Cost-effectiveness of ten commonly used antipsychotics in first-episode schizophrenia in the UK: economic evaluation based on a de-novo discrete event simulation model

Supplementary materials

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Supplementary sections

Supplementary section 1. Simulation of hypothetical cohorts for base-case and scenario analyses

For the base-case analyses on patients with first-episode schizophrenia, a hypothetical cohort of 1000 participants were simulated primarily based on the summary characteristics of study population from Smith et al1, which assessed the metabolic profiles of the young people with first episode psychosis in the UK. For the scenario analyses on patients with non-first-episode schizophrenia, a hypothetical cohort of 1000 participants were simulated primarily based on the summary characteristics of study population from the STAR trial2, which compared aripiprazole with standard treatment (especially olanzapine) for people with schizophrenia. Other published studies on patients with schizophrenia and assumptions were used to support the simulation of the hypothetical cohorts (Table SS1). Each attribute of an individual was simulated independently based on the data type of the covariate: continuous covariates were simulated using the normal distribution based on the population mean and standard deviance; binary covariates were simulated using the Bernoulli distribution based on the population proportion; and categorical covariates were simulated using a generalized Bernoulli distribution based on the population proportion for each category.

Table SS1. Baseline characteristics of the target patients with schizophrenia for the simulation.

	First-episode schizophrenia cohort for base-case analyses		Non-first-episode schizophrenia cohort for the scenario analysis	
Attributes	**Mean (SD)/ Proportion**	**Source**	**Mean (SD)/ Proportion**	**Source**
Age, years	24.6 (3.9)	Smith 2020[1]	38.5 (10.9)	Barnett 2009[2]
Male	0.69	Smith 2020[1]	0.60	Barnett 2009[2]
Body mass index, kg/m2	27.8 (5.8)	Smith 2020[1]	27.2 (5.1)	Barnett 2009[2]
Total cholesterol, mg/dl	173.7 (34.7)	Smith 2020[1]	211.6 (42.5)	Barnett 2009[2]
HDL cholesterol, mg/dl	46.3 (11.6)	Smith 2020[1]	50.4 (15.4)	Barnett 2009[2]
Triglycerides, mg/dl	150.4 (97.3)	Smith 2020[1]	192.4 (141.6)	Barnett 2009[2]
Fasting glucose, mg/dl	90.1 (12.6)	Smith 2020[1]	97.4 (19.1)	Barnett 2009[2]
Systolic blood pressure, mmHg	125.8 (17.6)	Smith 2020[1]	131.7 (19.3)	Osborn 2015[3]
Current smoker	0.61	Smith 2020[1]	0.49	Osborn 2015[3]
Alcohol consumption, unit/week	1 (0)	Assumption	1 (0)	Assumption
Compliance				
Full	0.41	Gilmer 2004[4]	0.41	Gilmer 2004[4]
Partial	0.35	Gilmer 2004[4]	0.35	Gilmer 2004[4]
None	0.24	Gilmer 2004[4]	0.24	Gilmer 2004[4]
Parental history of diabetes	0	Assumption	0	Assumption
Use of antihypertensive therapy	0	Assumption	0.16	Smith 2013[5]
History of atrial fibrillation	0	Assumption	0.01	Smith 2013[5]
History of left ventricular hypertrophy	0	Assumption	0	Assumption
History of diabetes	0	Assumption	0.09	Smith 2013[5]
History of coronary heart disease	0	Assumption	0.06	Smith 2013[5]
History of stroke	0	Assumption	0.04	Smith 2013[5]

HDL, high density lipoprotein; SD, standard deviance

Supplementary section 2. Model structure of previous economic models in schizophrenia

We reviewed the model structure of the models for economic evaluation in schizophrenia[6-89], identified from previous systematic review[90] and an updated search in 2019[91]. We extracted information on the model structure, including branching points and branches for decision tree (DT) models, health states and transitions for cohort-level (CL) and patient-level (PL) Markov models (MM), and events for discrete event simulation (DES) model. Description analyses were performed on the extracted information for DT and CLMM models. For PLMM and DES model, the model structure of the original core model was described in detailed, since only two original core models were available in each of them. The difference between the adapted models and the original core model were summarized.

To compare the model structure in different types of model, the structural elements were grouped into pathway, which was used to represent the evolution of certain status. For example, assuming the pathway of schizophrenia disease progression is that, a stable patient may "relapse" and move to "Acute" status, then may "recover" and move back to the "Stable" status. In DT model, this can be represented by a branching point of "relapse?" followed by two branches of "no relapse" and "relapse", with "relapse" followed by another branching point of "remission?" further followed by two branches of "remission" and "no remission". In Markov model, this can be represented by the health states of "Stable" and "Acute", and the transition between them. In DES model, this can be represented by events of "Relapse" and "Remission", with both possible to happen after the other.

Decision tree model

Twenty-nine DT models (85.3% of all DT models) reported their model structure, evaluating 2 to 64 outcomes and 1 to 12 branching points with increasing model complexity. Most of them covered disease progression, treatment sequence and side effect. Most had branching points at relapse, response, discontinuation, and adherence. Other rare structures were applied, including different side effects, suicide and employability. The relapse branch was composed of stable and relapse, with around half of them further classifying relapse depending on the necessity of hospitalization. The response branch was composed of response and no response. The discontinuation branch was composed of continuation, discontinuation, with discontinuation sometimes followed by a switch or dose increase or discontinuing medication all together. The adherence branch was composed of adherent, non-adherent, and sometimes partially adherent. (Table SS1)

Table SS1. Branching points in the decision tree models

Pathway	Branching point	Level	Branch
Disease progression	Relapse (n=21)	2	• relapse, stable (or no relapse, relapse) • exacerbation, stable • hospitalization, stable
		3	• exacerbation, hospitalization, stable (or relapse requiring hospitalization, relapse not requiring hospitalization, stable)
	Response (n = 12)	2	• no response, response • clinical deterioration, response • inadequate response, response
Treatment behaviour	Discontinuation (n = 19)	2	• continue, discontinue • continue, switch • switch, discontinue medication all together
		3	• continue, increase dose, switch • continue, switch, discontinue medication all together
		4	• continue, discontinue medication all together, switch due to side effect, switch due to lack of efficacy
	Adherence (n = 11)	2	• adherent, non-adherent
		3	• adherent, non-adherent, partially adherent
Side effect	Diabetes (n=2)	2	• no, yes
	metabolic syndrome (n=2)	2	• no, yes
	EPS (n=2)	2	• no, yes
	Therapy acceptability (n=1)	2	• no, yes
	Anticholinergic use (n=1)	2	• no, yes
	Diabetes complications (n=1)	7	• no complication, amputation, fatal MI, heart failure, ischemic heart disease, non-fatal MI, non-fatal stroke
	Side effect (n=1)	4	• no side effect, diabetes, EPS, intolerance glucose, weight gain
Others	Employability(n=1)	2	• no, yes
	Hospitalization (n=2)	2	• discharge from hospital, remain hospitalization
	Suicide (n=2)	2	• no suicide, suicide attempt/completion

EPS: extrapyramidal symptom; MI: myocardial infarction

Cohort-level Markov model

Thirty-one CLMM models (91% of all CLMM models) reported their structure, considering Markov health states from 2 to 33. Most of them reported the structure considering death and disease progression. Other pathways included presence of side effects, treatment lines, treatment status, setting of care, and adherence levels. Most models reported a structure with overall death, whereas others considered suicide specifically. There were seven ways of classification for schizophrenia health state, with 2-state classification of stable and relapse most used (Table SS2). Eight CLMM models did not include disease states, focused on the transition between the composite health states from parts of pathways of side effects, settings of care, treatment lines and treatment status.

Table SS2. Health states considered in the CLMM models

Pathway	Health states	N
Disease progression	schizophrenia, remission	2
	stable, relapse	14
	stable, non-stable, relapse	3
	no symptom, mix symptom, positive symptom, negative symptom, relapse	2
	residual, relapse	1
	PANSS improve >30%, PANSS improve 20%-30%, no response, post-relapse response, first relapse, subsequent relapse	2
	Mohr-Lenert health states 1-8	1
Side effect (SE)	no SE, SE	3
	no irreversible SE, irreversible SE	1
	no EPS, EPS	2
	no SE, tardive dyskinesia, agranulocytosis	2
	no SE, myocardial infarction, stroke	1
	no SE, metabolic syndrome, diabetes, coronary heart disease	1
	no SE, diabetes, stroke, CHD, hypertension, comorbidities (n=2,3,4)	1
Treatment sequence	comparator, clozapine	1
	≥ 2 lines of treatments	3
	3 lines of treatments	3
	4 lines of treatments	3
Treatment status	Treated, untreated	6
Setting of care	inpatient, outpatient	8
	hospitalization, outpatient intensive care, outpatient mild care	1
Adherence	adherent, non-adherent	3
	adherent, partially adherent, non-adherent	2
Survival	death, alive	21
	suicide, no suicide	5

CHD: coronary heart disease; EPS: extrapyramidal symptom; PANSS: positive and negative symptom scale; SE: side effect

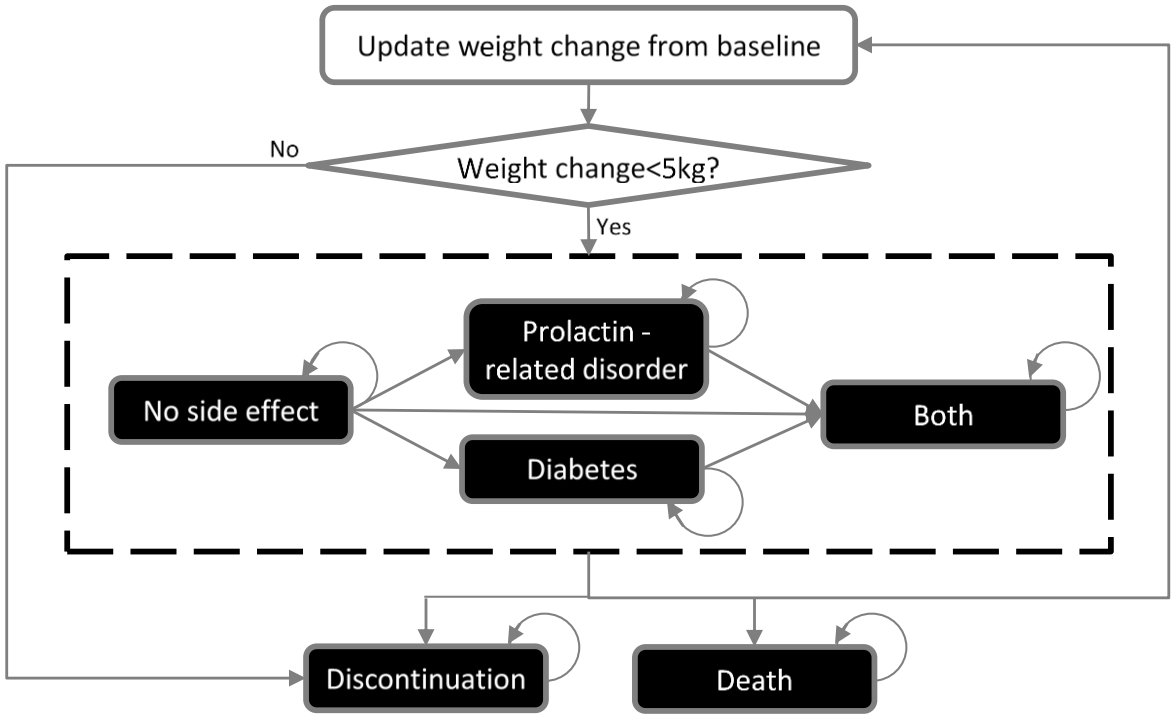
Patient-level Markov model

Among PLMM models, two were original[52,76], whereas the others adapted the model by Furiak et al.[52].

Core PLMM model by Vera-Llonch et al[76]

Figure SS1 shows the recreated structure for the model by Vera-Llonch et al[76]. This model focused on treatment side effects. It considered the transition among six health states including "No side effect", "Prolactin-related disorder only", "Diabetes only", "Both prolactin-related disorder and diabetes", "Discontinuation" and "Death" at monthly cycle over 1-year timeframe. Patients differed in baseline weight and body mass index (BMI), with weight changed depending on baseline BMI, treatment taken and months on treatment. A weight change >5 kg might lead to treatment discontinuation.

