A time trade-off study to develop health-related utility data for the impact of geographic atrophy on patients



¹Michele Intorcia, ²Sarah Hill, ²Hema Moor, ³Sujata Sarda, ²Yemi Oluboyede

¹Apellis Switzerland GmbH, Zug, Switzerland, ²Putnam, London, United Kingdom, ³Apellis Pharmaceuticals, Waltham, Massachusetts, USA

Objective

The aim of this study was to develop health-related utility data that would be suitable for use in cost-effectiveness models for novel therapies for the treatment of geographic atrophy (GA) using the time trade-off (TTO) stated preference approach.

Introduction

- Age-related macular degeneration (AMD) is a chronic degenerative disease of the retina in older people that leads to potentially irreversible vision loss¹. Late AMD comprises 2 forms: neovascular AMD (nAMD; also known as wet AMD) and GA (also known as advanced atrophic AMD).
- GA impairs health-related quality of life (HRQoL), and those living with GA also experience psychological impacts due to their symptoms².
- Data that failed quality checks (e.g., any respondents who valued the impaired health state greater than "full health" or valued all health states equally) were removed prior to analysis.

Results

Sample

- A total of 712 respondents met the quality control criteria and were included in the base-case utility valuation sample. The sample demographic characteristics are displayed in **Table 1**.
- Most of the sample had no experience of GA or advanced dry AMD.

Table 1. Demographic characteristics of respondent sample

Characteristic	Base case sample, n=712	UK population ^a
Sex		
Female	374 (53%)	51%
Male	332 (47%)	49%
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Table 2. Mean utility values for each health state vignette

	>75 EDTRS letters	75-66 EDTRS letters	65-51 EDTRS letters	50-36 EDTRS letters	<36 EDTRS letters
Mean utility (SD)	0.85 (0.24)	0.69 (0.40)	0.54 (0.48)	0.35 (0.56)	0.14 (0.56)
SE	0.009	0.015	0.018	0.021	0.021
Median utility (IQR)	0.98 (0.20)	0.82 (0.48)	0.68 (0.50)	0.50 (0.77)	0.28 (0.60)
Range	-0.57 to 1	-1 to 1	-1 to 1	-1 to 1	-1 to 0.98
Respondents, n	712	712	712	712	712

Abbreviations: EDTRS, Early Treatment Diabetic Retinophathy Study; IQR, interquartile range; SD, standard deviation; SE, standard error

- The largest difference in utility (0.21) between consecutive health states was observed between the health states associated with 50 to 36 EDTRS letters and <36 EDTRS letters.
- Greater variation in valuations for each health state was observed as health state severity increased. The highest proportion of values clustering at -1 (i.e., the lowest valuation possible) and 0 (i.e.,

- Currently, there are only 2 treatments approved in the United States for the treatment of GA due to AMD: SYFOVRE[®] and IZERVAY[™].
- There is a lack of published utility values for patients with GA due to AMD. Such utility values are required to conduct economic evaluations of therapies for GA.
- Measuring the HRQoL of patients with GA using the EQ-5D³ may not be appropriate because it has been recognised that the EQ-5D inadequately covers important aspects of health related to visual impairment. The National Institute for Health and Care Excellence (NICE) has recognised that alternative methods to generate utilities are acceptable in circumstances where the EQ-5D is inadequate⁴.

Methods

- Five vignette health state descriptions were developed based on results from qualitative interviews⁵, existing literature, and expert review to reflect a range of GA condition severities characterized by binocular best-corrected visual acuity (BCVA).
- BCVA is assessed using the Snellen chart or Early Treatment Diabetic Retinopathy Study (ETDRS) chart and is often expressed in ETDRS letters. The vignettes aimed to describe the HRQoL of a patient with GA based on how their condition affects their vision and daily life.
- A TTO survey was developed using an online hosting platform and was administered to a representative sample of the UK adult public (n=1000). The TTO valuation method is a preference-based measure that allows the determination of "true" values people assign to specific health states⁶. The aim of a TTO is to determine the amount of healthy time (typically, full health) the valuer would be willing to forego to avoid living in an impaired health state.
- Online recruitment for the survey occurred between 27 July 2023 and 12 August 2023. The sample size was informed by the EuroQol Valuation Technology protocol for TTO valuation studies⁷.

