

A Systematic Literature Review on the Humanistic Burden of Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema

Key Clinical Question

How does vision loss from neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) affect quality of life (QoL), mobility, and other patient-reported and humanistic outcomes?

Introduction

- Visual impairment has been linked to a decline in QoL, but limited research has been conducted on real-world humanistic outcomes in patients diagnosed with retinal diseases, including nAMD and DME
- Understanding humanistic outcomes in patients with nAMD and DME can provide a more holistic understanding of disease burden and patient experience, beyond traditional elements of value

Methods

- A systematic literature search was conducted using Medline, Embase, and Cochrane Library between 2011–2021 to identify studies that quantified ≥ 1 humanistic and patient-reported outcome of interest, including vision-related QoL, QoL, activities of daily living, productivity, and indirect costs/financial burden for vision-impaired patients with nAMD or DME in real-world/observational studies
- Two researchers (RP and DT) independently screened studies for eligibility

Conclusions

- Patients with nAMD and DME experience poor QoL and impaired activities of daily living in real-world settings, including difficulty in general vision, driving, reading, distance activities, social functioning, role difficulties, dependency, and color vision
- Limitations:** Smaller sample size, heterogeneity in study designs, patient populations, and outcome measures limit interpretability and cross-trial comparisons
- Further research on the impact of humanistic burden of nAMD and DME, including how the changing treatment landscape may impact that burden, is warranted

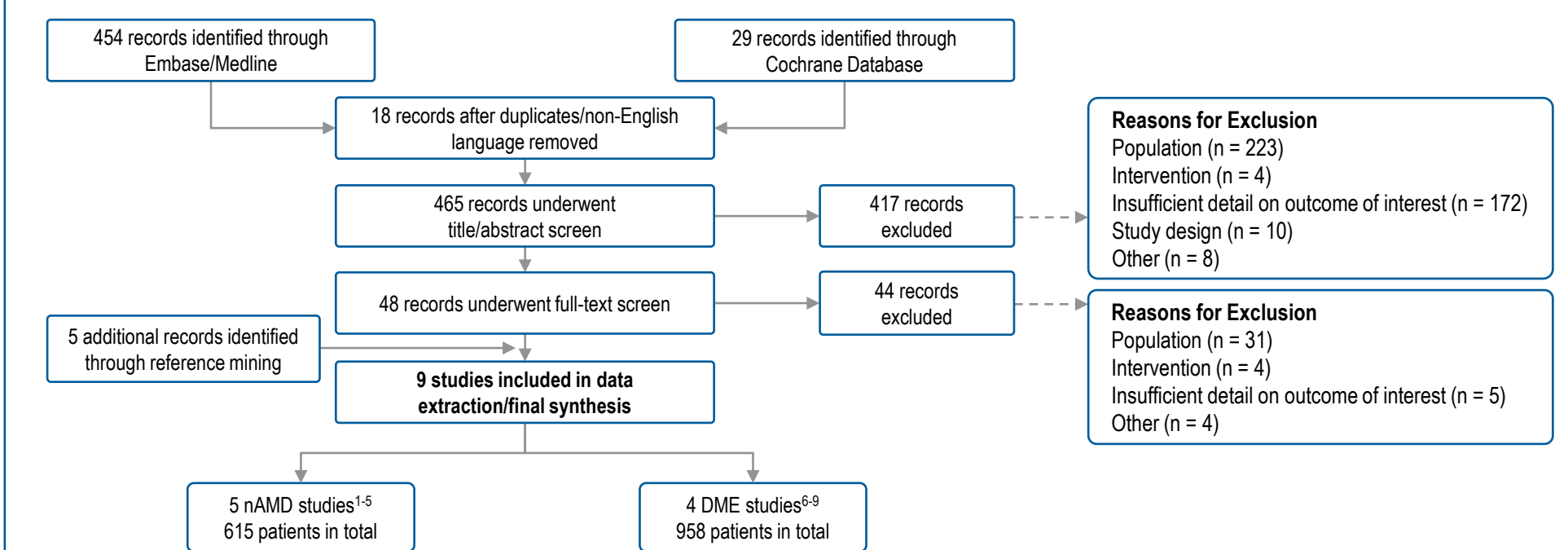
1. Systematic Literature Review Methodology

