

Supplementary Materials: Cost-Effectiveness of Treatment Optimisation with Biomarkers for Immunotherapy in Solid Tumours: A Systematic Review

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Supplement Box S1. Search Strategy

Query	Keywords (in Mesh OR Title and Abstract)	PubMed	Embase
#1	Antibodies, monoclonal	234,701	534,564
#2	Immunotherapy	315,085	230,610
#3	(nivolumab/ipilimumab[Title/Abstract])	9,625	32,770
	OR		
	ipilimumab[Title/Abstract])		
	OR		
	durvalumab[Title/Abstract])		
	OR		
#3	atezolizumab[Title/Abstract])	9,625	32,770
	OR		
	nivolumab[Title/Abstract])		
	OR		
	pembrolizumab[Title/Abstract])		
	OR		
#3	"Ipilimumab"[Mesh]) OR "durvalumab" [Supplementary Concept]) OR "avelumab" [Supplementary Concept]) OR "atezolizumab" [Supplementary Concept]) OR "Nivolumab"[Mesh]) OR "pembrolizumab" [Supplementary Concept]	9,625	32,770
	OR		
	OR		
	OR		
	OR		
	OR		
#4	Immune checkpoint inhibitor	27,009	22,451
#5	Neoplasms	3,340,811	3,956,642
#6	Cancer	3,785,562	3,707,300
#7	Carcinoma	911,084	1,209,542
#8	Tumor OR Tumor	1,283,887	1,580,661
#9	Target therapy OR Chemotherapy	406,424	772,722
#10	Biomarkers OR PD-1 OR Programmed Death 1 OR PD-L1 OR Programmed Death Ligand 1 OR IL-6 OR Interleukin-6 OR CTLA-4	404,251	565,451
#11	Cost benefit analysis	82,517	60,024
#12	Cost effectiveness	109,292	162,052
#13	Cost utility	4,773	10,928
#14	Economic evaluation	85,211	251,560
#15	Quality of life	327,312	495,744
#16	1 OR 2 OR 3 OR 4	110,915	297,320
#17	5 OR 6 OR 7 OR 8	3,073,490	3,573,285
#18	11 OR 12 OR 13 OR 14 OR 15	386,004	652,103
#19	16 AND 17	71,773	140,761
#20	19 AND 9 AND 10	3,763	10,894
#21	20 AND 18	164	566

Supplement Box S2. Search Syntaxes

PubMed

("antibodies monoclonal"[Title/Abstract] OR "Immunotherapy"[Title/Abstract] OR ("nivolumab ipilimumab"[Title/Abstract] OR "Ipilimumab"[Title/Abstract]) OR "durvalumab"[Title/Abstract] OR "atezolizumab"[Title/Abstract] OR "Nivolumab"[Title/Abstract] OR "pembrolizumab"[Title/Abstract] OR "Ipilimumab"[MeSH Terms] OR "durvalumab"[Supplementary Concept] OR "avelumab"[Supplementary Concept] OR "atezolizumab"[Supplementary Concept] OR "Nivolumab"[MeSH Terms] OR "pembrolizumab"[Supplementary Concept] OR "immune checkpoint inhibitor"[Title/Abstract]) AND ("Neoplasms"[Title/Abstract] OR "Cancer"[Title/Abstract] OR "Carcinoma"[Title/Abstract] OR "Tumor"[Title/Abstract] OR "Toumor"[Title/Abstract]) AND ("target therapy"[Title/Abstract] OR "Chemotherapy"[Title/Abstract]) AND ("Biomarkers"[Title/Abstract] OR "PD-1"[Title/Abstract] OR "programmed death 1"[Title/Abstract] OR "PD-L1"[Title/Abstract] OR "programmed death ligand 1"[Title/Abstract] OR "IL-6"[Title/Abstract] OR "Interleukin-6"[Title/Abstract] OR "CTLA-4"[Title/Abstract]) AND ("cost benefit analysis"[Title/Abstract] OR "cost effectiveness"[Title/Abstract] OR "cost utility"[Title/Abstract] OR "economic evaluation"[Title/Abstract] OR "quality of life"[Title/Abstract]) Sort by: Publication Date