There here buy	0 (170)	
Other	1 (0%)	-
Age, years		
18-24	84 (12%)	11%
25-34	114 (16%)	19%
35-44	109 (15%)	18%
45-54	139 (20%)	19%
≥55	266 (37%)	32%
Region		
London	87 (12%)	13%
England - Midlands	162 (23%)	25%
Northern England	184 (26%)	23%
Northern Ireland	5 (1%)	3%
Scotland	58 (8%)	8%
Southern England	186 (26%)	22%
Wales	30 (4%)	5%
Education		
Primary school	3 (0%)	
Secondary school	140 (20%)	
Further education below degree	230 (32%)	
University degree	210 (29%)	
Post-graduate degree	111 (16%)	
Other qualification	17 (2%)	
Prefer not to say	1 (0%)	
Ethnicity		
White	625 (88%)	
Mixed ethnic groups	22 (3%)	
Asian or Asian British	41 (6%)	
Black	19 (3%)	
Another ethnic group	5 (1%)	
Self-reported health status		
Very good	125 (18%)	
Good	342 (48%)	
Fair	187 (26%)	
Bad	48 (7%)	
Very bad	10 (1%)	
Experience of geographic atrophy		
I have dry AMD/GA	31 (4%)	
A family member has dry AMD/GA	106 (15%)	

equivalent to being dead) was observed for the most severe health state (<36 EDTRS letters) (n=56 and n=148, respectively).

Regression analyses

- Most covariates included in the model were not significant predictors of utility, and those that were shown to be predictors of utility were not consistent across health states.
- Covariates that significantly (p<0.05) predicted higher utility values were self-reported poor health for the most severe health state and having experience of GA from a family member or friend for the 50 to 36 EDTRS letters health state. Additionally, both being in employment and not working predict higher utility values for the 2 mildest health states (both, p<0.05).
- Self-reporting very poor health strongly predicts (p<0.01) a lower utility for the 65 to 51 EDTRS letters health state.

Table 3. Results from Tobit regression model, by health state

			Coefficient (SE)		
Covariate ^a	>75 EDTRS	75-66 EDTRS	65-51 EDTRS	50-36 EDTRS	<36 EDTRS
	letters	letters	letters	letters	letters
Sex					
Male	-0.031 (0.02)	-0.040 (0.03)	-0.003 (0.04)	0.057 (0.04)	0.090 (0.05)
Prefer not to say	0.034 (0.11)	0.238 (0.19)	0.385 (0.22)	0.326 (0.27)	0.234 (0.27)
Other	0.166 (0.24)	0.366 (0.41)	0.045 (0.49)	-0.092 (0.59)	0.029 (0.60)
Self-reported heal	th				
Very good	-0.032 (0.02)	-0.088* (0.04)	-0.099 (0.05)	-0.007 (0.06)	0.037 (0.06)
Fair	-0.000 (0.02)	-0.056 (0.04)	-0.013 (0.04)	0.005 (0.05)	-0.020 (0.06)
Poor	0.021 (0.04)	0.057 (0.06)	0.076 (0.08)	0.139 (0.09)	0.251** (0.09)
Very poor	-0.089 (0.08)	-0.144 (0.13)	-0.596*** (0.16)	-0.167 (0.19)	-0.343 (0.20)
Experience with G	A or dry AMD				
I have dry AMD or	0.004 (0.04)	0 100 (0 07)	0.010* (0.00)	0 044* (0 44)	0 152 (0 11)
GA	0.024 (0.04)	0.128 (0.07)	0.216 (0.09)	0.241 (0.11)	0.155 (0.11)
A family member					
or close friend has	-0.041 (0.02)	-0.019 (0.04)	0.100 (0.05)	0.169** (0.06)	0.100 (0.06)
dry AMD or GA					
Unsure	0.047 (0.03)	0.039 (0.06)	0.044 (0.07)	0.139 (0.08)	0.102 (0.08)
Employment statu	IS				
In employment	0.225** (0.08)	0.355** (0.14)	0.077 (0.16)	0.013 (0.20)	0.403* (0.20)
In education	0.193* (0.09)	0.164 (0.16)	0.044 (0.19)	-0.236 (0.23)	0.177 (0.24)
Not working	0.266*** (0.08)	0.381** (0.14)	0.075 (0.16)	-0.032 (0.20)	0.396 (0.20)
Full-time					
parent/caregiver or	0.192* (0.09)	0.262 (0.16)	0.171 (0.19)	-0.117 (0.23)	0.355 (0.24)
on parental leave					
More than 1	0 224* (0 00)	0 240* (0 46)	0 107 (0 10)	0 033 (0 33)	0 100* (0 22)
occupation	0.224 (0.09)	0.340 (0.10)	0.107 (0.19)	0.033 (0.23)	0.490 (0.23)
Constant	0.642*** (0.08)	0.382** (0.14)	0.448** (0.16)	0.266 (0.20)	-0.356 (0.20)
Observations	712	712	712	712	712