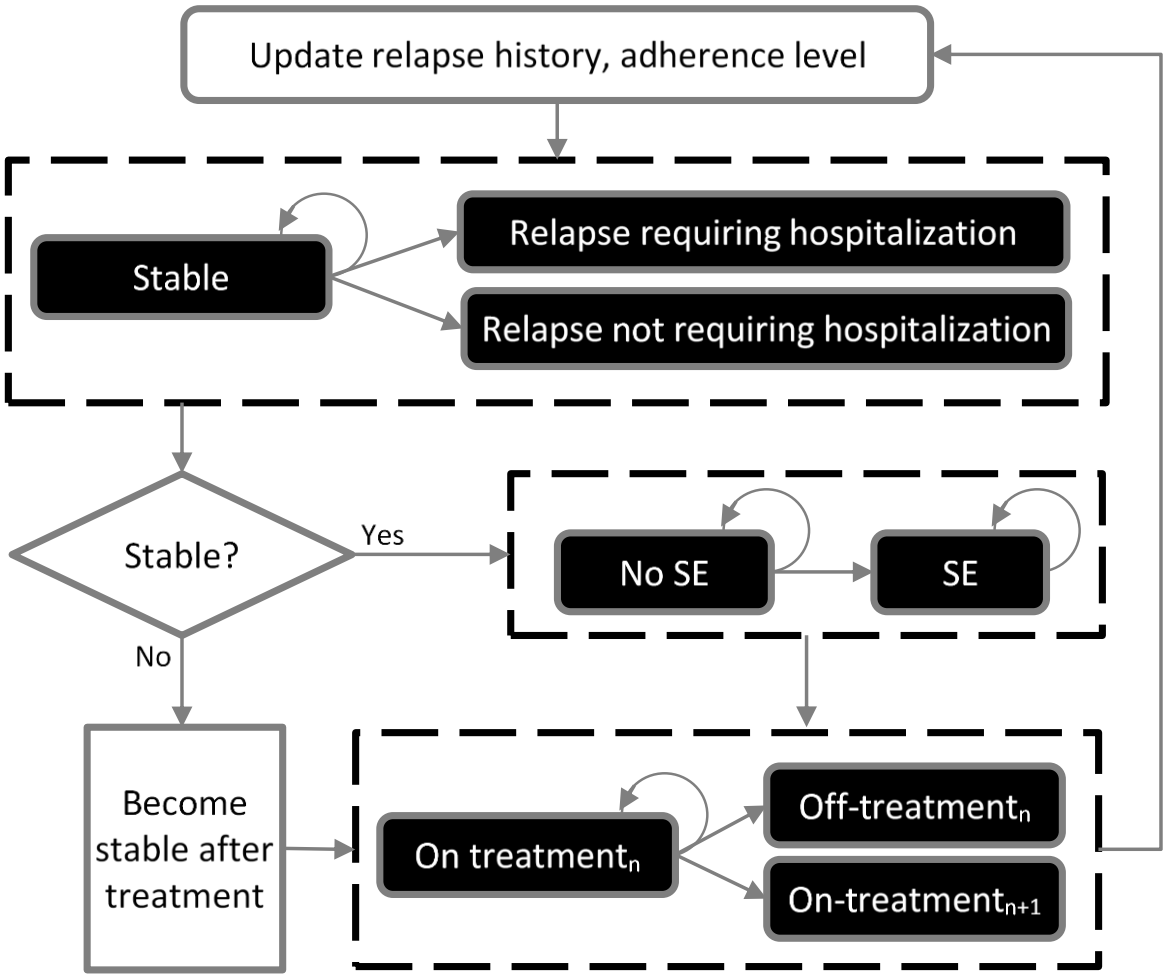
Figure SS1. Recreated model structure for the PLMM model by Vera-Llonch et al



Core PLMM model by Furiak et al[52]

Figure SS2 shows the recreated structure for the model by Furiak et al[52] . This model covered the pathways of disease progression, side effects and treatment discontinuation, and modelled at 3-month cycle over 1-year timeframe. For disease progression, there were three health states: stable, relapse requiring or not requiring hospitalization. The side effect (SE) presented in the structure included weight gain, EPS, diabetes and hyperlipidaemia, each with 2 health states (with and without SE). Treatment discontinuation included continuation, discontinuing medication all together, and switch to the next line of treatment. Patients differed from each other in adherence level in baseline. As the cycle advanced, patients would have different risk of relapse either requiring or not requiring hospitalization, with varying number of previous relapses, adherence levels, treatments status. Patients would also have different probability of treatment switch and discontinuation depending on current state in schizophrenia, SE, and treatment status.

Figure SS2. Recreated model structure of the PLMM model by Furiak et al



SE: side effect. The SE shown in the structure only included irreversible SE within the 1-year timeframe, including weight gain, EPS, diabetes, hyperlipidaemia.

Other non-core PLMM model

The other models[6,41,46] adapted the model structure by Furiak et al[52] with very limited changes in the model structure. Another model by Furiak et al[46] made a minor structural change, adding hyperprolactinemia and tardive dyskinesia as irreversible side effects. The others basically changed the model input due to the change of compared treatments and the change of country of analysis in their models.

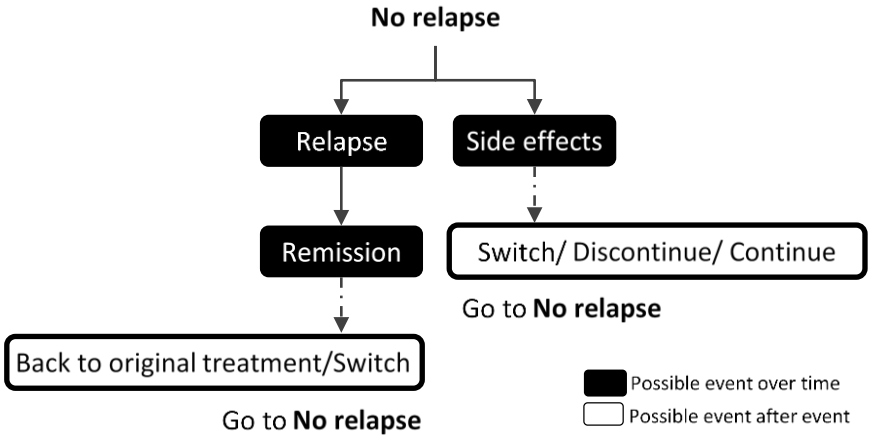
Discrete event simulation model

Among DES models, two were original[25,70], whereas the others adapted the model by Heeg et al.[70].

Core DES model by Dilla et al[20]

Figure SS3 shows the recreated structure for the model by Dilla et al. This model covered the pathways of disease progression, side effect and treatment status. Relapse was reported as the only event in the pathway of disease progression, though remission should be also included in the model. Presence of side effects was also reported as the only event in the pathway of side effect, with side effects possibly considered as irreversible. In the pathway of treatment status, patients were possible to discontinue, switch or return to original treatments after relapse or side effects. Time seems advanced with relapse and the presence of side effects. Events in treatment status possibly happened right after relapse or presence of side effect, and remission possibly happened after certain period or ratio of time from the most recent relapse. Patients differ from each other mainly on the time spent on the health states in each pathway.

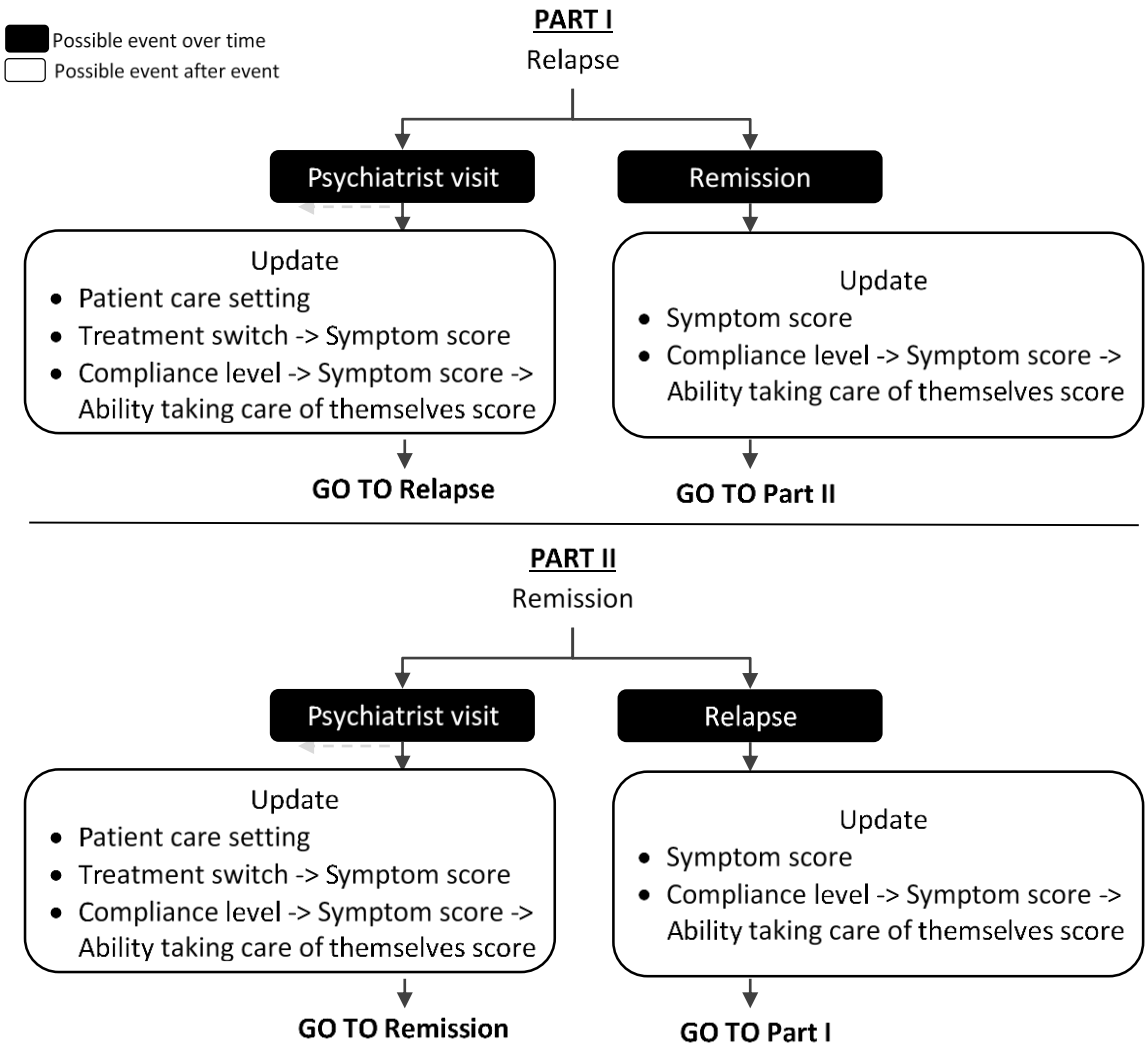
Figure SS3. Recreated model structure for the DES model by Dilla et al



Core DES model by Heeg et al[70]

Figure SS4 shows the recreated structure for the model by Heeg et al[70]. This model covered multiple pathways, including disease progression, psychiatrist visit, treatment sequence, compliance, symptom score, patient care setting and ability of taking care of themselves. In disease progression pathway, patients may relapse from remission, or remission from relapse. In psychiatrist visit pathway, patients would move forward from the first to the next several visits after relapse and back to the first visit after relapse when they visit the psychiatrist after relapse. The model time advanced by time to remission, relapse and psychiatrist visit, and ended at the target timeframe or death. The transition in the other pathways happened right after these events. Patients differed from each other initially in the following characteristics: disease severity; risk of self-harming or harming others; possibility of side effect; and social and environmental factors with impact on their treatment location.

Figure SS4. Recreated model structure for the DES model by Heeg et al



The other model[34,48,50,53,54,58,68,74] adapted the model by Heeg et al[70], with very limited changes in the model structure. Another model by Heeg et al[54] made a minor structural change, adding another compliance level and another line of treatment for switch. The others basically changed the model input due to the change of compared treatments (original: typical antipsychotic treatment with different compliance levels; adaptation: risperidone long-acting injection vs. others, branded risperidone vs. generic risperidone, different atypical antipsychotics, paliperidone extended release vs. others) and the change of country of analysis (original: the UK; adaptation: Canada, Germany, Spain, and Sweden) in their models.

Supplementary section 3. Time to event simulation with an example of time to relapse simulation.