EMBASE

(cost AND benefit AND analysis:ti,ab,kw OR (cost AND effectiveness:ti,ab,kw) OR (cost AND utility:ti,ab,kw) OR (economic AND evaluation:ti,ab,kw) OR (quality AND of AND life:ti,ab,kw)) AND (target AND therapy:ti,ab,kw OR chemotherapy:ti,ab,kw) AND (biomarkers:ti,ab,kw OR 'pd 1':ti,ab,kw OR (programmed AND death AND 1:ti,ab,kw) OR 'pd l1':ti,ab,kw OR (programmed AND death AND ligand AND 1:ti,ab,kw) OR 'il 6':ti,ab,kw OR 'interleukin 6':ti,ab,kw OR 'ctla 4':ti,ab,kw) AND ((antibodies AND monoclonal:ti,ab,kw OR immunotherapy:ti,ab,kw OR (immune AND checkpoint AND inhibitor:ti,ab,kw)) AND [embase]/lim OR ((nivolumab:ti,ab,kw OR ipilimumab:ti,ab,kw OR durvalumab:ti,ab,kw OR atezolizumab:ti,ab,kw OR pembrolizumab:ti,ab,kw OR avelumab:ti,ab,kw) AND [embase]/lim)) AND (neoplasms:ti,ab,kw OR cancer:ti,ab,kw OR carcinoma:ti,ab,kw OR tumor:ti,ab,kw OR toumor:ti,ab,kw) AND [embase]/lim

Supplementary Table S1. Key features of economic methods for the overall included studies

Study Reference, year	Study design	Type of Economic evaluation	Perspective used in the analysis	Type of costs included	Reference year of costs	Sensitivity analysis
Barbier MC et al., 2021 ⁹	Markov model	Cost-effectiveness analysis	Switzerland third-party payer	Direct health costs	CHF without reference to the year	One-way and probabilistic
Chang WC et al. 2021 ⁶⁷	De novo partitioned-survival model	Cost-utility analysis	Taiwan third-party payer	Direct health costs	2020 New Taiwan dollars (NT\$)	One-way
Cheng S et al 2021 ³³	Partitioned survival model	Cost-effectiveness analysis	US and China third-party payer	Direct health costs	2021 US dollars	One-way and probabilistic
Liu X et al 2021 ⁶²	Partitioned survival model	Cost-effectiveness analysis	Chinese third-party payer	Direct health costs	2021 US dollars	One-way and probabilistic
Liu G et al 2021 ³⁴	Decision-analytic model	Cost-effectiveness analysis	Chinese third-party payer	Direct health costs	2019 US dollars	One-way and probabilistic
Hu H et al 2021 ¹²	Markov model	Cost-effectiveness analysis	US third-party payer	Direct health costs	US dollars without reference to the year	One-way
Shi Y et al 2021 ⁶⁸	Partitioned survival model	Cost-effectiveness analysis	US third-party payer	Direct health costs	2021 US dollars	One-way and probabilistic

Cai Y et al 2021 ³⁵	Survival analysis and partitioned survival model	Cost- effectiveness analysis	China third- party payer	Direct health costs	2020 US dollars using the exchange rate: 1 US dollar = 6.4721 Chinese yuan renminbi.	Deterministic and probabilistic
Qin S et al 2021 ⁴⁷	Markov model	Cost- effectiveness analysis	US third-party payer	Direct health costs	2021 US dollars	One-way and probabilistic
Peng Y et al 2021 ⁴⁸	Markov model	Cost- effectiveness analysis	China third- party payer	Direct health costs	2021 US dollars	One-way and probabilistic
Qiao L et al 2021 ¹³	Markov model	Cost- effectiveness analysis	China third- party payer	Direct health costs	2020 US dollars	Deterministic and probabilistic
Yang SC et al 2021 ³⁶	Markov model	Cost- effectiveness analysis	US third-party payer	Direct health costs	2020 US dollars	One-way deterministic
Wurcel V et al 2021 ⁵⁶	Partitioned survival model	Cost- effectiveness analysis	Argentina social security perspective	Direct health costs	2020 Argentinian pesos	One-way deterministic
Insinga RP et al 2021 ¹¹	Markov model	Cost- effectiveness analysis	US third-party payer	Direct health costs	2019 US dollars	One-way and probabilistic
Peng Y et al 2021 ³⁷	Markov model	Cost- effectiveness analysis	US third-party payer	Direct health costs	2020 US dollars	Deterministic
Liu Q et al 2021 ¹⁴	Markov model	Cost- Effectiveness Analysis based on the 3-year follow-up	US third-party payer	Direct health costs	2021 US dollars	Univariate and probabilistic
Panje CM et al 2020 ¹⁵	Markov model	Cost- Effectiveness Analysis; lifetime horizon	Switzerland third-party payer	Direct health costs	2019 CHF	One-way deterministic
Wan N et al 2020 ³⁸	Markov model	Cost- effectiveness Analysis; lifetime horizon	US and China third-party payer	Direct health costs	2018 US dollars	Univariate and probabilistic
Weng X et al 2020 ⁶³	Markov model	Cost-Utility Analysis; lifetime horizon	US third-party payer	Direct health costs	2019 US dollars	One-way and probabilistic
Weng X et al 2020 ¹⁶	Markov model	Cost- Effectiveness Analysis; 10 years horizon	US payer perspective	Direct health costs	US dollars without reference to the year	One-way and probabilistic