- The survey contained basic demographic questions, an instructional video, an example TTO practice exercise, and the main valuation task, in which the 5 vignettes were presented in a randomized order to minimize bias⁸.
- Mean utility values for each vignette health state were calculated and subgroup analyses were conducted to examine how groups of the UK population with differing characteristics value the different health states. A regression analysis was conducted using a Tobit model to explore participant characteristics that may affect utility valuations.

Jnsure 57 (8%)	10	518 (73%)
	Jnsure	57 (8%)

Abbreviations: AMD, age-related macular degeneration; GA, geographic atrophy ^aFrom 2021 UK census

Time trade-off utility data

- Mean utility values followed a clinically plausible pattern: mean health state utility values decreased as health states became more severe (see Table 2).
- The mean and median utility values calculated for each health state were all positive. A non-linear decrease in mean utility values toward the more severe health states was observed.

Abbreviations: AMD, age-related macular degeneration; EDTRS, Early Treatment Diabetic Retinopathy Study; GA, geographic atrophy; SE, standard error

*p<0.1 **p<0.05 ***p<0.01

^aReference categories for categorical covariates: sex, female; self-reported health, good; experience with GA or dry AMD, no experience; employment status, other employment status/prefer not to say

Figure 1. Subgroup analyses of utility values by health status, experience of geographic atrophy, and age



No statistically significant differences were observed between the utility values offered by respondents with poor or fair self-reported health compared with respondents with good self-reported health.



- → Aged ≥55 years Aged <55 years 0.9 0.8 8.0 value 0.0 0.5 0.4 Mean 0.2 0.1 50-36 <36 letters >75 letters 75-66 65-51 letters letters letters
- Few respondents reported personal or familial experience of GA [n=31 (4%) and n=106 (15%), respectively].
- Respondents with personal experience of GA assigned higher utility values to all health states except the mildest (>75 EDTRS letters).
 For the 3 most severe health states, the difference in mean utility
- Respondents aged ≥55 years assigned similar mean utility values to each health state compared with the sample aged <55 years.
- The only difference in mean utility values identified as statistically significant (p>0.05) between age subgroups was observed for the valuation of the mildest health state (>75 EDTRS letters), although

valuation by experience subgroup was significant (p<0.05).

the absolute difference in means was small (0.03).

Strengths, limitations, and conclusions

- This study is the first vignette valuation study using the TTO approach to value condition-specific utilities for people living with GA. The study followed the NICE recommendations for best practice in vignette development⁸, and the results from this study demonstrated there was substantial and non-linear disutility associated with the progression of GA when characterized by vision loss. The study followed the NICE recommendations for best practice in vignette development to generate 5 health states depicting GA disease progression based on binocular BCVA⁹. These health states were valued using a large sample of the UK public as recommended by NICE guidelines for the generation of health-related utility data to be included in economic evaluations³.
- A limitation of this study is the use of an online self-completion valuation approach. This approach was chosen to collect a large sample in a time- and resource-efficient manner, and measures were taken to ensure high-quality data was collected, such as including an instruction video (which respondents had to watch in its entirety) on the TTO methodology; including a practice TTO task; and performing several data quality checks at both the time of data collection and the analysis stage.
- The generated utility values demonstrate face validity; a decrease in mean utility value was observed as vision impairment increased. Both mean and median utility values for all health states were positive, suggesting that, on average, all health states were considered better than being dead.
- The large difference in utility values between the mildest and most severe health states demonstrate a large perceived impact on HRQoL as GA progresses and vision impairment increases.

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Michele Intorcia, michele.intorcia@apellis.com

Contact information:

SH, YO, and HM: receiving funding from Apellis Pharmaceuticals to conduct this research MI and SS: employees of Apellis Pharmaceuticals and own stock in the company