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Supplementary materials:

Evaluating the use, performance and acceptability of utility measurement approaches in geographic atrophy, a severe vision disorder

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Table of abbreviations

Abbreviation	Full form
AMD	Age-related macular degeneration
BCVA	Best-corrected visual acuity
BSE	Better-seeing eye
CADTH	Canadian Agency for Drugs and Technologies in Health
CDR	Canadian Drug Review
CI	Confidence interval
CS	Contrast sensitivity
ERG	Evidence Review Group
ETDRS	Early Treatment Diabetic Retinopathy Study
FRI	Functional Reading Independence
GA	Geographic atrophy
HRQL	Health-related quality of life
HTA	Health technology assessment
HUI-3	Health Utilities Index-3
ICER	Institute for Clinical and Economic Review
LLVA	Low luminance visual acuity
MNRead	Minnesota Low-Vision Reading Test
MRS	Maximum reading speed
NICE	National Institute for Health and Care Excellence
NSF	Non-subfoveal
QoL	Quality of life
SD	Standard deviation
SF	Subfoveal
SF-6D	Short Form-6 Dimension
SG	Standard gamble
SMC	Scottish Medicines Consortium
TTO	Time trade-off
VA	Visual acuity
VFQ-UI	Visual Function Questionnaire-25
VFQ-25	Visual Function Questionnaire-Utilities Index
WSE	Worst-seeing eye

Search strategies

Table 1. Search strategy for search 1a

Search date: 23/01/24

		Search results
Geographic atrophy (GA) terms (adapted from Sarda et al., 2021)[1]		
1	exp Geographic Atrophy/ OR (age-related macular degeneration and atrophic).ti. OR ((dry age-related macular degeneration or dry macular degeneration or dry AMD) AND (advanced or late stage)).ti. OR geographic atroph*.ti,ab. OR atrophic age-related macular degeneration.ti,ab. OR atrophic AMD.ti,ab. OR advanced dry age-related macular degeneration.ti,ab. OR advanced dry AMD.ti,ab. OR (((dry or atroph$) adj3 ("age related macular degeneration$" or macular degeneration$ or maculopath$ or AMD)) and (advanced or late stage)).ti,ab.	6348
Dry age-related macular degeneration (AMD) terms (adapted from Schultz et al., 2021)[2]		
2	dry age related macular degeneration.ti,ab. OR dry AMD.ti,ab. OR d-AMD.ti,ab. OR atrophic macular degeneration.ti,ab. OR non-exudative age-related macular degeneration.ti,ab. OR nonexudative age-related macular degeneration.ti,ab. OR non-exudative AMD.ti,ab. OR nonexudative AMD.ti,ab.	3669
Utility terms (adapted from Glanville et al., 2009)[3]		
3	exp Quality of Life/ OR quality of life.ti,kf. OR ((instrument or instruments) adj3 quality of life).ab. OR Quality-Adjusted Life Year/ OR quality adjusted life.ti,ab,kf. OR (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf. OR exp Short form 36/ OR (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. OR (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6 or sf 6d).ti,ab,kf. OR (sf8 or sf 8 or sf eight or sfeight or shortform8 or short form8 or shortform 8 or short form 8 or shortform eight or short form eight).ti,ab,kf. OR (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. OR (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. OR (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. OR (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf. OR (pqol or qls).ti,ab,kf. OR (health adj3 (utilit* or status)).ti,ab,kf. OR (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf. OR (preference* adj3 (valu* or measur* or health or life or	1323070

	estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf. OR disutilit*.ti,ab,kf. OR Standard Gamble/ OR standard gamble*.ti,ab,kf. OR time trade-off method/ OR (time trade off or time tradeoff).ti,ab,kf. OR tto.ti,ab,kf. OR (hui or hui1 or hui2 or hui3).ti,ab,kf. OR (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf. OR (vfq or vfq25 or neivfq or visual function* questionnaire).ti,ab,kf. OR (((vfq or vfq25 or neivfq or visual function* questionnaire) and (map*)) or (vfq ui or vfqui or visual function* questionnaire utilit* index)).ti,ab,kf.	
4	1 or 2	8749
5	3 and 4	287
6	Deduplicate	207

Table 2. Search strategy for search 1b

Search date: 25/01/2024

		Search results
AMD terms (from Yeong et al., 2020)[4]		
1	exp Macular Degeneration/ OR exp Geographic Atrophy/ OR (macular degeneration or maculopathy or AMD or ARMD or geographic atrophy).tw.	106199
Utility terms (adapted from Glanville et al., 2009)[3]		
2	exp Quality of Life/ OR quality of life.ti,kf. OR ((instrument or instruments) adj3 quality of life).ab. OR Quality-Adjusted Life Year/ OR quality adjusted life.ti,ab,kf. OR (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf. OR exp Short form 36/ OR (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. OR (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6 or sf 6d).ti,ab,kf. OR (sf8 or sf 8 or sf eight or sfeight or shortform8 or short form8 or shortform 8 or short form 8 or shortform eight or short form eight).ti,ab,kf. OR (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. OR (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. OR (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. OR (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf. OR (pqol or qls).ti,ab,kf. OR (health adj3 (utilit* or status)).ti,ab,kf. OR (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf. OR (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf. OR disutilit*.ti,ab,kf. OR Standard Gamble/ OR standard gamble*.ti,ab,kf. OR time trade-off method/ OR (time trade off or time tradeoff).ti,ab,kf. OR tto.ti,ab,kf. OR (hui or hui1 or hui2 or hui3).ti,ab,kf. OR (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf. OR (vfq or vfq25 or neivfq or visual function* questionnaire).ti,ab,kf. OR (((vfq or vfq25 or neivfq or visual function* questionnaire) and (map*)) or (vfq ui or vfqui or visual function* questionnaire utilit* index)).ti,ab,kf.	1335711
Review terms (from CADTH Search Filters Database, 2024)[5]		
3	(systematic review or meta-analysis).pt. OR meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ or network meta-analysis/ OR ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf. OR ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf. OR ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf. OR (data synthes* or data extraction* or data abstraction*).ti,ab,kf.	1766240