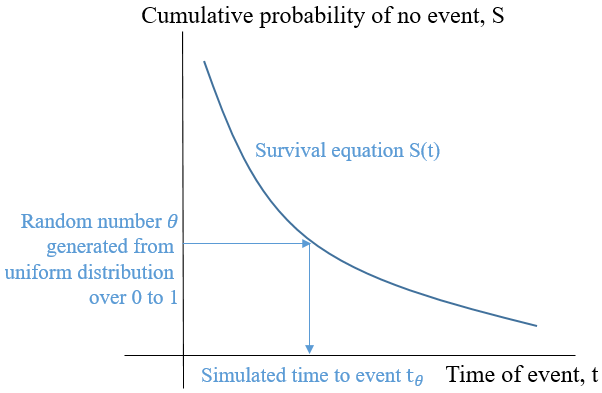
To simulate a time to event for an individual, we

- firstly determined the time to event equation based on the survival equation reflecting the cumulative probability of no event ($S(t)$) over time (t) and the individual characteristics
- secondly generated a random number (θ) between 0 and 1 assuming it is the random probability of the event happening $S(t_\theta)$ at a particular time (t_θ)
- last derived the event time by identifying the corresponding time at the random probability of the event happening based on the time to event equation for this individual

Figure SS illustrate the above process. Take the simulation of time to relapse as an example, we

- firstly determined the time to relapse equation of the individual
    - Time to relapse was assumed following exponential distribution, therefore given the characteristics of an individual the rate (r) of relapse over time (t)is constant
    - The cumulative probability of no relapse $S(t) = \exp^{-rt}$
    - The above equation could be converted to: $t = \frac{-\ln(S(t))}{r}$
- secondly drew a random number (θ) between 0 and 1, assuming it is the random cumulative probability of no relapse $S(t_\theta)$
- last derived the time to relapse for this individual $t_\theta = \frac{-\ln(\theta)}{r}$

Figure SS. Illustrative example of time to event simulation.



Supplementary section 4. Illustration of the use of the DES model.

To facilitate the use of the DES model, an RShiny webpage was developed with a case application to illustrate its use (available at https://livedataoxford.shinyapps.io/shiny_des_schizophrenia/), allowing users to perform economic evaluation of antipsychotics by modifying the treatment profiles and filling the data of a patient or a cohort of patients. The default patient was a 25-year old man with schizophrenia remitting from their first episode, being a non-smoker, not consuming any alcohol, partially compliant to antipsychotics, with the following metabolic profiles (BMI: 25 kg/m^2; total cholesterol: 150 mg/dl; HDL cholesterol: 40 mg/dl; Triglyceride: 140 mg/dl; fasting glucose: 80 mg/dl; systolic blood pressure: 120 mmHg), and without any following treatment or disease histories: use of antihypertensive treatment, atrial fibrillation, left ventricular hypertrophy, CHD, stroke, diabetes and parental diabetes. The default comparison was olanzapine compared with risperidone-LAI both as second-line treatment following first-line amisulpride, which were the undominated scenarios from the 90 treatment sequences in the base-case analyses (Table S4). Compared with olanzapine scenario, over ten years, risperidone-LAI scenario led to both higher QALYs (0·009) and higher costs (£2629), with an ICER of £298,465/QALY and net monetary benefit of £-2452 at a WTP of £20,000/QALY, indicating risperidone-LAI scenario was not cost-effective for this person.

Supplementary tables

Supplementary table 1. Number of prescriptions of atypical antipsychotics in the UK over 2014-2022

Atypical	2014	2015	2016	2017	2018	2019	2020	2021	2022
Oral product									
Amisulpride	396,244	401,170	405,509	403,363	403,682	403,457	409,740	399,643	396,371
Aripiprazole	721,923	820,177	925,007	1,028,029	1,131,199	1,252,622	1,369,540	1,484,867	1,572,613
Cariprazine	NA	NA	NA	NA	5	272	1,188	1,943	2,855
Lurasidone	91	2,702	6,975	12,759	16,581	21,230	26,769	32,044	37,748
Olanzapine	2,171,475	2,255,063	2,345,511	2,398,850	2,445,795	2,489,579	2,564,452	2,599,771	2,607,892
Paliperidone[a]	1,277	1,630	1,644	1,927	2,123	2,408	2,839	3,450	3,685
Quetiapine	2,577,302	2,811,606	3,082,370	3,322,969	3,517,655	3,735,141	4,013,204	4,200,612	4,315,352
Risperidone	1,621,477	1,682,245	1,722,382	1,744,097	1,761,325	1,766,177	1,784,804	1,772,142	1,772,200
Long acting injection (LAI) product									
Aripiprazole	NA	3,116	5,162	7,977	10,535	12,580	14,565	15,359	15,127
Olanzapine[a]	128	180	204	256	251	385	451	489	567
Paliperidone	5,451	7,823	9,828	11,520	12,336	13,349	14,314	14,738	14,830
Risperidone	28,266	25,185	22,469	19,747	17,314	15,052	12,976	10,973	9,647

Data obtained from Prescription Cost Analysis (PCA) – England database[92]

[a]: Oral paliperidone and depot olanzapine were not included in the present study as they were not commonly used in the current practice though they have been available since 2014. NA: not available;