Wu B et al 2020 ⁶⁴	Markov model	Cost- Effectiveness Analysis; 10 years horizon	US third-party payer	Direct health costs	2018 US dollars	One-way and probabilistic
Zhou K et al 2020 ⁵⁷	Markov model	Cost-utility analysis	US third-party payer	Direct health costs	2019 US dollars	One-way deterministic
Criss SD et al 2020 ³⁹	Markov model	Cost-utility analysis over 5 years	US third-party payer	Direct health costs	2019 US dollars	Deterministic and probabilistic
Lauren B et al 2020 ⁶⁹	Markov model	Cost-utility analysis lifetime	US third-party payer	Direct health costs	2018 US dollars	One-way and probabilistic
Liu Q et al 2020 ⁴⁰	Partitioned survival model	Cost-utility analysis	China third- party payer	Direct health costs	2018 US dollars	One-way
Parmar A et al 2020 ⁵⁴	Markov model	Cost- effectiveness analysis	Canada third- party payer	Direct health costs	2018 Canadian dollars	One-way and probabilistic
Rothwell B et al 2020 ¹⁷	Partitioned-survival model	Cost- effectiveness analysis	England third- party payer	Direct health costs	2015 English pounds	One-way and probabilistic
Li J et al 2020 ¹⁸	Partitioned survival model	Cost- effectiveness analysis	US third-party payer	Direct health costs	2019 US dollars	One-way and probabilistic
Aziz MIA et al 2020 ⁴¹	Decision-analytic model	Cost- effectiveness analysis	Singapore third-party payer	Direct health costs	Singapore SGD dollars without reference to the year	One-way and probabilistic
Hale O et al 2020 ⁴⁹	Partitioned survival model	Cost- Effectiveness Analysis; a time horizon of 15 yr (lifetime)	US third-party payer	Direct health costs	2018 US dollars	Deterministic
Wu B et al 2020 ¹⁹	Markov model	Cost- Effectiveness Analysis; 20 years horizon	US and China third-party payer	Direct health costs	2018 US dollars	One-way, two-way and probabilistic
Patterson K et al 2019 ⁵⁰	Markov model	Cost- Effectiveness Analysis; lifetime	Sweden third- party payer	Direct health costs	2018 Euro	One-way and probabilistic
Reinhorn D et al 2019 ⁵³	Markov model	Cost- Effectiveness Analysis; 10 years horizon	US third-party payer	Direct health costs	2017 US dollars	One-way and probabilistic
Longjiang S et al 2019 ²⁰	Markov model	Cost- effectiveness Analysis;	US third-party payer	Direct health costs	2016 US dollars	Univariate and probabilistic