	OR (handsearch* or hand search*).ti,ab,kf. OR (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf. OR (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf. OR (meta regression* or metaregression*).ti,ab,kf. OR (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw. OR (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. OR (cochrane or (health adj2 technology assessment) or evidence report).jw. OR (comparative adj3 (efficacy or effectiveness)).ti,ab,kf. OR (outcomes research or relative effectiveness).ti,ab,kf. OR ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf. OR (meta-analysis or systematic review).mp. OR (multi* adj3 treatment adj3 comparison*).ti,ab,kf. OR (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf. OR umbrella review*.ti,ab,kf. OR (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf. OR (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf. OR (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.	
4	1 and 2 and 3	347
5	Limit date from 2009-Current	311
6	Deduplicate	235

Table 3. Search strategy for search 2

Search date: 26/03/24

Database	Search string	Results
ClinicalTrials.gov	AREA[ConditionSearch] Dry Age-related Macular Degeneration OR Geographic Atrophy AND AREA[Phase] EXPAND[Term] COVER[FullMatch] (“Phase 2” OR “Phase 3” OR “Phase 4” OR “Not Applicable”)	193
EU Clinical Trials Register	Dry Age-related Macular Degeneration OR Geographic Atrophy. Limit to Phase II, III or IV.	24

Table 4. Search strategy for search 3

Search date: 16/04/24

		Search results
GA terms (adapted from Sarda et al., 2021)[1]		
1	exp Geographic Atrophy/ OR (age-related macular degeneration and atrophic).ti. OR ((dry age-related macular degeneration or dry macular degeneration or dry AMD) AND (advanced or late stage)).ti. OR geographic atroph*.ti,ab. OR atrophic age-related macular degeneration.ti,ab. OR atrophic AMD.ti,ab. OR advanced dry age-related macular degeneration.ti,ab. OR advanced dry AMD.ti,ab. OR (((dry or atroph$) adj3 ("age related macular Degeneration$" or macular degeneration$ or maculopath$ or AMD)) and (advanced or late stage)).ti,ab.	6,547
Dry AMD terms (adapted from Schultz et al., 2021)[2]		
2	dry age related macular degeneration.ti,ab. OR dry AMD.ti,ab. OR d-AMD.ti,ab. OR atrophic macular degeneration.ti,ab. OR non-exudative age-related macular degeneration.ti,ab. OR nonexudative age-related macular degeneration.ti,ab. OR non-exudative AMD.ti,ab. OR nonexudative AMD.ti,ab.	3,753
Utility measure terms *(including terms related to SF-36, SF-6, SF-8, SF-12, SF-16, SF-20, HUI, EQ-5D, VFQ-25 and VFQ-UI)*		
3	exp Short form 36/ or (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. or (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6 or sf 6d).ti,ab,kf. or (sf8 or sf 8 or sf eight or sfeight or shortform8 or short form8 or shortform 8 or short form 8 or shortform eight or short form eight).ti,ab,kf. or (sf8 or sf 8 or sf eight or sfeight or shortform8 or short form8 or shortform 8 or short form 8 or shortform eight or short form eight).ti,ab,kf. or (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. or (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. or (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. or (hui or hui1 or hui2 or hui3).ti,ab,kf. or (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf. or (vfq or vfq25 or neivfq or visual function* questionnaire).ti,ab,kf. or (((vfq or vfq25 or neivfq or visual function* questionnaire) and map*) or (vfq ui or vfqui or visual function* questionnaire utilit* index)).ti,ab,kf.	191,603
Psychometric terms (from Terwee et al., 2009)[6]		
4	(instrumentation or methods).mp OR (validation study or comparative study).mp. OR exp Psychometrics/ OR psychometr*.tw. OR (clinimetr* or clinometr*).mp. OR exp Outcome Assessment, Health Care/ OR outcome assessment.tw. OR outcome measure*.mp. OR exp Observer Variation/ OR	27,237,183

	observer variation.tw. OR exp Health Status Indicators/ OR exp Reproducibility of Results/ OR reproducib*.tw. OR exp Discriminant Analysis/ OR (reliab* or unreliab* or valid* or coefficient of variation or coefficient or homogeneity or homogeneous or internal consistency).tw. OR (cronbach* and (alpha or alphas)).tw. OR (item and (correlation* or selection* or reduction*)).tw. OR agreement.mp. OR precision.mp. OR imprecision.mp. OR precise values.mp. OR test-retest.tw. OR (test and retest).tw. OR (reliab* and (test or retest)).tw. OR stability.tw. OR (interrater or inter-rater or intrarater or intra-rater).tw. OR (intertester or inter tester or intratester or intra-tester).tw. OR (interobserver or inter-observer or intraobserver or intra-observer).tw. OR (intertechnician or inter-technician or intratechnician or intra-technician).tw. OR (interexaminer or inter-examiner or intraexaminer or intra-examiner).tw. OR (interassay or inter-assay or intraassay or intra-assay).tw. OR (interindividual or inter-individual or intraindividual or intra-individual).tw. OR (interparticipant or inter-participant or intraparticipant or intra-participant).tw. OR kappa.tw. OR kappas.tw. OR repeatab*.mp. OR ((replicab* or repeated) and (measure or measures or findings or result or results or test or tests)).mp. OR (generaliza* or generalisa*).tw. OR concordance.tw. OR (intraclass and correlation*).tw. OR discriminative.tw. OR known group.tw. OR (factor analysis or factor analyses or factor structure or factor structures).tw. OR dimension*.tw. OR subscale*.tw. OR (multitrait and scaling and (analysis or analyses)).tw. OR item discriminant.tw. OR interscale correlation*.tw. OR (error or errors).tw. OR individual variability.tw. OR interval variability.tw. OR rate variability.tw. OR (variability and (analysis or values)).tw. OR (uncertainty and (measurement or measuring)).tw. OR standard error of measurement.tw. OR sensitiv*.tw. OR responsive*.tw. OR (limit and detection).tw. OR minimal detectable concentration.tw. OR interpretab*.tw. OR ((minimal or minimally or clinical or clinically) and (important or significant or detectable) and (change or difference)).tw. OR (small* and (real or detectable) and (change or difference)).tw. OR meaningful change.tw. OR ceiling effect.tw. OR floor effect.tw. OR item response model.tw. OR IRT.tw. OR rasch.tw. OR differential item functioning.tw. OR DIF.tw. OR computer adaptive testing.tw. OR item bank.tw. OR cross-cultural equivalence.tw.	
5	1 or 2	9,001
6	3 and 4 and 5	104
7	Deduplicate	74

