

Appendix 1. Summary of the efficacy and safety measures included within the analysis

Measure	Measure description	Interpretation
Efficacy outcome measures		
MMSE	Assesses cognitive function by evaluating a patient’s memory and mental abilities.	Greatest increase from baseline would indicate the most effective treatment for improving cognitive function.
NPI-10	Detects, quantifies, and tracks changes of psychiatric symptoms in a population with dementia.	Greatest decrease from baseline would indicate the most effective treatment for improving neuropsychiatric symptoms.
UPDRS	<p>Assesses the progression of Parkinson’s disease symptoms. This measure is divided into 4 parts.</p> <p>Part III was primarily used in the included studies to objectively assess motor function by clinician rating of parkinsonian signs identified during clinical examination.</p> <p>Part II is a patient/caregiver reported questionnaire exploring motor function. It was used in 1 study and treated as being a comparable assessment of motor function for the purposes of this NMA.²⁴</p>	Greatest decrease from baseline would indicate the most effective treatment for improving motor function.
Safety outcome measures		
Overall rate of AEs	<p>Provides the most general assessment of the safety of a medicine/intervention.</p> <p>This includes all recorded adverse events, whether related to the drug being administered or not.</p>	<p>The rate of any AE occurring within each study’s timeframe was assessed. This was presented as a percentage likelihood of an event occurring for an individual.</p> <p>Within the NMA the odds ratios are also calculated. An odds ratio greater than one means a higher rate of AEs with respect to the comparator, while the converse is true for a ratio below one.</p>

<p>Overall discontinuation rate</p>	<p>The overall discontinuation rate provides the rate at which patients stopped the treatment course prematurely for any reason. The value is based on the number of patients recorded as discontinuing the treatment at any point within the studies time horizon.</p> <p>The two most common reasons to discontinue are intolerable adverse events or a lack of drug efficacy.</p>	<p>The rate is given for the likelihood of discontinuation. This was given as a percentage likelihood of an event occurring for an individual.</p> <p>Within the NMA the odds ratios are also calculated. An odds ratio greater than one means a higher rate of discontinuation with respect to the comparator, while the converse is true for a ratio below one.</p>
<p>Discontinuation due to AEs</p>	<p>Discontinuations due to AEs represent the rate at which patients discontinued specifically due to adverse event(s). This is given by the number of discontinuations due to AEs out of the total patient population on a treatment.</p> <p>Focusing only on those discontinuations that occur due to adverse events helps to better understand the tolerability profile of a medicine/intervention.</p>	<p>The rate is given for the likelihood of a discontinuation coded as being due to AEs. This was given as a percentage likelihood of an event occurring for an individual.</p> <p>Within the NMA the odds ratios are also calculated. An odds ratio greater than one means a higher rate of discontinuation due to AEs with respect to the comparator, while the converse is true for a ratio below one.</p>
<p>Psychiatric events</p>	<p>The measure captures all reported psychiatric events that occurred on each treatment within the study time horizon. This has not been limited to only drug-related events.</p> <p>There may be a strong correlation between symptom effects that lead to a deterioration in cognitive functions and the risk of psychiatric events occurring.</p>	<p>The values used in the NMA are the likelihood of a psychiatric event occurring for an individual given the treatment received.</p> <p>Within the NMA the odds ratios are also calculated. An odds ratio greater than one means a higher rate of psychiatric events with respect to the comparator, while the converse is true for a ratio below one.</p>

Appendix 1. Analyses run for each included outcome measure

Measure	Base-case	Sensitivity 1	Sensitivity 2	Sensitivity 3
MMSE	Random Effects	Fixed effect	Pool the results for donepezil across all dosages	Exclude studies with a mixed patient population
NPI-10	Random effects	Fixed effect	Inclusion of NPI-12 measure	Exclude studies with a mixed patient population
UPDRS	Random Effects	Fixed effect	Pool the results for donepezil across all dosages	Exclude studies with a mixed patient population
Overall rate of AEs	Random effects	Fixed effect	Pool the results for donepezil across all dosages	Exclude studies with a mixed patient population
Overall discontinuation rate	Random effects	Fixed effect	Pool the results for donepezil across all dosages	Exclude studies with a mixed patient population
Discontinuation due to AEs	Random effects	Fixed effect	Exclusion of study with 0 events	Exclude studies with a mixed patient population
Psychiatric events	Random effects	Fixed effect	Pool the results for donepezil across all dosages	Exclude studies with a mixed patient population