Supplementary table 2. Model input for the base-case, DSA and PSA analyses

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Annual probability of relapse	0.72	0.65	0.77	Beta	137.55	54.17	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: amisulpride oral vs. placebo	0.19	0.10	0.39	Lognorm	-1.65	0.36	Ostuzzi 2022[94], Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: aripiprazole oral vs. placebo	0.32	0.14	0.56	Lognorm	-1.14	0.35	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: cariprazine oral vs. placebo	0.65	0.16	1.14	Lognorm	-0.43	0.50	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: lurasidone oral vs. placebo	0.63	0.25	1.02	Lognorm	-0.46	0.36	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: olanzapine oral vs. placebo	0.20	0.09	0.38	Lognorm	-1.61	0.37	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: quetiapine oral vs. placebo	0.47	0.24	0.72	Lognorm	-0.76	0.28	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: risperidone oral vs. placebo	0.29	0.14	0.49	Lognorm	-1.24	0.32	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: clozapine oral vs. placebo	0.06	0.03	0.11	Lognorm	-2.82	0.30	Essali 2009[95], Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: aripiprazole LAI vs. placebo	0.32	0.14	0.57	Lognorm	-1.14	0.36	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: paliperidone LAI vs. placebo	0.31	0.16	0.48	Lognorm	-1.17	0.28	Schneider-Thoma 2022[93]
Risk ratio of relapse by treatment: risperidone LAI vs. placebo	0.25	0.12	0.47	Lognorm	-1.39	0.35	Schneider-Thoma 2022[93]
Hazard ratio of relapse by compliance: partial vs. full	1.79	1.31	2.43	Lognorm	0.58	0.16	Gilmer 2004[4]
Hazard ratio of relapse by compliance: none vs. full	2.59	1.88	3.56	Lognorm	0.95	0.16	Gilmer 2004[4]
Duration of relapse, years	0.50	0.38	0.63	Norm	0.50	0.06	NICE 2014[96] (Range: ±25%)
Annual probability of discontinuation using amisulpride oral	0.25	0.16	0.38	Beta	13.71	41.72	Ostuzzi 2022[94], Schneider-Thoma 2022[93]
Annual probability of discontinuation using aripiprazole oral	0.46	0.33	0.58	Beta	27.02	31.85	Schneider-Thoma 2022[93]
Annual probability of discontinuation using cariprazine oral	0.61	0.35	0.82	Beta	9.64	6.11	Schneider-Thoma 2022[93]
Annual probability of discontinuation using lurasidone oral	0.51	0.35	0.67	Beta	19.49	18.54	Schneider-Thoma 2022[93]
Annual probability of discontinuation using olanzapine oral	0.27	0.18	0.36	Beta	25.79	70.53	Schneider-Thoma 2022[93]
Annual probability of discontinuation using quetiapine oral	0.42	0.31	0.54	Beta	27.60	38.00	Schneider-Thoma 2022[93]
Annual probability of discontinuation using risperidone oral	0.31	0.21	0.41	Beta	24.94	56.56	Schneider-Thoma 2022[93]
Annual probability of discontinuation using clozapine oral	0.33	0.22	0.49	Beta	14.96	30.64	Kishimoto 2019[97], Schneider-Thoma 2022[93]
Annual probability of discontinuation using aripiprazole LAI	0.36	0.26	0.47	Beta	27.37	48.76	Schneider-Thoma 2022[93]
Annual probability of discontinuation using paliperidone LAI	0.43	0.33	0.51	Beta	47.39	63.24	Schneider-Thoma 2022[93]
Annual probability of discontinuation using risperidone LAI	0.34	0.23	0.47	Beta	19.58	37.31	Schneider-Thoma 2022[93]
Proportion of switch after relapse	0.50	0.25	0.75	Beta	7.18	7.18	Assumption
Proportion of acute EPS using amisulpride oral	0.28	0.18	0.38	Beta	20.78	52.76	Leucht 2013[98], Schneider-Thoma 2022[93]
Proportion of acute EPS using aripiprazole oral	0.41	0.22	0.59	Beta	11.17	15.81	Schneider-Thoma 2022[93]
Proportion of acute EPS using cariprazine oral	0.36	0.15	0.57	Beta	6.61	11.89	Schneider-Thoma 2022[93]
Proportion of acute EPS using lurasidone oral	0.19	0.09	0.44	Beta	3.43	14.73	Schneider-Thoma 2022[93]
Proportion of acute EPS using olanzapine oral	0.04	0.01	0.23	Beta	0.52	11.56	Schneider-Thoma 2022[93]
Proportion of acute EPS using quetiapine oral	0.21	0.12	0.39	Beta	7.49	27.93	Schneider-Thoma 2022[93]
Proportion of acute EPS using risperidone oral	0.26	0.13	0.48	Beta	6.15	17.67	Schneider-Thoma 2022[93]
Proportion of acute EPS using clozapine oral	0.06	0.02	0.13	Beta	5.11	73.58	Leucht 2013[98], Schneider-Thoma 2022[93]
Proportion of acute EPS using aripiprazole LAI	0.45	0.26	0.62	Beta	13.23	16.08	Schneider-Thoma 2022[93]
Proportion of acute EPS using paliperidone LAI	0.35	0.23	0.53	Beta	13.16	24.42	Schneider-Thoma 2022[93]
Proportion of acute EPS using risperidone LAI	0.27	0.14	0.53	Beta	4.98	13.41	Schneider-Thoma 2022[93]
Proportion of weight gain using amisulpride oral	0.27	0.13	0.45	Beta	7.84	21.08	NICE 2014[96]
Proportion of weight gain using aripiprazole oral	0.13	0.07	0.22	Beta	9.29	63.00	NICE 2014[96]
Proportion of weight gain using cariprazine oral	0.21	0.06	0.71	Beta	1.00	3.87	Ostuzzi 2022[94], NICE 2014[96]
Proportion of weight gain using lurasidone oral	0.19	0.05	0.67	Beta	0.99	4.26	Ostuzzi 2022[94], NICE 2014[96]
Proportion of weight gain using olanzapine oral	0.36	0.25	0.47	Beta	26.43	46.15	NICE 2014[96]
Proportion of weight gain using quetiapine oral	0.40	0.13	1.00	Beta	1.53	2.30	Ostuzzi 2022[94], NICE 2014[96]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Proportion of weight gain using risperidone oral	0.18	0.09	0.29	Beta	9.93	45.59	NICE 2014[96]
Proportion of weight gain using clozapine oral	0.26	0.21	0.31	Beta	88.27	256.52	Essali 2009[95], NICE 2014[96]
Proportion of weight gain using aripiprazole LAI	0.13	0.07	0.22	Beta	9.29	63.00	NICE 2014[96]
Proportion of weight gain using paliperidone LAI	0.18	0.08	0.30	Beta	7.96	36.90	NICE 2014[96]
Proportion of weight gain using risperidone LAI	0.18	0.09	0.29	Beta	9.93	45.59	NICE 2014[96]
Proportion of sedation using amisulpride oral	0.03	0.01	0.05	Beta	10.07	347.52	Leucht 2013[98], Schneider-Thoma 2022[93]
Proportion of sedation using aripiprazole oral	0.01	0.01	0.03	Beta	7.41	521.88	Schneider-Thoma 2022[93]
Proportion of sedation using cariprazine oral	0.01	0.00	0.02	Beta	3.57	353.91	Ostuzzi 2022[94], Schneider-Thoma 2022[93]
Proportion of sedation using lurasidone oral	0.02	0.01	0.05	Beta	4.81	194.14	Schneider-Thoma 2022[93]
Proportion of sedation using olanzapine oral	0.03	0.02	0.05	Beta	11.54	378.42	Schneider-Thoma 2022[93]
Proportion of sedation using quetiapine oral	0.06	0.04	0.09	Beta	15.90	267.98	Schneider-Thoma 2022[93]
Proportion of sedation using risperidone oral	0.02	0.01	0.04	Beta	7.94	328.37	Schneider-Thoma 2022[93]
Proportion of sedation using clozapine oral	0.15	0.09	0.24	Beta	13.83	76.82	Leucht 2013[98], Schneider-Thoma 2022[93]
Proportion of sedation using aripiprazole LAI	0.04	0.01	0.12	Beta	2.42	53.36	Schneider-Thoma 2022[93]
Proportion of sedation using paliperidone LAI	0.04	0.02	0.08	Beta	5.15	141.94	Schneider-Thoma 2022[93]
Proportion of sedation using risperidone LAI	0.01	0.01	0.03	Beta	5.13	341.16	Schneider-Thoma 2022[93]
Proportion of sexual dysfunction using amisulpride oral	0.03	0.01	0.07	Beta	3.00	106.00	Schmidt-Kraepelin 2022[99], Serretti 2011[100]
Proportion of sexual dysfunction using aripiprazole oral	0.27	0.17	0.39	Beta	17.00	45.00	Serretti 2011[100]
Proportion of sexual dysfunction using cariprazine oral	0.01	0.01	0.01	Beta	20	2028	Schmidt-Kraepelin 2022[99], Serretti 2011[100]
Proportion of sexual dysfunction using lurasidone oral	0.00	NA	NA	NA	NA	NA	Clayton 2018[101]
Proportion of sexual dysfunction using olanzapine oral	0.40	0.39	0.42	Beta	1421	2100	Serretti 2011[100]
Proportion of sexual dysfunction using quetiapine oral	0.15	0.13	0.17	Beta	213	1233	Serretti 2011[100]
Proportion of sexual dysfunction using risperidone oral	0.45	0.43	0.48	Beta	864	1038	Serretti 2011[100]
Proportion of sexual dysfunction using clozapine oral	0.53	0.43	0.62	Beta	58.00	52.00	Serretti 2011[100]
Proportion of sexual dysfunction using aripiprazole LAI	0.27	0.17	0.39	Beta	17.00	45.00	Serretti 2011[100]
Proportion of sexual dysfunction using paliperidone LAI	0.57	0.38	0.73	Beta	17.16	13.17	Potkin 2017[102], Serretti 2011[100]
Proportion of sexual dysfunction using risperidone LAI	0.45	0.43	0.48	Beta	864	1038	Serretti 2011[100]
Annual probability of tardive dyskinesia using amisulpride oral	0.02	0.00	0.05	Beta	3.26	134.30	Carbon 2018[103]
Annual probability of tardive dyskinesia using aripiprazole oral	0.02	0.00	0.04	Beta	2.64	154.16	Carbon 2018[103]
Annual probability of tardive dyskinesia using cariprazine oral	0.05	0.00	0.09	Beta	4.03	82.00	Assume = Lurasidone
Annual probability of tardive dyskinesia using lurasidone oral	0.05	0.00	0.09	Beta	4.03	82.00	Carbon 2018[103]
Annual probability of tardive dyskinesia using olanzapine oral	0.03	0.02	0.04	Beta	29.25	993.97	Carbon 2018[103]
Annual probability of tardive dyskinesia using quetiapine oral	0.02	0.00	0.05	Beta	4.51	178.29	Carbon 2018[103]
Annual probability of tardive dyskinesia using risperidone oral	0.02	0.01	0.03	Beta	16.69	687.16	Carbon 2018[103]
Annual probability of tardive dyskinesia using clozapine oral	0.04	0.02	0.06	Beta	10.80	251.80	Carbon 2018[103]
Annual probability of tardive dyskinesia using aripiprazole LAI	0.02	0.00	0.04	Beta	2.64	154.16	Carbon 2018[103]
Annual probability of tardive dyskinesia using paliperidone LAI	0.02	0.01	0.03	Beta	16.69	687.16	Assume = Risperidone
Annual probability of tardive dyskinesia using risperidone LAI	0.02	0.01	0.03	Beta	16.69	687.16	Carbon 2018[103]
Proportion of agranulocytosis using clozapine	0.01	0.01	0.01	Beta	93	12667	Munro 1999[104]
Mean difference of BMI (kg/m2) by treatment: amisulpride oral vs. placebo	1.66	0.18	3.14	Norm	1.66	0.76	Deepak 2015[105]
Mean difference of BMI (kg/m2) by treatment: aripiprazole oral vs. placebo	-0.22	-0.81	0.37	Norm	-0.22	0.30	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: cariprazine oral vs. placebo	0.83	0.00	1.66	Norm	0.83	0.42	Greger 2021[107]
Mean difference of BMI (kg/m2) by treatment: lurasidone oral vs. placebo	0.24	0.08	0.41	Norm	0.24	0.08	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: olanzapine oral vs. placebo	1.07	0.90	1.25	Norm	1.07	0.09	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: quetiapine oral vs. placebo	0.70	0.44	0.96	Norm	0.70	0.13	Pillinger 2020[106]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Mean difference of BMI (kg/m2) by treatment: risperidone oral vs. placebo	0.56	0.42	0.70	Norm	0.56	0.07	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: clozapine oral vs. placebo	1.02	0.27	1.78	Norm	1.02	0.39	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: aripiprazole LAI vs. placebo	-0.22	-0.81	0.37	Norm	-0.22	0.30	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: paliperidone LAI vs. placebo	0.56	0.42	0.70	Norm	0.56	0.07	Pillinger 2020[106]
Mean difference of BMI (kg/m2) by treatment: risperidone LAI vs. placebo	0.56	0.42	0.70	Norm	0.56	0.07	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: amisulpride oral vs. placebo	8.11	-13.90	30.12	Norm	8.11	11.23	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: aripiprazole oral vs. placebo	2.32	-1.93	5.79	Norm	2.32	1.97	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: cariprazine oral vs. placebo	-3.47	-9.27	2.70	Norm	-3.47	3.05	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: lurasidone oral vs. placebo	-1.16	-0.58	3.47	Norm	-1.16	1.03	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: olanzapine oral vs. placebo	15.44	11.97	18.92	Norm	15.44	1.77	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: quetiapine oral vs. placebo	11.97	7.34	16.22	Norm	11.97	2.27	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: risperidone oral vs. placebo	2.32	-1.16	5.79	Norm	2.32	1.77	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: clozapine oral vs. placebo	21.62	10.04	33.20	Norm	21.62	5.91	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: aripiprazole LAI vs. placebo	2.32	-1.93	5.79	Norm	2.32	1.97	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: paliperidone LAI vs. placebo	2.32	-1.16	5.79	Norm	2.32	1.77	Pillinger 2020[106]
Mean difference of total cholesterol (mg/dL) by treatment: risperidone LAI vs. placebo	2.32	-1.16	5.79	Norm	2.32	1.77	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: amisulpride oral vs. placebo	-3.86	-12.74	5.41	Norm	-3.86	4.63	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: aripiprazole oral vs. placebo	1.54	0.00	3.09	Norm	1.54	0.79	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: cariprazine oral vs. placebo	0.77	-1.54	3.09	Norm	0.77	1.18	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: lurasidone oral vs. placebo	0.77	-1.93	3.47	Norm	0.77	1.38	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: olanzapine oral vs. placebo	-0.39	-1.54	1.16	Norm	-0.39	0.69	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: quetiapine oral vs. placebo	0.39	-1.16	1.93	Norm	0.39	0.79	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: risperidone oral vs. placebo	0.39	-0.77	1.93	Norm	0.39	0.69	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: clozapine oral vs. placebo	-4.48	-6.81	-2.15	Norm	-4.48	1.19	Gupta 2014[108]
Mean difference of HDL cholesterol (mg/dL) by treatment: aripiprazole LAI vs. placebo	1.54	0.00	3.09	Norm	1.54	0.79	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: paliperidone LAI vs. placebo	0.39	-0.77	1.93	Norm	0.39	0.69	Pillinger 2020[106]
Mean difference of HDL cholesterol (mg/dL) by treatment: risperidone LAI vs. placebo	0.39	-0.77	1.93	Norm	0.39	0.69	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: amisulpride oral vs. placebo	7.96	-44.25	60.18	Norm	7.96	26.64	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: aripiprazole oral vs. placebo	1.77	-6.19	9.73	Norm	1.77	4.06	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: cariprazine oral vs. placebo	0.88	-11.50	12.39	Norm	0.88	6.10	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: lurasidone oral vs. placebo	0.00	-12.39	11.50	Norm	0.00	6.10	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: olanzapine oral vs. placebo	40.71	32.74	48.67	Norm	40.71	4.06	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: quetiapine oral vs. placebo	28.32	18.58	38.94	Norm	28.32	5.19	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: risperidone oral vs. placebo	3.54	-3.54	10.62	Norm	3.54	3.61	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: clozapine oral vs. placebo	86.73	42.48	131.86	Norm	86.73	22.80	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: aripiprazole LAI vs. placebo	1.77	-6.19	9.73	Norm	1.77	4.06	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: paliperidone LAI vs. placebo	3.54	-3.54	10.62	Norm	3.54	3.61	Pillinger 2020[106]
Mean difference of triglycerides (mg/dL) by treatment: risperidone LAI vs. placebo	3.54	-3.54	10.62	Norm	3.54	3.61	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: amisulpride oral vs. placebo	-8.29	-24.86	8.47	Norm	-8.29	8.50	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: aripiprazole oral vs. placebo	2.34	-0.90	5.59	Norm	2.34	1.65	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: cariprazine oral vs. placebo	4.68	-0.90	10.45	Norm	4.68	2.90	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: lurasidone oral vs. placebo	-5.23	-9.91	-0.54	Norm	-5.23	2.39	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: olanzapine oral vs. placebo	3.60	-0.72	6.67	Norm	3.60	1.88	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: quetiapine oral vs. placebo	1.62	-1.98	5.23	Norm	1.62	1.84	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: risperidone oral vs. placebo	1.44	-1.08	3.96	Norm	1.44	1.29	Pillinger 2020[106]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Mean difference of fasting glucose (mg/dL) by treatment: clozapine oral vs. placebo	18.92	7.39	30.63	Norm	18.92	5.93	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: aripiprazole LAI vs. placebo	2.34	-0.90	5.59	Norm	2.34	1.65	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: paliperidone LAI vs. placebo	1.44	-1.08	3.96	Norm	1.44	1.29	Pillinger 2020[106]
Mean difference of fasting glucose (mg/dL) by treatment: risperidone LAI vs. placebo	1.44	-1.08	3.96	Norm	1.44	1.29	Pillinger 2020[106]
Mean difference of SBP (mmHg) by treatment: amisulpride oral vs. placebo	1.17	-3.03	5.37	Norm	1.17	2.14	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: aripiprazole oral vs. placebo	0.84	-3.32	5.00	Norm	0.84	2.12	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: cariprazine oral vs. placebo	4.17	0.40	7.94	Norm	4.17	1.93	Greger 2021[107]
Mean difference of SBP (mmHg) by treatment: lurasidone oral vs. placebo	-1.59	-2.77	-0.41	Norm	-1.59	0.60	Greger 2021[107]
Mean difference of SBP (mmHg) by treatment: olanzapine oral vs. placebo	1.28	-0.15	2.71	Norm	1.28	0.73	Greger 2021[107]
Mean difference of SBP (mmHg) by treatment: quetiapine oral vs. placebo	2.60	0.00	5.20	Norm	2.60	1.33	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: risperidone oral vs. placebo	2.60	0.00	5.20	Norm	2.60	1.33	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: clozapine oral vs. placebo	3.90	-2.59	10.39	Norm	3.90	3.31	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: aripiprazole LAI vs. placebo	0.84	-3.32	5.00	Norm	0.84	2.12	Gupta 2014[108]
Mean difference of SBP (mmHg) by treatment: paliperidone LAI vs. placebo	2.60	0.00	5.20	Norm	2.60	1.33	Assume = Risperidone
Mean difference of SBP (mmHg) by treatment: risperidone LAI vs. placebo	2.60	0.00	5.20	Norm	2.60	1.33	Gupta 2014[108]
Intercept of logistic regression of diabetes	-5.52	0.00	0.00	NA	0.00	0.00	Wilson 2007[109]
Odds ratio of diabetes by age (50-64 vs. <50, year)	0.98	0.64	1.50	Lognorm	-0.02	0.22	Wilson 2007[109]
Odds ratio of diabetes by age (>=65 vs. <50, year)	0.92	0.54	1.59	Lognorm	-0.08	0.28	Wilson 2007[109]
Odds ratio of diabetes by male	0.99	0.70	1.41	Lognorm	-0.01	0.18	Wilson 2007[109]
Odds ratio of diabetes by parental diabetes (yes vs. no)	1.76	1.17	2.64	Lognorm	0.57	0.21	Wilson 2007[109]
Odds ratio of diabetes by BMI (25-30 vs. <25, kg/m2)	1.35	0.78	2.34	Lognorm	0.30	0.28	Wilson 2007[109]
Odds ratio of diabetes by BMI (?30 vs. <25, kg/m2)	2.50	1.45	4.30	Lognorm	0.92	0.28	Wilson 2007[109]
Odds ratio of diabetes by SBP > 130/85 mmHg OR receiving therapy	1.65	1.10	2.46	Lognorm	0.50	0.21	Wilson 2007[109]
Odds ratio of diabetes by HDL (men: < 40 mg/dL; women: <50 mg/dL)	2.57	1.75	3.77	Lognorm	0.94	0.20	Wilson 2007[109]
Odds ratio of diabetes by triglyceride level >= 150 mg/dL	1.78	1.22	2.59	Lognorm	0.58	0.19	Wilson 2007[109]
Odds ratio of diabetes by fasting glucose level >= 100 mg/dL	7.25	4.89	10.74	Lognorm	1.98	0.20	Wilson 2007[109]
Intercept of accelerated failure time weibull model of incident CHD in male	12.79	6.40	19.18	Norm	12.79	3.26	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by age (year)	0.96	0.94	0.98	Lognorm	-0.04	0.01	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by ln (total cholesterol/HDL)	0.39	0.24	0.62	Lognorm	-0.95	0.24	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by ln (SBP) (lnmmHg)	0.36	0.20	0.66	Lognorm	-1.02	0.31	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by If antihypertensive, (200 - SBP) * (SBP - 110) / 100 (mmHg)	0.98	0.97	1.00	Lognorm	-0.02	0.01	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by diabetes	0.64	0.39	1.05	Lognorm	-0.44	0.25	D'Agostino 2000[110]
Accelerated ratio of incident CHD in male by current smoker	0.55	0.40	0.74	Lognorm	-0.60	0.15	D'Agostino 2000[110]
Scale of accelerated failure time weibull model of incident CHD in male	0.78	0.00	0.00	NA	0.00	0.00	D'Agostino 2000[110]
Intercept of accelerated failure time weibull model of incident CHD in female	20.97	10.49	31.45	Norm	20.97	5.35	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by age (year)	0.94	0.89	1.00	Lognorm	-0.06	0.03	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by menopause	0.02	0.00	0.40	Lognorm	-3.85	1.50	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by age AND menopause (year)	1.08	1.01	1.14	Lognorm	0.07	0.03	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by ln (total cholesterol/HDL)	0.53	0.32	0.91	Lognorm	-0.63	0.27	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by ln (SBP) (lnmmHg)	0.11	0.03	0.33	Lognorm	-2.24	0.57	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by (200 - SBP) * (SBP - 110) / 100 (mmHg) AND using antihypertensive therapy	0.91	0.75	1.09	Lognorm	-0.10	0.09	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by diabetes	0.59	0.37	0.95	Lognorm	-0.52	0.24	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by current smoker	0.69	0.50	0.94	Lognorm	-0.38	0.16	D'Agostino 2000[110]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Accelerated ratio of incident CHD in female by ln (triglycerides) (ln mg/dL)	1.31	1.01	1.69	Lognorm	0.27	0.13	D'Agostino 2000[110]
Accelerated ratio of incident CHD in female by alcohol (ow/wk)	1.05	1.00	1.12	Lognorm	0.05	0.03	D'Agostino 2000[110]
Scale of accelerated failure time weibull model of incident CHD in female	0.75	0.00	0.00	NA	0.00	0.00	D'Agostino 2000[110]
Intercept of accelerated failure time weibull model of subsequent CHD in male	5.00	2.50	7.49	Norm	5.00	1.27	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in male by age (year)	0.99	0.97	1.00	Lognorm	-0.01	0.01	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in male by ln (total cholesterol/HDL)	0.51	0.33	0.78	Lognorm	-0.67	0.22	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in male by diabetes	0.74	0.52	1.04	Lognorm	-0.30	0.17	D'Agostino 2000[110]
Scale of accelerated failure time weibull model of subsequent CHD in male	1.00	0.00	0.00	NA	0.00	0.00	D'Agostino 2000[110]
Intercept of accelerated failure time weibull model of subsequent CHD in female	13.54	5.50	21.57	Norm	13.54	4.10	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in female by age (year)	0.98	0.94	1.01	Lognorm	-0.02	0.02	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in female by ln (total cholesterol/HDL)	0.43	0.20	0.92	Lognorm	-0.83	0.38	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in female by ln (SBP) (lnmmHg)	0.25	0.05	1.30	Lognorm	-1.37	0.83	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in female by diabetes	0.46	0.26	0.80	Lognorm	-0.78	0.28	D'Agostino 2000[110]
Accelerated ratio of subsequent CHD in female by current smoker	0.69	0.40	1.19	Lognorm	-0.37	0.27	D'Agostino 2000[110]
Scale of accelerated failure time weibull model of subsequent CHD in female	1.03	0.00	0.00	NA	0.00	0.00	D'Agostino 2000[110]
Rate of exponential model of stroke in male	0.00	0.00	0.00	NA	0.00	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in male by age (centre at 50 per 10 years)	1.05	1.03	1.07	Lognorm	0.05	0.01	D'Agostino 1994[111]
Hazard ratio of stroke in male by SBP (centred at 110 per 10 mmHg)	1.02	1.01	1.02	Lognorm	0.02	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in male by (200 - SBP) * (SBP - 110) / 100 (mmHg) AND using antihypertensive therapy	1.00	1.00	1.00	Lognorm	0.00	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in male by CVD	1.73	1.68	1.78	Lognorm	0.55	0.02	D'Agostino 1994[111]
Hazard ratio of stroke in male by left ventricular hypertrophy	2.20	1.26	3.84	Lognorm	0.79	0.28	D'Agostino 1994[111]
Hazard ratio of stroke in male by Current smoker	1.69	1.27	2.23	Lognorm	0.52	0.14	D'Agostino 1994[111]
Hazard ratio of stroke in male by atrial fabriation	1.82	1.01	3.29	Lognorm	0.60	0.30	D'Agostino 1994[111]
Hazard ratio of stroke in male by diabetes	1.41	0.97	2.04	Lognorm	0.34	0.19	D'Agostino 1994[111]
Rate of exponential model of stroke in female	0.00	0.00	0.00	NA	0.00	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in female by age (centre at 50 per 10 years)	1.07	1.05	1.09	Lognorm	0.07	0.01	D'Agostino 1994[111]
Hazard ratio of stroke in female by SBP (centred at 110 per 10 mmHg)	1.02	1.01	1.02	Lognorm	0.02	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in female by (200 - SBP) * (SBP - 110) / 100 (mmHg) AND using antihypertensive therapy	1.00	1.00	1.00	Lognorm	0.00	0.00	D'Agostino 1994[111]
Hazard ratio of stroke in female by CVD	1.55	1.17	2.07	Lognorm	0.44	0.15	D'Agostino 1994[111]
Hazard ratio of stroke in female by left ventricular hypertrophy	2.24	1.39	3.60	Lognorm	0.81	0.24	D'Agostino 1994[111]
Hazard ratio of stroke in female by current smoker	1.72	1.29	2.29	Lognorm	0.54	0.15	D'Agostino 1994[111]
Hazard ratio of stroke in female by atrial fabriation	3.06	1.95	4.80	Lognorm	1.12	0.23	D'Agostino 1994[111]
Hazard ratio of stroke in female by diabetes	1.75	1.25	2.45	Lognorm	0.56	0.17	D'Agostino 1994[111]
SMR of death in schizophrenia in male	4.10	2.80	5.90	Lognorm	1.41	0.19	Reininghaus 2014[112]
SMR of death in schizophrenia in female	2.80	1.60	5.10	Lognorm	1.03	0.30	Reininghaus 2014[112]
Proportion of death at stroke in male	0.26	0.26	0.27	Beta	7882	21974	Seminog 2019[113]
Proportion of death at stroke in female	0.29	0.21	0.29	Beta	142.71	358.02	Seminog 2019[113]
Proportion of death at CHD in male	0.08	0.08	0.08	Beta	16823	198181	Asaria 2017[114]
Proportion of death at CHD in female	0.12	0.12	0.12	Beta	15872	113269	Asaria 2017[114]
Proportion of death at agranulocytosis	0.02	0.00	0.00	Beta	2.00	91.00	Munro 1999[104]
Utility weight at stable state of schizophrenia	0.81	0.74	0.88	Beta	97.72	23.37	Lenert 2004[115]
Utility weight at relapse state of schizophrenia	0.54	0.42	0.65	Beta	38.40	32.76	Lenert 2004[115]
Utility weight by agranulocytosis	0.46	0.20	0.90	Beta	3.12	3.67	Week 1991[116]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Utility decrement due to EPS	-0.04	-0.06	-0.03	Norm	-0.04	0.01	Millier 2014[117]
Utility decrement due to sedation	-0.02	-0.03	0.00	Norm	-0.02	0.01	Millier 2014[117]
Utility decrement due to sexual dysfunction	-0.02	-0.04	0.00	Norm	-0.02	0.01	Millier 2014[117]
Utility decrement due to weight gain	-0.02	-0.04	-0.01	Norm	-0.02	0.01	Millier 2014[117]
Utility decrement due to tardive dyskinesia	-0.04	-0.06	-0.03	Norm	-0.04	0.01	Assume = EPS
Utility decrement due to diabetes	-0.15	-0.19	-0.11	Norm	-0.15	0.02	Briggs 2008[118]
Utility decrement due to CHD	-0.06	-0.07	-0.04	Norm	-0.06	0.01	Clarke 2002[119]
Utility decrement due to stroke	-0.16	-0.22	-0.11	Norm	-0.16	0.03	Clarke 2002[119]
Annual drug tariff of amisulpride oral	86	64	107	Gamma	61.47	1.40	BNF 79[120] [Range: ±25%]
Annual drug tariff of aripiprazole oral	24	18	30	Gamma	61.47	0.39	BNF 79[120] [Range: ±25%]
Annual drug tariff of cariprazine oral	1048	786	1310	Gamma	61.47	17.05	BNF 79[120] [Range: ±25%]
Annual drug tariff of lurasidone oral	1183	888	1479	Gamma	61.47	19.25	BNF 79[120] [Range: ±25%]
Annual drug tariff of olanzapine oral	23	17	29	Gamma	61.47	0.37	BNF 79[120] [Range: ±25%]
Annual drug tariff of quetiapine oral	93	70	117	Gamma	61.47	1.52	BNF 79[120] [Range: ±25%]
Annual drug tariff of risperidone oral	160	120	200	Gamma	61.47	2.60	BNF 79[120] [Range: ±25%]
Annual drug tariff of clozapine oral	868	651	1085	Gamma	61.47	14.12	BNF 79[120] [Range: ±25%]
Annual drug tariff of aripiprazole LAI	2645	1984	3306	Gamma	61.47	43.03	BNF 79[120] [Range: ±25%]
Annual drug tariff of paliperidone LAI	3772	2829	4715	Gamma	61.47	61.36	BNF 79[120] [Range: ±25%]
Annual drug tariff of risperidone LAI	1375	1031	1718	Gamma	61.47	22.36	BNF 79[120] [Range: ±25%]
Cost per episode of agranulocytosis	858	644	1073	Gamma	61.47	13.96	NHS reference 2020[121] [Range: ±25%]
Cost per episode of EPS	225	168	281	Gamma	61.47	3.65	NICE 2014[96], NHS reference 2020[121], BNF79[120] [Range: ±25%]
Cost per episode of sedation	39	29	49	Gamma	61.47	0.63	Assumption, PSSRU 2020[122] [Range: ±25%]
Cost per episode of sexual dysfunction	39	29	49	Gamma	61.47	0.63	
Cost per episode of weight gain	98	74	123	Gamma	61.47	1.59	
Cost per episode of tardive dyskinesia	225	168	281	Gamma	61.47	3.65	Assume = EPS
Annual cost of CHD in people without prior CVD in year of CHD	4530	4232	4828	Norm	4530	152	Zhou 2023[123]
Annual cost of CHD in people without prior CVD in 1 year after CHD	560	464	656	Norm	560	49	Zhou 2023[123]
Annual cost of CHD in people without prior CVD in 2 years after CHD	380	297	463	Norm	380	42	Zhou 2023[123]
Annual cost of CHD in people without prior CVD in ≥3 years after CHD	350	283	417	Norm	350	34	Zhou 2023[123]
Annual cost of CHD in people with prior CVD in year of CHD	5840	5393	6287	Norm	5840	228	Zhou 2023[123]
Annual cost of CHD in people with prior CVD in 1 year after CHD	940	664	1216	Norm	940	141	Zhou 2023[123]
Annual cost of CHD in people with prior CVD in 2 years after CHD	600	433	767	Norm	600	85	Zhou 2023[123]
Annual cost of CHD in people with prior CVD in ≥3 years after CHD	600	433	767	Norm	600	85	Zhou 2023[123]
Annual cost of stroke in people without prior CVD in year of stroke	5950	5677	6223	Norm	5950	139	Zhou 2023[123]
Annual cost of stroke in people without prior CVD in 1 year after stroke	1420	1205	1635	Norm	1420	110	Zhou 2023[123]
Annual cost of stroke in people without prior CVD in 2 years after stroke	770	631	909	Norm	770	71	Zhou 2023[123]
Annual cost of stroke in people without prior CVD in ≥3 years after stroke	670	537	803	Norm	670	68	Zhou 2023[123]
Annual cost of stroke in people with prior CVD in year of stroke	6600	6178	7022	Norm	6600	215	Zhou 2023[123]
Annual cost of stroke in people with prior CVD in 1 year after stroke	1610	1317	1903	Norm	1610	149	Zhou 2023[123]
Annual cost of stroke in people with prior CVD in 2 years after stroke	1240	984	1496	Norm	1240	131	Zhou 2023[123]
Annual cost of stroke in people with prior CVD in ≥3 years after stroke	1240	984	1496	Norm	1240	131	Zhou 2023[123]
Annual cost of diabetes in people without prior CVD in < 10 years after diabetes	520	495	545	Norm	520	13	Zhou 2023[123]
Annual cost of diabetes in people without prior CVD in ≥10 years after diabetes	650	603	697	Norm	650	24	Zhou 2023[123]
Annual cost of diabetes in people with prior CVD in < 10 years after diabetes	650	579	721	Norm	650	36	Zhou 2023[123]