Eligibility criteria

Table 5. Eligibility criteria for search 1a

	Inclusion criteria	Exclusion criteria
Population	• Individuals with a diagnosis of GA or dry AMD	• Individuals with a diagnosis of wet AMD • Combined AMD population (unless stratified by type of AMD)
Intervention/comparator	• N/A	• N/A
Outcome	• Utility methods/measures • Non-preference based health-related quality of life (HRQL) measures with known mapping algorithms for utility estimation • Utility values	• Non-preference based HRQL measures without known mapping algorithms for utility estimation
Study	• Interventional or non-interventional research studies generating utilities in GA or dry AMD • Studies reporting the development of economic models for treatments indicated in GA or dry AMD that include utility values	• N/A
Record type	• Journal articles • Conference proceedings • Guidelines	• Case studies, comments, non-research letters or editorials • Grey literature
Language	• English language	• Non-English language

Table 6. Eligibility criteria for search 1b

	Inclusion criteria	Exclusion criteria
Population	• Individuals with a diagnosis of AMD	• Individuals with a diagnosis of any other vision disorder (unless stratified by type of vision disorder)
Intervention/comparator	• N/A	• N/A
Outcome	• Utility methods/measures • Non-preference based HRQL measures with known mapping algorithms for utility estimation • Utility values	• Non-preference based HRQL measures without known mapping algorithms for utility estimation
Study	• Reviews of interventional or non-interventional research studies reporting utility values in AMD	• Primary research
Record type	• Journal articles	• Conference proceedings • Case studies, comments, non-research letters, editorials or guidelines • Grey literature
Language	• English language	• Non-English language

Table 7. Eligibility criteria for search 2

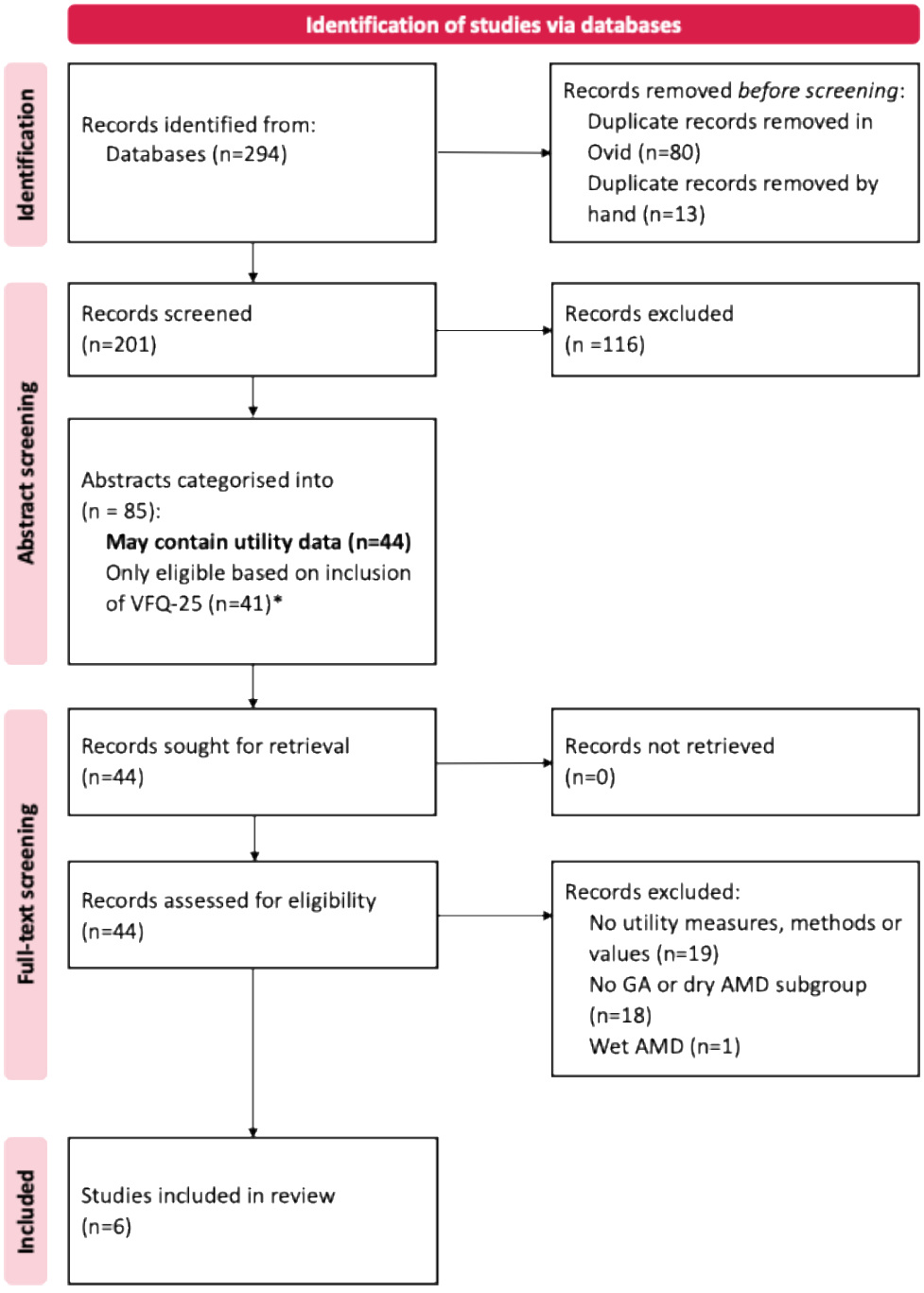
	Inclusion criteria	Exclusion criteria
Population	• Individuals with a diagnosis of GA or dry AMD	• Individuals with a diagnosis of wet AMD • Combined AMD population (unless stratified by type of AMD)
Intervention/comparator	• N/A	• N/A
Outcome	• Utility measures • Non-preference based HRQL measures with known mapping algorithms for utility estimation • Utility values	• Non-preference based HRQL measures without known mapping algorithms for utility estimation
Study	• Interventional or non-interventional research studies using utility measures in GA or dry AMD	• N/A
Trial phase	• Phases II, III, IV or not applicable	• Phase I