		lifetime (30 years)				
Wan X et al 2019 ⁴²	Partitioned-survival model	Cost-effectiveness and cost-utility analysis over 10 years	US third-party payer	Direct health costs	2018 US dollars	Univariate deterministic and multivariate probabilistic
Zhou K et al 2019 ⁴³	Markov model	Cost-effectiveness analysis	China third-party payer	Direct health costs	2019 US dollars	Deterministic
Bhadhuri A et al 2019 ²¹	Partitioned-survival model	Cost-effectiveness and cost-utility analysis over 20 years	Switzerland third-party payer	Direct health costs	2018 CHF	One-way deterministic and probabilistic
Chouaid C et al 2019 ²²	Partitioned-survival model	Cost-effectiveness and cost-utility analysis; lifetime	France third-party payer	Direct health costs	2017 Euro	One-way deterministic
Criss SD et al 2019 ⁵¹	Microsimulation model	Cost-effectiveness analysis	US third-party payer	Direct health costs	2017 US dollars	One-way deterministic
Huang M et al 2019 ²³	Partitioned survival model	Cost-effectiveness analysis	US third-party payer	Direct health costs	2019 US dollars	One-way and two-way deterministic
Insinga RP et al 2019 ³¹	Markov model	Cost-effectiveness analysis	US third-party payer	Direct health costs	2018 US dollars	One-way probabilistic
Liu M et al 2019 ⁵⁸	Markov model	Cost-Effectiveness Analysis, duration of 2 years	China and US third-party payer	Direct health costs	2018 US dollars	Probabilistic
Loong HH et al 2019 ³⁰	Markov model	Cost-Effectiveness Analysis; 1 mo over a 10-yr time horizon	Hong Kong	Direct health costs	Hong Kong (HK) dollars	Univariate and probabilistic
Liao W et al 2019 ⁴⁴	Markov model	Cost-Effectiveness Analysis	China third-party payer	Direct health costs	2017 US dollars	Univariate
Meng Y et al 2018 ⁶⁵	Markov model	Cost-utility analysis lifetime	England third-party payer	Direct health costs	2017 british pounds	Probabilistic
Sarfaty M et al 2018 ⁵²	Markov model	Cost-utility analysis	US third-party payer	Direct health costs	2016 US dollars	Univariate and probabilistic

Sarfaty M et al 2018 ⁵⁵	Markov model	Cost-Effectiveness Analysis; 1 mo over a 5-yr time	US, UK, Canada and Australia third-party payer	Direct health costs	2017 US dollars	Univariate and probabilistic
Tarhini A et al 2018 ⁶⁶	Markov model	Cost-utility analysis over lifetime	US third-party payer	Direct health costs	2016 US dollars	Deterministic and probabilistic
Zargar M et al 2018 ⁵⁹	Cohort based, state transition model	Cost-utility analysis over 5 years	Canada third-party payer	Direct health costs	2016 Canadian dollars	Univariate and probabilistic
Aguiar P et al 2018 ⁴⁵	Markov model	Cost-Effectiveness over 5 years and budget impact	Argentina, Brazil and Peru third-party payer	Direct health costs	US dollars without reference to the year	None
Hirschmann A et al 2018 ⁶⁰	Markov model	Cost-effectiveness over 60 months	Switzerland third-party payer	Direct health costs	2018 CHF	Univariate and probabilistic
Hu x et al 2018 ³²	Markov model	Cost-Effectiveness and cost-utility analysis	UK third-party payer	Direct health costs	2017 British pounds	Univariate and probabilistic
Insinga RP et al 2018 ²⁵	Cohort based simulation model	Cost-utility analysis; lifetime	US third-party payer	Direct health costs	2017 US dollars	Univariate and probabilistic
Georgieva M et al 2018 ²⁶	Bayesian Markov model	Cost-utility analysis; lifetime	US and UK third-party payer	Direct health costs	2018 US dollars	Probabilistic
Ward MC et al 2017 ⁶¹	Markov model	Cost-utility analysis over 36 months	US third-party payer	Direct health costs	2017 US dollars	Univariate and probabilistic
Aguiar PN Jr et al 2017 ²⁷	RCT-based model	Cost-utility analysis	South America third-party payer	Direct health costs	US dollars without reference to the year	None
Huang M et al 2017 ²⁹	Partitioned survival model	Cost-effectiveness and cost-utility analysis; lifetime	US third-party payer	Direct health costs	2016 US dollars	Univariate and probabilistic
Matter-Walstra K et al 2016 ⁴⁶	Markov model	Cost-utility analysis	Switzerland third-party payer	Direct health costs	2016 CHF	Univariate and probabilistic

Abbreviations: Swiss francs (CHF); Randomized controlled trial (RCT); United States (US); United Kingdom (UK)