Model parameter	Base-case	DSA parameter		PSA parameter			Source
		Low	High	Distribution	Alpha	Beta	
Annual cost of diabetes in people with prior CVD in ≥10 years after diabetes	810	713	907	Norm	810	50	Zhou 2023[123]
Cost of death due to CHD or stroke in people without prior CVD	1460	1135	1785	Norm	1460	166	Zhou 2023[123]
Cost of death due to CHD or stroke in people with prior CVD	2700	2226	3174	Norm	2700	242	Zhou 2023[123]
Cost of death due to the other reasons in people without prior CVD	5740	5514	5966	Norm	5740	115	Zhou 2023[123]
Cost of death due to the other reasons in people with prior CVD	6240	5805	6675	Norm	6240	222	Zhou 2023[123]
Annual cost of schizophrenia state of stable	6648	3324	9971	Gamma	15	433	NICE 2014[96], PSSRU 2020[122] [Range: ±50%]
Annual cost of schizophrenia state of relapse at non-acute phase	5321	2660	7981	Gamma	15	346	
Cost of managing acute phase of a relapse episode	28645	14323	42968	Gamma	15	1864	

BMI, Body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DSA, deterministic sensitivity analysis; EPS, extrapyramidal symptom; HDL, high density lipoprotein; PSA, probabilistic sensitivity analysis; SBP, systolic blood pressure; SMR, standardized mortality ratio.