- A systematic literature review was performed based on PRISMA and NICE guidelines
- Medline, Embase, and Cochrane Library were searched between 2011–2021 using the following terms^a:
 - Disease area of interest:** Wet or neovascular or exudative age-related macular degeneration; diabetic macular edema; diabetic retinopathy; retinal vein occlusion
 - Outcomes of interest:** Quality of life or health-related quality of life; vision related quality of life; mobility – driving, falls, fractures, or injuries; scene viewing or face recognition; time off work or work productivity; depression or anxiety; activities of daily living, including reading or leaving the house; indirect costs or financial burden

Eligibility Criteria

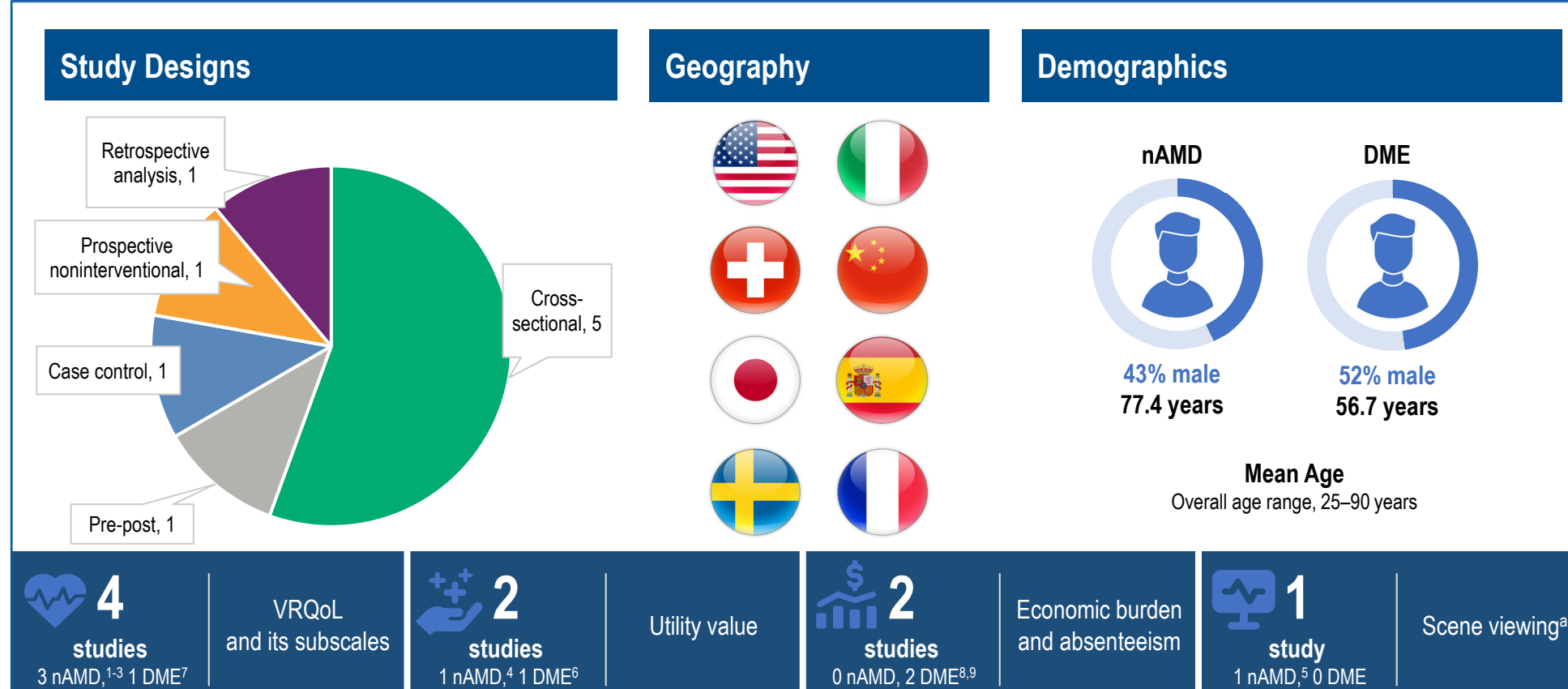
Population	Outcomes	Exclusions
Patients with vision impairment diagnosed with the following diseases: <ul style="list-style-type: none"> nAMD^b DME^c Diabetic retinopathy^c Retinal vein occlusion^b 	Humanistic and Patient-Reported Outcomes <ul style="list-style-type: none"> QoL or health-related QoL Mobility (driving, falls, fractures, or injuries) Scene viewing and face recognition Depression or anxiety Activities of daily living Time off from work or work productivity Indirect costs or financial burden 	Studies in disease conditions other than nAMD and DME and not providing sufficient detail on at least 1 outcome of interest were excluded
Intervention		
<ul style="list-style-type: none"> No intervention/treatment Patients may be receiving standard-of-care treatment 		
Comparator(s)		
<ul style="list-style-type: none"> Any 		