Table 8. Eligibility criteria for search 3

	Inclusion criteria	Exclusion criteria
Population	• Individuals with a diagnosis of GA or dry AMD	• Individuals with a diagnosis of wet AMD • Combined AMD population (unless stratified by type of AMD)
Intervention/comparator	• N/A	• N/A
Outcome	• Psychometric properties including known groups validity, convergent validity and responsiveness	• N/A
Study	• Studies assessing the psychometric properties of utility measures in GA or dry AMD	• N/A
Record type	• Journal articles	• Conference proceedings • Case studies, comments, non-research letters, editorials or guidelines • Grey literature
Language	• English language	• Non-English language

PRISMA flow diagrams

Figure 1. PRISMA flow diagram for search 1a



*Studies were cross-checked with articles citing either of the development papers for the Visual Function Questionnaire-Utility Index (VFQ-UI)[7,8], which can be used to derive utilities from Visual Function Questionnaire-25 (VFQ-25) data. None of the studies cited the development papers so were excluded at this stage based on the assumption that the VFQ-UI was not used to derive utilities.

Figure 2. PRISMA flow diagram for search 1b

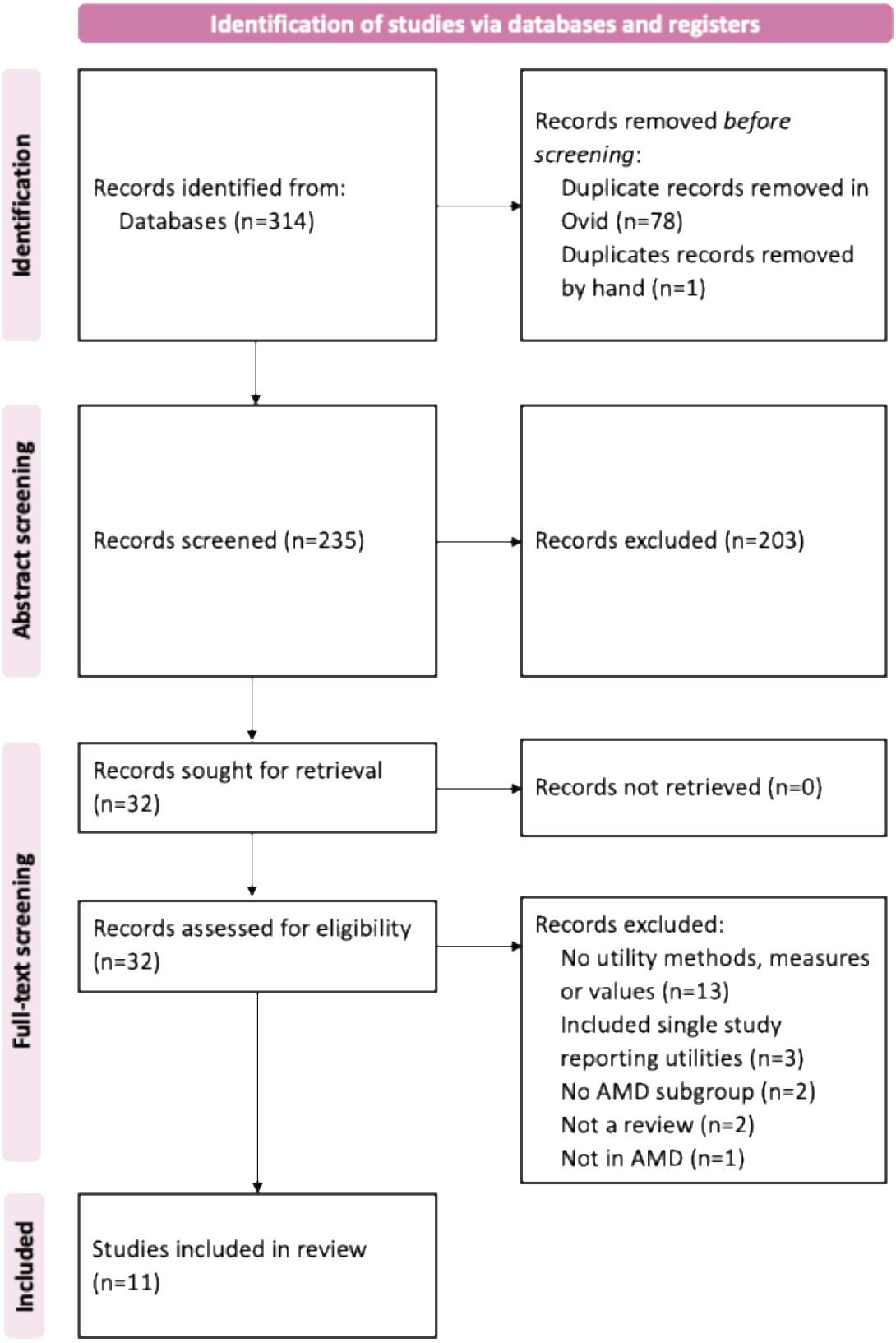


Figure 3. PRISMA flow diagram for search 2

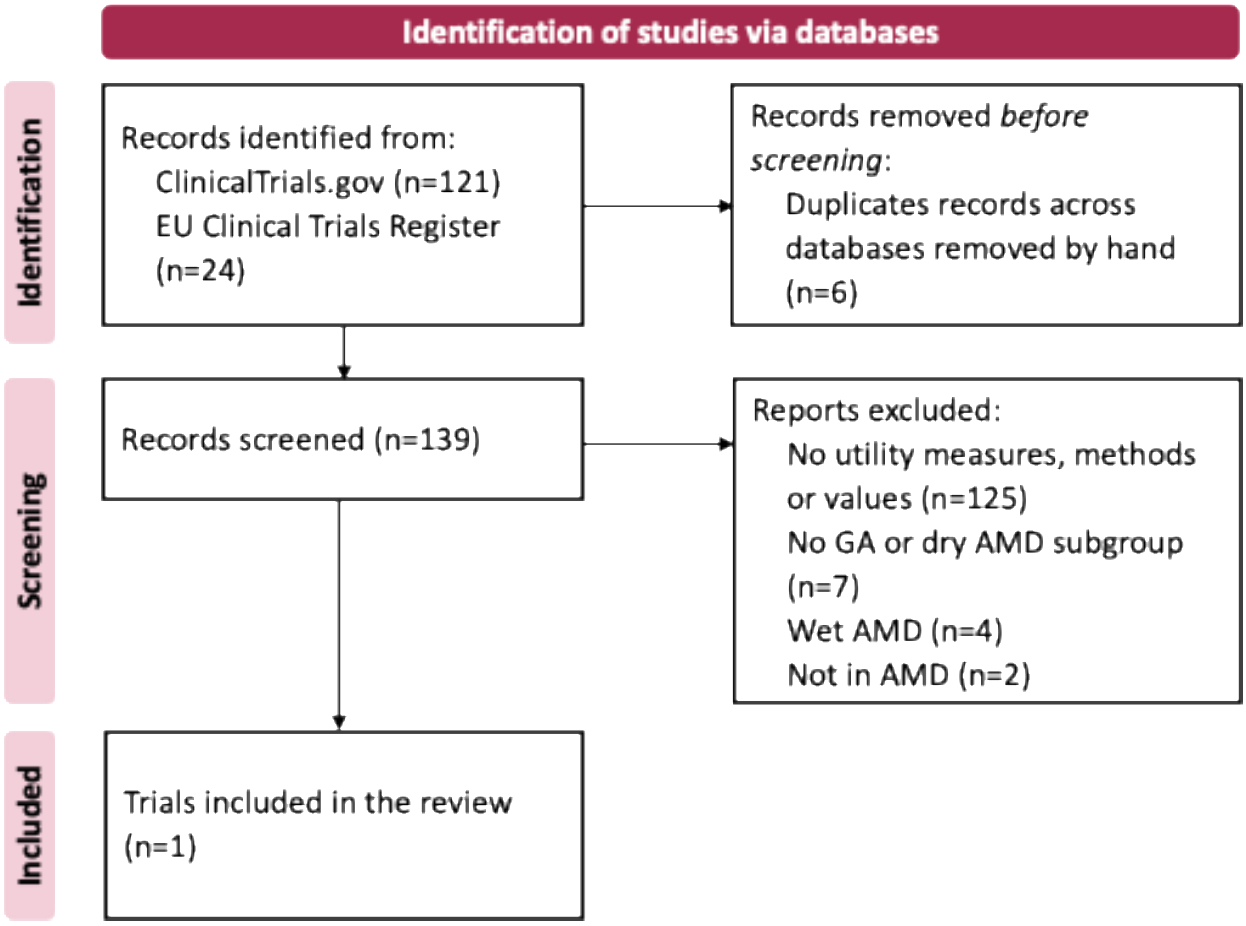
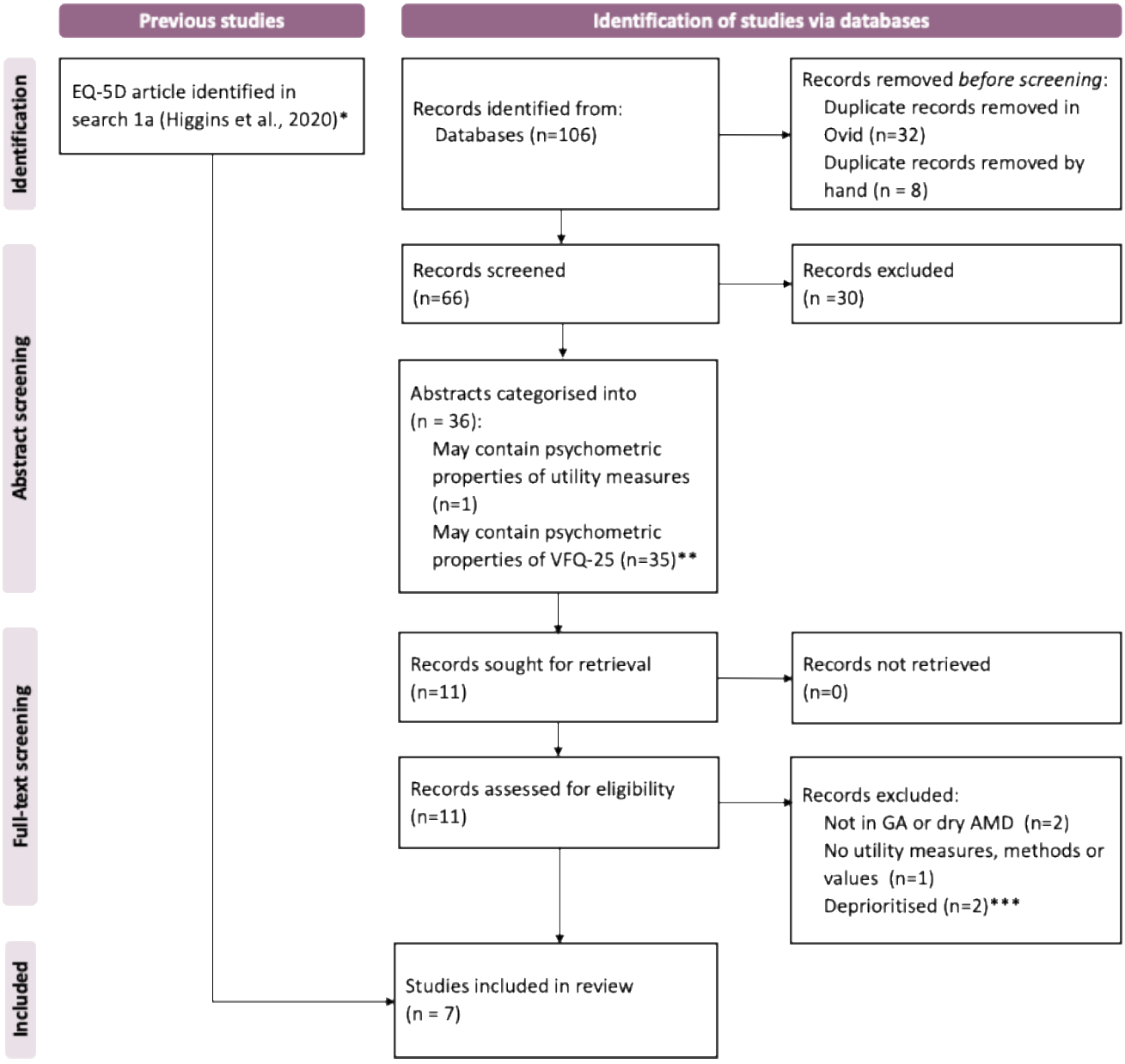