Supplementary table 3. Base-case incremental outcomes over 10 years under compared first-line antipsychotics

Reference	Ranking at WTP £20K/QALY	Incremental costs (£) / Incremental QALYs [ICER, £/QALY] compared to the reference								
		AMI	**RIS-LAI**	**ARI-LAI**	**OLA**	**PAL-LAI**	**RIS**	**ARI**	**LUR**	**QUE**
AMI	1	..	..	..	..	..	..	..	..	..
RIS-LAI	3	-6500 / 0.038	..	..	..	..	..	..	..	..
ARI-LAI	5	-13500 / 0.052	-7000 / 0.014	..	..	..	..	..	..	..
OLA	2	-1900 / 0.064	**4600 / 0.026 [179300]**	**11600 / 0.012 [955300]**	..	..	..	..	..	..
PAL-LAI	7	-17800 / 0.070	-11300 / 0.032	-4300 / 0.019	-15900 / 0.006	..	..	..	..	..
RIS	4	-10200 / 0.074	-3700 / 0.037	**3300 / 0.023 [144400]**	-8300 / 0.011	**7600 / 0.004 [1818000]**	..	..	..	..
ARI	6	-15600 / 0.095	-9100 / 0.057	-2100 / 0.044	-13700 / 0.031	**2200 / 0.025 [87700]**	-5400 / 0.021	..	..	..
LUR	8	-26500 / 0.125	-20000 / 0.087	-13000 / 0.073	-24600 / 0.061	-8700 / 0.054	-16300 / 0.050	-10900 / 0.029	..	..
QUE	9	-20300 / 0.132	-13700 / 0.094	-6800 / 0.080	-18400 / 0.068	-2500 / 0.061	-10100 / 0.057	-4700 / 0.036	**6200 / 0.007 [898700]**	..
CAR	10	-27200 / 0.174	-20700 / 0.137	-13700 / 0.123	-25400 / 0.111	-9500 / 0.104	-17000 / 0.100	-11600 / 0.079	-700 / 0.050	-7000 / 0.043

Both costs and QALY were discounted; Costs, incremental costs and ICER were round to 100; QALYs and incremental QALYs were round to 0.001.
References and comparators sorted by decreasing QALYs (thus incremental QALYs were all positive). ICER was not estimated if incremental costs was negative (reference was dominated).
Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; ICER, incremental cost-effectiveness ratio; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone; WTP. Willingness to pay

Supplementary table 4. Cost-effectiveness results across all the scenarios.

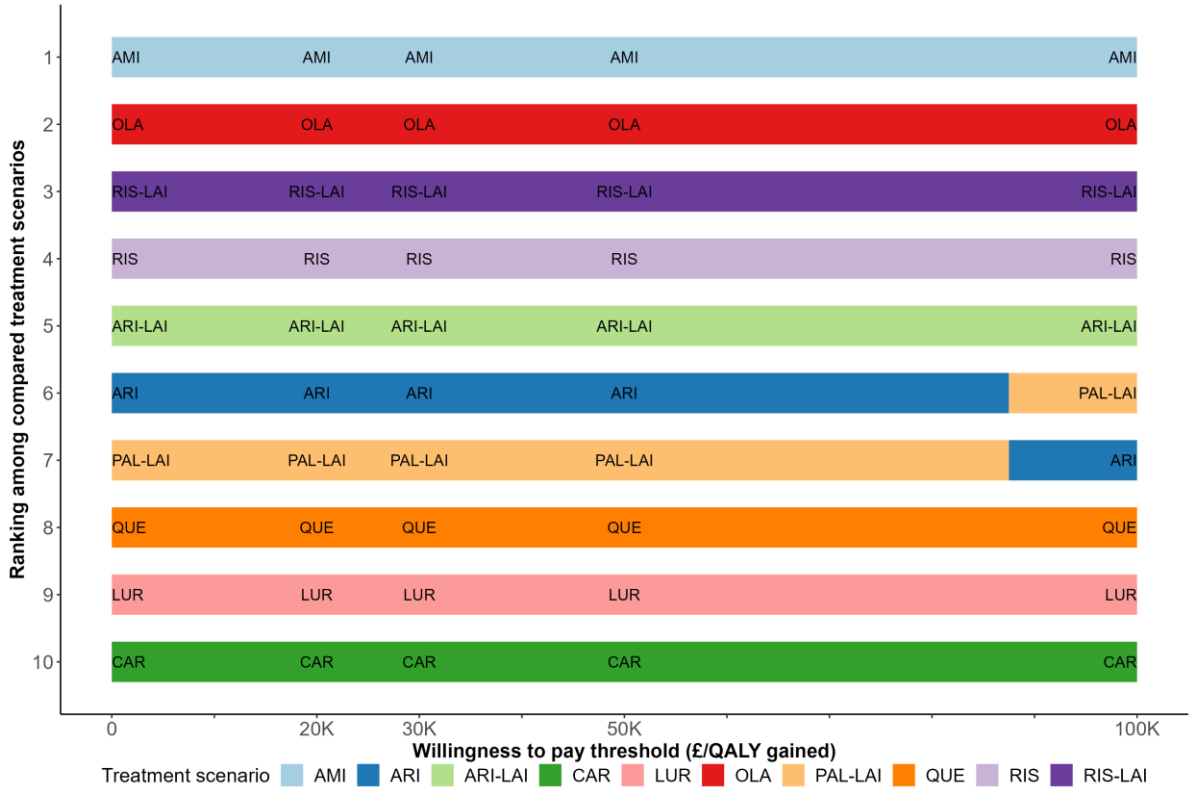
Scenario		Outcome		Incremental outcome		ICER
1st line	2nd line	Cost (£)	QALY	Cost (£)	QALY	(£/QALY gained)
Undominated scenarios						
AMI	**OLA**	138,218	6.153	-	-	-
AMI	**RIS-LAI**	141,318	6.156	3,100	0.003	909,148
All scenarios						
AMI	**OLA**	138,218	6.153	-	-	-
OLA	**AMI**	139,101	6.099	883	-0.054	Dominated
AMI	**RIS-LAI**	141,318	6.156	3,100	0.003	909,148
OLA	**RIS-LAI**	143,192	6.091	1,873	-0.066	Dominated
AMI	**RIS**	143,306	6.133	1,987	-0.023	Dominated
RIS-LAI	**AMI**	143,858	6.127	2,540	-0.029	Dominated
RIS-LAI	**OLA**	144,791	6.115	3,473	-0.041	Dominated
OLA	**RIS**	145,217	6.067	3,899	-0.089	Dominated
AMI	**ARI-LAI**	146,172	6.146	4,854	-0.010	Dominated
AMI	**ARI**	146,507	6.118	5,189	-0.039	Dominated
RIS	**AMI**	147,067	6.091	5,748	-0.065	Dominated
RIS	**OLA**	148,077	6.077	6,759	-0.079	Dominated
OLA	**ARI-LAI**	148,160	6.081	6,842	-0.076	Dominated
OLA	**ARI**	148,484	6.053	7,165	-0.103	Dominated
AMI	**PAL-LAI**	149,387	6.136	8,068	-0.020	Dominated
AMI	**QUE**	149,811	6.098	8,493	-0.059	Dominated
RIS-LAI	**RIS**	150,021	6.095	8,703	-0.062	Dominated
ARI-LAI	**AMI**	150,940	6.115	9,621	-0.041	Dominated
OLA	**PAL-LAI**	151,425	6.071	10,107	-0.085	Dominated
RIS	**RIS-LAI**	151,622	6.082	10,304	-0.075	Dominated
OLA	**QUE**	151,855	6.033	10,537	-0.123	Dominated
ARI-LAI	**OLA**	151,914	6.102	10,595	-0.055	Dominated
ARI	**AMI**	152,249	6.072	10,930	-0.084	Dominated
RIS-LAI	**ARI-LAI**	153,349	6.107	12,031	-0.049	Dominated
ARI	**OLA**	153,352	6.057	12,034	-0.099	Dominated
RIS-LAI	**ARI**	153,438	6.079	12,119	-0.077	Dominated
AMI	**LUR**	154,843	6.084	13,524	-0.072	Dominated
AMI	**CAR**	155,213	6.069	13,894	-0.088	Dominated
PAL-LAI	**AMI**	155,395	6.097	14,077	-0.060	Dominated
ARI-LAI	**RIS-LAI**	155,598	6.104	14,280	-0.052	Dominated
PAL-LAI	**OLA**	156,392	6.083	15,074	-0.073	Dominated
RIS-LAI	**PAL-LAI**	156,667	6.097	15,349	-0.059	Dominated
RIS-LAI	**QUE**	156,841	6.059	15,523	-0.097	Dominated
QUE	**AMI**	156,926	6.034	15,608	-0.122	Dominated
OLA	**LUR**	156,999	6.019	15,680	-0.138	Dominated
RIS	**ARI-LAI**	157,105	6.071	15,787	-0.086	Dominated
ARI	**RIS-LAI**	157,189	6.061	15,870	-0.095	Dominated
RIS	**ARI**	157,371	6.039	16,053	-0.117	Dominated
OLA	**CAR**	157,391	6.006	16,073	-0.151	Dominated
ARI-LAI	**RIS**	157,442	6.080	16,124	-0.076	Dominated
QUE	**OLA**	158,046	6.018	16,728	-0.138	Dominated
ARI	**RIS**	159,356	6.033	18,038	-0.123	Dominated
PAL-LAI	**RIS-LAI**	160,167	6.086	18,849	-0.071	Dominated
RIS	**PAL-LAI**	160,680	6.060	19,361	-0.097	Dominated
ARI-LAI	**ARI**	160,981	6.064	19,662	-0.092	Dominated
RIS	**QUE**	161,057	6.017	19,738	-0.139	Dominated
PAL-LAI	**RIS**	162,047	6.060	20,729	-0.096	Dominated
QUE	**RIS-LAI**	162,078	6.023	20,760	-0.133	Dominated
RIS-LAI	**LUR**	162,097	6.043	20,779	-0.113	Dominated
RIS-LAI	**CAR**	162,508	6.029	21,190	-0.128	Dominated
ARI	**ARI-LAI**	163,024	6.049	21,705	-0.107	Dominated
LUR	**AMI**	163,318	6.046	22,000	-0.110	Dominated
CAR	**AMI**	164,035	5.990	22,716	-0.167	Dominated
QUE	**RIS**	164,352	5.995	23,034	-0.162	Dominated
ARI-LAI	**PAL-LAI**	164,387	6.083	23,069	-0.074	Dominated
LUR	**OLA**	164,536	6.026	23,217	-0.130	Dominated
ARI-LAI	**QUE**	164,545	6.042	23,226	-0.114	Dominated
CAR	**OLA**	165,251	5.972	23,932	-0.184	Dominated
PAL-LAI	**ARI-LAI**	165,641	6.074	24,322	-0.082	Dominated
PAL-LAI	**ARI**	165,676	6.044	24,358	-0.113	Dominated
RIS	**LUR**	166,596	6.001	25,277	-0.155	Dominated
ARI	**PAL-LAI**	166,800	6.037	25,481	-0.119	Dominated
RIS	**CAR**	167,018	5.985	25,700	-0.171	Dominated
ARI	**QUE**	167,044	5.992	25,726	-0.164	Dominated
QUE	**ARI-LAI**	168,197	6.011	26,878	-0.145	Dominated
QUE	**ARI**	168,369	5.977	27,050	-0.180	Dominated