Study Identification and Attrition



^a Word variations were searched with AND/OR conditional criteria. Limits applied: not animal/in vitro; limited to observational studies, registry, systematic reviews and meta-analysis; limited to English language. ^b Only included studies that explicitly note nAMD/wet AMD and diabetic retinopathy if it included presence of DME. ^c Studies were excluded if there was no specific mention of DME, including "proliferative disease"/neovascularization in the macula. AMD, age-related macular degeneration; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; NICE, National Institute for Health and Care Excellence; PICO, patient, problem or population, intervention, comparison, control or comparator, outcome(s); PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; QoL, quality of life; VRQoL, vision-related quality of life.

2. Studies Identified From Literature Review



^a Target object recognition within congruent and incongruent backgrounds. DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; VRQoL, vision-related quality of life.

3. General Themes for Humanistic Outcomes in Studies of Patients With nAMD or DME

Although different study designs and patient populations limit cross-trial comparison, most studies reported an overall decrease in VRQoL and other activities of daily living in patients with nAMD or DME

- Poor VRQoL with low utility values in patients with nAMD and DME
- Difficulty in activities of daily living captured by subscales of VRQoL and NEI VFQ-25
- Patients with DME experience a burden of permanent disability, affecting employees' direct and indirect costs across a range of benefits, and employee absenteeism
- Visual acuity and contrast sensitivity were positively correlated with activities of daily living in patients with nAMD

DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; NEI VFQ-25, National Eye Institute Visual Function Questionnaire-25; VRQoL, vision-related quality of life.

4. Humanistic Outcomes in Studies of Patients With nAMD

Overall, patients with nAMD had poor VRQoL ¹⁻⁵	Patients reported difficulties across 7 VRQoL subscale domains ¹⁻³	Contrast sensitivity and visual acuity were positively correlated with activities of daily living	For scene viewing, patients performed better when the target object, background, and context were consistent ²	Living with nAMD was reported to cause a substantial decrease in patient utility values ⁴
One study reported a dramatic increase in the rate of VRQoL decline after the development of advanced nAMD (before: 0.49 ± 2.91 vs after: 3.30 ± 5.58; P < 0.001 ¹)	<ul style="list-style-type: none"> General vision Reading fine print Driving in traffic Reading bills Driving during day Reading newspaper Driving at night 	Contrast sensitivity was positively correlated with activities of daily living for both distance and near distance (r = 0.67, r = 0.59; P < 0.001), measured by NEI VFQ-25 ^{2,3} . A significant Pearson and partial correlation was observed between QoL with visual acuity (r = 0.34; P < 0.001) and contrast sensitivity (r = 0.28; P < 0.001), but was lower for reading ability variables (P > 0.10). ² Another study reported similar results ³	Patients with nAMD performed better (ie, shorter response times) in scene viewing when the target object (animal, furniture pieces) was consistent with background and context (indoor scenes, natural scenes) compared with those without nAMD (response time difference [f-value]: 159 ms [11.5]; P < 0.002) ²	nAMD was reported to cause a substantial decrease in patient utility values. One study reported an overall linear trend in increasing utility values as BCVA in the better-seeing eye improved (TTO: 0.598; 95% CI, 0.518, 0.677; SG: 0.695; 95% CI, 0.609, 0.781) ⁴