Figure 4. PRISMA flow diagram for search 3



*Higgins et al. (2020)[9]

**Of the n=35 records that were categorised as containing VFQ-25 data, n=10 were prioritised for full-text screening based on condition (GA only) and publication type (journal articles only).

***Two additional studies were de-prioritised for data extraction. One review article referenced primary research articles already included in the review and one primary research article conducted the same assessment of convergent validity in the same data set as a study already included in the review.

Summary data extraction tables

Table 9. Overview of studies reporting utility data in GA or dry AMD (search 1a)

Author (date)	Design	Utility method or measure	Measurement population (N)	Utility values (mean, SD)
Enoch et al. (2023)[10]	Cross-sectional	EQ-5D-5L administered verbally during interviews	Individuals with GA (n=30)	Not reported*
Crabb et al. (2021)[11]	Cross-sectional	Four different sized simulated scotomas applied to films of everyday scenes were valued using time trade-off (TTO)	Individuals with normal vision (n=75)	**Very large scotoma:** Participants traded 5.0 (2.7) years of perfect health to avoid ten years of life with the very large scotoma** **Very small scotoma:** Participants traded 1.9 (1.4) years of perfect health to avoid ten years of life with the very small scotoma **Realistic central scotoma obscuring 5% of the film:** Participants traded 2.6 (1.9) years of perfect health to avoid ten years of life with the scotoma obscuring 5% of the film **Realistic central scotoma obscuring 8% of the film:** Participants traded 3.5 (2.1) years of perfect health to avoid ten years of life with the scotoma obscuring 8% of the film
Higgins et al. (2020)[9]* **	Cross-sectional	EQ-5D (version not reported) administered at baseline	Individuals with no macular disease (n=11), early or intermediate AMD (n=16) and GA (n=22)	No macular disease = 0.81 Early or intermediate AMD = 0.88 GA = 0.82

*Additional information requested from authors; ** TTO values were reported as the number of years of perfect health traded to avoid 10 years in the health state, rather than a 0-1 utility value; ***Identified via a review paper that was identified through the search (Aggarwal et al., 2023)[12]

Table 10. Overview of cost-effectiveness studies including utilities in GA (search 1a)

Author (date)	Utilities derived from	Method or measure used to derive utilities in the elicitation studies	Utility values used in economic model	
Patel et al. (2024)[13]	Calculated from Brown et al. (2003)[14] but no further details provided	Not clear	The utility change from 20/63 to 20/400 was 0.255 This utility loss was assumed to be linear	
Joyner et al. (2023)[15]	Claxton et al. (2014)[16] and an Apellis Pharmaceuticals data on file referenced Claxton study references Czoski-Murray et al. (2009)[17]	EQ-5D (version not reported and no further details provided)	**Base utility (all GA)** ≥76 letters = 0.82 66-75 letters = 0.75 51-65 letters = 0.69 36-50 letters = 0.63 ≤35 letters = 0.56	**Base utility (extrafoveal GA**)** ≥76 letters = 0.82 66-75 letters = 0.73 51-65 letters = 0.66 36-50 letters = 0.59 ≤ 5 letters = 0.50
Singh et al. (2022)[18]	Better-seeing eye (BSE) utilities from Czoski-Murray et al. (2009)[17]***	Healthy participants (n=108) valued three AMD states simulated using contact lenses with TTO	Non-subfoveal (NSF) > 250 microns = 0.84 NSF 1-249 microns = 0.82 Subfoveal (SF) ≤20/40 = 0.80 20/40 < SF <20/200 = 0.67 SF≥20/200 = 0.53	

**Defined as patients whose GA lesions were ≥250 µm from the foveal center; ***Utilities in Singh et al. (2022)[18] from Claxton et al. (2014)[16] and BSE utilities in Claxton et al. (2014)[16] from Czoski-Murray et al. (2009)[17]

Table 11. Overview of clinical trial in dry AMD using EQ-5D (search 2)

EudraCT number	Study sponsor	Design	Condition	N	Treatment	Utility measure	Assessment schedule
2017-003899-31	Dobecure, S.L.	Randomised, single-blind, sham-controlled, 2x2 cross over phase III clinical trial	Dry AMD	60	Dicynone (Etamsylate), intravitreal use	EQ-5D-5L **Note:** VFQ-25 also included	Baseline, 90 days and 180 days

Table 12. Overview of studies including assessments of known-groups validity for VFQ-25 in GA (search 3)