Scenario		Outcome		Incremental outcome		ICER
1st line	2nd line	Cost (£)	QALY	Cost (£)	QALY	(£/QALY gained)
LUR	**RIS-LAI**	168,845	6.031	27,526	-0.126	Dominated
PAL-LAI	**QUE**	169,323	6.022	28,004	-0.134	Dominated
CAR	**RIS-LAI**	169,629	5.977	28,310	-0.179	Dominated
ARI-LAI	**LUR**	170,018	6.027	28,700	-0.130	Dominated
ARI-LAI	**CAR**	170,425	6.011	29,107	-0.145	Dominated
LUR	**RIS**	171,121	6.000	29,802	-0.156	Dominated
CAR	**RIS**	171,861	5.947	30,542	-0.209	Dominated
QUE	**PAL-LAI**	172,170	5.999	30,851	-0.158	Dominated
ARI	**LUR**	172,882	5.976	31,564	-0.180	Dominated
ARI	**CAR**	173,315	5.958	31,996	-0.198	Dominated
PAL-LAI	**LUR**	174,912	6.006	33,593	-0.151	Dominated
LUR	**ARI-LAI**	175,228	6.018	33,910	-0.139	Dominated
PAL-LAI	**CAR**	175,332	5.990	34,014	-0.167	Dominated
LUR	**ARI**	175,337	5.980	34,019	-0.177	Dominated
CAR	**ARI-LAI**	176,076	5.965	34,758	-0.192	Dominated
CAR	**ARI**	176,117	5.930	34,799	-0.227	Dominated
QUE	**LUR**	178,330	5.935	37,012	-0.221	Dominated
QUE	**CAR**	178,799	5.917	37,481	-0.240	Dominated
LUR	**PAL-LAI**	179,381	6.003	38,063	-0.153	Dominated
LUR	**QUE**	179,427	5.954	38,109	-0.203	Dominated
CAR	**QUE**	180,219	5.904	38,901	-0.253	Dominated
CAR	**PAL-LAI**	180,237	5.952	38,919	-0.205	Dominated
LUR	**CAR**	186,190	5.914	44,871	-0.242	Dominated
CAR	**LUR**	186,557	5.887	45,239	-0.270	Dominated

Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; ICER, incremental cost effectiveness ratio; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

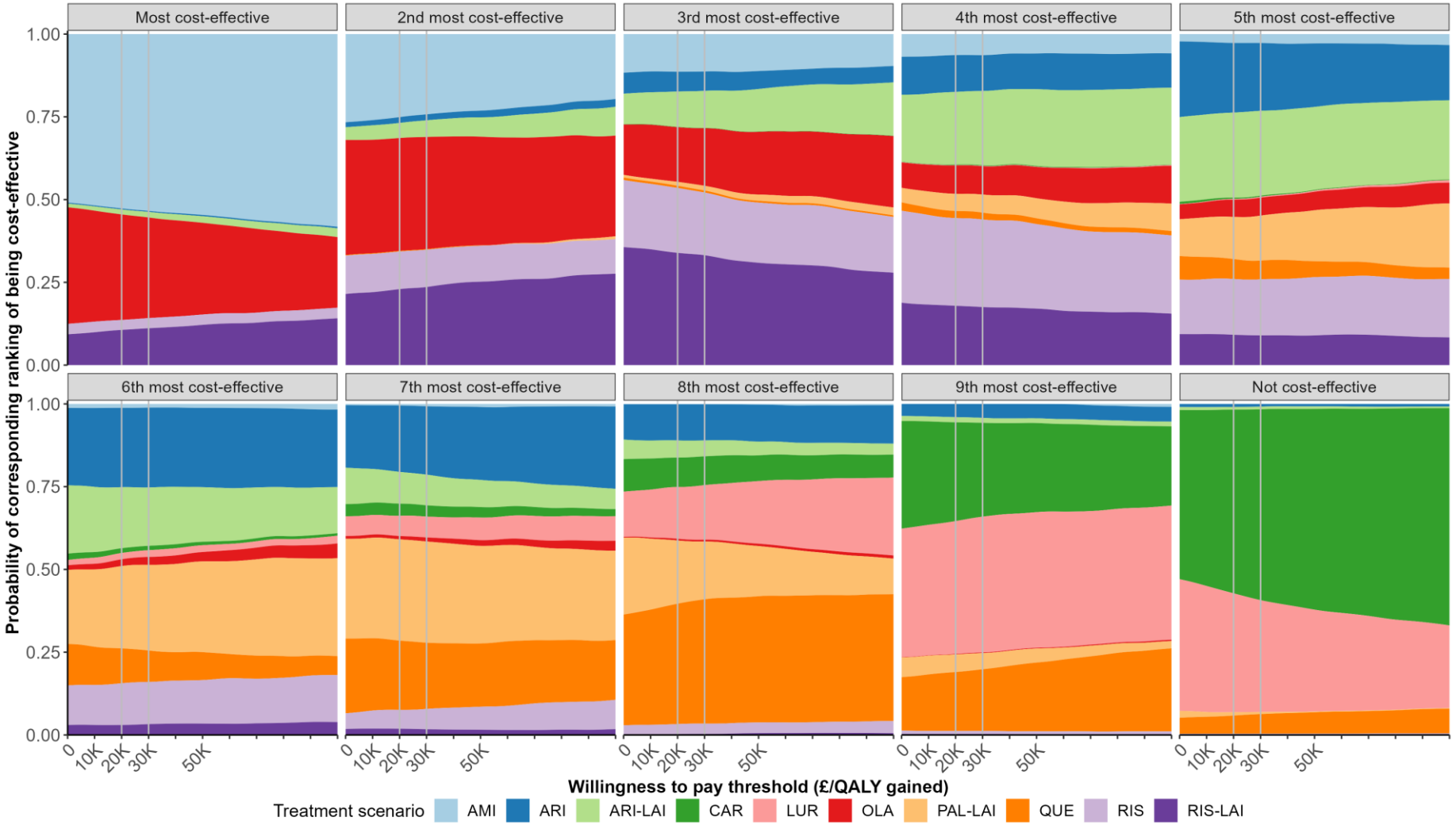
Supplementary figures

Supplementary figure 1. Base-case rankings of cost-effectiveness among first-line antipsychotics



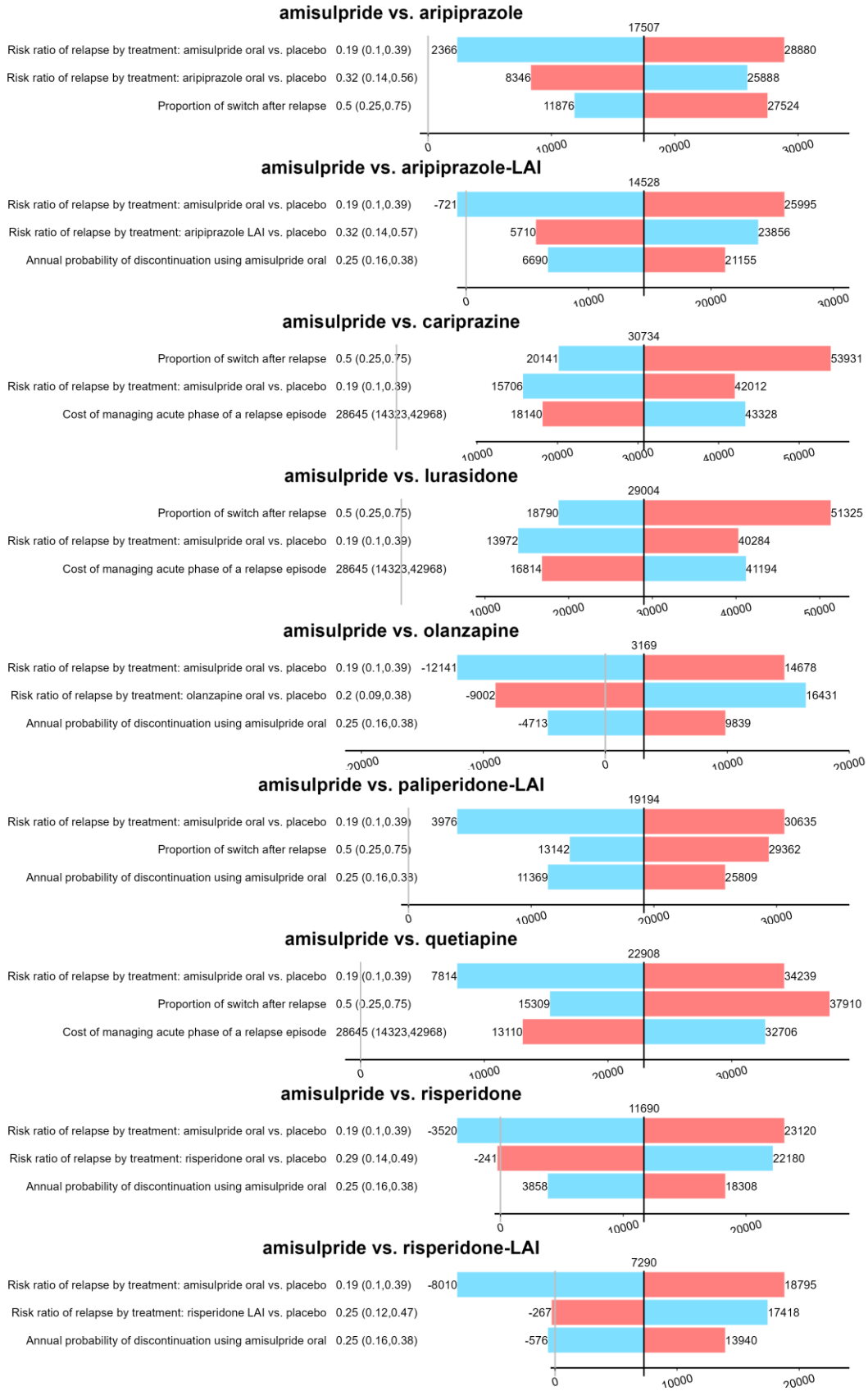
Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

Supplementary figure 2. Probabilistic sensitivity analyses results of the ranking among comparators



Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

Supplementary figure 3. Top 3 impactful inputs (n=263) on NMB at £20K/QALY in AMI vs. others

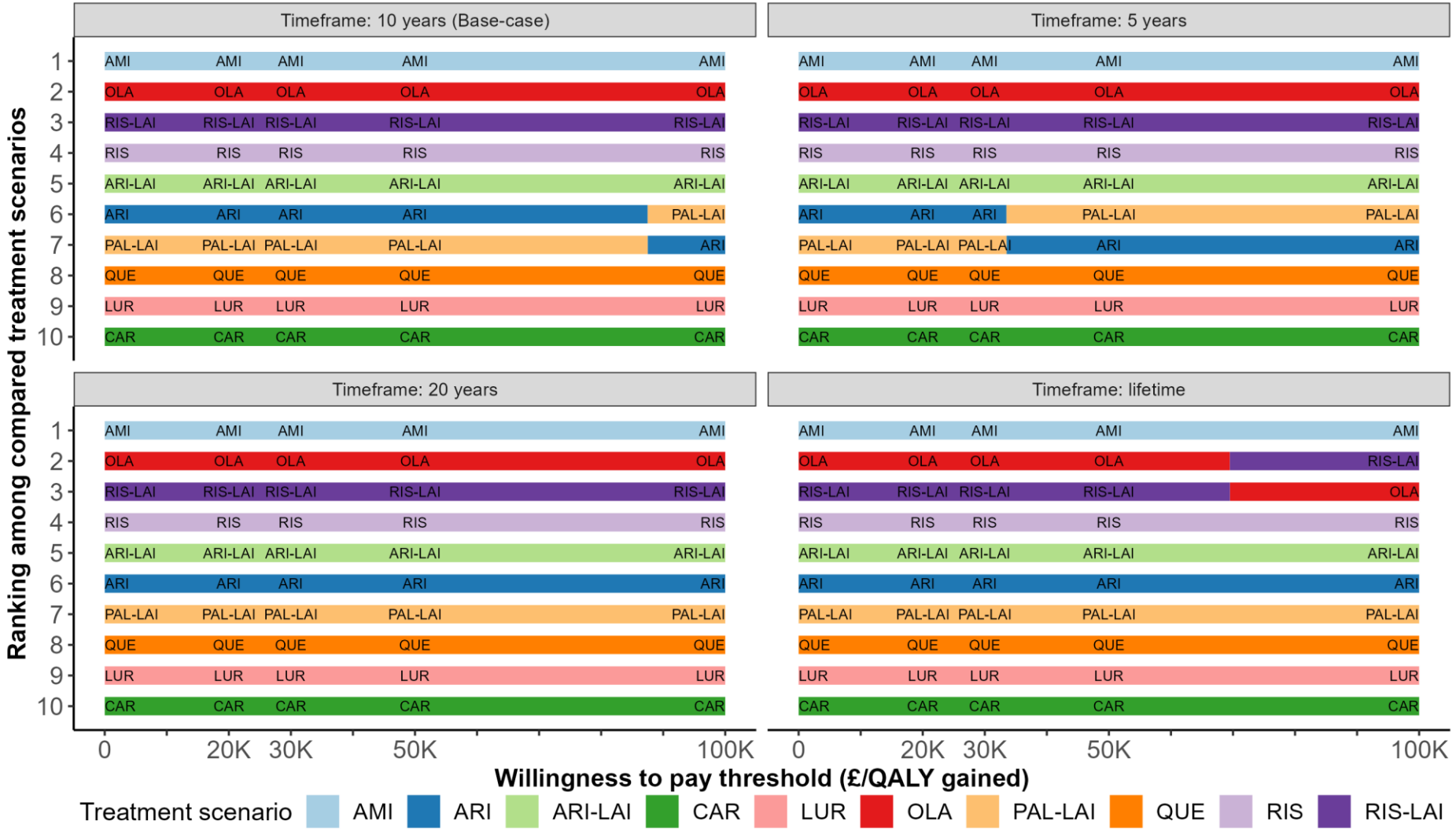


Blue (Red) bar is the result when input takes its upper (lower) range; Black vertical line is the base-case result. AMI, amisulpride; LAI, long-acting injection; NMB, net monetary benefit; QALY, quality-adjusted life year;
Comparison between other pairs of included antipsychotics is similar (results not shown)