BCVA, best-corrected visual acuity; nAMD, neovascular age-related macular degeneration; NEI VFQ-25, National Eye Institute Visual Function Questionnaire-25; QoL, quality of life; SG, standard gamble; TTO, time tradeoff; VRQoL, vision-related quality of life.

5. Humanistic Outcomes in Studies of Patients With DME

Patients with diabetes with visual impairment due to DME had low scores for NEI VFQ-25 and SF-36 on general health subscale ⁷	Patients reported difficulties across 8 VRQoL subscale domains ⁷	DME was independently associated with lower utility values assessed by both patients and ophthalmologists ⁶	Burden of permanent disability was observed in patients with DME, with significant impact on employee costs and a detrimental impact on absenteeism ^{8,9}
Patients with DME had significantly lower scores than patients with normal vision for near activities overall, across subscales, and the composite score (mean [f-value]: 78.13 [9.86]; P < 0.001) ⁷ . Similar association was seen in the post hoc analysis of patients with moderate or severe visual impairment due to DME compared with patients with normal vision (P < 0.05). No relationships were found between retinopathy severity and NEI VFQ-25 scales ⁷	<ul style="list-style-type: none"> Near Activities: 66.23 (4.53); P = 0.002 Distance Activities: 74.54 (8.47); P < 0.001 Dependency: 93.48 (3.50); P = 0.038 Driving: 72.02 (12.45); P < 0.001 Social Functioning: 87.5 (10.58); P < 0.001 Role Difficulties: 78.07 (10.85); P < 0.001 Color Vision: 91.18 (3.78); P = 0.029 Peripheral Vision: 77.68 (5.78); P = 0.006 Values are mean (f-value) ⁷	Utility values for DR with vision loss were low, as assessed by patients (TTO: 0.81; SD: 0.10; RS: 0.81; SD: 0.11) and their ophthalmologists (TTO: 0.93; SD: 0.07; RS: 0.95; SD: 0.04) ⁶ . Patients reported significantly lower utility values than ophthalmologists (P < 0.01) ⁶ . Significant predictors of patients' utility values included visual acuity in the affected eye, presence of DME, and unemployment ⁶	Burden of permanent disability was observed in patients with DME, with significant impact on employee direct and indirect costs across a range of benefits, as well as the detrimental impact on employee absenteeism (mean [range] cost: €7051 [0–320,502] vs €1052 [0–147,034]; P = 0.01) ⁸ . However, no statistically significant differences were observed in the indirect occupational costs annualized by patient, related to temporary occupational disability (P = 0.535) ⁹ . DME and DR were associated with substantial direct medical cost and absenteeism among medically insured employees ⁹

DME, diabetic macular edema; DR, diabetic retinopathy; NEI VFQ-25, National Eye Institute Visual Function Questionnaire-25; RS, rating scale; SF-36, Short Form-36; TTO, time tradeoff; VRQoL, vision-related quality of life.

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Financial Disclosures

- RP: Former Employee: Genentech, Inc., during the conduct of this study
- EK: Employee: Genentech, Inc., University of Washington
- VG, DT: Employee: Genentech, Inc.

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