Author (date)	Sample (N)	Key findings
Patnaik et al. (2021)[19]	Early/intermediated AMD (n=294) Unilateral GA (n=31) Bilateral GA (n=84) Unilateral wet AMD (n=137) Bilateral wet AMD (n=31)	Patients with unilateral and bilateral GA had significantly lower mean VFQ-25 composite scores than patients with early/intermediate AMD (81.7 [SD, 2.5] and 71.3 [SD, 1.5] vs 89.9 [SD, 0.8] respectively; p<0.05). The unliteral and bilateral wet AMD groups had relatively higher mean VFQ-25 composite scores compared with the GA group (86.1 [SD, 1.2] and 82.9 [SD, 2.5] respectively).
Patel et al. (2020)[20]	GA (n=137) Non-GA (n=52)	Patients with GA had significantly lower mean VFQ-25 composite scores than those in the non-GA group (53.1 [SD, 19.05] vs 84.5 [SD, 6.55]; p<0.001).*
Burguera-Gimenez et al. (2020)[21]	GA (n=32) Control group (n=31)	Patients with GA had significantly lower mean VFQ-25 composite scores than those in the control group (46.67 [SD, 16.34] vs 89.62 [SD, 3.19] respectively; p<0.001).**
Sivaprasad et al. (2018)[22]	GA (n=100): Maximum reading speed (MRS) <80 wpm (n=38-41) MRS ≥80 wpm (n=48-54)*** FRI <2.5 (n=39-44) FRI ≥2.5 (n=45-50)	Mean maximum Minnesota Low-Vision Reading test (MNRead) reading speed of ≥80 wpm was associated with higher VFQ-25 scores than mean maximum reading MNR reading speed of <80 wpm (composite: 68.8 vs 53.0; near activities: 60.1 vs 34.6; and distance activities: 64.6 vs 45.7; all p<0.0001). Mean Functional Reading Independence (FRI) index score of >2.5 was also associated with higher VFQ-25 scores than mean FRI index score of <2.5 (composite: 69.8 vs 51.8; near activities: 61.0 vs 34.2; and distance activities: 66.7 vs 43.0; all p<0.0001).***

*Patients with GA also had significantly lower VFQ-25 subscale scores for near activities, distance activities, dependency, driving, social functioning, mental health, role difficulties, colour vision, and peripheral vision than those with non-GA conditions; **Patients with GA also has significantly lower VFQ-25 scores in all subscales tested compared with the control group; ***Known-groups validity was not demonstrated for the monocular outcomes GA lesion size and best-correct visual acuity (BCVA), with the exception that a BCVA Early Treatment Diabetic Retinopathy Study (ETDRS) letter score greater than the median of 48 (approximate Snellen equivalent: 20/125) was associated with a higher VFQ-25 near activities score (53.2 vs 43.7; P=0.03).

Table 13. Overview of studies including assessments of convergent validity for VFQ-25 in GA (search 3)

Author (date)	N	Key findings
Kunzel et al. (2024)[23]	82	The most significant associations with VFQ-25 scores for distance and near activities subscale scores were observed in the inner lower and inner left subfields of the BSE, respectively. For patients with foveal-sparing GA, the low luminance visual acuity (LLVA) of the BSE stood out as the most influential variable across all VFQ-25 subscales.
Burguera-Gimenez et al. (2020)[21]	32	Moderate and strong correlations in the GA group were found between MRS (r=0.787) (p<0.01), contrast sensitivity (CS) spatial frequency 3 cpd (r=0.441) (p<0.05), CS spatial frequency 6 cpd (r=0.524) (p<0.01), fixation P1 (r=0.379) (p<0.05), macular sensitivity (r=0.484) (p<0.05) and atrophic area (r =–0.689) (p<0.01), and the VFQ-25 composite score.
Sivaprasad et al. (2018)[22]	00	Strong (0.60-0.79) or moderate (0.40-0.59) correlations were detected between baseline VFQ-25 scores (composite, near activities, and distance activities) and binocular maximum MNRead reading speed (r=0.61, 0.69, and 0.57, respectively) and the FRI index score (r=0.69, 0.73, and 0.64, respectively).
Ahluwalia et al. (2022)[24]	161	Mean composite VFQ-25 scores were not associated with total area of atrophy in the better (β, –0.53; 95%CI, –1.11 to 0.05; p=0.07) or worse eye (β, 0.12; 95%CI, –0.32 to 0.55; p=0.59). However, area of atrophy in the central 1-mm-diameter zone of the better eye was significantly associated with mean composite VFQ-25 scores when the ETDRS subfields were examined individually (β, –14.57; 95%CI, –27.12 to –2.02; p=0.023), grouped into quadrants (β, –18.35; 95%CI, –30.03 to –6.67; p=0.002), inner and outer zones (β, –17.26; 95%CI, –29.38 to –5.14; p=0.006), or vertical and horizontal zones (β, –18.97; 95%CI, –30.18 to –7.77; p=0.001).

Table 14. Overview of study including assessments of convergent validity for EQ-5D in GA (search 3)

Author (date)	N	Key findings
Higgins et al. (2020)[9]	22	EQ-5D (version not reported) index score was not significantly correlated with reaction time or total correct responses across all visual function tasks.

Table 15. Overview of appraisals in wet AMD and RPE65-mediated IRD submitted to NICE (search 4)

Appraisal details		Utility data			
Treatment (indication) *Sponsor Year*	**Appraisal decision**	**Manufacturer's submission: Utility method or measure and population**	**Evidence Review Group (ERG): Utility method or measure and population**	**Key feedback and conclusions from appraisal committee**	**Appraisal committee preferred utility values**
Ranibizumab (wet AMD) *Novartis 2008*	Recommended	**Method:** TTO (direct elicitation)* **Population:** Not reported **Note:** HUI-3-derived utilities also available but not used as base-case.	**Method:** TTO **Population:** Patients with AMD (n=80)*	Indicated it is more appropriate to use utility values derived using a generic instrument. Noted utility values derived from a study using the HUI-3[25] which reported a small utility difference between two health states with markedly different VAs. Agreed that the HUI-3 may not fully capture the impact of AMD on patients' quality of life (QoL).	**Manufacturer's** utility values considered most plausible.
Afilbercept (wet AMD) *Bayer Pharma 2013*	Recommended	**Measure:** EQ-5D **Population:** Patients with wet AMD[26]	**Note:** Considered manufacturer's model a WSE model and conducted separate analyses for a BSE and WSE model.	No feedback reported on the utility data.	**ERG's** approach considered more reasonable.