Supplementary Table S2. Quality appraisal of individual included studies according to GRADE scale

Study Reference, year	Quality appraisal (GRADE scale) (n=59 studies)	
	Scoring	Appraisal
Barbier MC et al., 2021 ⁹	High ⊕⊕⊕⊕	The true effect lies close to that of the estimate of the effect.
Chang WC et al. 2021 ⁶⁷	Moderate ⊕⊕⊕○	Rarity of disease. Such low disease prevalence may result in heterogeneity of disease diagnosis and treatment effect.
Cheng S et al 2021 ³³	High ⊕⊕⊕⊕	The true effect lies close to that of the estimate of the effect.
Liu X et al 2021 ⁶²	Moderate ⊕⊕⊕○	Limitation related to generalizability.
Liu G et al 2021 ³⁴	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Hu H et al 2021 ¹²	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Shi Y et al 2021 ⁶⁸	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Cai Y et al 2021 ³⁵	High ⊕⊕⊕⊕	The true effect lies close to that of the estimate of the effect
Qin S et al 2021 ⁴⁷	High ⊕⊕⊕⊕	The true effect lies close to that of the estimate of the effect
Peng Y et al 2021 ⁴⁸	Moderate ⊕⊕⊕○	Limitation related to generalizability.
Qiao L et al 2021 ¹³	Moderate ⊕⊕⊕○	Bias in the economic results. The effect estimate as the true effect is likely to be close to the estimate of the effect.
Yang SC et al 2021 ³⁶	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Wurcel V et al 2021 ⁵⁶	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Insinga RP et al 2021 ¹¹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Peng Y et al 2021 ³⁷	Moderate/Low ⊕⊕○ ○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Liu Q et al 2021 ¹⁴	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Panje CM et al 2020 ¹⁵	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Wan N et al 2020 ³⁸	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.

Weng X et al 2020 ⁶³	Moderate/Low ⊕⊕○○	Limitation related to generalizability. The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Study Reference, year	Scoring	Appraisal
Weng X et al 2020 ¹⁶	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Wu B et al 2020 ⁶⁴	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Zhou K et al 2020 ⁵⁷	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Criss SD et al 2020 ³⁹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Lauren B et al 2020 ⁶⁹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Liu Q et al 2020 ⁴⁰	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Parmar A et al 2020 ⁵⁴	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Rothwell B et al 2020 ¹⁷	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Li J et al 2020 ¹⁸	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect
Aziz MIA et al 2020 ⁴¹	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Hale O et al 2020 ⁴⁹	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Wu B et al 2020 ¹⁹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Patterson K et al 2019 ⁵⁰	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Reinhorn D et al 2019 ⁵³	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Longjiang She et al 2019 ²⁰	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Wan X et al 2019 ⁴²	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Zhou K et al 2019 ⁴³	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Bhadhuri A et al 2019 ²¹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.

Chouaid C et al 2019 ²²	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Criss SD et al 2019 ⁵¹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Huang M et al 2019 ²³	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Study Reference, year	Scoring	Appraisal
Insinga RP et al 2019 ³¹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Liu M et al 2019 ⁵⁸	Moderate ⊕⊕⊕○	Limitation related to generalizability.
Loong HH et al 2019 ³⁰	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Liao W et al 2019 ⁴⁴	Moderate/Low ⊕⊕○ ○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Meng Y et al 2018 ⁶⁵	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Sarfaty M et al 2018 ⁵²	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Sarfaty M et al 2018 ⁵⁵	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Tarhini A et al 2018 ⁶⁶	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Zargar M et al 2018 ⁵⁹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Aguiar P et al 2018 ⁴⁵	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Hirschmann A et al 2018 ⁶⁰	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Hu x et al 2018 ³²	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Insinga RP et al 2018 ²⁵	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Georgieva M et al 2018 ²⁶	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Ward MC et al 2017 ⁶¹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
Aguiar PN Jr et al 2017 ²⁷	Moderate ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is quite different.
Huang M et al 2017 ²⁹	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.

Matter-Walstra K et al 2016 ⁴⁶	Moderate/High ⊕⊕⊕○	The effect estimate as the true effect is likely to be close to the estimate of the effect.
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