Supplementary figure 4. Top 3 impactful inputs (n=263) on incremental QALYs in AMI vs. others

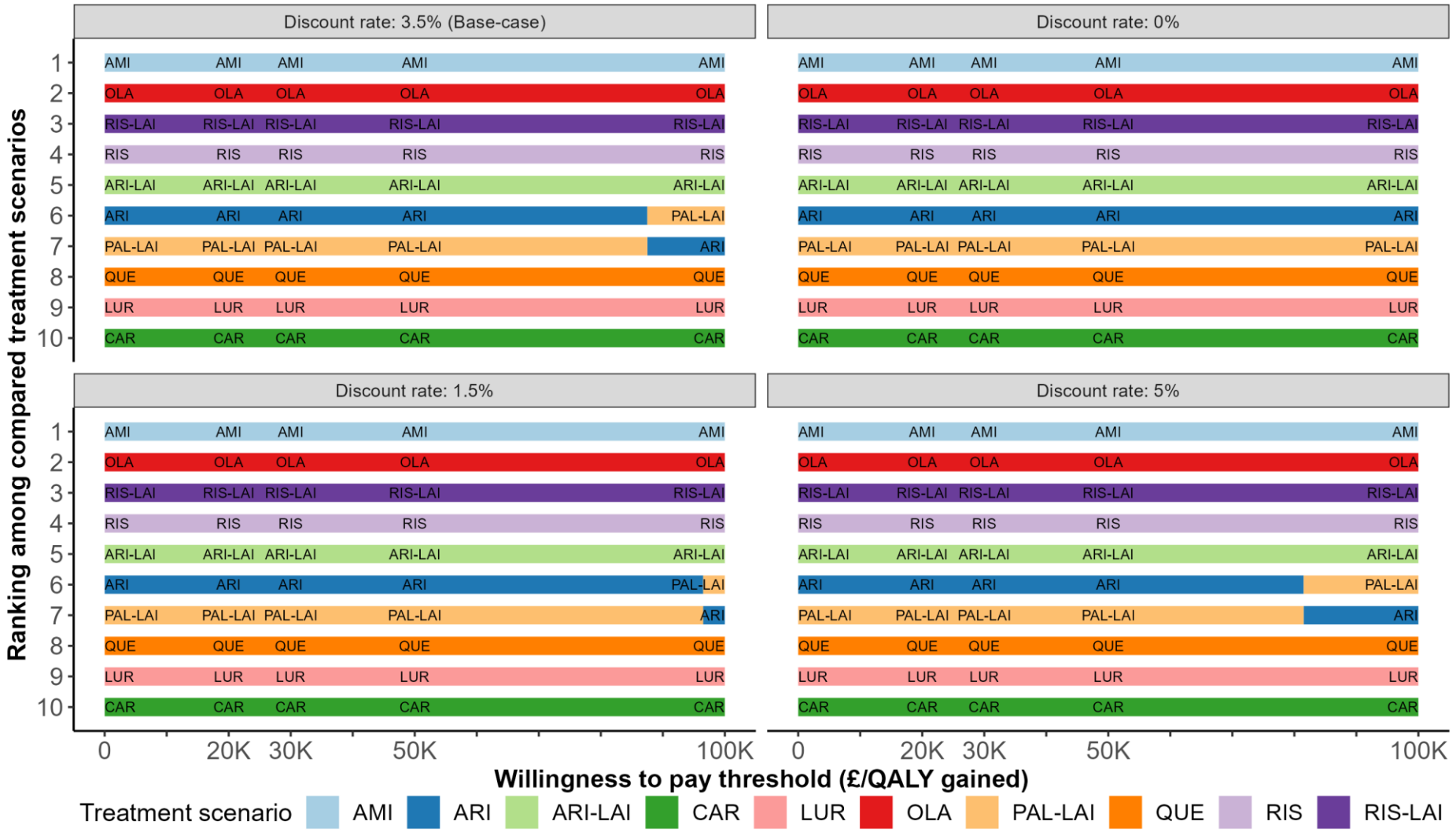
Blue (Red) bar is the result when input takes its upper (lower) range; Black vertical line is the base-case result. AMI, amisulpride; LAI, long-acting injection; QALY, quality-adjusted life year;
Comparison between other pairs of included antipsychotics is similar (results not shown)

Supplementary figure 5a. Scenario analyses results with different analytical timeframes



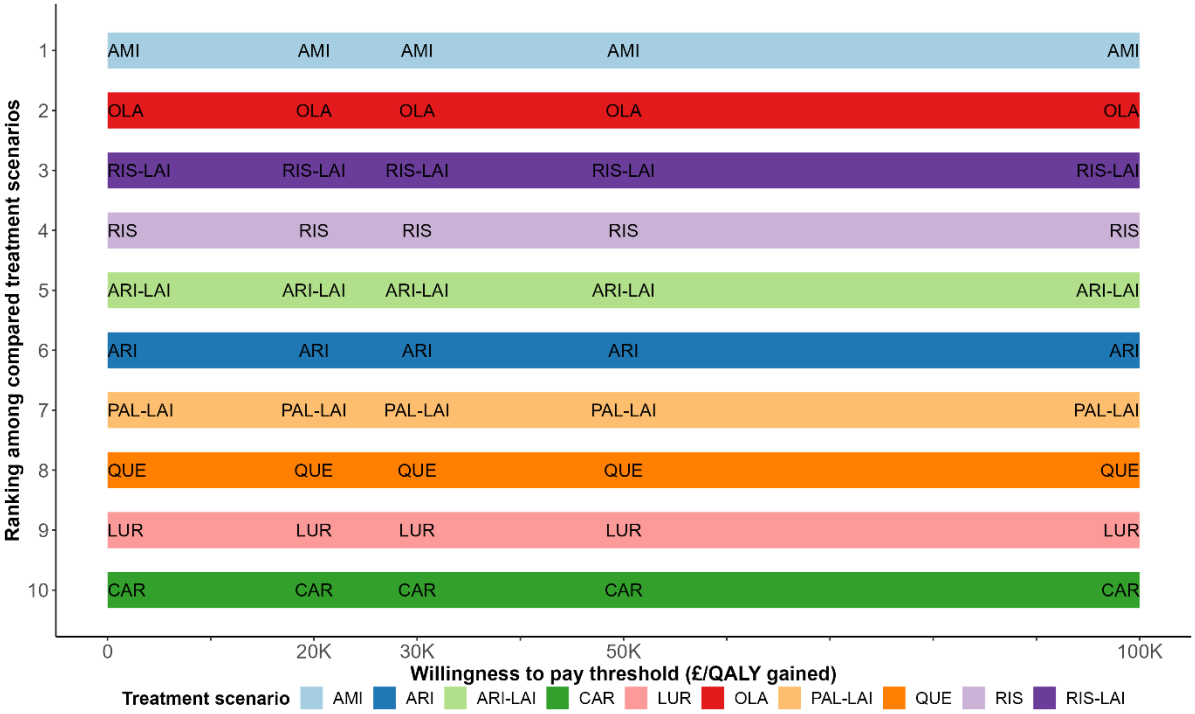
Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

Supplementary figure 5b. Scenario analyses results with different discount rates



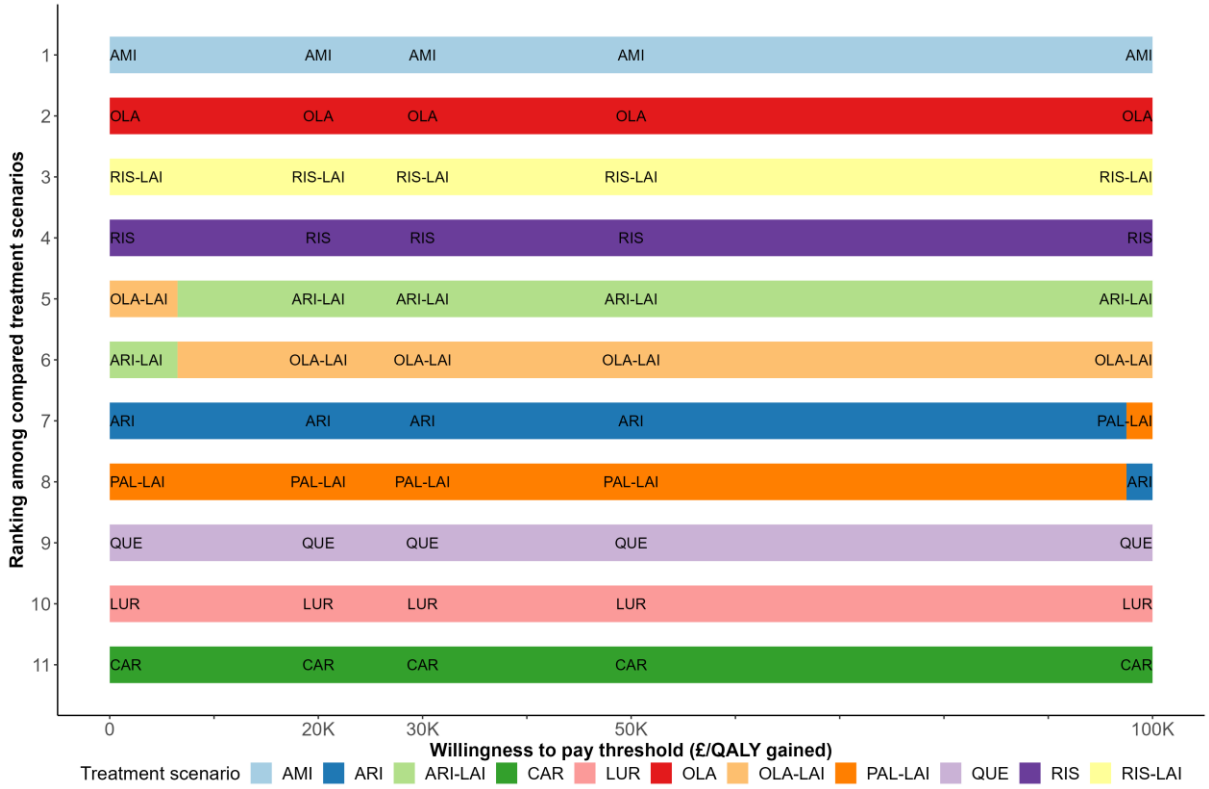
Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

Supplementary figure 6. Scenario analyses results comparing antipsychotics as second-line treatment in non-first-episode schizophrenia



Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

Supplementary figure 7. Scenario analyses results including olanzapine-LAI into the comparison among first-line antipsychotics in first-episode schizophrenia



We used different inputs of treatment profiles for olanzapine-LAI than oral olanzapine in risk ratio on relapse prevention (0.29 vs. 0.20), annual probability of discontinuation (0.35 vs. 0.27), and annual drug costs (£3426 vs. £23) based on the recent NMA[93] and BNF drug tariff[120].

Treatment is an oral one if its name is not followed by "LAI"; AMI, amisulpride; ARI, aripiprazole; CAR, cariprazine; LAI, long-acting injection; LUR, lurasidone; OLA, olanzapine; PAL, paliperidone; QALY, quality-adjusted life year; QUE, quetiapine; RIS, risperidone;

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