			BSE model: TTO in people with impaired vision* **WSE model:** Consistent with manufacturer's submission		
Voretigene neparvovec (RPE65-mediated IRD) *Novartis 2019*	Recommended	**Measure:** Vignettes valued using HUI-3 **Population:** Clinicians[27] **Note:** EQ-5D derived utilities also collected but not used as base-case.	**Measure:** TTO **Population:** General UK population[7] **Note:** TTO looked at eight health states with varying degrees of vision problems defined by six items of the VFQ-25.	Noted that manufacturer's methods were limited due to small sample size and possibility of clinicians focusing on issues related to vision loss rather than all areas of a patient's life, which may have led to underestimating QoL. Concluded that manufacturer's HUI-3 values lacked face validity. Considered that the EQ-5D values were more appropriate because of the potential focus on vision by the clinicians.	Neither source of data considered sufficiently robust. In the absence of further evidence, would consider that the utility values fell between the ERG's base case and the manufacturer's EQ-5D values.

*Reference not clear or not provided

Table 16. Overview of appraisals in wet AMD and RPE65-mediated IRD submitted to SMC (search 4)

Appraisal details		Utility data	
Treatment (indication) *Sponsor Year*	**Appraisal decision**	**Manufacturer's submission: Utility method or measure and population**	**Key feedback and conclusions from appraisal committee**
Ranibizumab (wet AMD) *Novartis 2007*	Recommended	**Method:** TTO **Population:** General public*	The TTO results were noted as differing from others in the literature but did not appear unreasonable.
Afilbercept (wet AMD) *Bayer Pharma 2013*	Recommended	**Measure:** EQ-5D **Population:** Patients with wet AMD[26]	No feedback reported on the utility data.
Voretigene neparvovec (RPE65-mediated IRD) *Novartis 2019*	Specific recommendations not provided	**Measure:** Vignettes valued using HUI-3 **Population:** Clinicians[27] **Note:** EQ-5D derived utilities also collected but not used as base-case.	Noted that the utilities were based on a small sample of clinician responses and subject to several limitations. Noted that the utility score for the worst health state in the model using HUI-3 was worse than death, which lacks face validity. Considered that this may be due to the higher focus of the HUI-3 instrument on visual dimensions compared to EQ-5D and a potential bias of retina specialists surveyed to place a higher value on this dimension.

*Reference not provided

Table 17. Overview of appraisals in wet AMD and RPE65-mediated IRD submitted to CADTH (search 4)

Appraisal Details		Utility Data		
Treatment (indication) ***Sponsor*** ***Year***	**Appraisal decision**	**Manufacturer's submission: Utility method or measure and population**	**CADTH Common Drug Review (CDR): Utility method or measure and population**	**Key feedback and conclusions from appraisal committee**
Ranibizumab (wet AMD) *Novartis* *2008*	Recommended	Not reported*	CDR re-analysis included "more conservative estimates for utility".	Noted that the methodology employed in the utility study appears to have some significant limitations such as the design and the population.
Brolucizumab (wet AMD) *Novartis* *2019*	Recommended	**Measure:** EQ-5D **Population:** Not reported**	Not reported	No feedback reported on the utility data.
Faricimab (wet AMD) *Roche* *2022*	Recommended	**Method:** AMD states simulated using contact lenses valued using TTO **Population:** Healthy participants[17]	Not reported	No feedback reported on the utility data.
Voretigene neparvovec (RPE65-mediated IRD) *Novartis* *2020*	Recommended	**Measure:** Vignettes valued using EQ-5D **Population:** Retina specialists[27]	Clinical experts consulted by CADTH completed the manufacturer's utility elicitation exercise and estimates were pooled with the manufacturer's data.	The estimation of the utilities was noted as a key limitation, given that the manufacturer elicited them from physician proxies as opposed to patients or members of the public.

*Utilities based on a confidential study sponsored by the manufacturer; **Reference not provided

Table 18. Overview of appraisals in wet AMD and RPE65-mediated IRD submitted to ICER (search 4)

Appraisal details		Utility data	
Treatment (indication) ***Sponsor*** ***Year***	**Appraisal decision**	**Manufacturer's submission: Utility method or measure and population**	**Key feedback and conclusions from appraisal committee**
Voretigene neparvovec (RPE65-mediated IRD) *Novartis* *2018*	Specific recommendations not provided	**Method:** Vignettes valued using SG **Population:** Patients with diabetic retinopathy[28]	Noted that as QoL data specific to RPE65-mediated IRD were not available, the manufacturer used utility values from other retinal disease populations which are often older and may have led to biased QoL estimates.

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Links to HTA appraisals

National Institute for Health and Care Excellence (NICE)

- Ranibizumab: https://www.nice.org.uk/guidance/ta155
- Aflibercept: https://www.nice.org.uk/guidance/ta294
- Voretigene neparvovec: www.nice.org.uk/guidance/hst11 and https://www.nice.org.uk/guidance/hst11/evidence/committee-papers-pdf-6908685661

Scottish Medicines Consortium (SMC)

- Ranibizumab: https://www.scottishmedicines.org.uk/media/2217/ranibizumab_10mgmlsolution_intravitreali njection_lucentis_38107.pdf
- Aflibercept: https://www.scottishmedicines.org.uk/media/1217/aflibercept_eylea_final_march_2013_amen ded_030413_for_website.pdf
- Voretigene neparvovec: https://www.scottishmedicines.org.uk/media/5280/assessment-explained-voretigene-luxturna.pdf

Canadian Agency for Drugs and Technologies in Health (CADTH)

- Ranibizumab: https://www.cadth.ca/ranibizumab
- Brolucizumab: https://www.cadth.ca/brolucizumab
- Faricimab: https://www.cadth.ca/faricimab
- Voretigene neparvovec: https://www.cadth.ca/voretigene-neparvovec

Institute for Clinical and Economic Review (ICER)

- Voretigene neparvovec: https://icer.org/assessment/inherited-retinal-disease-2018/