusion ¹
Alexeyeva <i>et al.</i> , 2001 [74]	Published before 2005
Almond <i>et al.</i> , 1998 [75]	Published before 2005
Almond <i>et al.</i> , 2000 [76]	Published before 2005
Andrews <i>et al.</i> , 2003 [77]	Partial economic evaluation
Annemans <i>et al.</i> , 2012 [78]	Partial economic evaluation
Arteaga Duarte <i>et al.</i> , 2019 [79]	Not English
Barnett <i>et al.</i> , 2012 [80]	Not modelling study
Barnett <i>et al.</i> , 2015 [81]	Different population
Basu <i>et al.</i> , 2018 [82]	Not economic evaluation
Bera <i>et al.</i> , 2014 [83]	Cost consequences analysis
Bettinger <i>et al.</i> , 2007 [84]	Not modelling study
Bobes <i>et al.</i> , 2004 [85]	Published before 2005
Bouvy <i>et al.</i> , 2012 [86]	Different population
Byrom <i>et al.</i> , 1998 [87]	Published before 2005
Carswell <i>et al.</i> , 2010 [88]	Not modelling study
Colombo <i>et al.</i> , 2008 [89]	Cost consequences analysis
Davies <i>et al.</i> , 1993 [90]	Published before 2005
Davies <i>et al.</i> , 1998 [91]	Published before 2005
Davies <i>et al.</i> , 2007 [92]	Not modelling study
Davies <i>et al.</i> , 2008 [93]	Not modelling study
de Menil <i>et al.</i> , 2015 [94]	Not modelling study
Dickey <i>et al.</i> , 2004 [95]	Not modelling study
Druais <i>et al.</i> , 2017 [96]	Not English
Duggan <i>et al.</i> , 2003 [97]	Published before 2005
Edwards <i>et al.</i> , 2005 a [98]	Cost consequences analysis
Edwards <i>et al.</i> , 2005 b [99]	Cost consequences analysis
Edwards <i>et al.</i> , 2008 [100]	Cost consequences analysis
Edwards <i>et al.</i> , 2012 [101]	Cost consequences analysis
Einarson <i>et al.</i> , 2013 [102]	Not modelling study
Emsley <i>et al.</i> , 2004 [103]	Published before 2005
Frey <i>et al.</i> , 2014 [104]	Cost consequences analysis
Ganguly <i>et al.</i> , 2003 [105]	Published before 2005
Glazer <i>et al.</i> , 1996 [106]	Published before 2005
Glennie <i>et al.</i> , 1997 [107]	Published before 2005
Gozlan <i>et al.</i> , 2018 [108]	Not English

Grande <i>et al</i> , 2020 [109]	Review paper
Grieve <i>et al</i> , 2008 [110]	Not modelling study
Haby <i>et al</i> , 2004 [111]	Published before 2007
Hansen <i>et al</i> , 2002 [112]	Published before 2005
Heeg <i>et al</i> , 2005 [113]	Cost consequences analysis
Henrique <i>et al</i> , 2020 [114]	Review paper
Janssen <i>et al</i> , 2011 [115]	Not modelling study
Johnson-Masotti <i>et al</i> , 2000 [116]	Different population
Joshi <i>et al</i> , 2015 [117]	Partial economic evaluation
Kaaya <i>et al</i> , 2013 [118]	Review paper
Karki <i>et al</i> , 2001 [119]	Not modelling study
Keks <i>et al</i> , 1997 [120]	Review paper
Kongsakon <i>et al</i> , 2005 [121]	Cost consequences analysis
Langley-Hawthorne <i>et al</i> , 1997 [122]	Partial economic evaluation
Launois <i>et al</i> , 1998 [123]	Published before 2005
Laurier <i>et al</i> , 1997 [124]	Published before 2005
Lecomte <i>et al</i> , 2000 [125]	Published before 2005
Leitao <i>et al</i> , 2006 [126]	Partial economic evaluation
Lin <i>et al</i> , 2001 [127]	Not modelling study
Lin <i>et al</i> , 2015 [128]	Partial economic evaluation
Matheson <i>et al</i> , 1994 [129]	Published before 2005
Mauskopf <i>et al</i> , 1999 [130]	Published before 2005
Mauskopf <i>et al</i> , 2002 [131]	Published before 2005
McCrone <i>et al</i> , 2009 [132]	Partial economic evaluation
McCrone <i>et al</i> , 2013 [133]	Cost consequences analysis
Mehta <i>et al</i> , 2017 [134]	Not modelling study
Mihalopoulos <i>et al</i> , 1999 [135]	Not modelling study
Mihalopoulos <i>et al</i> , 2004 [136]	Published before 2006
Mortimer <i>et al</i> , 2003 [137]	Published before 2005
NCCMH (CBT) <i>et al</i> , 2014 [43]	Partial economic evaluation
NCCMH (early intervention service) <i>et al</i> , 2014 [43]	Partial economic evaluation
NCCMH (family intervention) <i>et al</i> , 2014 [43]	Partial economic evaluation
Nemeth <i>et al</i> , 2018 [138]	Review paper
Norton <i>et al</i> , 2006 [139]	Not economic evaluation
Oh <i>et al</i> , 2001 a [140]	Published before 2005
Oh <i>et al</i> , 2001 [141]	Published before 2005
O'Malley <i>et al</i> , 2011 [142]	Partial economic evaluation

Osborn <i>et al</i> , 2019 [143]	Not economic evaluation
Palmer <i>et al</i> , 1998 [144]	Published before 2005
Palmer <i>et al</i> , 2002 [145]	Published before 2005
Patel <i>et al</i> , 2013 [146]	Not modelling study
Petit <i>et al</i> , 2003 [147]	Not modelling study
Quintero <i>et al</i> , 2016 [148]	Partial economic evaluation
Rajagopalan <i>et al</i> , 2013 a [149]	Cost consequences analysis
Rajagopalan <i>et al</i> , 2013 b [150]	Cost consequences analysis
Richardson <i>et al</i> , 2015 [151]	Different population
Rosenheck <i>et al</i> , 2016 [152]	Not modelling study
Seghers <i>et al</i> , 2015 [153]	Not modelling study
Serretti <i>et al</i> , 2009 [154]	Cost consequences analysis
Tilden <i>et al</i> , 2002 [155]	Published before 2005
Valmaggia <i>et al</i> , 2009 [156]	Cost consequences analysis
Vera-Llonch <i>et al</i> , 2004 [157]	Cost consequences analysis
Verma <i>et al</i> , 2011 [158]	Not economic evaluation
Wang <i>et al</i> , 2004 [159]	Published before 2005
Ward <i>et al</i> , 2013 [160]	Cost consequences analysis
Windmeijer <i>et al</i> , 2006 [161]	Not modelling study
Winkler <i>et al</i> , 2018 [162]	Partial economic evaluation
Yu <i>et al</i> , 2009 [163]	Not modelling study
Zhou <i>et al</i> , 2018 [164]	Review paper
Zito <i>et al</i> , 1995 [165]	Not economic evaluation

Notes:

1. A study can be excluded from the systematic review for more than one reason. In table 6 we only reported the primary reason for exclusion for each study.

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